WEBVTT

1
00:00:18.800 --> 00:00:20.029
Drew Kasper: Morning.

2
00:00:20.070 --> 00:00:27.530
Drew Kasper: Welcome to the new technology. Add on payment or end Tap Town Hall meeting for fiscal year, two thousand and twenty, four.

3
00:00:27.660 --> 00:00:29.999
Drew Kasper: I'm. Your host drew Casper

4
00:00:30.590 --> 00:00:33.340
Drew Kasper: with the division of new technology.

5
00:00:37.690 --> 00:00:48.430
Drew Kasper: Thank you all for being here with us today. This is an exciting time of year for us. We spend many hours with your applications, and it's really nice to hear from and interact with you all in our live setting.

6
00:00:48.590 --> 00:00:49.999
Drew Kasper: We began.

7
00:00:50.170 --> 00:00:59.279
Drew Kasper: I'd like to cover some basics for today's events. In the event that we experience any major technical issues you can reach out via the new tech mailbox.

8
00:00:59.580 --> 00:01:03.000
Drew Kasper: That's N. E. W. T. E. C. H.

9
00:01:11.460 --> 00:01:25.190
Drew Kasper: And many of you are are already familiar with the new tech mailbox. Um. Those of you who have communicated with us through that for and have purposes you'll already know that mailbox.

10
00:01:25.200 --> 00:01:34.209
Drew Kasper: We'll do our best to keep you apprised of what's happening in the event of a technical issue. If you communicate with

us through that mailbox,

11
00:01:34.220 --> 00:01:37.169
Drew Kasper: the of data, volume and bandwidth it.

12
00:01:37.630 --> 00:01:53.809
Drew Kasper: Such a large group of people, the standard for today will be to not activate your video unless you are presenting presenters are welcome to activate your cameras and project video during your presentation, but otherwise we'd appreciate it. If you do not activate your cameras.

13
00:01:54.140 --> 00:02:05.090
Drew Kasper: All attendees may submit their questions, using the Q. And a feature at the bottom of the screen or by using the raise hand zoom function. You'll see a button down at the bottom for raise hand

14
00:02:05.590 --> 00:02:10.790
Drew Kasper: for those of you who are only dialed in by telephone and not on a computer.

15
00:02:10.979 --> 00:02:20.460
Drew Kasper: You can email your questions to us at that. Cms new Tech email box, the one I had mentioned new tech at Cms. Hhs Gov.

16
00:02:20.830 --> 00:02:29.090
Should pertain to substantial clinical improvement of the technologies being presented which we sometimes refer to as in

17
00:02:29.100 --> 00:02:30.010
Yeah, I

18
00:02:30.490 --> 00:02:36.710
Drew Kasper: as a reminder, there are three main criterion for new technology and on payment, eligibility,

19
00:02:36.760 --> 00:02:47.479
Drew Kasper: newness, cost, and substantial clinical improvement over existing services or technologies. We're here today to talk about the substantial clinical improvement criterion. Specifically.

20
00:02:49.750 --> 00:02:52.480
Drew Kasper: Also, I do want to mention um.

21
00:02:53.000 --> 00:03:04.579
Drew Kasper: Anyone has more generalized comments about and tab you could be welcome to email those to that mailbox as well

22
00:03:05.940 --> 00:03:20.199
Drew Kasper: for him. This is consideration in the Ifs proposed rule. Public comments must be submitted to Cms. In writing via email to New Tech, at Cms. Ah. Hhs. Gov: with the subject line Town Hall comment,

23
00:03:20.580 --> 00:03:33.419
Drew Kasper: and then we'd appreciate it. If you'd include the technology name the theory of the technology associated with your comment. All comments must be received by five Pm. On Thursday, December twenty second,

24
00:03:33.910 --> 00:03:35.319
Drew Kasper: two thousand and twenty two.

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00:03:35.580 --> 00:03:43.379
Drew Kasper: Even if you raised a verbal comment during the Town hall today. You must send the written comment to ensure consideration in the proposed rule.

26
00:03:44.260 --> 00:03:59.849
Drew Kasper: We have a very full agenda, so i'm going to get right into introducing our keynote speaker for this morning, Who? I would like to thank very much for taking the time to speak to us today. He's the director of the technology coding and pricing group, which is where our division tips.

27
00:04:00.160 --> 00:04:02.960
Drew Kasper: Ladies and gentlemen, Mr. Jason Bennett,

28
00:04:06.800 --> 00:04:12.079
Jason Bennett: Thank you, Drew. Thank you for the introduction and appreciate all of you joining us today.

29

00:04:12.120 --> 00:04:29.649
Jason Bennett: I understand that this is our twentieth annual. Ah, ips in Tech Town Hall meeting, and I want to acknowledge the many years that Cms. Has been facilitating this Town Hall meeting and hearing from

30
00:04:29.660 --> 00:04:37.150
applicants such as yourself in working to advance medical technology in the hospital inpatient setting

31
00:04:37.290 --> 00:04:47.640
Jason Bennett: before we turn to some specific presentation. I want to just touch a little bit on how this program operates and our vision for this program,

32
00:04:47.850 --> 00:05:06.049
Jason Bennett: as you know cms is committed to driving innovation to tackle our health system challenges and promote value-based person-centered care. We really are focused on the best means of our beneficiary in ensuring that beneficiaries have access to the best possible

33
00:05:06.060 --> 00:05:24.480
Jason Bennett: therapies and services that will improve their, and may help them maintain their their quality of life and their health in the settings, in their homes, and in the settings that they find themselves in any particular time,

34
00:05:24.660 --> 00:05:33.070
Jason Bennett: and so that that leads us to the conversation of of Really? Why we have intap in our perspective payment system,

35
00:05:33.350 --> 00:05:38.959
Jason Bennett: as you likely know, we pay for. We pay hospitals using

36
00:05:38.970 --> 00:05:54.960
Jason Bennett: what are known as drgs or diagnosis-related groups. These are large bundles that are inclusive of the drugs and the devices, the biological and other aspects

37
00:05:54.970 --> 00:06:04.649
that the hospital would be providing in that inpatient setting for the

treatment and care of the particular beneficiary.

38
00:06:05.160 --> 00:06:23.470
Jason Bennett: What that means is that we have a lag in our data as new technologies as potentially such as those that you are um developing have come to market as our payments. Our perspective payment may not yet reflect those costs in the system.

39
00:06:23.730 --> 00:06:37.769
Jason Bennett: So, as a result, we have, as Congress, provided, you know, statute the intap program which allows us a period of typically two to three years to better

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00:06:37.810 --> 00:06:43.150
Jason Bennett: develop the pricing and and cost information that we need

41
00:06:43.180 --> 00:07:01.829
Jason Bennett: to to ensure that we're paying appropriately in the hospital in-patient setting. And because these bundles reflect, care. What we're really looking for is when there is a care and care, change a change to the typical standard of care or change to that care model

42
00:07:01.840 --> 00:07:18.389
Jason Bennett: where the quality of the care is improving. And so that's why we focus today on substantial clinical improvement and looking to see when there are new technologies that are bringing those kinds of changes to the hospital inpatient setting,

43
00:07:18.400 --> 00:07:34.389
Jason Bennett: that when hospitals choose to adopt those and and provide those services, and in care to the patients that we see them. Um! The benefit of crewing to to the beneficiary, and then that the hospital is is appropriately paid.

44
00:07:35.070 --> 00:07:39.359
Jason Bennett: We're seeing a continued interest in the intap program.

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00:07:39.470 --> 00:07:58.649
Jason Bennett: There has been close to a fifty percent increase in applications from just last year, and one hundred percent increase from three years ago, and we are pleased to be hearing from. I believe

it will be twenty. One of you today in which your

46
00:07:58.660 --> 00:08:13.410
Jason Bennett: device, or drug or biological is representing a potential, substantial clinical improvement based on our criteria, and we look forward to hearing those presentations and in dialogue with you today

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00:08:14.900 --> 00:08:25.139
Jason Bennett: want to acknowledge the team that is with you. Here we have a very strong team of analysts, clinicians, physicians,

48
00:08:25.360 --> 00:08:27.160
Jason Bennett: epidemiologists.

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00:08:27.290 --> 00:08:36.859
Jason Bennett: We have a pharmacists and non-position practitioners as well who will be asking questions

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00:08:36.870 --> 00:08:52.690
Jason Bennett: and looking to get your input through through this process today, as well as throughout the public comment period that we have in the proposed rule and and developing our final analysis and final decision making,

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00:08:52.900 --> 00:09:06.869
Jason Bennett: We also have. This team has also been able to develop a new online format for the submission of application that we unveiled this year, and we appreciate your doing so. It really helps us to have our application

52
00:09:06.880 --> 00:09:16.719
Jason Bennett: one one spot, and be able to maintain an electronic file that's related to years to your product.

53
00:09:16.790 --> 00:09:36.109
Jason Bennett: It also is helping us to post more information related to the substantial clinical improvement in related to your applications overall. We think this additional public posting of information will help you share with the broader, clinical and scientific community

54
00:09:36.120 --> 00:09:55.870
Jason Bennett: the advances that your device or your drug or your biological, your product, is potentially bringing to the market, and also be able to get more robust feedback from the from the public, from ah, other peers from others, in that

55
00:09:55.880 --> 00:10:01.679
the clinical and scientific community about how they think your product will

56
00:10:02.010 --> 00:10:20.640
Jason Bennett: perform, and and will address care in the broader setting, and we think that this is a benefit for all involved, and we appreciate your your understanding and your work in sharing information with us that that will facilitate that

57
00:10:21.790 --> 00:10:23.720
Jason Bennett: one of the Uh.

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00:10:23.990 --> 00:10:34.229
Jason Bennett: Ah considerations that we would ask for you to think about is that we do have a large volume of applications as I mentioned earlier, just as we've had in the last couple of cycles.

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00:10:34.380 --> 00:10:45.879
Jason Bennett: This means that as we approach the final rule, our time becomes very focused and very precious to work on those that

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00:10:46.430 --> 00:11:04.910
Jason Bennett: have the appropriate Fda marketing authorization by the July first deadline. And so we really would ask that if you find yourself in a circumstance where, in your discussions with the food and drug administration, your product is not going to receive

61
00:11:04.920 --> 00:11:17.889
Jason Bennett: the appropriate marketing authorization by July the first. And you become aware of that, we ask that you reach out and contact us and discuss potentially withdrawing the application.

62
00:11:18.130 --> 00:11:34.279
Jason Bennett: Consideration. The sooner that we know that the more we

will be able to focus our resources, our time, our energies on products that may meet those standards, and that have those marketing authorization in place.

63
00:11:34.290 --> 00:11:48.159
Jason Bennett: It also allows us to spend additional time and additional resources looking at other areas of responsibility, whether that's in the hospital, outpatient setting or advanced diagnostic laboratory tests

64
00:11:48.170 --> 00:12:07.200
Jason Bennett: in stage renal disease or other areas where there's new and emerging technology that warrant a product review or some additional policy thinking in consideration. And so we we appreciate your recognition of

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00:12:07.250 --> 00:12:24.989
Jason Bennett: the the the value of the time of the the team that is here with you today. We certainly want to make sure that we give full consideration to all products; that we will have a a marketing authorization by July first,

66
00:12:25.000 --> 00:12:41.450
Jason Bennett: and for those that may not be able to reach that that date this year that we can can try to focus as effectively as we can than on on our other work.

67
00:12:42.110 --> 00:12:57.789
Jason Bennett: So with that we we do look forward to engaging with you all today on the clinical merits of the application, and welcome your questions as well as your comments on how this process is going, and I look forward to the continued engagement

68
00:12:57.800 --> 00:13:10.809
Jason Bennett: throughout this fiscal year rule-making cycle, and also on a personal that want to wish you a happy New Year. And as Stephen's greetings as we enter that that part of our year

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00:13:10.930 --> 00:13:13.949
Jason Bennett: with that drew, i'll turn it back over to you.

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00:13:16.080 --> 00:13:18.219

Drew Kasper: Thank you very much, Jason,

71
00:13:19.510 --> 00:13:23.109
for your remarks, and for taking the time to be with us here today,

72
00:13:24.310 --> 00:13:35.180
Drew Kasper: we will have an opportunity for public comments related to each technology being considered for a new technology. Add on payments after each presentation throughout the day.

73
00:13:35.650 --> 00:13:41.550
Drew Kasper: But we'll begin today with public comments from Mr. Richard Christ from Adzanet

74
00:13:42.330 --> 00:13:45.420
Drew Kasper: Price. You may now unmute your mic.

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00:13:48.730 --> 00:14:00.080
Richard Price: Well, thank you very much, Drew. And good morning, everyone. Um, Richard Wright, Senior Vice President Um, in the payment and healthcare Delivery department at Athens,

76
00:14:00.230 --> 00:14:02.310
Richard Price: and um

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00:14:03.400 --> 00:14:19.069
Richard Price: for those of you who do not know. Ah! Adrim is an association of member companies who produce on the medical devices, diagnostic products and health information systems

78
00:14:19.080 --> 00:14:28.180
Richard Price: that are transforming health care through earlier detection, less invasive procedures and more effective treatments.

79
00:14:28.200 --> 00:14:40.249
Richard Price: I want to begin my comments by first expressing our appreciation to speak today briefly about our recommendations for and-tap process improvements.

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00:14:40.260 --> 00:14:55.240

Richard Price: Ah, we also want to. Ah, thank the Cms for responding to several of the recommendations and issues we have brought to these Town Hall meetings over the past several years.

81
00:14:55.490 --> 00:15:10.759
Richard Price: We come today with five and tap process improvement recommendations which I will briefly summarize, and I have already submitted a more complete discussion of these issues for your consideration

82
00:15:10.860 --> 00:15:12.560
Richard Price: our first recommendation

83
00:15:12.900 --> 00:15:32.520
Richard Price: and tap permits Fda approved or cleared follow-on products to qualify for ah add on payment, provided the follow-on product uses a mechanism of action substantially similar to the approved applicant's mechanism of action.

84
00:15:32.530 --> 00:15:40.250
Richard Price: And the Icd ten procedure code accurately describes the Far-on technology

85
00:15:40.520 --> 00:15:47.939
Richard Price: aimed asks that cms issue sub-regulatory guidance

86
00:15:47.980 --> 00:15:57.760
Richard Price: to clarify the criteria for a product to qualify for and tap as a follow-on technology under the traditional and tab pathway

87
00:15:57.770 --> 00:16:10.880
Richard Price: this would apply to all technologies under the traditional pathway, including technologies with digital components, such as artificial intelligence and algorithms

88
00:16:11.120 --> 00:16:17.690
Richard Price: manufacturers and hospitals need objective criteria to assess the materiality

89
00:16:17.700 --> 00:16:22.210

Richard Price: of those distinctions for n-tap applicability,

90
00:16:22.220 --> 00:16:29.980
Richard Price: and whether the technology falls within a particular Icd Ten Pcs code,

91
00:16:29.990 --> 00:16:47.730
Richard Price: rather than establish a formal application or approval process for follow-on products. We ask that Cms. Of Cms issue guidance for stakeholders to mitigate ambiguity and enhance access to innovative technologies.

92
00:16:47.790 --> 00:16:49.880
Richard Price: Our second recommendation

93
00:16:49.890 --> 00:17:06.299
Richard Price: adamant believes that cms could provide more flexibility under the N-tab process than it does currently for n-tap applications that do not receive fda approval by July first of a given year

94
00:17:06.410 --> 00:17:24.379
Richard Price: under current regulations. As you heard Mr. Bennett refer to. If an applicant's product does not receive Fda approval by July, there is no opportunity for that product to receive and tap

95
00:17:24.390 --> 00:17:32.930
Richard Price: until the subsequent fiscal year. Thus, if a product that would otherwise meet the requirements for entail

96
00:17:33.040 --> 00:17:34.290
Richard Price: um

97
00:17:34.610 --> 00:17:45.930
Richard Price: ah! Does not receive Fda approval until shortly after July the first, and here we specifically suggest

98
00:17:46.420 --> 00:17:59.120
Richard Price: any time during July or August the product will be ineligible for n-tab payments until October of the following year, and another n-tap application is required,

99
00:17:59.130 --> 00:18:03.899
Richard Price: as in that believes the July. The first deadline can be extended

100
00:18:03.910 --> 00:18:22.229
Richard Price: until September first, to allow Cms. To make a file determination on and tap applications where Fda approval is not received until after on July. But sometime in July or August until September First,

101
00:18:22.270 --> 00:18:30.370
Richard Price: we've had companies in this situation. That's why we bring this recommendation to you for consideration.

102
00:18:30.420 --> 00:18:39.540
Richard Price: While Cms. Would not use the Ips's final rule published by August the first to make an n-tap determination

103
00:18:39.550 --> 00:18:55.559
Richard Price: on the applicant's new technology. It could supplement the Ips final rule with an additional final rule or notice published sometime prior to the October first beginning of the fiscal year.

104
00:18:56.470 --> 00:18:58.440
Richard Price: Our third recommendation,

105
00:18:58.450 --> 00:19:12.709
Richard Price: Avamet, has supported Cms's conditional and tap approval, alternative pathway for add on payments or certain antimicrobial products that do not receive Fda approval by July first.

106
00:19:12.720 --> 00:19:23.760
Richard Price: These products receive conditional approval for Intel, the quarter following Fda approval. If it occurs after the July first deadline.

107
00:19:23.900 --> 00:19:40.769
Richard Price: Avphabet believes this conditional approval pathway should be extended to all technologies that have been approved or cleared by Fda through the breakthrough device program and not limited

to antimicrobial products.

108
00:19:40.780 --> 00:19:55.780
Richard Price: These breakthrough technologies fill critical needs for Medicare beneficiaries, just as microbial products do cms stated in previous rule, making that the agency would consider

109
00:19:55.790 --> 00:20:01.599
Richard Price: expanding the policy, as they gained experience with conditional approval

110
00:20:01.610 --> 00:20:15.500
Richard Price: of n-tap for antimicrobial products. We believe that Cms. Has had sufficient time to evaluate conditional approval that it has been successful.

111
00:20:15.510 --> 00:20:22.579
Richard Price: Ensuring Medicare beneficiaries have access to these technologies as soon as possible.

112
00:20:22.590 --> 00:20:39.179
Richard Price: Innovative breakthrough approved devices should not have to weigh over a full year to reapply for intap because they fail to obtain Fda approval by the current jurisdictions. Our fourth recommendation,

113
00:20:39.720 --> 00:20:54.429
Richard Price: current Federal regulations provide an alternative streamline pathway for Ah! And tap approval for drugs designated by the Fda as qualified infectious disease products

114
00:20:54.440 --> 00:21:04.589
Richard Price: or approved by Fda under the limited population pathway for antimicrobial and anti-fungal drugs program.

115
00:21:04.790 --> 00:21:09.570
Richard Price: The n-tap program singles out these products for special treatment

116
00:21:09.580 --> 00:21:14.540
Richard Price: in recognition. Of their importance to the health of

medicare beneficiaries

117
00:21:14.800 --> 00:21:32.040
Richard Price: on the same premise we ask Cms to extend similar special treatment to New Ivds used to assist in detection and diagnosis of serious life, threatening infections and appropriate treatment for them.

118
00:21:32.070 --> 00:21:45.410
Richard Price: The Covid, nineteen pandemic, has highlighted the critical importance of diagnostic tests for public health in identifying and mitigating the spread of infectious diseases,

119
00:21:45.420 --> 00:22:01.599
Richard Price: and the same incentives that exist for treatment of infectious disease should extend to the products used to detect and diagnose infectious disease and identify appropriate treatments,

120
00:22:01.630 --> 00:22:03.910
Richard Price: and our final recommendation

121
00:22:04.080 --> 00:22:22.800
Richard Price: fathomed has applauded Cls's decision to increase the add-on payments for approved and Tap um to sixty five percent of the difference between the standard Msdrg Payment and the cost of the procedure. With the new technology.

122
00:22:22.810 --> 00:22:34.590
Dr. James Boron: However, we continue to believe that the add on payment level for approved end tasks should be increased to eighty percent or at a minimum to the seventy five percent level

123
00:22:34.600 --> 00:22:46.940
Richard Price: Cms provides to medical products designated as Qidp or approved under the lpad pathway that I referenced above

124
00:22:47.020 --> 00:22:52.800
Richard Price: our concern is that hospitals find the sixty five percent, add-on payment

125
00:22:52.810 --> 00:23:08.769

Brenda Hudson: insufficient to cover the cost, of using the new technologies with their having to absorb the thirty five percent of the cost of the new technology not being covered by.

126
00:23:08.780 --> 00:23:23.589
Richard Price: We believe that this higher level would mitigate these losses. Further encourage adoption of new technologies by hospitals, and continue to provide incentives for hospitals to act as food producers.

127
00:23:23.600 --> 00:23:31.289
Richard Price: And with that we thank you again for this opportunity to comment, and i'll turn it back to you, Drew.

128
00:23:36.380 --> 00:23:39.969
Drew Kasper: Okay, Thank you very much for your comments, Mr. Price.

129
00:23:41.380 --> 00:23:45.119
Drew Kasper: Is there anyone else that would like to give public comments

130
00:23:50.900 --> 00:23:53.559
Drew Kasper: anything in the Q. A.

131
00:23:56.340 --> 00:23:59.219
Drew Kasper: Not seeing anything in the new tech mailbox.

132
00:24:07.650 --> 00:24:10.760
Drew Kasper: I don't see any raised hands.

133
00:24:14.090 --> 00:24:15.320
Okay.

134
00:24:20.100 --> 00:24:24.200
Drew Kasper: A reminder for all attendees. When you submit

135
00:24:24.330 --> 00:24:29.889
Drew Kasper: the questions, using the two and a feature at the bottom of the screen, or you can use the raise hand feature in zoom,

136
00:24:29.900 --> 00:24:38.509
and we will either unmute you, or if you are a participant responsible for managing your own new function,

137
00:24:38.520 --> 00:24:57.620
Drew Kasper: then you could unmute yourself at that time those who are dialed in by telephone. You may email your requests. That is, those who are dialed in by telephone only. So not on the computer. You can email your requests to the new tech mailbox at New Tech, at Gms. Hhs. Go.

138
00:24:58.220 --> 00:25:12.690
Drew Kasper: We will now move on to fiscal year, twenty, twenty, four, and tap application presenters. I'd like to remind the presenters that we've allotted exactly ten minutes for each presentation, after which we'll have questions from the public,

139
00:25:12.820 --> 00:25:16.449
Drew Kasper: then from Cms, with responses from presenters.

140
00:25:16.560 --> 00:25:19.849
Drew Kasper: Ms. Will advance the slides for each presentation

141
00:25:20.050 --> 00:25:24.189
Drew Kasper: presenters should indicate when to advance to the next slide,

142
00:25:25.660 --> 00:25:28.859
Drew Kasper: and we'll now hear from presenters

143
00:25:29.180 --> 00:25:34.290
Drew Kasper: for the glorified and the the application. You may now unmute your phone.

144
00:25:36.280 --> 00:25:47.499
Dr. Michael Dickinson: Hello, everyone. My name is Michael Dickinson. I'm, a hematologist at Peter Mccallum Cancer Centre and Royal Melbourne Hospital in Melbourne, Australia, and I'm. Presenting on glo fitomap.

145

00:25:47.600 --> 00:25:49.460
Dr. Michael Dickinson: Next slide, please.

146
00:25:49.670 --> 00:25:59.829
Dr. Michael Dickinson: Glyphetamab is a t cell engaging by specific antibody with a novel two to one structure that is efficacious and has a manageable safety profile.

147
00:25:59.840 --> 00:26:13.210
Dr. Michael Dickinson: And here we are using it for treatment of patients with relapsed and refractory to fuselage b cell lymphoma, who have received at least two prior systemic therapies. Next slide, please

148
00:26:13.770 --> 00:26:19.910
Dr. Michael Dickinson: diffuse large b cell Lymphoma is the most common form of non-hodgkin lymphoma in America.

149
00:26:20.150 --> 00:26:28.110
Dr. Michael Dickinson: It is an aggressive and rapidly progressive disease that involves the malignant proliferation of B. Lymphocytes.

150
00:26:28.410 --> 00:26:34.160
Dr. Michael Dickinson: It is predominantly a disease of older people with a Median age of sixty six.

151
00:26:35.260 --> 00:26:46.719
Dr. Michael Dickinson: The rate of new cases in the United States is five point six, one one hundred thousand people per year, and the death rate is one per one point. Eight one hundred thousand people per year.

152
00:26:47.100 --> 00:27:03.340
Dr. Michael Dickinson: The five-year relative survival of sixty, four point six and the incidence of diffusage visa lymphoma is projected to increase by eleven percent from two thousand and twenty to two thousand and twenty five, because of the aging population

153
00:27:03.350 --> 00:27:09.159
Dr. Michael Dickinson: and the underlying high incidence rate of diffuse large-based lymphoma in older people.

154
00:27:09.440 --> 00:27:20.759
Dr. Michael Dickinson: This application focuses on diffuse large bs lymphoma, where patients have received two prior lines of therapy, which is a cohort of substantial, unmet clinical need.

155
00:27:20.860 --> 00:27:22.539
Dr. Michael Dickinson: Next slide, please.

156
00:27:24.670 --> 00:27:41.159
Dr. Michael Dickinson: Most patients with diffuse large vesselymphoma are cured with their first therapy, but approximately forty percent of patients are not, and from here on in the prognosis is poor. A proportion of patients will have disease that is refractory for online therapy,

157
00:27:41.170 --> 00:27:53.430
Dr. Michael Dickinson: while others will relapse typically in the first two years standard therapy for patients with their first relapse is either autologous stem cell transplantation, or chimeric antigen receptor T. Cells.

158
00:27:53.440 --> 00:28:07.069
Dr. Michael Dickinson: I mentioned earlier that this is a disease of older patients. And so it goes That autologous stem cell transplantation which requires very intensive chemotherapy, is often not deliverable to a patient with relapse Disease,

159
00:28:07.080 --> 00:28:26.129
Dr. Michael Dickinson: chimeric antigen receptor t cells require specialised treatment. Centers may have long wait times for evaluation and manufacturing, and may require patient travel and these factors, taken together, can limit the applicability of this treatment to a significant proportion of patients with relapsed disease.

160
00:28:26.180 --> 00:28:41.030
Dr. Michael Dickinson: The Median survival of patients who receive a second line of treatment has been estimated to be as low as ten to twelve months, while those who require a third line of treatment have a Median survival of four to six months.

161
00:28:41.120 --> 00:28:42.819
Dr. Michael Dickinson: Next slide, please.

162
00:28:44.880 --> 00:28:59.999
Dr. Michael Dickinson: There are drugs available for patients who have relapsed to fuselage v. Cell lymphoma, but these have been evaluated in populations that may not address the area of need, and have largely been evaluated before the era of car T cells,

163
00:29:00.010 --> 00:29:05.330
Dr. Michael Dickinson: or in populations where few patients have received autologous stem cell transplantation,

164
00:29:05.870 --> 00:29:13.540
Dr. Michael Dickinson: taphysitomay, lenolidomide is a long-term treatment that has a moderate rate of treatment discontinuation due to toxicity

165
00:29:13.590 --> 00:29:28.260
Dr. Michael Dickinson: polituzamab bender and must bend. A mustine and retoxmap is active, but may cause peripheral neuropathy, while Selenix or and longhous Tuxamand Teserine have complete remission rates that to my mind are lower than ideal.

166
00:29:28.540 --> 00:29:30.269
Dr. Michael Dickinson: Next slide, please

167
00:29:31.520 --> 00:29:44.829
Dr. Michael Dickinson: car t cells do induce a favorable complete remission rate, but they have important limitations. This treatment requires custom manufacturing for each patient and delivery in a specialized treatment center.

168
00:29:45.110 --> 00:30:00.189
Dr. Michael Dickinson: There are bottlenecks for patients who wish to access cartes, especially for those whose current treatment is not in a carte treatment centre. The process of referral and review may require a weight as well as significant travel, for some patients

169
00:30:00.200 --> 00:30:12.720
Dr. Michael Dickinson: cell collection and manufacturing slots may also require a weight, and manufacturing takes weeks. Such delays for treatment can place a patient with this aggressive disease at risk of progression.

170
00:30:12.870 --> 00:30:31.279
Dr. Michael Dickinson: Added to that car t cells have significant toxicities. You can see in this table that the rate of cytokine release syndrome for one product is more than ninety percent, and the rate of severe neurologic toxicity which may require an intensive nursing environment, can be as high as a third.

171
00:30:31.560 --> 00:30:44.629
Dr. Michael Dickinson: These toxicities need to be managed in specialist treatment centres which require a patient to be in, but hospitalised, or within an hour of the hospital for a month, which may mean relocation of the for treatment.

172
00:30:44.640 --> 00:31:03.319
Dr. Michael Dickinson: Twelve States have no available carte sites, and these issues that significantly limit the applicability of this technology. So, taken together, there's a significant need for new options, with rapid accessibility, higher complete remission rates, and a management a manageable safety profile.

173
00:31:03.330 --> 00:31:04.939
Dr. Michael Dickinson: Next slide, please

174
00:31:05.940 --> 00:31:15.710
Dr. Michael Dickinson: buffetimab is an off-the-shelf t cell engaging by a specific antibody that is unique from others due to its potency-increasing, two-to-one structure,

175
00:31:15.720 --> 00:31:29.199
Dr. Michael Dickinson: meaning that it binds two cd twenty molecules on the surface of B cells, one cd three molecule or the surface of T cells leading to c. Cell activation, proliferation and lymphoma cell death

176
00:31:29.390 --> 00:31:36.910
Dr. Michael Dickinson: where fitimab has a long half-life and importantly it's been developed with a fixed duration treatment schedule.

177
00:31:37.050 --> 00:31:45.570
Dr. Michael Dickinson: Glyphidimab will be used to treat patients with

relapse and refractory. Diffuse large visa lymphoma, who have progressed after two prior lines of therapy

178
00:31:45.600 --> 00:31:47.370
Dr. Michael Dickinson: next slide, please.

179
00:31:48.810 --> 00:31:58.550
Dr. Michael Dickinson: The Dose Expansion Study of Glfidamab included patients with various forms of diffuse large b cell Lymphoma, who had received at least two prior therapies

180
00:31:58.660 --> 00:32:17.599
Dr. Michael Dickinson: for mitigation of cytokine release syndrome. The Anti, cd Twenty antibody of inner Tusa may is given as a single flat dose for the first site, and the target dose of giftedomat. Thirty milligrams is reached in two steps, separated by a week, where Fiddimap is delivered intravenously,

181
00:32:18.100 --> 00:32:30.430
Dr. Michael Dickinson: where fit a map is given every three weeks for a fixed course, twelve cycles, or just under, but every three weeks for a fixed course of twelve cycles, which takes us to just under nine months of treatment,

182
00:32:30.800 --> 00:32:47.339
Dr. Michael Dickinson: because complete remission is a prerequisite for cure. In this aggressive lymphoma our primary endpoint was complete response, determined by an independent committee and the study was powered to show an improvement against a historical control.

183
00:32:47.640 --> 00:33:07.050
Dr. Michael Dickinson: This trial there are three minutes remaining. This trial included a heavily treated population that reflects what we see in the clinic a meeting of three prior therapies, but eighty-six percent were refractory to the last therapy, and accordingly inflicting current treatment patterns a third at prior car t cell therapy

184
00:33:07.390 --> 00:33:09.050
Dr. Michael Dickinson: next slide, please.

185
00:33:09.790 --> 00:33:26.769

Dr. Michael Dickinson: The complete remission rate was thirty, nine point four, and the median duration of follow up was twelve point. Six months responses are achieved rapidly at forty-two days, and patients had a similar complete response. Rate Regardless of prior therapies.

186
00:33:27.170 --> 00:33:28.939
Dr. Michael Dickinson: Next slide, please.

187
00:33:29.330 --> 00:33:44.840
Dr. Michael Dickinson: The median duration of response was eighteen point four months. These responses were durable. Eighty percent of complete responses were ongoing at the data cut off date, and the estimated twelve month. Complete remission rate is seventy, seven point six percent.

188
00:33:44.850 --> 00:33:50.100
Dr. Michael Dickinson: This is striking because patients are completely off therapy at just under nine months.

189
00:33:50.320 --> 00:33:52.059
Dr. Michael Dickinson: Next slide. Please.

190
00:33:52.720 --> 00:34:03.949
Dr. Michael Dickinson: The median-progression-free survival was four point nine months, and crucially in this population the median overall survival. Was eleven point five five months next slide, please.

191
00:34:04.600 --> 00:34:23.789
Dr. Michael Dickinson: There was a manageable safety, profile, medium dose intensity was one hundred percent, only three point. Two percent of patients discontinued due to a related ae after cytokine release Syndrome Neutropenia was the most common ae, that this was not complicated by serious infection, nor was it dose lunity.

192
00:34:23.870 --> 00:34:25.639
Dr. Michael Dickinson: Next slide, please.

193
00:34:26.420 --> 00:34:36.430
Dr. Michael Dickinson: Cytokine release. Syndrome is a syndrome caused by the activation of T. Lymphocytes, which can cause fever, hypertension, and a syndrome similar to infection.

194
00:34:36.489 --> 00:34:49.789
Dr. Michael Dickinson: It occurred in sixty-three percent of patients, and was grade two in eleven percent and grade three and only three point nine percent of patients, and it becomes very um one after the remaining

195
00:34:49.800 --> 00:34:55.379
Dr. Michael Dickinson: late. Neurologic events only occurred in two point six percent of patients. The

196
00:34:55.580 --> 00:34:57.309
Dr. Michael Dickinson: next slide, please,

197
00:34:57.810 --> 00:35:07.980
Dr. Michael Dickinson: in summary glyphetamine delivered clinically meaningful outcomes with a manageable safety profile in relapse and refractory to fuselage-based lymphoma.

198
00:35:07.990 --> 00:35:20.090
Dr. Michael Dickinson: In this heavily pre-treated cohort. Thirty nine point four percent of patients achieved a complete response, and these complete responses were durable after a fixed course treatment.

199
00:35:20.100 --> 00:35:40.079
Dr. Michael Dickinson: It was well tolerated with a low rate of treatment, discontinuation, and the most frequent adverse event, the cytokine release syndrome, the majority being grade one or fever occurring on the initial dose, and rarely occurring after the third dose. It is a promising off-the-shelf big duration, treatment,

200
00:35:40.090 --> 00:35:52.849
Dr. Michael Dickinson: and treatment can be completed in just eight point three months, and with that i'd like to move to the final slide and thank everyone for listening to the presentation, and I welcome any questions.

201
00:35:54.610 --> 00:35:56.899
Drew Kasper: Thank you very much for your presentation.

202
00:35:57.120 --> 00:36:00.269
Drew Kasper: Are there any questions from the public?

203
00:36:00.460 --> 00:36:04.200
Drew Kasper: And this may include other applicants as well

204
00:36:05.120 --> 00:36:08.859
Drew Kasper: any questions from Cms. After this. But right now, looking for questions

205
00:36:08.980 --> 00:36:10.170
on the public,

206
00:36:10.540 --> 00:36:13.489
Drew Kasper: I see one in the Q. And A.

207
00:36:14.290 --> 00:36:24.390
Drew Kasper: I typically view Dl. Bcl. Treated in the outpatient setting. Could you please. Let us know what your inpatient utilization will be.

208
00:36:24.810 --> 00:36:40.049
Dr. Michael Dickinson: Yes, sure. So um. At the moment we typically admit patients after the first cycle of treatment, so patients receive a dose of a binatus amount as an outpatient for cytokine releasingro mitigation.

209
00:36:40.060 --> 00:36:55.270
Dr. Michael Dickinson: The first dose of Glaffitam is two point five milligrams and patients are admitted for observation. After that first dose. If patients do not have cytokine release syndrome, they require no further admissions.

210
00:36:55.280 --> 00:37:04.339
Dr. Michael Dickinson: The rate of cytokine release and growing reduces after each dose, and so this will be an almost entirely outpatient treatment.

211
00:37:09.970 --> 00:37:11.069
Drew Kasper: Thank you.

212
00:37:17.600 --> 00:37:19.629

I am not

213
00:37:20.220 --> 00:37:23.660
raised hands with our attendees.

214
00:37:24.060 --> 00:37:27.590
Drew Kasper: No no questions in the new tab

215
00:37:28.510 --> 00:37:31.360
Drew Kasper: in tap uh mailbox.

216
00:37:31.370 --> 00:37:41.379
Drew Kasper: And so with that i'd like to open it up to Cms for questions. If someone from the public has a question. It's not too late, but we're opening it up now. Also for Cms questions.

217
00:37:54.170 --> 00:37:56.299
Andrew Wang: There are no questions from Cms:

218
00:37:58.690 --> 00:38:00.180
Drew Kasper: Okay, Thank you.

219
00:38:01.290 --> 00:38:06.150
Drew Kasper: The last call for questions from the public or anyone. At this point

220
00:38:07.450 --> 00:38:17.400
Dr. Michael Dickinson: something in the Q. And A. Um. If time allows, I can provide a slightly expanded answer to that question. I was very mindful that we were coming up on time.

221
00:38:18.940 --> 00:38:21.520
Drew Kasper: Oh, sure, yeah, go ahead.

222
00:38:21.530 --> 00:38:37.740
Dr. Michael Dickinson: Yeah. So I just wanted to to further address that outpatient question. So, um, we have developed a risk that identifies patients who are at high risk of cytokine release syndrome and those patients who are most likely to develop a feeder.

223
00:38:37.760 --> 00:38:49.040
Dr. Michael Dickinson: We have also explored in a cohort in the presented in the in the study that we've done of patients who have had dex amethystone retreat

224
00:38:49.050 --> 00:38:59.020
Dr. Michael Dickinson: in that patient cohort, cytokine, release, syndrome of more than of grade. Two or above did not occur after the first dose of Glyphin,

225
00:38:59.030 --> 00:39:14.130
Dr. Michael Dickinson: and this and the risk score that has been developed. The clinical risk score that's been developed is very sensitive and specific about identifying patients who might be at risk of cytokine release syndrome. So this will help physicians ah

226
00:39:14.140 --> 00:39:23.999
Dr. Michael Dickinson: profile! Whether their patients are likely to require further observation, and will assist in management and of resourcing

227
00:39:24.010 --> 00:39:48.769
Dr. Michael Dickinson: and in addition, one feature about low food demand that perhaps distinguishes it amongst the other by-specific antibodies is that the timing of cytokine release syndrome is very very predictable, occurring ten hours after the infusion, which means that ah doctors are able to anticipate resource utilization in the management of their age.

228
00:39:53.970 --> 00:39:57.229
Drew Kasper: Thank you for that additional information, and Dr. Dickinson,

229
00:39:59.490 --> 00:40:06.640
Drew Kasper: with that I'm going to do one last check here, and nothing new in the chat

230
00:40:07.700 --> 00:40:11.599
Drew Kasper: in the intent mailbox, no new raised hands.

231
00:40:12.050 --> 00:40:13.979

Drew Kasper: And so with that

232
00:40:14.540 --> 00:40:21.630
Drew Kasper: we will now hear from presenters for the Ep cortemab technology, the

233
00:40:21.660 --> 00:40:24.379
Drew Kasper: you may now unmute your mics.

234
00:40:25.030 --> 00:40:27.459
Dr. Jon Ukropec: Okay, thank you. Can you hear me, Drew.

235
00:40:28.080 --> 00:40:29.359
Drew Kasper: I can. Thanks

236
00:40:29.870 --> 00:40:31.089
Dr. Jon Ukropec: great. Thank you.

237
00:40:31.100 --> 00:40:43.890
Dr. Jon Ukropec: Good morning, and thank you for the opportunity to present Freddamas for the treatment of third line, plus relapse for factory detail. Lymphoma. My name is Johnny Krofik. I'm. The head of u s medical affairs and hematology agenda.

238
00:40:44.000 --> 00:40:45.279
Dr. Jon Ukropec: Next slide, please.

239
00:40:47.860 --> 00:40:49.239
Dr. Jon Ukropec: That's what i'm

240
00:40:49.450 --> 00:41:00.550
Dr. Jon Ukropec: is a full-length ig. One by a specific Antibodies derived from humanized human anti-human cb three and human anti-cd twenty monoclonal Antibodies

241
00:41:00.620 --> 00:41:06.270
Dr. Jon Ukropec: that have been eloquently engineered to induce t-cell mediated killing of malignant b cells.

242

00:41:06.680 --> 00:41:17.649
Dr. Jon Ukropec: Fredomat is currently under consideration by the Fda for the treatment of relapse or factory and large b cell. Lymphoma for patients who have failed at least two prior therapies.

243
00:41:18.370 --> 00:41:23.209
Dr. Jon Ukropec: Large B cell Lymphoma is an aggressive subtype, as you heard from Dr. Dickinson,

244
00:41:23.500 --> 00:41:32.340
Dr. Jon Ukropec: it's a subtype of non hodgkin's lymphoma, and in the Us. It has limited treatment, options, and remains. A high, unmet medical need,

245
00:41:32.570 --> 00:41:34.750
Dr. Jon Ukropec: subcutaneous at critical,

246
00:41:34.800 --> 00:41:44.820
Dr. Jon Ukropec: has been shown to achieve deep and durable responses with a manageable safety profile, and i'll go through some of that data in the course of this presentation.

247
00:41:44.860 --> 00:41:46.190
Dr. Jon Ukropec: Next slide, please.

248
00:41:48.970 --> 00:41:53.639
Dr. Jon Ukropec: Large B cell. Lymphoma is an aggressive constellation of B cell lymphomas.

249
00:41:53.790 --> 00:42:08.949
Dr. Jon Ukropec: You heard from Dr. Dickinson about the fuselage B cell. That is the predominant subtype in large B cell. It also includes primary media's final high-grade b cell lymphoma, molecular grade, three B

250
00:42:09.510 --> 00:42:10.709
as well

251
00:42:10.720 --> 00:42:15.490
Dr. Jon Ukropec: the average onset is approximately after sixty five years of age

252
00:42:15.540 --> 00:42:22.460
Dr. Jon Ukropec: for those patients who don't seek treatment, they typically succumb to the aggressive disease within the first year.

253
00:42:22.760 --> 00:42:27.670
Dr. Jon Ukropec: Unfortunately, the relative survival is only about sixty. Five percent

254
00:42:28.200 --> 00:42:29.569
Dr. Jon Ukropec: next slide, please.

255
00:42:31.280 --> 00:42:41.770
Dr. Jon Ukropec: The treatment of large B-cell Lymphoma largely utilizes regiments used for its diffuse search vessel, and Dr. Dickinson did a great job of reviewing those options,

256
00:42:42.070 --> 00:42:53.169
Dr. Jon Ukropec: while chemo immunotherapy is the predominant therapy in first line in the United States there is no clear standard of care for relapse, refractory, large b cell lymphoma,

257
00:42:54.730 --> 00:43:02.569
Dr. Jon Ukropec: with the recent approvals of carte in the Us. They do offer another potential for cure After the frontline treatment,

258
00:43:02.660 --> 00:43:09.349
Dr. Jon Ukropec: however, many patients are in eligible due to serious comorbidities or rapidly progressing disease,

259
00:43:09.960 --> 00:43:22.060
Dr. Jon Ukropec: and they require active therapy pre-authorizations, coupled with a long and complex manufacturing process, result in protracted waiting periods to receive their cardi therapy

260
00:43:22.250 --> 00:43:29.980
Dr. Jon Ukropec: addition, intense safety. Monitoring requires distreatment, modality to be limited to specialized tertiary centers. The

261

00:43:30.850 --> 00:43:38.519
Dr. Jon Ukropec: this often relegates the therapy to patients who are fit enough, and can withstand delays in receiving active treatment

262
00:43:39.360 --> 00:43:42.720
Dr. Jon Ukropec: as patients progress through the different lines of therapy.

263
00:43:43.070 --> 00:43:44.360
Dr. Jon Ukropec: In the Us.

264
00:43:44.620 --> 00:43:56.529
Dr. Jon Ukropec: The predominant therapy is a chemo-based regimen their remission time becomes shorter and shorter. Therefore novel therapies are needed for patients receiving third line, and beyond a treatment

265
00:43:57.080 --> 00:43:58.439
Dr. Jon Ukropec: next slide, please

266
00:44:01.520 --> 00:44:09.919
Dr. Jon Ukropec: the schematic on the left detects that pertinent binding to Cd. Three on cytotoxic T cells and Cd. Twenty on B cells.

267
00:44:11.020 --> 00:44:18.469
Dr. Jon Ukropec: This leads to conformational change of the molecule, activating the cytotoxic t cell and killing the malignant B cell

268
00:44:18.870 --> 00:44:29.710
Dr. Jon Ukropec: in the appcore and nhl one dose expansion cohort subcutaneous Ferritom was well tolerated and drove strong responses across multiple-patient subtypes

269
00:44:30.930 --> 00:44:32.290
Dr. Jon Ukropec: next slide, please.

270
00:44:34.390 --> 00:44:47.729
Dr. Jon Ukropec: So looking at that for Nhl, one which was our pivotal trial, and and and specifically the one hundred and fifty seven patients in the dose expansion cohort. The Median age was sixty. Four.

271
00:44:47.740 --> 00:45:02.439
Dr. Jon Ukropec: About half of the patients were sixty, five years and older. Eighty nine percent of patients had diffuse large b-cell of that seventy percent were nervous de novo, twenty nine percent were transformed from indolent disease,

272
00:45:02.450 --> 00:45:09.999
Dr. Jon Ukropec: six percent high-grade three percent primary media style and three percent molecular grade Threeb.

273
00:45:10.790 --> 00:45:17.520
Dr. Jon Ukropec: The median time, from initial diagnosis to first dose of that pyramid was one point six years

274
00:45:18.100 --> 00:45:19.760
Dr. Jon Ukropec: over this time

275
00:45:20.100 --> 00:45:24.450
Dr. Jon Ukropec: patients receive the medium of three prior lines of therapy.

276
00:45:24.590 --> 00:45:28.709
Dr. Jon Ukropec: Fifty. One percent of those patients were refractory to primary disease.

277
00:45:31.470 --> 00:45:37.459
Dr. Jon Ukropec: Prior carte therapy was used in thirty. Nine percent of the patient population in this study

278
00:45:37.490 --> 00:45:52.520
Dr. Jon Ukropec: want to highlight for the audience that this particular patient population have a four prognosis, and, in fact, three-quarters of the patients that were entered into the into the study, had progressed within six months of their carte therapy.

279
00:45:53.400 --> 00:45:54.690
Dr. Jon Ukropec: Next slide, please.

280
00:45:57.310 --> 00:46:05.330

Dr. Jon Ukropec: Looking at the safety from this pivotal study, after it has demonstrated low rates of treatment-related adverse events.

281
00:46:05.470 --> 00:46:10.869
Dr. Jon Ukropec: They were typically low-grade, and occurred early in treatment within the first three cycles.

282
00:46:10.940 --> 00:46:14.049
Dr. Jon Ukropec: The incidents declined over time the

283
00:46:14.830 --> 00:46:26.109
Dr. Jon Ukropec: credit-time release. Syndrome is an adverse event that is characterized within this class of drug, and, as you can see, the majority were low-grade

284
00:46:26.800 --> 00:46:42.869
Dr. Jon Ukropec: these patients typically experienced crs within the first several doses of receiving apparatus, the Median time. The onset was approximately twenty hours, and all patients resolved, and this is not discontinued due to So Crs.

285
00:46:42.880 --> 00:46:48.929
There was one patient, however, that did withdrawal consent. While experience a grade one. Drs event,

286
00:46:49.390 --> 00:46:59.080
Dr. Jon Ukropec: twenty one percent of patients experienced the grade. Three or hired Nitrienia. These were effectively managed according to local protocols and leveraged growth actors,

287
00:46:59.090 --> 00:47:02.519
Dr. Jon Ukropec: hierarchy. It was also observed, independent of Crs

288
00:47:02.730 --> 00:47:09.059
Dr. Jon Ukropec: fatigue, diarrhea injection, site reaction nausea and anemia were also observed. The

289
00:47:09.620 --> 00:47:23.030
Dr. Jon Ukropec: icons is also an adverse event that is associated with this class of drug. Ten patients experienced an Icann event. Nine were grade, one and two, and resolved one patient,

290
00:47:23.870 --> 00:47:26.299
Dr. Jon Ukropec: and experience a grade five

291
00:47:26.650 --> 00:47:42.569
Brenda Hudson: against events. This was confounded by multiple factors, which included excess of opioid use for grade three paint. Here, I tell you, this elevated ammonia levels and multifoal cerebral in parts in the setting. There are three minutes remaining

292
00:47:43.870 --> 00:47:54.899
Dr. Jon Ukropec: medium follow-up of the study. It was ten point seven months. The meeting number of treatment cycles were five. This will continue to increase as thirty, two percent are still on study.

293
00:47:55.150 --> 00:48:06.329
Dr. Jon Ukropec: Fifty eight patients discontinued therapy, and the majority were due to disease progression. In this highly refractory population. Seven percent discontinued through the aes.

294
00:48:06.410 --> 00:48:11.200
Dr. Jon Ukropec: Four percent went on to transplant three percent with your consent.

295
00:48:11.550 --> 00:48:12.909
Dr. Jon Ukropec: Next slide, please.

296
00:48:15.590 --> 00:48:25.600
Dr. Jon Ukropec: Epcoretim that drives deep and durable complete responses which is the focus of the response desired in this patient population in the Swim Lane plot below,

297
00:48:25.820 --> 00:48:29.620
Dr. Jon Ukropec: you'll see patients who achieved a complete response

298
00:48:29.730 --> 00:48:46.600
Dr. Jon Ukropec: or or any response. Were quick within the first six weeks, for those patients who achieved a partial response and continued on therapy. We saw the deepening of response, particularly after nine months of therapy patients were still achieving a complete response.

299
00:48:46.610 --> 00:48:56.569
Dr. Jon Ukropec: The line indicates those patients that were continuing therapy in the study as of the data cut off those links without ours of patients that went on the transplant

300
00:48:57.090 --> 00:49:00.680
Dr. Jon Ukropec: sixty, three percent of patients achieved an overall response,

301
00:49:00.730 --> 00:49:14.150
Dr. Jon Ukropec: thirty, nine percent, a complete response to put this in the context by Dr. Gil Sales from memorial. So Kettering reported at Ash earlier this week from a pulled analysis in scholar one a third line

302
00:49:14.160 --> 00:49:23.400
Dr. Jon Ukropec: plus patients receiving chemotherapy. It's based regiments, thirty four percent and achieved an overall response. Four percent of the Cr.

303
00:49:23.410 --> 00:49:30.799
Dr. Jon Ukropec: This is consistent with reports from real-world evidence where complete response was seen in about nine percent of the patients

304
00:49:30.810 --> 00:49:33.809
Brenda Hudson: medium time it's possible for me.

305
00:49:34.350 --> 00:49:37.020
Dr. Jon Ukropec: And the meeting duration was not reached. The

306
00:49:37.430 --> 00:49:38.490
Dr. Jon Ukropec: next slide.

307
00:49:39.740 --> 00:49:45.920
Dr. Jon Ukropec: This Kathleen Meyer on the left-hand side you'll see the itp population, and at nine months

308
00:49:45.990 --> 00:49:50.400

Dr. Jon Ukropec: about forty percent of the patients were still in progression free.

309
00:49:50.440 --> 00:49:56.290
Dr. Jon Ukropec: This was mainly driven as seen in the right-hand panel for those patients who were in the complete response.

310
00:49:56.300 --> 00:50:01.690
Dr. Jon Ukropec: Eighty nine percent of patients were in A in a complete response. By nine months the

311
00:50:01.880 --> 00:50:13.670
Dr. Jon Ukropec: an updated ash by Tesla Phillips reported that seventy nine percent of those patients are still in a completed response with the Median follow-up of fifteen point seven months with single asian fredomat.

312
00:50:14.810 --> 00:50:16.140
Dr. Jon Ukropec: Next slide, please.

313
00:50:17.270 --> 00:50:23.890
Dr. Jon Ukropec: Similarly, looking at a pre-specified analysis that pretty much demonstrated that you can see across

314
00:50:24.000 --> 00:50:33.540
Dr. Jon Ukropec: variety of different patient subtypes regardless of age, disease, and the the most difficult and challenging to treat population post-car tea

315
00:50:34.340 --> 00:50:35.420
Dr. Jon Ukropec: next slide.

316
00:50:36.600 --> 00:50:54.789
Dr. Jon Ukropec: In conclusion, that perdemat demonstrated an impressive clinical benefit in patients being treated with this aggressive challenging to treat refracting disease in the pivotal trial. Single agent, Fredomat demonstrated deep and durable responses, was well tolerated with a few discontinuations due to the adverse events,

317
00:50:54.800 --> 00:50:59.380

Dr. Jon Ukropec: the patient population representative of those seen in the United States. The

318
00:51:00.100 --> 00:51:04.960
Dr. Jon Ukropec: that credit map has the potential to become the first and class subcutaneously admitted service.

319
00:51:06.590 --> 00:51:16.610
Dr. Jon Ukropec: Rt: Sorry of the Shells P. Cell engaging therapy intended to treat patients in third line and beyond large b cell. Lymphoma.

320
00:51:16.640 --> 00:51:19.730
Dr. Jon Ukropec: Thank you for your attention, and happy to take any questions.

321
00:51:20.380 --> 00:51:22.450
Drew Kasper: Thank you for your presentation.

322
00:51:22.710 --> 00:51:25.349
Drew Kasper: Are there any questions from the public?

323
00:51:26.150 --> 00:51:34.649
Drew Kasper: This may include other applicants. We'll take questions from Cms. After this, any questions from the public

324
00:51:43.020 --> 00:51:47.250
Drew Kasper: seeing any raised hands or questions in the Q. And A.

325
00:51:47.450 --> 00:51:54.630
Drew Kasper: Yet, and I do want to take a moment. We've had a lot of people join us since I last stated this. So,

326
00:51:54.640 --> 00:52:07.739
Drew Kasper: as a reminder, all attendees can submit questions using the Q. And a feature at the bottom of your screen, or you can use the raise hand feature in zoom, and we will either unmute you, or if you are a participant. You may unmute yourself

327
00:52:07.750 --> 00:52:25.030

Drew Kasper: for those who are dialed in by telephone only, and not on a computer. You can email your questions to the Cms new tech mailbox at New Tech at Cms. Dot. Hhs dot Gov. As N. E. W. Pch at Cms. Dot

328
00:52:26.750 --> 00:52:33.119
Drew Kasper: with that um. Returning to questions from the public. I'm. Going to take one more scan.

329
00:52:33.760 --> 00:52:35.669
Dr. Jon Ukropec: Nothing in the Q. A.

330
00:52:36.560 --> 00:52:38.700
Drew Kasper: No. Raised hands

331
00:52:39.740 --> 00:52:41.120
Drew Kasper: and

332
00:52:42.110 --> 00:52:47.980
Drew Kasper: no new emails in the new technology. So with that we'll open up questions to Cms as well.

333
00:52:49.800 --> 00:52:58.359
Andrew Wang: Hi, this is Andrew. Thank you so much for the presentation. One question Cms. Had was under continuing three.

334
00:52:58.370 --> 00:53:20.479
Andrew Wang: The applicant submits. Ah, the the results for the outcomes for Ah, at the core of the map. Um, which are conference proceedings rather than peer-reviewed publications. We're we are um, asking, or wondering if you had any additional peer-reviewed data that compares elementary fence to f core to map with some sort of matching across the population for comparability purposes.

335
00:53:21.810 --> 00:53:36.690
Dr. Jon Ukropec: So thank you for the question. I I was remiss in not stating that this data is not only the basis for the filing in the Us. But has also been accepted, and is in press at the Journal of Clinical on Ecology.

336
00:53:37.100 --> 00:53:50.930
Dr. Jon Ukropec: So yes, it has been accepted. An analysis and

comparison has been done with the current standards of care, and that was part of what was presented at the American Society hematology as well.

337
00:53:52.860 --> 00:53:55.180
Dr. Jon Ukropec: Does that answer your question, Andy.

338
00:53:55.390 --> 00:53:57.090
Andrew Wang: Yes, thank you so much.

339
00:54:31.780 --> 00:54:38.610
There are no new questions in the Q. And A. Or the new tech mailbox, and no raised hands.

340
00:54:40.970 --> 00:54:42.330
Drew Kasper: But with that

341
00:54:46.010 --> 00:54:49.179
Drew Kasper: we will now move on. Thank you.

342
00:54:49.750 --> 00:54:55.889
Dr. Jon Ukropec: Thank you, and we'll now hear from presenters for the septicide rapid application.

343
00:54:56.420 --> 00:54:58.450
Drew Kasper: You may now unmute your phone.

344
00:55:01.640 --> 00:55:15.070
Dr. Roy Davis: Good morning. My name is Ray Davis, and I am Cmo at the immune Express. Thank you for the opportunity to present our host respond. Since this diagnostic step to a rapid and discuss its impact on Sepsis clinical care and outcomes.

345
00:55:15.320 --> 00:55:16.959
Dr. Roy Davis: Next slide, please.

346
00:55:18.660 --> 00:55:22.870
Dr. Roy Davis: In the next ten minutes I will briefly review the burden of sepsis in the Us.

347
00:55:22.960 --> 00:55:35.250
Dr. Roy Davis: And discuss its diagnostic challenges, review the scepticite solution and its clinical validation, and then review how septicide, rapid adds substantial clinical improvement to care and outcomes.

348
00:55:36.400 --> 00:55:37.770
Dr. Roy Davis: Next slide, please,

349
00:55:39.250 --> 00:55:45.510
Dr. Roy Davis: in two thousand and nineteen. In the Us. There were one point, seven million hospitalizations diagnosed as Cetis.

350
00:55:45.620 --> 00:55:55.610
Dr. Roy Davis: It is the number one cause of hospital mortality with approximately three hundred and fifty thousand deaths per year, and this ranked is the number one most expensive medical condition

351
00:55:55.620 --> 00:55:58.700
Dr. Roy Davis: costing approximately forty, one billion dollars a year

352
00:56:05.210 --> 00:56:06.649
Dr. Roy Davis: next slide, please.

353
00:56:08.900 --> 00:56:10.820
Dr. Roy Davis: Appropriate management of sepsis

354
00:56:10.830 --> 00:56:16.200
Dr. Roy Davis: dependent upon early diagnosis to allow for rapid initiation of treatment.

355
00:56:20.610 --> 00:56:25.889
Dr. Roy Davis: This remains the major challenge presenting major towns pretending for diagnosis.

356
00:56:26.080 --> 00:56:34.319
Dr. Roy Davis: Presenting signs and symptoms are non-specific There is no diagnostic test that differentiates sepsis from non-infectious ideology

357
00:56:34.380 --> 00:56:40.310
Dr. Roy Davis: present biomarkers such as white, count, Crp, etc. Are non-specific

358
00:56:40.830 --> 00:56:50.069
Dr. Roy Davis: blood Cultures remain the gold standard, but are only positive at best in thirty percent of patients and results take twenty, four to seventy two hours.

359
00:56:50.430 --> 00:56:58.429
Dr. Roy Davis: Delays in diagnosis impacts appropriate clinical intervention, resulting in increased morbidity and mortality.

360
00:56:59.400 --> 00:57:00.550
Dr. Roy Davis: Next slide, please

361
00:57:03.960 --> 00:57:05.540
Dr. Roy Davis: tips your site rapid

362
00:57:05.670 --> 00:57:08.249
Dr. Roy Davis: measures M. Rna and white blood cells

363
00:57:08.330 --> 00:57:14.510
Dr. Roy Davis: quantifies the expression in two white cell genes, and is specific to infection and systemic information

364
00:57:14.870 --> 00:57:18.359
Dr. Roy Davis: independent of the type of pathogen that's causing the infection,

365
00:57:18.590 --> 00:57:22.059
Dr. Roy Davis: and is not reliant on finding the pathogen in the blood sample

366
00:57:24.030 --> 00:57:24.790
sixty minutes

367
00:57:24.800 --> 00:57:26.299
Dr. Roy Davis: for a result,

368
00:57:26.410 --> 00:57:32.209
Dr. Roy Davis: and translates the results into a clinical risk Score from one to fifteen called the Safety Score

369
00:57:32.500 --> 00:57:39.859
Dr. Roy Davis: reports. The likelihood of Cpsis is independent of severity, and the actual borisms are seen in one hundred percent of secession of sepsis

370
00:57:42.410 --> 00:57:43.480
Dr. Roy Davis: next slide, please.

371
00:57:47.210 --> 00:57:55.749
Dr. Roy Davis: Septicide rapid was validated, and Fda cleared as a sepsis diagnosing in a multi-center and retrospective and prospect of clinical study

372
00:57:55.950 --> 00:58:03.350
Dr. Roy Davis: primary objective want to demonstrate septicide rapid ability to differentiate tips from non-infectious series

373
00:58:03.930 --> 00:58:13.160
Dr. Roy Davis: inclusion criteria where patients presenting with two service criteria and starting on antibiotics as there is no gold standard for the comparison.

374
00:58:13.410 --> 00:58:23.359
Dr. Roy Davis: The comparator was a retrospective diagnosis of sepsis or serious by three leaders and sepsis in the United States. Following review of the clinical data at discharge

375
00:58:25.060 --> 00:58:26.250
Dr. Roy Davis: next slide, please.

376
00:58:27.790 --> 00:58:31.060
Dr. Roy Davis: The results of the validation study are shown in this side.

377
00:58:31.130 --> 00:58:37.599

Dr. Roy Davis: Four hundred and nineteen patients were included in the study consensus. Diagnosis of substance by the panel was used.

378
00:58:37.960 --> 00:58:43.939
Dr. Roy Davis: The graph on the left shows the increasing probability of sepsis with increasing safety score.

379
00:58:44.510 --> 00:58:56.159
Dr. Roy Davis: The probability of sepsis falls into four bands with band, one having less than a ten percent chance of sepsis with a sensitivity of ninety, four percent and a negative predictive value of ninety, one,

380
00:58:56.720 --> 00:59:05.819
Dr. Roy Davis: four scores have an eighty percent probability of sepsis with specificity of ninety percent and a positive predictive value of eighty One percent

381
00:59:06.380 --> 00:59:07.790
Dr. Roy Davis: next slide, please.

382
00:59:10.080 --> 00:59:23.369
Dr. Roy Davis: The upper left graph on the show slide shows the area under the curve of a septicite. Rapid's ability to differentiate sepsis from series in the full cohort, resulting in an area of the curve of zero point eight five.

383
00:59:23.380 --> 00:59:37.829
Dr. Roy Davis: The lower graph is the prospect of cohort, in which the test was performed on-site at the time of clinical assessment, showing an a you see of zero point nine. You grow up on the right and the A, you see, for differentiating captures from sewers

384
00:59:37.840 --> 00:59:52.920
Dr. Roy Davis: of the fourteen most common clinical variables used in sepsis diagnosis, either alone or in combination. Compared to the septiscore. As you can see, septicide rapid, simply score alone, or in combination outperforms all of the present clinical tools

385
00:59:53.240 --> 00:59:54.459
Dr. Roy Davis: next slide please

386
00:59:56.150 --> 01:00:11.060
Dr. Roy Davis: septicide rapid addresses, the need for rapid accurate differentiation of substance from non-infectious systemic information with actual results in about one hour step to site, rapid outperformance current clinically available tools to suspect their subscriptions,

387
01:00:11.250 --> 01:00:15.989
Dr. Roy Davis: increasing s to score correlates with increased likelihood of culture. Positivity

388
01:00:16.010 --> 01:00:17.240
Dr. Roy Davis: Next slide, please.

389
01:00:19.760 --> 01:00:24.390
Dr. Roy Davis: How does a hypocrite rapid improve the care of the suspicion of this patient

390
01:00:24.440 --> 01:00:36.070
Dr. Roy Davis: so have to say, a rapid alone, or in combination of superior and differentiating sepsis from service. Current clinical screening tools, such as sirs, Q. Sofa, et cetera, are very sensitive, but not specific

391
01:00:36.190 --> 01:00:46.940
Dr. Roy Davis: the addition of septicaid, rapid to the triaged suspected substance. Patient provides early rapid-specific diagnosis. Allowing for appropriate treatment within the one to three hours

392
01:00:47.310 --> 01:00:48.469
Dr. Roy Davis: it's a period

393
01:00:49.030 --> 01:01:04.950
Dr. Roy Davis: septicide. Rapid results allow for early antibody decisions to be made early. Appropriate antibiotics decreases mortality, while a low score may support no census diagnosis which will impact the use of antibiotics addressing antibiotic stewardship.

394
01:01:06.640 --> 01:01:11.450
Dr. Roy Davis: These results are actionable. Much sooner than the cultures or results for molecular education,

395
01:01:12.350 --> 01:01:18.039
Dr. Roy Davis: post-respons, tests or biomunkers such as Crp are a little about even certain kind of conditions.

396
01:01:18.420 --> 01:01:28.129
Dr. Roy Davis: Scepticite record has been shown to perform well in diagnosing sexes and patients with malignancy on antineoplasting drugs, or on immunosuppressants,

397
01:01:28.370 --> 01:01:33.660
Dr. Roy Davis: high-risk, post-operative surgical patients have been followed and diagnosed with census

398
01:01:33.880 --> 01:01:34.979
Dr. Roy Davis: by this test

399
01:01:35.200 --> 01:01:37.379
Dr. Roy Davis: and also in covid nineteen patients

400
01:01:37.500 --> 01:01:40.979
Dr. Roy Davis: who develop secondary or primary bacterial infections,

401
01:01:42.170 --> 01:01:54.490
Dr. Roy Davis: septicide, rapid outperforms, all current sepsis diagnostics allowing for early actionable diagnosis for the latest c of zero point eight five driving early therapy and appropriate culture of its collection,

402
01:01:55.560 --> 01:01:56.610
Dr. Roy Davis: the positive perception

403
01:01:57.710 --> 01:02:01.589
Dr. Roy Davis: with a one-hour turnaround time, the sip to school guides the condition, the

404
01:02:01.760 --> 01:02:09.409
Dr. Roy Davis: a reassess of additional diagnostic ideologies besides sexes thus improving diagnostic stewardship practices.

405
01:02:10.470 --> 01:02:13.669
Brenda Hudson: There are three remaining

406
01:02:14.370 --> 01:02:15.819
Dr. Roy Davis: next slide, please.

407
01:02:16.780 --> 01:02:19.530
Dr. Roy Davis: How does sipasite, rapid improve outcomes?

408
01:02:19.990 --> 01:02:31.719
Dr. Roy Davis: Septicide? Rapid aids such as antibiotic initiation consistent with the current guideline. The recent twenty, twenty, one surviving Texas campaign management guidelines recommend antibiotic initiation

409
01:02:31.750 --> 01:02:33.750
Dr. Roy Davis: based on the senses. Likelihood

410
01:02:34.160 --> 01:02:42.739
Dr. Roy Davis: high likelihood suggests antibiotics with one hour and four patients which fit in this criteria with an eighty one percent probability of census

411
01:02:42.980 --> 01:02:48.600
Dr. Roy Davis: possible sepsis antibiotics to be given within three hours. Ban three and four patients with

412
01:02:50.290 --> 01:02:54.360
Dr. Roy Davis: low likelihood of sepsis. The recommendation is differ. Antibiotics

413
01:02:54.410 --> 01:02:57.419
Dr. Roy Davis: and monitor band, one and two patients

414
01:02:59.810 --> 01:03:05.810
Dr. Roy Davis: safety score probability bands, aids, clinician and meeting guidelines and impacting outcome

415
01:03:08.680 --> 01:03:15.739

Dr. Roy Davis: substrate rapid our installations in complying with step one and surviving sessions campaign three. Our bundle recommendations

416
01:03:15.750 --> 01:03:29.009
Dr. Roy Davis: most common standard reasons for non-compliance is uncertainty of diagnosis or additional time needed to confirm the diagnosis. The one hour Turnaround time aids in addressing these two concerns and improving

417
01:03:29.130 --> 01:03:37.789
Dr. Roy Davis: outcomes by meeting these compliance standards. Legislature confirmed that early. An appropriate investigation of the source of the infection

418
01:03:38.140 --> 01:03:48.370
Dr. Roy Davis: proves patients. A response to therapy and outcome. A higher steps is probability results within one hour would guide the connection to implemented source control embedding outcome.

419
01:03:49.770 --> 01:03:51.000
Dr. Roy Davis: Next slide, please,

420
01:03:52.840 --> 01:03:54.160
Dr. Roy Davis: in summary

421
01:03:54.670 --> 01:04:01.660
Dr. Roy Davis: septicite rapid is the only technology to accurately differentiate sepsis versus non-effective systemic information in one hour.

422
01:04:02.520 --> 01:04:11.279
Brenda Hudson: Sepsis rate rapid. Also outperforms currently use sepsis diagnostic tools Consistently there is one minute remaining

423
01:04:11.450 --> 01:04:24.829
Dr. Roy Davis: consistently achieving a rock's values of eight point zero point eight, three, zero point, eight, seven across various patient cohorts, and in multiple studies this rapid, turnaround time allows for early steps of identification,

424

01:04:25.140 --> 01:04:28.149
Dr. Roy Davis: an appropriate intervention and suspecting sepsis patients

425
01:04:28.200 --> 01:04:36.490
Dr. Roy Davis: driving prompt source control investigation. All of which combined is documented to improve patient outcomes and clinical care

426
01:04:37.160 --> 01:04:41.970
Dr. Roy Davis: septicide record provides action will result by a suspected sepsis patient.

427
01:04:41.980 --> 01:04:46.219
Dr. Roy Davis: Well, before blood, culture or molecular pathogen detection results.

428
01:04:48.450 --> 01:04:52.989
Dr. Roy Davis: Thank you for time and intention. I'd like to address any questions that come up.

429
01:05:02.200 --> 01:05:04.160
Drew Kasper: Thank you for your presentation.

430
01:05:04.470 --> 01:05:07.979
Drew Kasper: Are there any questions from the public?

431
01:05:08.130 --> 01:05:24.509
Drew Kasper: And we haven't been getting a lot of questions from the public. So i'm going to say, Um, what's open up to both public for cms? Are there any questions from the public or Cms, and this could include other applicants that have questions as well. Um, please raise your hand or use

432
01:05:26.210 --> 01:05:27.839
of zoom,

433
01:05:37.880 --> 01:05:39.990
Drew Kasper: and I see a raised hand.

434

01:05:42.810 --> 01:05:46.280
Drew Kasper: Um, amber, amber. Go ahead and unmute.

435
01:05:47.240 --> 01:05:59.069
Amber Woodruff: Good morning. Thank you. Um. Everybody for your presentations this morning. My name is Amber Woodruff, and I'm. From Cms. And my question is, you mentioned other sepsis diagnostic.

436
01:05:59.240 --> 01:06:07.129
Amber Woodruff: Can you discuss whether a sepsicide lab is also used for this purpose, and whether it would be an appropriate comparator?

437
01:06:08.590 --> 01:06:12.350
Dr. Roy Davis: So i'm not sure what your question is addressing

438
01:06:15.710 --> 01:06:17.380
Amber Woodruff: so? Um,

439
01:06:17.430 --> 01:06:23.930
Amber Woodruff: yes, for sub-site rapid you. You mentioned that there might be some other um

440
01:06:24.040 --> 01:06:28.720
Dr. Roy Davis: not as efficient diagnostic tools.

441
01:06:28.730 --> 01:06:31.789
Amber Woodruff: Um! Can you discuss whether sub-site lab

442
01:06:31.860 --> 01:06:37.799
Amber Woodruff: is used for this purpose, and whether it would be an appropriate comparator to sub-site rapid.

443
01:06:37.860 --> 01:06:49.050
Dr. Roy Davis: The Sepside lab was our predicate for the scepticide rapid test. Tipzine Lab was a binge test. Time sent around. Time was approximately four to six hours to come on

444
01:06:49.580 --> 01:07:08.489
Dr. Roy Davis: complexity, and we thought it was not appropriate to introduce this clinically. We modified that, and put this into a

cartridge basis and a one-out turnaround time which has obvious clinical outcome impact and usability. So it is basically, the same test, but modified.

445
01:07:08.500 --> 01:07:11.050
Dr. Roy Davis: You have a good turnaround time.

446
01:07:12.140 --> 01:07:17.839
Amber Woodruff: Thank you. Um. One follow up question. Was sub-site lab ever available in the Us.

447
01:07:18.120 --> 01:07:30.670
Dr. Roy Davis: Step aside. Lab was cleared by the Fda and available, but not used, as we felt from a marketing standpoint. From a clinical standpoint it was really not of value except for research conditions.

448
01:07:31.120 --> 01:07:32.380
Amber Woodruff: Thank you.

449
01:07:38.200 --> 01:07:42.009
Drew Kasper: Thank you. Are there any other questions from the public or Cms

450
01:07:44.120 --> 01:07:47.769
Drew Kasper: for you to type them into the Q. And a feature in zoom

451
01:07:48.160 --> 01:07:51.320
Drew Kasper: or use the raise hand function to be unmuted.

452
01:07:53.270 --> 01:07:57.189
Drew Kasper: Do not see any raised hands.

453
01:08:02.410 --> 01:08:05.140
Drew Kasper: There are no new questions in the Q. A.

454
01:08:07.110 --> 01:08:17.699
Drew Kasper: And there are no new questions via the new tech airbox. Okay? Well, with that, Thank you again for your presentation.

455

01:08:19.290 --> 01:08:21.029
Dr. Roy Davis: Thank you. And

456
01:08:21.340 --> 01:08:26.889
Drew Kasper: we will now hear from presenters for the vest technology application.

457
01:08:32.310 --> 01:08:34.020
Dr. Daniel Goldstein: Good morning. Can you hear me?

458
01:08:35.080 --> 01:08:45.780
Drew Kasper: We can thank you perfect. Thank you, Casper. Ah! On behalf of vascular graph solutions and myself. I want to thank Cms for the opportunity to share with you

459
01:08:46.359 --> 01:09:01.519
Dr. Daniel Goldstein: the data that has been gathered from clinical trials and real world experience, with a unique device that is designed as an external support, scaffolding for saff and his vein graph the most commonly used conduits for corn a by-based surgery worldwide.

460
01:09:01.710 --> 01:09:14.290
Dr. Daniel Goldstein: I would like to disclose that I am one of the national kobe eyes for the ongoing best clinical trial, which is being run in collaboration with the Nih's Cardi Thoracic surgery network. Next slide, please.

461
01:09:16.490 --> 01:09:28.230
Dr. Daniel Goldstein: As a background information. It is important to appreciate that coronary's disease impacts a large number of Americans, and remains the number one cause of death in the United States and Western societies.

462
01:09:28.359 --> 01:09:33.200
Dr. Daniel Goldstein: The estimated total cost of caring for people with this disease is exorbitant.

463
01:09:33.510 --> 01:09:46.859
Dr. Daniel Goldstein: Cornay bypass surgery remains the goldstander treatment for patients with severe coronary. Already disease, and accounts for two hundred thousand procedures per year. For the past

several years in the United States.

464
01:09:47.210 --> 01:09:54.840
Dr. Daniel Goldstein: During this operation disease coronary arteries are bypassed with arterial grafts, and with saff and his main grass,

465
01:09:55.310 --> 01:10:10.469
Dr. Daniel Goldstein: the latter constitute the most commonly used Conrad with an average of two point, two, seven. It's Vane grass for operation, therefore, approximately four hundred and fifty thousand. Sapphon, as being graphs are created per year next slide, please.

466
01:10:12.930 --> 01:10:20.729
Dr. Daniel Goldstein: Failure of these graphs constitutes the major limitation to the long-term success of coronary bypass surgery,

467
01:10:21.150 --> 01:10:26.880
Dr. Daniel Goldstein: the biological process underpinning staff and his vein Graph failure are well described.

468
01:10:27.210 --> 01:10:45.500
Dr. Daniel Goldstein: Early failure, occurring within hours to days after cornet. Bypass surgery is related to technical factors like poor conduits, a traumatic harvest of the conduit, pinking or compression of the graph, and is characterized by thrombotic oclusion.

469
01:10:45.830 --> 01:10:57.849
Dr. Daniel Goldstein: The more chronic and insidious graph failure which you see here on this graph occurs as a result of the development of intimal hyperplasia. Starting several months to one year after surgery

470
01:10:58.370 --> 01:11:08.589
Dr. Daniel Goldstein: By ten years after surgery, fifty percent of the Stephan as being grass are completely occluded, and half of the remaining Peyton ones are severely diseased.

471
01:11:08.950 --> 01:11:10.830
Dr. Daniel Goldstein: The best device

472
01:11:10.940 --> 01:11:14.809

Dr. Daniel Goldstein: targets, the biological process of internal hyperplasia.

473
01:11:20.670 --> 01:11:38.490
Dr. Daniel Goldstein: The only prophylaxis against the development of saphon as being graph failure is the use of aspirin and statins, both of which have had a limited impact, however, and thus there remains in our met clinical need to forestole or mitigate the development of the sephon is vein graph failure.

474
01:11:38.640 --> 01:11:40.179
Dr. Daniel Goldstein: Next slide, please.

475
01:11:41.830 --> 01:11:59.120
Dr. Daniel Goldstein: The problem with suffering is being graph. Failure is that it can lead to adverse clinical events, including a recurrence of engineer and or myocardial infarction and the ensuing need for rivascarization to treat that angular or mycard infection and or death.

476
01:11:59.340 --> 01:12:08.679
Dr. Daniel Goldstein: The frequency of these events, at one and five years after surgery are depicted here along with the health care costs associated with these treatments.

477
01:12:09.550 --> 01:12:10.840
Next slide.

478
01:12:12.880 --> 01:12:31.909
Dr. Daniel Goldstein: The vest device is a proprietary cobalt chronium scent that is deployed outside the staff. It's been graph at the time of surgery. It requires no more than a couple of minutes to deploy, and it does not require the surgeon to change the way he or she performs the operation.

479
01:12:32.110 --> 01:12:37.040
Dr. Daniel Goldstein: More than seven thousand such devices in several countries have been implanted.

480
01:12:37.240 --> 01:12:40.969
Dr. Daniel Goldstein: The device is seeing Mark approved in the European Union.

481
01:12:41.170 --> 01:12:53.459
Dr. Daniel Goldstein: We will go over some of the salient clinical outcome data that has been accumulated from four randomized clinical trials, five road registries, and featured in fifteen peer review publications.

482
01:12:53.680 --> 01:13:01.039
Dr. Daniel Goldstein: Importantly, there is no other device in the market or under investigation anywhere to our knowledge.

483
01:13:01.540 --> 01:13:02.900
Dr. Daniel Goldstein: Next slide

484
01:13:04.730 --> 01:13:21.700
Dr. Daniel Goldstein: the data shown here as being prepared for a manuscript. It shows that the use of the device was associated with a reduction of nearly fifty percent in the instance of very early graph failure, as shown in cat scans that were performed one week after surgery.

485
01:13:21.710 --> 01:13:29.210
Dr. Daniel Goldstein: Now I just share with you that this device was designed to mitigate internal hyperplasia. In process. It occurs much later on.

486
01:13:29.310 --> 01:13:45.519
Dr. Daniel Goldstein: So this was a surprise, and we believe that the beneficial effect is likely related to the avoidance of pinking or compression of the saffon as vingraft as it exes the order, providing a smooth lie on the epicarial surface of the heart,

487
01:13:47.580 --> 01:13:51.990
Dr. Daniel Goldstein: or the non-surgeons in the audience. If you can see this is my model heart.

488
01:13:52.290 --> 01:14:09.170
Dr. Daniel Goldstein: This year is a sacrificing graph sort of street to the right coronary circulation this year. It's a sapphire and graph to the Circle Flex. And this here is a memorial that you know, is used to bypass the interior descending artery. You can imagine it would The chest is closed,

489
01:14:15.080 --> 01:14:27.429
Dr. Daniel Goldstein: it can kink it can be compressed, et cetera. So, having this outside scaffolding, perhaps creates a smooth, a lie and a more uniform lie. So those things are less likely to happen

490
01:14:28.840 --> 01:14:30.190
Dr. Daniel Goldstein: Next Slide

491
01:14:32.120 --> 01:14:48.990
Dr. Daniel Goldstein: Data from two randomized clinical trials conducted in the United Kingdom show a significant reduction in into the hypoplasia, as measured by intravascular ultrasound, a significant improvement, and the uniformity of the saffron who's in graph something you know, is strong predictive of grass area

492
01:14:49.000 --> 01:15:04.149
Dr. Daniel Goldstein: and clinically, it's a a reduction in the need for ischemic drivenary. Vascarization so the numbers are too small to achieve significance as the follow-up required to collect sufficient data necessitates several years of observation. Next slide

493
01:15:06.190 --> 01:15:14.190
Dr. Daniel Goldstein: to focus on the clinical, critical, clinical outcome with scheme, a given and vascarization. You see here data from three different sources

494
01:15:14.200 --> 01:15:31.060
Dr. Daniel Goldstein: from Europe, the United States and the Uk. At different post-operative time points, and these show a consistent reduction on this mace event, and the impact appears to increase over time with the greatest impact. Scene at the four and a half year. Study

495
01:15:31.130 --> 01:15:32.700
Dr. Daniel Goldstein: next slide, please.

496
01:15:33.610 --> 01:15:36.490
Brenda Hudson: There are three minutes remaining

497
01:15:36.500 --> 01:15:55.469

Dr. Daniel Goldstein: additional non-randomized but prospectively acquired data from two studies in Europe show a very low rate of me for erascarization. Up to years all these patients in these two series receive at least one best device. These rates are lower than those reported in cost, effectiveness. Models next slide

498
01:15:56.920 --> 01:16:13.369
Dr. Daniel Goldstein: displayed. Here is the same information from prior slides in a different way, showing the relative reduction in Iskemia ribbon vascarization, based on three clinical, random randomized clinical trials at different time points after coronary bypass surgery next slide.

499
01:16:15.040 --> 01:16:31.880
Dr. Daniel Goldstein: Most recently preliminary data from an analysis conducted in South Africa, looking at adverse events and mortality from a large insurance company database, with a five-year follow-up of two hundred and fifty, three best recipients, and over five thousand control cabbages for out best

500
01:16:31.890 --> 01:16:43.190
Dr. Daniel Goldstein: demonstrates a lower O God, mortality and incidence of adverse events among the series of at least one best device. Clearly more granular data is necessary in upcoming.

501
01:16:43.200 --> 01:16:48.519
Dr. Daniel Goldstein: But this preliminary data hint at the possibility of benefit over a long-term follow-up

502
01:16:48.560 --> 01:16:49.840
Dr. Daniel Goldstein: next slide.

503
01:16:50.590 --> 01:17:09.490
Dr. Daniel Goldstein: This additional data displays survival and a Ben-free survival among the seventy-four patients enroll in the Austrian study, which I just showed earlier documenting the benefit and early graph occlusion. Both curves are quite favorable with three-year survival and a battery survival in the ninety percent range.

504
01:17:09.920 --> 01:17:11.279
Dr. Daniel Goldstein: Next slide.

505

01:17:13.210 --> 01:17:34.690
Dr. Daniel Goldstein: So The totality of the data thus far accumulated suggests that the use of the best device can one unexpectedly provide a reduction in early graph failure and two resulting a reduction in the rate of repeated rascization that extends at least to five years when compared to data from the literature in benefit, they can potentially translate into sizeable while savings.

506
01:17:35.150 --> 01:17:37.939
Brenda Hudson: There is one remaining.

507
01:17:39.190 --> 01:17:41.240
Dr. Daniel Goldstein: Thank you. Next slide.

508
01:17:43.950 --> 01:17:49.669
Dr. Daniel Goldstein: Thank you for your attention, and there are several members of Bgs on the line, and we're happy to take questions.

509
01:17:53.950 --> 01:17:55.080
Drew Kasper: All right.

510
01:17:56.490 --> 01:17:58.549
Drew Kasper: Thank you for your presentation.

511
01:17:58.710 --> 01:18:03.450
Drew Kasper: Are there any questions from the public or from Cms.

512
01:18:05.090 --> 01:18:10.219
Drew Kasper: Include questions from other applicants, and you can use the Q. And a function,

513
01:18:10.870 --> 01:18:15.470
Drew Kasper: or you can use the raise hand function.

514
01:18:20.960 --> 01:18:36.469
Drew Kasper: You want to just remind folks that if you are a panelist, you will be in charge of your immune function. So if you're not talking, we appreciate you making sure that your phone is muted during their presentations.

515

01:18:38.230 --> 01:18:42.009
Drew Kasper: I don't see any new questions in the Q. And A.

516
01:18:42.820 --> 01:18:46.420
Drew Kasper: We're open to questions from the public or Cms.

517
01:18:46.840 --> 01:18:49.740
Drew Kasper: There are no raised hands

518
01:18:49.780 --> 01:18:51.050
Drew Kasper: in the

519
01:18:52.300 --> 01:18:53.570
Drew Kasper: the group

520
01:18:54.350 --> 01:18:58.130
Drew Kasper: and no raised hands and the panelists grew.

521
01:18:59.510 --> 01:19:01.160
Drew Kasper: There are

522
01:19:01.200 --> 01:19:05.710
Drew Kasper: no new questions in the Cms. New Tech mailbox.

523
01:19:08.170 --> 01:19:10.559
Drew Kasper: The last call for questions.

524
01:19:13.600 --> 01:19:18.060
Drew Kasper: Can I see a raised hand from Edina. Adina, please go ahead and unmute,

525
01:19:18.840 --> 01:19:27.899
Adina Hersko: So can you talk about the surgical procedure itself, Whether other aspects of cells were tested, such as pump. Use no touch, procedures, et cetera.

526
01:19:28.920 --> 01:19:44.899
Dr. Daniel Goldstein: Thank you. Excellent question. Just so. You probably don't know. But the the design of the trial required within

patient randomization. So we avoid any biological ah differences from patient to patient, or the way that operation was conducted in one place or another.

527
01:19:44.910 --> 01:20:03.200
Dr. Daniel Goldstein: Um! Everything that was done was sort of what I showed you like. We always do, Coronavirus, and the only difference is so. We create the what we call the distal and asthmosis first was a connection, or the vain to the artery, and then we simply slide this device, which is already pre-measured according to elect to the vein

528
01:20:03.210 --> 01:20:12.190
Dr. Daniel Goldstein: and then perform the vonsel mon estimosa. So there's nothing that changes in the way the surgeon does the operation in terms of five best views or any other variable.

529
01:20:14.520 --> 01:20:20.129
Adina Hersko: Thank you. Can you also talk about whether any adjustments

530
01:20:20.150 --> 01:20:22.830
Adina Hersko: to the p-values were made for multiple comparisons

531
01:20:23.760 --> 01:20:25.019
Dr. Daniel Goldstein: or

532
01:20:27.830 --> 01:20:30.080
Adina Hersko: sorry there are multiple comparisons

533
01:20:30.120 --> 01:20:31.990
Adina Hersko: for multiple comparisons.

534
01:20:32.290 --> 01:20:36.620
Dr. Daniel Goldstein: Yeah, I'm going to the fair that the for that question to

535
01:20:36.640 --> 01:20:39.649
Dr. Daniel Goldstein: uh road time, or someone from Vgs

536
01:20:49.630 --> 01:20:50.800

Dr. Daniel Goldstein: y'all,

537
01:20:56.250 --> 01:21:00.829
Dr. Daniel Goldstein: I guess there's no already on the line to answer the multiple

538
01:21:00.940 --> 01:21:04.139
Dr. Daniel Goldstein: the p-values that you refer to, as in which trial

539
01:21:04.510 --> 01:21:10.169
Drew Kasper: what we can really make sure that they are is yeah

540
01:21:10.920 --> 01:21:14.090
Drew Kasper: is E. I a l orion of

541
01:21:14.100 --> 01:21:15.890
Drew Kasper: I all around you. Zoom: Yeah,

542
01:21:15.900 --> 01:21:16.930
Eyal Orion: I'm: here.

543
01:21:17.800 --> 01:21:19.959
Drew Kasper: Yeah, Sorry. I

544
01:21:20.190 --> 01:21:27.239
Eyal Orion: Yeah, it's good. Can you please repeat the questions which comparison comparative analysis did you refer to at dinner?

545
01:21:28.280 --> 01:21:35.900
Adina Hersko: Yeah, we had a question about the multiple comparisons, and if any adjustments were made to the p-values for that,

546
01:21:36.770 --> 01:21:40.340
Eyal Orion: the p-values in the pivotal study are swimming. To

547
01:21:42.440 --> 01:21:53.899
Eyal Orion: Yeah. So of course, we have done several sub-analyses the primary, and both analysis of the pivotal study was a reduction in

itimal hyperplasia at one year

548
01:22:05.430 --> 01:22:12.459
Eyal Orion: to the data which showed a subgroup of patients like diabetics, for example, the benefit even double.

549
01:22:27.980 --> 01:22:29.019
Thank you,

550
01:22:30.110 --> 01:22:39.950
Dr. Daniel Goldstein: Adina, the the The details of the statistical analysis, I presume again, from the pivotal trial, are published

551
01:22:40.490 --> 01:22:43.989
Dr. Daniel Goldstein: in jam, a cardiology. So you can refer to that there

552
01:22:44.000 --> 01:23:02.349
Eyal Orion: and just just to add on this, remember that the the unique design was within patient randomization. So we didn't randomize two different groups. The comparison, the comparisons you've seen, and all the inputs was within the same patient. Ah! Two veins within the same patients, one with a device, one without

553
01:23:05.920 --> 01:23:08.649
Drew Kasper: Rotam. You are also unmuted.

554
01:23:11.020 --> 01:23:17.120
Drew Kasper: You should be momentarily here. I've asked that you be unmuted. Yeah, you could do unmute rotem.

555
01:23:17.130 --> 01:23:18.730
Rotem Katzenellenbogen: Thank you.

556
01:23:18.740 --> 01:23:22.900
Rotem Katzenellenbogen: Thank you. J. A. Lore on our already replied Thank you.

557
01:23:33.900 --> 01:23:37.450
Drew Kasper: Hey? Do we have any other questions

558
01:23:38.530 --> 01:23:40.380
Drew Kasper: in the public or Cms.

559
01:23:46.460 --> 01:23:51.169
Drew Kasper: Be no additional raised hands from panelists or attendees?

560
01:23:53.010 --> 01:23:56.860
Drew Kasper: There are no new questions in the new tech mailbox.

561
01:23:58.300 --> 01:24:02.029
Drew Kasper: There are no new questions in the Q. And A.

562
01:24:03.350 --> 01:24:04.360
Drew Kasper: Hey?

563
01:24:05.030 --> 01:24:08.789
Drew Kasper: All right, folks. So with that

564
01:24:08.910 --> 01:24:12.130
Drew Kasper: we will now be heading into

565
01:24:13.000 --> 01:24:14.650
Drew Kasper: break period.

566
01:24:14.840 --> 01:24:23.150
Drew Kasper: We are six minutes ahead of schedule. Excuse me, so we have until ten, forty, five.

567
01:24:23.620 --> 01:24:29.039
Drew Kasper: Please be back and ready to go for ten, forty five folks. Thank you.

568
01:24:31.830 --> 01:24:38.029
Drew Kasper: Continue to just be logged in and walk away from your computer for the next twenty minutes.

569

01:26:14.540 --> 01:26:15.760
Drew Kasper: Anyone

570
01:26:16.880 --> 01:26:19.410
Drew Kasper: and anyone who um

571
01:26:19.470 --> 01:26:32.090
Drew Kasper: is logging on via telephone. Rather not logging on to your computer, but just on the telephone. You can email us this new attack at Dms. Hhs. Gov: If you have a question.

572
01:26:32.100 --> 01:26:35.519
Drew Kasper: You're not long, then, to be able to submit it

573
01:26:37.120 --> 01:26:39.060
Drew Kasper: through the through the zoom.

574
01:26:39.230 --> 01:26:48.889
Drew Kasper: We do ask also that if you're not presenting that you please ensure that your phone is muted. There is a zoom function for me that you can use

575
01:26:51.320 --> 01:26:53.539
Drew Kasper: with that

576
01:26:54.120 --> 01:26:55.809
Drew Kasper: by two.

577
01:26:58.010 --> 01:27:00.090
Drew Kasper: Welcome Our next presenters.

578
01:27:00.720 --> 01:27:08.469
Drew Kasper: We'll now hear from presenters for the

579
01:27:10.130 --> 01:27:38.300
Dr. Robert Stevens: thank you Drove. Ah, good morning. I'm. Robbie Stevens, the Vice President and head of Medical barriers at series. Therapeutics. We thank Cms. For allowing us to present this in tab application for Sierra one hundred and nine, an investigational microbiome therapeutic to prevent recurrent cluster diocese diplomacy,

which I will shorten to see depth infection throughout my presentation. Next slide, please shows my disclosures,

580
01:27:38.370 --> 01:27:40.809
Dr. Robert Stevens: and then the next slide. Please.

581
01:27:41.000 --> 01:27:58.309
Dr. Robert Stevens: Recurrent sea death. Infection has a high unmet need, and is associated with significant morbidity and mortality. Patients can experience up to fifteen episodes of watery diary of per day, requiring them to be home bound and tethered to the toilet.

582
01:27:58.320 --> 01:28:03.290
Dr. Robert Stevens: This results in a markedly diminished quality of life for the individual patient

583
01:28:03.300 --> 01:28:12.539
Dr. Robert Stevens: about one in four patients experience recurrent infections and over twenty thousand patients died per year. To this infection. Next slide

584
01:28:13.130 --> 01:28:34.310
Dr. Robert Stevens: an initial recurrence is a sign that the microbiome is disrupted and may need repair. The twenty five percent of patients that enter a recurrent cycle is the focus of our N-tab application. With c. One hundred and nine It is important to stop this cycle, recurrent infection and repair the microbiome, as shown on the next slide.

585
01:28:35.980 --> 01:28:51.560
Dr. Robert Stevens: The first illustration in the upper left is a healthy, diverse, gut microbiome but the combination of antibiotics causing disruption of this microbiome, coupled with exposure to c div scores, leads to infection

586
01:28:51.570 --> 01:29:07.669
Dr. Robert Stevens: a two-pronged treatment shown in the gray shaded box in the rights portion of this slide is needed, starting with antibiotics to kill a vegetative bacteria, followed by microbiome repair to increase microbial diversity.

587
01:29:07.680 --> 01:29:19.480

Dr. Robert Stevens: Up until now microbiome repair has been with fecal microbiota, transplantation, or fmt, which is whole donor derived stool next slide.

588
01:29:20.060 --> 01:29:26.500
Dr. Robert Stevens: But fmt is an unapproved product associated with several safety issues

589
01:29:26.630 --> 01:29:43.299
Dr. Robert Stevens: issued by the Fda warning of the potential risk of transmission of infectious pathogens. Therefore safer products are needed that undergo rigorous clinical development and demonstrate the safety and efficacy in preventing recurrent, c. Death infection.

590
01:29:43.310 --> 01:29:48.849
Dr. Robert Stevens: One such live by logic. Product is Cer. One hundred and nine next slide

591
01:29:49.250 --> 01:30:18.500
Dr. Robert Stevens: moving clockwise from the upper left. I will describe how, c. One hundred and nine prevents recurrency deep infection. In nearly ninety percent of patients as a well-tolerated safety profile is administered or orally with a low pill burden of four capsules once daily. For three days. The Fda granted priority Review for the biologic license application for C one hundred and nine with a Padua action, date of April twenty sixth, two thousand and twenty-three

592
01:30:18.570 --> 01:30:19.949
Dr. Robert Stevens: next slide

593
01:30:20.900 --> 01:30:36.319
Dr. Robert Stevens: seer one hundred and nine is a purified consortia of donor-drived firm, acute scores, and it is the extraction and purification of the firm. Acute scores that supports a new technology advancement. For this live by logic.

594
01:30:36.330 --> 01:30:55.130
Dr. Robert Stevens: Fermakutes are key bacteria. In preventing sea dips for germination and growth. They are resistant to gastric acidity, which allows for an oral formulation taken by mouth, avoiding a procedure for drug administration, such as a colonoscopy or rectal animal,

595
01:30:55.140 --> 01:31:10.239
Dr. Robert Stevens: a key component of the technology in manufacturing c. One hundred and nine is the process in activates vegetative bacteria, parasites, fungi, and viruses, including Sars Cov. Two next slide.

596
01:31:11.580 --> 01:31:27.689
Dr. Robert Stevens: For the remainder of the presentation I will discuss the phase three data that support how se. One hundred and nine provides a substantial clinical improvement to standard of care treatment with antibiotics for recurrency. Death next slide

597
01:31:30.970 --> 01:31:32.589
Dr. Robert Stevens: next slide, please.

598
01:31:36.280 --> 01:31:40.389
Dr. Robert Stevens: Ecos four hundred and three was a phase three randomized, controlled trial,

599
01:31:40.400 --> 01:31:54.379
Dr. Robert Stevens: where one hundred and eighty-two patients were toxin-positive C diagnosis, thus confirming patients had true infection and having symptom resolution. After receiving ten to twenty, one days of standard of care antibiotics,

600
01:31:54.390 --> 01:32:14.269
Dr. Robert Stevens: we're randomized to sear one hundred and nine or placebo or oral capsules once daily for three days following administration of ten ounces of magnesium citrate. To remove any residual antibiotic in the gut. The trial was powered to demonstrate superiority. Next slide

601
01:32:15.130 --> 01:32:30.449
Dr. Robert Stevens: this table is the demographics of a study population, where I will call your attention to subject age. On the third line over half of the subjects were sixty, five years of age or greater, which is an age cohort of interest to Cms.

602
01:32:30.610 --> 01:32:32.059
Dr. Robert Stevens: Next slide

603
01:32:32.840 --> 01:32:53.230
Dr. Robert Stevens: the Bar charts to illustrate the primary efficacy results at eight weeks, showing that Se. One hundred and nine was superior to placebo in reducing risk of recurrency, gift, infection in the left bar charts, twelve percent of c. One hundred and nine subjects had a recurrence compared to forty percent or placebo.

604
01:32:53.240 --> 01:33:04.990
Dr. Robert Stevens: This absolute difference of twenty-eight percent is the largest delta reported for any phase two or three randomized controlled trial with a live biologic product.

605
01:33:05.000 --> 01:33:15.680
Dr. Robert Stevens: The bar chart on the right shows the opposite result to recurrence rate, which is eighty eight percent of subjects at a sustained clinical response to C, one hundred and nine

606
01:33:15.690 --> 01:33:30.990
Dr. Robert Stevens: Not shown on the slide is the number needed to treat for Co. One hundred and nine, which was three point six. So for every four patients treated with C, one hundred and nine, one case of recurrency gift would be prevented. Next slide

607
01:33:31.490 --> 01:33:43.980
Dr. Robert Stevens: recurrence rates in subjects sixty, five years of age or older, are shown in the left bar chart. Seventeen percent of Se. One hundred and nine and forty, six percent of placebo patients have recurrence.

608
01:33:44.030 --> 01:34:03.270
Dr. Robert Stevens: This is an absolute difference of twenty, nine, and consistent with the twenty, eight percent difference for the overall study population that I showed on the previous slide. These findings reveal that C one and I a similar efficacy across the eight adult age spectrum Next slide

609
01:34:04.600 --> 01:34:15.780
Brenda Hudson: this cabin. My analysis scrapes the natural history of recurrence. Following antibiotic discontinuation. There are three,

610
01:34:16.380 --> 01:34:22.379
Dr. Robert Stevens: mostly different recurrences occurred rapidly

within a couple weeks two

611
01:34:22.390 --> 01:34:40.510
Dr. Robert Stevens: separation between Sierra, one hundred and nine, depicted in the Orange line and Placebo, The black line is observed within a few days following antibiotics, highlighting the importance of early Se. One hundred and nine, and administration, in reducing risk of recurrent Cdi;

612
01:34:40.520 --> 01:34:53.859
Dr. Robert Stevens: and third, the magnitude of difference between Placebo and C one hundred and nine is maintained through the twenty-four weeks, attributing to the durability of response to Cer, one hundred and nine next slide

613
01:34:54.850 --> 01:34:59.389
Dr. Robert Stevens: the purported mechanism of C. One hundred and nine is depicted in these figures.

614
01:34:59.400 --> 01:35:10.349
Dr. Robert Stevens: The blue bars in the left panel shows the significant and grassment in the gut of the seer. One hundred and nine dose species at week one, and maintained through week eight,

615
01:35:10.360 --> 01:35:30.810
Dr. Robert Stevens: which leads to increases in secondary bio-acid metabolites shown in the middle panel that are needed to prevent c. Depths for germination that ultimately results in the observed clinical response shown in the right now, which is showing the superiority of Sierra, one hundred and nine to the citybo

616
01:35:30.820 --> 01:35:35.359
Dr. Robert Stevens: standard of care, Antibiotics Next slide

617
01:35:36.200 --> 01:35:47.890
Dr. Robert Stevens: seer, one hundred and nine was well tolerated with a safety profile characterized in the table. The most common adversity. Events were gastrointestinal in nature, and were mild to moderate.

618
01:35:47.900 --> 01:35:58.619
Dr. Robert Stevens: Three deaths occurred on the seer, one hundred and

nine arm, and were reported as being unrelated to cer one hundred and nine by the blinded investigator. Next slide.

619
01:35:59.840 --> 01:36:13.829
Dr. Robert Stevens: Results of the ecosystem for open-label phase three study are consistent with the safety and efficacy findings recorded in the ecosystem. Three randomized control trial that I just reviewed

620
01:36:13.840 --> 01:36:35.210
Brenda Hudson: Ecos Four four is my first study, showing at least ninety sustained, showing at least ninety sustained clinical response that we gave, regardless of number of prior recurrent episodes, as shown in the figure. The sustained clinical response in first recurrent patients was ninety four percent

621
01:36:35.220 --> 01:36:38.290
and ninety percent for multiple recurrence,

622
01:36:38.300 --> 01:36:49.889
Dr. Robert Stevens: as in Ecos four, three, The most common adverse events in this open-labeled stoneup are gi related and mild to moderate in nature. None of the a deaths were determined to be related,

623
01:36:49.900 --> 01:37:08.639
Dr. Robert Stevens: or possibility related to this study plan. In the next slide my final slide to summarize clinical outcomes for recurrency. Depth can be significantly improved with the two prong treatment. Approach of antibiotics, followed by microbiome recovery, with se one hundred and nine

624
01:37:08.730 --> 01:37:17.520
Dr. Robert Stevens: c. One hundred and nine was superior to placebo in reducing recurrence. Validating this, four-based therapeutic approach

625
01:37:17.530 --> 01:37:27.489
Dr. Robert Stevens: Overall Sear, one hundred and nine was well tolerated, which might be expected, since firm, acute spores are normal residents of the healthy, gut microbiome,

626
01:37:27.500 --> 01:37:55.810

Dr. Robert Stevens: sir, one hundred and nine achieved high efficacy while mitigating risk of transmitting infectious agents through intensive donor screening and manufacturing processes. Lastly, if approved, seer, one hundred and nine, maybe may potentially be the first in class oral microbiome therapeutic serving as appropriate foundation therapy for a broad set of patients caught in the vicious cycle of recurrency, death, infection.

627
01:37:55.820 --> 01:37:56.940
Dr. Robert Stevens: Thank you,

628
01:37:58.920 --> 01:38:01.759
Drew Kasper: and thank you very much for your presentation.

629
01:38:01.920 --> 01:38:05.570
Drew Kasper: Are there any questions from the public or Cms?

630
01:38:06.740 --> 01:38:10.620
Drew Kasper: It's the Q. And A. Feature or the raise hand feature?

631
01:38:20.410 --> 01:38:23.990
Drew Kasper: See any new questions in the new tech mailbox.

632
01:38:26.900 --> 01:38:32.259
Drew Kasper: No questions in the Q. And A. Yet. And let's see here we do have a question.

633
01:38:32.580 --> 01:38:34.270
Drew Kasper: But please proceed, Adena.

634
01:38:35.540 --> 01:38:36.650
Adina Hersko: So

635
01:38:36.680 --> 01:38:50.900
Adina Hersko: you provide the rationale for exclusion out patients treated with as we talk from that from the trial, and whether there is any evidence demonstrating differences in recurrent patients treated with Epochromat and Sdr. One hundred and nine.

636
01:38:53.550 --> 01:39:10.919

Dr. Robert Stevens: Yes, we have no data on Ah, on the outcome of antibiotics with Beslok Toxomat, followed by Uh Sierra one hundred and nine. The rationale for not including a

637
01:39:10.930 --> 01:39:17.009
Dr. Robert Stevens: toxomab in the Protocol will require me to get back with you for that complete answer.

638
01:39:19.480 --> 01:39:20.739
Adina Hersko: Okay, thank you.

639
01:39:26.570 --> 01:39:30.799
Drew Kasper: We have any other questions from the public or from Cms.

640
01:39:33.000 --> 01:39:36.019
Drew Kasper: I'm. A scan. I'm not seeing any

641
01:39:36.190 --> 01:39:38.179
Drew Kasper: raised hands

642
01:39:41.460 --> 01:39:43.719
Drew Kasper: seeing anything in the Q. A.

643
01:39:46.190 --> 01:39:55.690
Drew Kasper: And i'm not seeing any new questions in the new tech mailbox for folks That would be perhaps only on the phone and not have access to the zoom features.

644
01:39:56.720 --> 01:39:58.969
Drew Kasper: Okay, So with that

645
01:40:00.610 --> 01:40:02.000
Drew Kasper: you again,

646
01:40:02.470 --> 01:40:10.899
Drew Kasper: and we will now hear from presenters from the Rbx two thousand six hundred and sixty technology application.

647
01:40:11.470 --> 01:40:13.250

Drew Kasper: And now unmute your phone.

648
01:40:23.700 --> 01:40:25.939
Dr. Paul Feuerstadt: Okay, can you hear me?

649
01:40:26.600 --> 01:40:29.200
Drew Kasper: We can thank you. Excellent!

650
01:40:29.210 --> 01:40:51.700
Dr. Paul Feuerstadt: Well, my name is Dr. Paul Weyerstadt. I'm. An assistant clinical professor of medicine at the Yale University School of Medicine and an attending gastroenterologist at the Pact Gastroenterology Center. I'm. Delighted to be here to present the new technology add on payment request for rbx twenty, six, sixty. Now, Fda approved as real iota a microviolent based

651
01:40:52.910 --> 01:40:56.570
Dr. Paul Feuerstadt: therapeutic suspension. Please advance the next slide.

652
01:40:57.560 --> 01:41:26.090
Dr. Paul Feuerstadt: It's really important to realize that when the original application for Ah Rbx twenty, six was submitted. It was not an Fbi from the product that achieved approval on November thirtieth two thousand and twenty two as the first microbiota-based live biotherapeutic product, with an indication of prevention of recurrence of ostrogitis, cibosal infection in individuals eighteen years of age and older following a standard of care, antimicrobial therapy, it is essential to understand.

653
01:41:26.100 --> 01:41:35.310
Dr. Paul Feuerstadt: Ah Rbx, two thousand six hundred and sixty, for now Rebiota is not a solitary therapy for the treatment of C. Deposal. Please advance to the next slide,

654
01:41:35.320 --> 01:41:51.210
Dr. Paul Feuerstadt: c. That of zeal is a major problem in the United States. It's estimated that about a half a million individuals test positive or Cd. To the deal on an annual basis, leaving a massive burden on our health person and our patients.

655
01:41:53.600 --> 01:42:14.189

Dr. Paul Feuerstadt: But fifty percent of those patients have community associated infection and fifty percent have healthcare Associated Infection seed at the seal is the most common health care. Associated infection accounting for an estimated fifteen point, five percent of all health care associated infections. It's more common than Dr. E. It's more common than M. Rsa.

656
01:42:14.200 --> 01:42:32.830
Dr. Paul Feuerstadt: Importantly, when patients are seeing the standard of care anti-microbial. A guideline recommended antimicrobial to treat an initial episode of Cinderella seal it's estimated that about thirty-five percent or up to thirty five percent. All those patients will, in fact, recover Once those that recur,

657
01:42:32.840 --> 01:43:01.369
Dr. Paul Feuerstadt: we need a fifty percent of the ones to occur after that, and an astounding sixty percent will go on to occur thereafter as patients get caught in this vicious cycle of recurrence after a current sector occurrence. Now the medicare population behaves as a specific burden. The Medicare population is the highest risk burden group as a being a risk factor for both initial infection and recurrent infection. In fact, up to ninety three percent of all people that succumb to seed it with steel infection

658
01:43:01.420 --> 01:43:04.930
Dr. Paul Feuerstadt: in the Medicare population next slide, please.

659
01:43:06.700 --> 01:43:09.790
Dr. Paul Feuerstadt: So how did we get here? How did this all work?

660
01:43:09.800 --> 01:43:30.769
Dr. Paul Feuerstadt: Well? Anybody who's had clinical training will know that a patient that has, c-def seal infection has a alteration in their microbiota and alteration in the microorganisms that live within their coal, see that it still has two main phases, a vegetative phase, and a score base. The vegetative base is a phase that releases toxins that essentially cause the abdominal mean the diarrhea

661
01:43:30.780 --> 01:43:49.949
Dr. Paul Feuerstadt: fingers that patients with a C different seal get importantly. See if you're the parents of microbials, such as Bangladesh, but axomycin. They are able to control the vegetative views, which is why, when patients are on these antimicrobials, they feel better alternatively the spore phase is able to elude the

antimicrobials,

662
01:43:49.960 --> 01:43:53.329
Dr. Paul Feuerstadt: and once we pull off that antimicrobial, the score fees

663
01:43:53.340 --> 01:44:22.050
Dr. Paul Feuerstadt: frequently remains within a patient's system. The deficiency that we see with the microbiota the deficiencies of the bacteroid needs and permit it is, is largely most present at the end of that antimicrobial force, and it's up to the patient's system to regrow the missing microbiota and replenish itself without further intervention. But unfortunately, about up to thirty, five percent of the time, initially forty to fifty percent with first returns and up to sixty percent is second or

664
01:44:22.060 --> 01:44:30.449
Dr. Paul Feuerstadt: and beyond it's unable to do that, we're unable to replenish on our own and patients get a recurrence next slide, please.

665
01:44:31.110 --> 01:44:40.530
Dr. Paul Feuerstadt: This is where our product, like Rebiota comes in. Rebiota is a broad consortium. It has both score and non-sploreforming bacteria.

666
01:44:40.540 --> 01:45:02.199
Dr. Paul Feuerstadt: It is created from human school that is processed. It's widely screened it under those good manufacturing procedures. It is rectally instilled as a single dose It takes about fifteen minutes to administer that dose, and it has about fifteen times ten to the eight microorganisms per Cc. To be administered in any office setting or in the hospital setting

667
01:45:02.210 --> 01:45:12.489
Dr. Paul Feuerstadt: in certain States could be administered by a medical assistant to be administered by a nurse broadly, or a physician, or advanced practice Provider. Next slide, please.

668
01:45:14.130 --> 01:45:28.090
Dr. Paul Feuerstadt: One of the biggest strengths associated with the data for Rebiota are the number of trials that it has gone through. I show you here a listing of three phase, two trials, two phase, three

trials, and a retrospective analysis.

669
01:45:28.100 --> 01:45:34.200
Dr. Paul Feuerstadt: And I want to point your attention to the phase. Two trial program where we see this study duration,

670
01:45:34.210 --> 01:45:48.570
Dr. Paul Feuerstadt: we see the punch cd two, and the Punch open. Label Study had up to twenty four months of follow up for both safety and efficacy largely different from the standard six-month follow-up that most other studies have undergone.

671
01:45:48.580 --> 01:46:10.589
Dr. Paul Feuerstadt: Now, when we look at the punching, a three program. We see again a prospect of randomized control trial and an open-label study, and the retrospective analysis is Interesting retrospective analysis is an analysis of patients that didn't meet criteria to answer into the study, or chose not to participate in clinical trials. They were given the product under Enforcement discretion, with an open access opportunity.

672
01:46:10.600 --> 01:46:20.179
Dr. Paul Feuerstadt: Most importantly. There was consistency of safety and efficacy across these trials. Next slide, please. When we look at the punch cd three data,

673
01:46:20.200 --> 01:46:31.669
Dr. Paul Feuerstadt: we're we're looking at a prospective, multi-center, randomized placebo controlled trial of patients that have had one or more recurrence of cedar seal. All that received a standard

674
01:46:31.680 --> 01:46:58.680
Dr. Paul Feuerstadt: their into microbial they had a washout period between the ends of the antimicrobial and intervention, and then they were randomized to and receive a placebo or rebiota. Importantly within this analysis the easy in an analysis, was performed. Since the phase two trial program had the same exact formulation of rebiota, no changing dosing, the same diagnostics, similar patient populations and similar safety and efficacy assessments.

675
01:46:58.690 --> 01:47:09.020
Dr. Paul Feuerstadt: The data could be leveraged through a Bayesian analysis if consistency of efficacy by the placebo and rebiota remains

across the that was achieved

676
01:47:09.030 --> 01:47:28.490
Brenda Hudson: the overall happiness in the Rebyota was seventy point, six percent versus fifty-seven point five percent The close to Your probability of superiority was point nine nine, one showing statistic significance and efficacy was shown for first recurrence, and beyond there were no significance, for during emerging adverse

677
01:47:28.500 --> 01:47:31.090
Dr. Paul Feuerstadt: with this next slide, please.

678
01:47:33.210 --> 01:47:52.880
Dr. Paul Feuerstadt: Rebyota has been assessed in a sustained fashion. This is the phase two data follow, and what we see is that six months of the patients who responded. Initially, ninety seven percent remain responsive. Ninety Five percent remain responsive at twelve and at twenty, four months ninety one percent remain responsive. So those who respond

679
01:47:53.960 --> 01:47:57.149
Dr. Paul Feuerstadt: respond in a hardy manner. Next slide please

680
01:48:00.090 --> 01:48:02.400
Dr. Paul Feuerstadt: different

681
01:48:03.720 --> 01:48:13.159
Dr. Paul Feuerstadt: or re-biota from fecal microbiot transplantation what differs is the factoring procedures the quality assurances associated with it and the

682
01:48:13.910 --> 01:48:17.750
Dr. Paul Feuerstadt: assistant safety and efficacy files. Fm: two

683
01:48:20.050 --> 01:48:26.070
Dr. Paul Feuerstadt: from a lot of heterogeneity. A treatment that's done in one location would be completely different than one that's done in another next slide, please.

684
01:48:27.060 --> 01:48:35.189
Dr. Paul Feuerstadt: So the bigger question comes up is, Well, what

are there specific subgroups that might benefit more from a product like Rebiota?

685
01:48:35.200 --> 01:48:53.989
Dr. Paul Feuerstadt: And the answer was put forward at a major digestive Disease Conference earlier this year in May, in San Diego, California, where subgroup analyses of the phase, three data looked at specific groups, age, gender, race number of episodes. Once again that consistency was fully there for re-biota

686
01:48:54.000 --> 01:49:07.919
Dr. Paul Feuerstadt: it consistently performed the reverse of safety and efficacy, no matter how you slice the data. So what about Bezlo Toxinab? Bezo Toxinab is a fully humanized monoclonal antibody designed to find toxin b in a specific matter

687
01:49:07.930 --> 01:49:16.980
Dr. Paul Feuerstadt: but Bezlo toxin. It can't be used in certain populations like a congested part failure population, since it's associated with exacerbations of congested art. Failure

688
01:49:17.190 --> 01:49:18.670
Dr. Paul Feuerstadt: next slide please.

689
01:49:20.470 --> 01:49:33.529
Dr. Paul Feuerstadt: So, putting all of this together, reviolate is the first microbiome to face live biotherapeutic product to be approved for the prevention of recurrence of clustereditis or c-defenseal infection.

690
01:49:33.540 --> 01:49:41.559
Brenda Hudson: It's indicated in one minute remaining. It's indicated in adults eighteen and over who have

691
01:49:41.570 --> 01:49:58.839
Dr. Paul Feuerstadt: recurrent c. To facil infection for the prevention of recurrence who are receiving a standard of care, anti-microbial. Importantly, we've seen consistent data across three phase two trials two phase, three trials and a retrospective open access. Analysis This is a major Step forward.

692
01:49:58.850 --> 01:50:02.050

Dr. Paul Feuerstadt: There are no specific subgroups that this should be limited to

693
01:50:02.430 --> 01:50:05.590
Dr. Paul Feuerstadt: thank you so much for your attention, and i'll accept any questions

694
01:50:10.510 --> 01:50:11.880
Drew Kasper: right.

695
01:50:12.350 --> 01:50:20.189
Drew Kasper: Thank you very much for your presentation. Are there any questions from the public or from Cms

696
01:50:21.100 --> 01:50:30.030
Drew Kasper: this time? You can raise a hand with questions, or you can type them into the Q. And a feature of the zoom webinar.

697
01:50:30.510 --> 01:50:35.300
Drew Kasper: Or if you've called in and don't have a computer, you can email us

698
01:50:37.140 --> 01:50:40.869
Drew Kasper: new tech at Cms. Hhs. Gov.

699
01:50:44.960 --> 01:50:47.450
I'm. Not to any raised hands yet.

700
01:50:48.900 --> 01:50:51.630
Drew Kasper: More questions in the Q. A.

701
01:50:52.650 --> 01:50:55.990
Drew Kasper: Looking at the new tech mailbox

702
01:50:59.320 --> 01:51:03.230
Drew Kasper: not have new questions in the new tech mailbox.

703
01:51:05.620 --> 01:51:09.229
Drew Kasper: I'm. Going to give it another moment in case folks are

still

704
01:51:09.550 --> 01:51:11.260
Drew Kasper: not working on

705
01:51:11.900 --> 01:51:14.269
Drew Kasper: into that raise hand feature

706
01:51:16.520 --> 01:51:20.010
Drew Kasper: no raised hands from,

707
01:51:21.450 --> 01:51:27.050
Drew Kasper: and what group of it and these and I see no raised hands from.

708
01:51:29.940 --> 01:51:31.300
Drew Kasper: Okay,

709
01:51:32.110 --> 01:51:35.229
Drew Kasper: All right. Well, thank you again very much,

710
01:51:35.840 --> 01:51:38.539
Drew Kasper: and we will not.

711
01:51:38.930 --> 01:51:45.589
Drew Kasper: We will now hear from presenters for the on the Tuba Civil technology application.

712
01:51:45.810 --> 01:51:48.510
Drew Kasper: You can now go ahead and unmute.

713
01:51:51.870 --> 01:51:55.129
Dr. Ronit Simantov: Thank you. This is Ronnie Simmon to.

714
01:51:55.140 --> 01:51:59.189
Dr. Ronit Simantov: I I will go off the video in order to preserve bandwidth.

715

01:52:00.630 --> 01:52:04.299
Dr. Ronit Simantov: I'll be talking about Oma Duba cell today. Next slide, please.

716
01:52:04.980 --> 01:52:11.330
Dr. Ronit Simantov: College of a cell is an investigational agent, and has not been approved by any agency. Next slide, please.

717
01:52:13.020 --> 01:52:22.529
Dr. Ronit Simantov: A tuba cell is a product the potential to serve as a donor source for patients in need of a bone marrow or hematopoetic stem cell transplant

718
01:52:23.060 --> 01:52:25.990
upon the approval it will be the first.

719
01:52:26.000 --> 01:52:40.670
Dr. Ronit Simantov: Fda approved advanced cell therapy to be used as a donor source for the treatment of patients with hematological lignancies like leukemia and lymphoma, we need an allogenic hemat and poetic stem cell transplant

720
01:52:40.940 --> 01:52:48.309
Dr. Ronit Simantov: when we do, a cell is currently under review. At Fda was a Pidua action. Date of May, the first two thousand and twenty.

721
01:52:48.480 --> 01:52:51.889
Dr. Ronit Simantov: Let's receive. Break through therapy designation as well as orphan

722
01:52:51.900 --> 01:52:53.369
Dr. Ronit Simantov: drug designation.

723
01:52:54.010 --> 01:53:03.929
Dr. Ronit Simantov: The full data of the Phase Iii study were published in blood in October, two thousand and twenty one, and I would refer to some of those data here today. Next slide, please.

724
01:53:05.740 --> 01:53:24.329
Dr. Ronit Simantov: The Minnesota has pioneered Nicotinami or Nam

technology as an approach to the expansion of stem cells. Historically, stem cells and culture have been notoriously difficult to culture. They differentiate in culture and become metabolically stressed.

725
01:53:24.340 --> 01:53:38.990
Dr. Ronit Simantov: What the tindamide technology does is it preserves or up, regulates transcription transcription factors that activate self-renewal and self-cycle regulation as well as Dna repair,

726
01:53:39.000 --> 01:53:46.419
Dr. Ronit Simantov: while down regulating inflammatory signals antoctic signals and reactive oxygen species

727
01:53:46.510 --> 01:54:02.730
Dr. Ronit Simantov: on the right is our cartoon that illustrates how the stem cells, cultured with the nam technology in Omaduba cell are resistant to oxidative stress and reactive oxygen species, environments

728
01:54:02.750 --> 01:54:12.600
Dr. Ronit Simantov: mimicking the environment of the bone marrow where de novo stem cell production takes place.

729
01:54:14.030 --> 01:54:19.450
Dr. Ronit Simantov: The time for processing and manufacturing and shipping on maduba cells depicted on this slide.

730
01:54:19.560 --> 01:54:27.780
Dr. Ronit Simantov: Owen-domo cell is created as a patient-specific cell therapy it uses umbilical core blood as a starting material

731
01:54:27.790 --> 01:54:31.720
Dr. Ronit Simantov: and that needs to be selected specifically for each patient.

732
01:54:31.730 --> 01:54:44.730
Dr. Ronit Simantov: Patients are identified and typed according to their hla, and that needs to be matched to a donor source. The umbilical core blood starting material for that specific patient

733

01:54:44.740 --> 01:54:52.639
Dr. Ronit Simantov: cord. Blood, however, has fewer matching requirements, or a less stringent matching requirement than other sources for Gorman or transplant.

734
01:54:53.340 --> 01:55:04.510
Dr. Ronit Simantov: Once the search is completed and a core blood unit is selected. It's shipped to our manufacturing site, where it undergoes culturing and processing,

735
01:55:04.520 --> 01:55:06.959
Dr. Ronit Simantov: and then is shipped to the transplant center

736
01:55:07.630 --> 01:55:09.989
Dr. Ronit Simantov: patients who undergo transplant,

737
01:55:10.000 --> 01:55:24.699
Dr. Ronit Simantov: undergo a conditioning regiment of chemotherapy and radiation prior to the infusion of Omiduous that renders their blood cell counts very very low or almost nonexistent. It basically eradicates their bone.

738
01:55:24.920 --> 01:55:37.170
Dr. Ronit Simantov: Patients are then infused with O Madubo cell as a donor cell source, and are monitored carefully until the there's hemat aquatic recovery, and they're stable enough to leave the hospital

739
01:55:37.330 --> 01:55:38.580
Dr. Ronit Simantov: next slide

740
01:55:40.240 --> 01:55:49.740
Dr. Ronit Simantov: Olympic, so it will expand the quality of donor sources and provide reliable access by a couple of things that are outlined on this slide.

741
01:55:49.750 --> 01:56:06.419
Dr. Ronit Simantov: First of all, because of the less stringent matching requirements, patients who might not be able to identify a donor source in the registries can potentially identify and don't, of course, to the poor blood registries. In fact, patients who are

742

01:56:06.430 --> 01:56:15.910
Dr. Ronit Simantov: on Caucasian have a much lower probability of identifying a source for bone marrow. Transplant from the adult donor registries

743
01:56:15.980 --> 01:56:18.630
Dr. Ronit Simantov: In the homosexual phase, we study

744
01:56:19.200 --> 01:56:31.320
Dr. Ronit Simantov: Twenty Four percent of the patients were of ethnic and racial minorities, signifying the ability of on the Duba cell to represent a donor source for those patients.

745
01:56:31.970 --> 01:56:44.789
Dr. Ronit Simantov: It also addresses barriers to the use of local cord blood, and though a portable that has been used as a donor source, but has a very small number of cells, and we're doing so does by increasing the number of cells in that

746
01:56:44.800 --> 01:56:57.269
Dr. Ronit Simantov: a donor source will make the dose adequate for adults and for others, and will improve the outcomes in patients because of stem cell numbers are higher next slide.

747
01:56:58.610 --> 01:57:03.150
Dr. Ronit Simantov: The data for this are found in the phase three global randomized study

748
01:57:03.330 --> 01:57:09.209
Dr. Ronit Simantov: patients enrolled in the study had high-risk, hematologic malignancies, like leukemia and lymphoma

749
01:57:09.220 --> 01:57:16.800
Dr. Ronit Simantov: they were eligible for an algebraic combat, poetic stem cell transplant but had no readily available match donor

750
01:57:16.930 --> 01:57:23.249
Dr. Ronit Simantov: one hundred and twenty five patients were randomized to receive either omen, duba, cell, or umbilical cord blood.

751

01:57:23.260 --> 01:57:37.690
Dr. Ronit Simantov: The primary endpoint for the study was time to neutrophil and grasp it for the time it took for the mutual count the absolute neutral account, a subset of white cells to reach at least five hundred cells per my earlier for three days in a row.

752
01:57:38.120 --> 01:57:40.580
Dr. Ronit Simantov: Secondary endpoints included

753
01:57:40.600 --> 01:57:49.779
Dr. Ronit Simantov: Platelet and grasp it. The time it comes to place to recover, as well as intersections and hospitalizations, as well as other safety and ffc endpoints next slide.

754
01:57:52.310 --> 01:57:56.489
Dr. Ronit Simantov: These are the results of the primary endpoint in one of the secondary endpoints,

755
01:57:56.500 --> 01:58:01.709
Dr. Ronit Simantov: transparent with oma Duba cell resulted in this significantly faster time to in graph it.

756
01:58:01.750 --> 01:58:13.480
Dr. Ronit Simantov: On the left is the Protocol population, showing the cumulative incidence of neutrophil and rasm with with Omiduba cell in the red, showing that patients who are transplanted with a do a cell,

757
01:58:13.990 --> 01:58:20.110
Dr. Ronit Simantov: we're able to recover The neutral counts faster than patients who are transplanted with cord blood,

758
01:58:20.150 --> 01:58:26.519
with a Median times neutral phone grassment of ten versus twenty days and a p-value of less than zero point zero zero one

759
01:58:26.840 --> 01:58:34.949
Dr. Ronit Simantov: ninja fill and grasp. It was accompanied by the faster recovery and platele and graph mint, which was also the

760
01:58:35.010 --> 01:58:42.409

Dr. Ronit Simantov: shorter in patients, were transplanted with ameduba cell than with cord blood, and it was statistically significant

761
01:58:42.590 --> 01:58:43.920
Dr. Ronit Simantov: next slide.

762
01:58:48.520 --> 01:58:58.240
Brenda Hudson: But recovery is important, because nutrients are important for the immune function of patients after transplant, and Indeed, we found our three-minute remaining

763
01:58:58.310 --> 01:59:01.589
Dr. Ronit Simantov: that patients who are transplanted with omen do we cell

764
01:59:01.600 --> 01:59:12.959
Dr. Ronit Simantov: had a so lower percentage of infections than patients transplanted with court and that included serious infections, factory or fungal, as well as viral infections. Next slide

765
01:59:15.010 --> 01:59:29.409
Dr. Ronit Simantov: the decreased percentage of patients with infections also translated to less time spent in the hospital. This slide shows the days alive and out of the hospital for patients. In the first One Hundred Days Post. Transplant

766
01:59:29.570 --> 01:59:36.530
Dr. Ronit Simantov: patients transplanted with Omega, so spent more time out of the hospital. This is statistically significant as well.

767
01:59:36.670 --> 01:59:37.830
Dr. Ronit Simantov: Excellent.

768
01:59:40.820 --> 01:59:54.730
Dr. Ronit Simantov: The study was not power to detect a difference in overall survival, but, as you can see on this council in my own, there's a trend towards improvement in survival, with a seventy-three percent survival rate in patients transplanted

769
02:00:00.270 --> 02:00:10.069

Dr. Ronit Simantov: and patient-reported outcome analyses showed clinically meaningful and sustained improvements, functional and overall. Well-being compared to the for and blood group.

770
02:00:10.430 --> 02:00:24.100
Dr. Ronit Simantov: An additional study looking at a retrospective analysis of patients transplanted in our phase one, two, and three studies from sustained hematopoesis. As long as ten years after transplant

771
02:00:24.170 --> 02:00:25.340
Dr. Ronit Simantov: excellent,

772
02:00:27.810 --> 02:00:31.889
Dr. Ronit Simantov: all the totality of the data shows that Omega so

773
02:00:32.560 --> 02:00:43.820
Dr. Ronit Simantov: has the potential to be the first patient-specific advanced cellular therapy donor source meaning a high unmet need for a diverse group of patients with humanological agencies who need transplant

774
02:00:44.250 --> 02:00:55.540
Dr. Ronit Simantov: the nam technology has an overall favorable benefit, risk profile providing high-quality stem cells and clinically meaningful clinical improvements in patients

775
02:00:56.230 --> 02:00:59.150
Brenda Hudson: with that I won't be.

776
02:00:59.260 --> 02:01:00.510
Dr. Ronit Simantov: Thank you.

777
02:01:09.660 --> 02:01:11.769
Dr. Ronit Simantov: Happy to take questions at this time.

778
02:01:21.870 --> 02:01:29.920
Drew Kasper: I see we do have some raised hands here. Let's start with Dr. Perry election.

779

02:01:30.820 --> 02:01:32.380
Perry Alexion: Good morning. Thank you.

780
02:01:32.770 --> 02:01:35.490
Dr. Ronit Simantov: Good morning. Thank you for your presentation.

781
02:01:35.820 --> 02:01:45.399
Perry Alexion: Does the use of the technology expand the potential for the umbilical cord? By? That is to say,

782
02:01:45.760 --> 02:01:57.710
Perry Alexion: are the the the the standards of use slower? Or is there still a threshold that must be met for the cord blood to be used in transplant? If the technology isn't is employed

783
02:01:59.300 --> 02:02:29.180
Dr. Ronit Simantov: support, but it is used in transplant and has to meet minimum standards in order to be used in transplant on its own. But the technology does is increases the ability of the cortex to be used by increasing the number of cells in that poor blood, but also has to be certain standards to be used in the manufacturing. But so standards the manufacturing. Then it proves upon the blood by increasing the numbers and maintaining stemness of the cells in the blood, so it can be used in larger patients

784
02:02:37.720 --> 02:02:39.990
Perry Alexion: Not clearly getting the answer i'm seeking

785
02:02:40.000 --> 02:02:51.269
Dr. Ronit Simantov: um that is to say, would would would cord blood be able to be used with the technology that otherwise would not be used in a transplant.

786
02:02:52.970 --> 02:03:12.560
Dr. Ronit Simantov: I understand. So when chords so cord blood is limited in this number of cells, so in certain patients, what would not be a a certain core blood unit would not be considered useful for those patients, because it just didn't have enough cells. If you then apply the technology to that unit of poor blood, it can be used

787
02:03:12.570 --> 02:03:18.679
Dr. Ronit Simantov: that patient, so it does increase the ability of

court to be used in patients with transplant.

788
02:03:26.420 --> 02:03:27.599
Perry Alexion: Okay, thank you.

789
02:03:29.810 --> 02:03:33.319
Drew Kasper: Okay. And we have another question from Valerie at all.

790
02:03:35.160 --> 02:03:46.530
Valerie Favela: Hi, We note that the Horowitz phase three article involved patients up to age sixty five. Can you clarify whether the outcome scene are generalizable to the Medicare population?

791
02:03:47.550 --> 02:04:03.699
Dr. Ronit Simantov: We have not studied patients older than the age of sixty, five at this time, but the patients who were in the older age range in the study did benefit to the same extent that patients who were younger. So we anticipate that older patients will,

792
02:04:03.710 --> 02:04:33.119
Dr. Ronit Simantov: if they are eligible for transplant, and have the diseases that don't make them acquire a transplant. We anticipate that that would provide a similar benefit, because those patients require a donor source just like the applications do. Um. And, in fact, those patients may actually be more susceptible to infections, and are at higher risk for prolonged Nujupenia. And so one would think that the older population actually could stand to benefit from all juices.

793
02:04:33.130 --> 02:04:34.099
It's about,

794
02:04:36.640 --> 02:04:37.830
Valerie Favela: thank you.

795
02:04:48.680 --> 02:04:52.169
Drew Kasper: Not seeing any raised hands

796
02:04:52.580 --> 02:04:57.950
Drew Kasper: from panelists and not seeing any raised hands from other attendees.

797
02:04:59.480 --> 02:05:01.980
Drew Kasper: There are no new questions in the Q. And A.

798
02:05:03.710 --> 02:05:08.190
Drew Kasper: And there are no new questions in the new tech mailbox.

799
02:05:09.490 --> 02:05:13.030
Drew Kasper: Okay? So last call for questions.

800
02:05:15.910 --> 02:05:19.130
Drew Kasper: And with that we thank you.

801
02:05:19.590 --> 02:05:26.220
Drew Kasper: We'll now hear from our presenters for the Turle Vaz or Turla Crescent

802
02:05:26.610 --> 02:05:28.500
Drew Kasper: technology application.

803
02:05:29.840 --> 02:05:31.460
Drew Kasper: Now go ahead and unmute

804
02:05:47.310 --> 02:05:55.269
Dr. Khurram Jamil: and Dr. Jamal, you you are still muted in zoom to look at Here, There we go

805
02:06:07.990 --> 02:06:11.979
Dr. Khurram Jamil: first. Sd. Approved treatment for Hrs in the country,

806
02:06:11.990 --> 02:06:17.049
and in order to preserve the bandwidth. I'll turn off the camera

807
02:06:19.780 --> 02:06:21.050
Dr. Khurram Jamil: next slide.

808
02:06:36.610 --> 02:06:43.899
Dr. Khurram Jamil: It has the highest mortality of any complication of

cirrhosis, as you can see from the captain. Mark curve the

809
02:06:43.970 --> 02:06:47.429
if left untreated, the medium survival is less than twod

810
02:06:48.700 --> 02:06:49.860
Dr. Khurram Jamil: next slide

811
02:07:07.900 --> 02:07:14.169
Dr. Khurram Jamil: again. These are head-to- our studies against moderate and of tritide combination, and or of enough.

812
02:07:14.680 --> 02:07:15.980
Dr. Khurram Jamil: Next slide

813
02:07:42.020 --> 02:07:43.139
Dr. Khurram Jamil: next slide

814
02:07:44.710 --> 02:07:59.410
Dr. Khurram Jamil: confirmed trial was the largest prospective receiver control study. It enrolled three hundred patients in two to one randomization to twenty percent or perceived to arm with open label. Arguments in both cohorts.

815
02:07:59.840 --> 02:08:05.769
Dr. Khurram Jamil: Subjects receive telepresence at one milligram every six hours. Iv. Bowlers;

816
02:08:05.900 --> 02:08:13.290
Dr. Khurram Jamil: and if the dose, if the treatment. Ah! Responses less than thirty percent on day four a dose could be increased.

817
02:08:13.960 --> 02:08:18.749
Dr. Khurram Jamil: Majority of sessions are enrolled in us, trials, more than fifty percent

818
02:08:18.830 --> 02:08:22.800
Dr. Khurram Jamil: centers and a handful of them were also involved in Canada.

819
02:08:23.340 --> 02:08:31.540
Dr. Khurram Jamil: These patients were very sick, as indicated by their males. Score of thirty, three, their sit and crack, you know, three point five

820
02:08:31.690 --> 02:08:33.999
Dr. Khurram Jamil: and child field class, c.

821
02:08:34.090 --> 02:08:38.590
Dr. Khurram Jamil: In two-thirds of the patient, which is the highest degree of advanced labor. Disease.

822
02:08:39.700 --> 02:08:43.249
Dr. Khurram Jamil: Forty percent of patients were transferred from at the hospital

823
02:08:49.220 --> 02:08:50.450
Dr. Khurram Jamil: next slide

824
02:08:52.420 --> 02:08:53.849
Dr. Khurram Jamil: confirm this also,

825
02:09:12.960 --> 02:09:21.739
Dr. Khurram Jamil: followed by at least ten days survival without any form of or T. During this period, as we can see perfect twice as many patients

826
02:09:22.330 --> 02:09:28.700
point on to repressing compared to February or element alone with a p-value of zero point, zero, zero, six

827
02:09:29.660 --> 02:09:30.789
Dr. Khurram Jamil: next slide.

828
02:09:32.560 --> 02:09:40.090
Dr. Khurram Jamil: There are four predefined Second V end points, and they capture incidents of such a as reversal, which is the most common

829
02:09:53.280 --> 02:09:54.440

Dr. Khurram Jamil: next slide,

830
02:09:56.390 --> 02:10:14.220
Dr. Khurram Jamil: as we can see self-presented subjects achieved highly statistical, significant results in three of those four secondary endpoints and even in verified that there is a we know, Waker and speed at thirty at least fifty percent of it achieved the secondary endpoint

831
02:10:15.220 --> 02:10:16.290
Dr. Khurram Jamil: next slide

832
02:10:19.070 --> 02:10:26.440
Dr. Khurram Jamil: insulin of real replacement, therapy or rrt through day ninety was a predefined endpoint in confirmed the

833
02:10:27.290 --> 02:10:39.449
Dr. Khurram Jamil: it's worth noting that Rrt carries far more morbidity in patient with advanced labour disease anti-compensation, such as hrs compared to a chronic initiative

834
02:10:43.670 --> 02:10:47.070
Dr. Khurram Jamil: as part of poracity in a grass-laver disease

835
02:11:01.470 --> 02:11:02.500
Dr. Khurram Jamil: next one.

836
02:11:02.820 --> 02:11:03.850
Dr. Khurram Jamil: It's like,

837
02:11:20.100 --> 02:11:24.060
Dr. Khurram Jamil: I don't roughly only twenty percent of patients, but transfer listed

838
02:11:24.090 --> 02:11:26.809
Dr. Khurram Jamil: even if you get it in a timely matter.

839
02:11:26.860 --> 02:11:30.589
Dr. Khurram Jamil: In fact, basically Us. Data in the country

840
02:11:37.610 --> 02:11:38.630
Dr. Khurram Jamil: next slide.

841
02:11:41.250 --> 02:11:45.600
Dr. Khurram Jamil: The majority of patients in confirmed were treated on a regular floor

842
02:11:45.790 --> 02:11:55.440
Dr. Khurram Jamil: selling-present or can be bears, unlike other proteins or suppressors, such as northern nesting or with the protein, does not require dose titration

843
02:11:55.560 --> 02:11:57.229
Dr. Khurram Jamil: for cardiac monitoring.

844
02:11:57.870 --> 02:12:03.839
Dr. Khurram Jamil: It can be also given as per for line, and does not require a central line for the integration.

845
02:12:04.320 --> 02:12:10.050
Dr. Khurram Jamil: Eighty five percent of subjects can confirm were treated on a regular floor or leverage unit

846
02:12:18.200 --> 02:12:21.300
significantly more in television cohort compared to the

847
02:12:22.810 --> 02:12:23.910
Dr. Khurram Jamil: next slide.

848
02:12:38.530 --> 02:12:39.599
Dr. Khurram Jamil: Second,

849
02:12:42.360 --> 02:12:45.869
Dr. Khurram Jamil: looking at a form of a competing in and out,

850
02:12:46.000 --> 02:12:56.100
Dr. Khurram Jamil: transport or t or dialysis, and that are unwanted outcomes. We can see that patients on telepresence, more subject for a life through day, nineteen

851
02:12:56.380 --> 02:13:00.369
without requiring r two. Then placebo alone.

852
02:13:00.650 --> 02:13:03.990
Brenda Hudson: There are three minutes remaining

853
02:13:04.120 --> 02:13:05.410
Dr. Khurram Jamil: next slide.

854
02:13:07.640 --> 02:13:19.960
Dr. Khurram Jamil: These These two slides are too badly for the benefit of such as reversal across three Us. Trials over the last fifteen years. We know patients who achieve the air transplant have roughly one hundred percent survival.

855
02:13:19.970 --> 02:13:24.499
Dr. Khurram Jamil: But the middle capital marker shows that those who are Hs reversal, the

856
02:13:24.720 --> 02:13:28.970
Dr. Khurram Jamil: and most people of transparents still had better survivor than both.

857
02:13:29.200 --> 02:13:31.669
Dr. Khurram Jamil: With No, it's just a so, and no deal with craftsman

858
02:13:32.770 --> 02:13:33.800
Dr. Khurram Jamil: next slide.

859
02:13:43.370 --> 02:13:45.690
Dr. Khurram Jamil: Those who had no adjustment

860
02:13:53.720 --> 02:13:54.760
Dr. Khurram Jamil: next slide

861
02:14:17.240 --> 02:14:18.469
Dr. Khurram Jamil: next slide.

862
02:14:20.490 --> 02:14:30.930
Dr. Khurram Jamil: We saw that in confirmed study compared to the two previous study, there was forty percent higher use of algebra in in patients before they were randomized to twenty p

863
02:14:31.240 --> 02:14:32.439
Dr. Khurram Jamil: next slide.

864
02:14:34.040 --> 02:14:50.650
Dr. Khurram Jamil: We also know that, based on the guideline changes ten years ago there has been increased use of algebra as an actual encouraging in managing session with us. But until the results from confirmed study came out, and also a reason. You were used to a tired, published same time last year.

865
02:14:50.660 --> 02:15:00.899
Dr. Khurram Jamil: They both highlighted the need for proper food management, and also those modifications and patients who have food overload and restory complications at the time of randomization

866
02:15:01.440 --> 02:15:04.270
Brenda Hudson: there is one minute remaining.

867
02:15:05.530 --> 02:15:06.670
Next slide.

868
02:15:07.670 --> 02:15:18.730
Dr. Khurram Jamil: We also find confirmed that patients who have three or more failing oriented baseline acl up, grade three at higher risk of developingatory complication on telegraph.

869
02:15:18.890 --> 02:15:35.900
Dr. Khurram Jamil: Hence this will be data curled Usb our label includes warnings around proper food management, intra-vascular food self monitoring also it recommends advisors against using a polyvare invasion who have

870
02:15:40.450 --> 02:15:42.630
Dr. Khurram Jamil: that you should be avoided

871

02:15:52.380 --> 02:16:10.010
Dr. Khurram Jamil: I don't know syndrome being patiently and state labour disease it's a first-hand treatment of option based on the Us. And its national treatment Guidelines confirms that we demonstrate a greater incidents of such a reversal lowering for dialogue says there was a higher incident of respiratory competition

872
02:16:17.200 --> 02:16:21.069
to present significant improvement in current We are center of scale.

873
02:16:24.550 --> 02:16:26.980
Dr. Khurram Jamil: I'll be happy to answer any questions.

874
02:16:35.570 --> 02:16:38.910
Drew Kasper: Hi! This is. Can you hear me?

875
02:16:40.340 --> 02:16:55.789
Dr. Khurram Jamil: Yes, I can hear you. Okay, I work at Cms. Um. Could you? Um comment on the similarity of the death rates at day ninety between the Placebo group and the Trump present group. Thank you.

876
02:16:57.280 --> 02:17:14.530
Um. There was traditionally no difference in mortality in two thousand and one, and the reason is that, especially especially with very advanced with a disease such as there was a node concern study thirty percent, in fact, only one complication which we are,

877
02:17:14.540 --> 02:17:29.429
Dr. Khurram Jamil: and these patients are at risk of dying of other complications, such as a pair of need sepsis severe, that against the collaborative to name it, and only the difference that can make in those long term outcomes is a

878
02:17:30.330 --> 02:17:32.960
Dr. Khurram Jamil: in the overall patient population. The

879
02:17:32.969 --> 02:17:46.499
Dr. Khurram Jamil: there was no difference in mortality, and we didn't expect a difference, and that's why mortality has never been studied as a primary and borne, or a secondary important in us.

880

02:17:52.250 --> 02:17:53.479
E L Hambrick: Thank you.

881
02:18:00.629 --> 02:18:06.640
Drew Kasper: And I believe that question was from Dr. Hamburg. Yes, okay. So that was the raised hand.

882
02:18:07.280 --> 02:18:10.189
Drew Kasper: Any other raised hands at the moment

883
02:18:11.330 --> 02:18:16.399
Drew Kasper: standing across other question avenues. There are no questions in the Q. And A.

884
02:18:17.580 --> 02:18:19.030
Drew Kasper: And

885
02:18:19.350 --> 02:18:37.209
Drew Kasper: there are no questions in the new tech mailbox for those that might not have computer access right now. They can use the new tech at Cms at Dot Hhs Gov. New tech at Cms dot dot Hhs Gov:

886
02:18:37.530 --> 02:18:44.489
Drew Kasper: you can use if you're on telephone only, and don't have access to the zoom Q. And A.

887
02:18:44.840 --> 02:18:47.289
Drew Kasper: Or raise hand features.

888
02:18:47.299 --> 02:19:04.369
Drew Kasper: So I don't see any new raised hands, and I don't see any new questions in the Q. And A. So again thank you for your presentation, and at this point we will be adjourning for a lunch break,

889
02:19:05.100 --> 02:19:11.510
Drew Kasper: after which we will return with Hepsado Kit after lunch at one thousand two hundred and thirty,

890
02:19:12.170 --> 02:19:15.510

Drew Kasper: you know. Feel free to leave your

891
02:19:15.900 --> 02:19:20.320
Drew Kasper: computer logged in and we'll see you back here

892
02:19:20.510 --> 02:19:21.639
Drew Kasper: and

893
02:19:21.930 --> 02:19:23.170
Drew Kasper: twelve thirty.

894
02:19:26.010 --> 02:19:28.259
Drew Kasper: Thank you to all of our morning presenters.

895
02:20:08.190 --> 02:20:24.620
Drew Kasper: Hello, everyone! We will begin again in just a minute. I just wanted to take a moment to remind everyone that while general attendees are muted and should use the raise hand function to be unmuted,

896
02:20:25.400 --> 02:20:32.620
Drew Kasper: the panelists, consisting of presenters and participants, are responsible for your own mute functions.

897
02:20:32.870 --> 02:20:51.679
Drew Kasper: So please do make sure you're muted when other people are speaking, and if we do hear background noise we may mute you in zoom. Um. So if you're using your other, your phone's mute feature and ple to be aware that you could be double muted when it is time for you to talk.

898
02:20:52.010 --> 02:21:05.700
Drew Kasper: Thanks very much, and we've just hit twelve, thirty. So we will now hear from presenters for the Hepsado Kit technology application. You may Now unmute your phone.

899
02:21:06.500 --> 02:21:07.670
Thank you.

900
02:21:07.750 --> 02:21:13.039

Dr. Johnny John: Good afternoon. My name is Dr. Johnny John and I'm here to present the hebsato kit

901
02:21:13.160 --> 02:21:14.699
Dr. Johnny John: next slide, please.

902
02:21:15.710 --> 02:21:19.689
Dr. Johnny John: Ocular momentum is approximately five percent of all melanomas,

903
02:21:19.700 --> 02:21:33.190
Dr. Johnny John: with a Us. Incidence of a of of approximately one thousand five hundred to one thousand six hundred cases per year, half of all ocular mallocations develop metastatic disease, and for ninety percent of these stations metastasis that curs and the liver,

904
02:21:33.200 --> 02:21:37.349
Dr. Johnny John: often with a diffuse or military pattern, Next slide, please.

905
02:21:39.110 --> 02:21:56.919
Dr. Johnny John: Patients Ah, once diagnosed with um have a have a difficult treatment to pad pathway. Ah! Once a patient develops metastatic. Ah! Ocular melanoma, the prognosis and outcomes are poor with a Median survival of ten to twelve months. Next slide, please.

906
02:21:58.860 --> 02:22:18.540
Dr. Johnny John: Current treatment. Optionism can be categorized into two categories. They could be liver-directed, for example, Trans. Bacterial chemonization and radiomization, or cert using y ninety or there could be systemic treatments, such as chemotherapy, immunotherapy or biological agents

907
02:22:18.840 --> 02:22:29.880
Dr. Johnny John: recently there was a first-time approval of an Ovid therapy for metastatic Yugoslav and earlier This year with the approval of kimtrack or tomentifest

908
02:22:30.970 --> 02:22:43.880
Dr. Johnny John: this approval did apply to a certain subset of patients with ocular malenoma, approximately forty five percent of patients that had a specific allele known as the Hla, a two genotype

909
02:22:43.890 --> 02:22:45.319
Dr. Johnny John: Next slide, please,

910
02:22:47.990 --> 02:22:52.320
Dr. Johnny John: we'll come back to the slide so we could skip this for the moment. Next slide, please.

911
02:22:53.590 --> 02:22:57.020
Dr. Johnny John: The Malfun kit is a drug device. Combination.

912
02:22:57.580 --> 02:23:07.400
Dr. Johnny John: The drug involved in the mealflow. Hexoto kit is malflu hydrochloride, which is given at a dose of three milligrams per kilogram. Ideal body. Weight

913
02:23:07.710 --> 02:23:17.300
Dr. Johnny John: The device is known as the hepatic delivery system, and consists of a catheters and a extra corporeal circuit along with a filter next slide, please.

914
02:23:19.220 --> 02:23:24.320
Dr. Johnny John: So this light provides a schematic of the of the hephatic delivery system.

915
02:23:24.560 --> 02:23:38.449
Dr. Johnny John: Access to the patient is through the moral axis. The infusion catheter is inserted into the thermal artery, and directly injects the high dose, novel, and hydrochloride into the liver.

916
02:23:38.830 --> 02:23:56.739
Dr. Johnny John: The efflux or blood flowing out of the river is collected by a second catheter that's introduced through the Memorial day, and it directs the blood through the extra corporeal circuit through the filters that you can see on the left. Here the two double filters and the the filtered blood.

917
02:23:56.750 --> 02:24:03.289
Dr. Johnny John: The mul of is removed is re injected into the patient through the internal jugular bay.

918
02:24:03.300 --> 02:24:04.720
Dr. Johnny John: Next slide, please.

919
02:24:07.070 --> 02:24:21.719
Dr. Johnny John: This is a slide to show that the current procedure that is employed for the meltdown Hds. Kit is in the current Nccn guidelines under the isolation profusion of the liver category.

920
02:24:21.960 --> 02:24:23.560
Dr. Johnny John: Next slide, please.

921
02:24:25.740 --> 02:24:33.189
Dr. Johnny John: The data that i'm going to present today comes from a global phase, three focused trial

922
02:24:33.200 --> 02:24:52.989
Dr. Johnny John: global phase, three trials known as the Focus trial. This was a trial that was conducted in in the United States and in countries in Western Europe there were twenty three centers and one hundred and two subjects were enrolled in the trial. Patients were treated every six to eight weeks, and a maximum of of cycles were allowed for for each, for each patient.

923
02:24:53.000 --> 02:24:54.550
Dr. Johnny John: Next slide, please.

924
02:24:56.900 --> 02:25:15.590
Dr. Johnny John: This is a quick schematic of what the trial um and design was. On the upper left. You can see that the trial started as a randomized trial with a one to one randomization for patients with Phd. And Bac. The best alternative car care are

925
02:25:15.600 --> 02:25:19.349
Dr. Johnny John: in the bacr, and patients were given one of four choices,

926
02:25:19.600 --> 02:25:32.199
Dr. Johnny John: a procedure known as liberties, and all sorts of things to a very specific thing and a chemotherapy.

927

02:25:32.290 --> 02:25:35.700
Dr. Arash Mostaghimi: That's one thing I want to pronounce once once the

928
02:25:36.280 --> 02:25:44.890
Dr. Johnny John: I. If you're not speaking, please do leave your home. We're hearing some background noise.

929
02:25:44.900 --> 02:25:46.940
Dr. Arash Mostaghimi: Okay, thank you.

930
02:25:48.300 --> 02:25:51.369
Dr. Johnny John: So the accomplishment. This is so,

931
02:25:51.810 --> 02:25:52.869
Dr. Arash Mostaghimi: and

932
02:25:53.610 --> 02:26:05.090
Dr. Johnny John: the initial trial design was amended when patients were withdrawing from the bac arm, and it was amended to a single arm trial that you can see the design presented bottom next slide, please.

933
02:26:08.190 --> 02:26:22.190
Dr. Johnny John: So the the primary endpoint for the trial was Orr objective response rate, followed by a duration of response. On the left you can see that the data that was obtained for the Php patients

934
02:26:22.200 --> 02:26:40.449
Dr. Johnny John: that received the hepsato kit, which was ninety One patients there were thirty-three patients that um showed a response for thirty, six point, three percent of patients with thirty-three point, three percent Orr in the Bac arm, which was thirty two patients. There were four responders or twelve point five percent

935
02:26:41.000 --> 02:27:00.260
Dr. Johnny John: in terms of disease control rate, which includes responders plus stable disease patients, sixty-seven of the ninety one patients who fell into this category for seventy-three point six percent Dcr for the bac arm. This was thirty, seven point five

936
02:27:00.270 --> 02:27:06.999

Dr. Johnny John: we've provided the p-values there, and you can see that they're statistically significant along with the confidence intervals

937
02:27:07.010 --> 02:27:08.169
Dr. Johnny John: on the right,

938
02:27:08.500 --> 02:27:26.790
Dr. Johnny John: the table that demonstrates the duration of response that was obtained during the trial. So the the response rate was durable in the Php population medium. Dr. Was fourteen months. We've provided the conferences for this in the bac.

939
02:27:26.800 --> 02:27:33.639
Dr. Johnny John: The number of patients that did obtain their response. This was not

940
02:27:33.650 --> 02:27:49.549
Dr. Johnny John: all together in the Php. Out of the ninety one patients we had thirty-three bases, that had a response of seven crs and twenty-six prs. In the bacr. There were four patients that had a response, and they were all the ours. Next slide. Please.

941
02:27:51.500 --> 02:27:58.490
Dr. Johnny John: This is a slide showing the progression of you survival Kaplan Meyer curve on the left. The Php. Patients are in the

942
02:27:58.500 --> 02:28:15.619
Dr. Johnny John: purple and the B. You see, patients are in the teal color on the right. We have the Median progression fee survival data, which was nine point zero, three months of the phrases a three point one, two months in the

943
02:28:15.640 --> 02:28:16.589
Dr. Johnny John: the p-value

944
02:28:16.600 --> 02:28:19.330
Brenda Hudson: there are three minutes remaining.

945
02:28:19.580 --> 02:28:25.320
Dr. Johnny John: P-value and Constant are also provided, and you can

see there's particularly significant. Next slide, please,

946
02:28:26.900 --> 02:28:35.709
Dr. Johnny John: in terms of overall solid rival. The study was not powered for overall survival, but the capital admire occur again is shown on the left Php. In the Bac arms.

947
02:28:35.720 --> 02:28:48.680
Dr. Johnny John: We are still following patients for overall progression and survival. But currently the Median Os is nineteen point two, five months of the Phr. Ah versus fourteen point four, nine months of the bacr next slide, please.

948
02:28:51.260 --> 02:29:05.750
Dr. Johnny John: In this slide we show the waterfall plots for both arms of the trot. The Php patients on the left. Each line there represents a patient any, any, any any line below the horizontal line indicates a decrease in the tumor.

949
02:29:05.760 --> 02:29:21.870
Dr. Johnny John: Um uh tumor of size observed for these patients, you can see that the the green lines there represent the seven complete responses that were observed in the Php patients under the right. We have a similar waterfall block, where the bac pitches next slide, please,

950
02:29:23.550 --> 02:29:42.599
Dr. Johnny John: in terms of safety or address events observed in the We are providing a table here of serious treatment, emergent diverse events that occurred in any category that was above five percent of patients. So this fell into three categories, schematological, respiratory, and cardiac

951
02:29:42.750 --> 02:29:55.969
Dr. Johnny John: There were no treatment-related deaths during the trial, and the majority of all adverse events, including series, are well-known expected and manageable by the treating physicians next slide please

952
02:29:57.270 --> 02:30:09.399
Dr. Johnny John: so in terms of reviewing the treatment options for available for the patients on this slide on the left, we have with the Hezato Kit. You can see that the high efficacy Orr is thirty, six

point, three percent

953
02:30:09.410 --> 02:30:27.910
Brenda Hudson: in terms of patients surviving over twelve months. It was seventy seven percent of the patients. It is repeatable, and it applies to all patients that that that have this disease. Next slide, please. There is one minute remaining in terms of a direct comparison to the recent approved Kim track. One

954
02:30:27.920 --> 02:30:43.680
Dr. Johnny John: ah or toventifest um to manifest is only for forty-five percent of patients that have this have have metastatic doctrine Malnoma you have to have the specific gene, and you can see that the data used for the approval, the page, all contractations for treatment by

955
02:30:43.690 --> 02:31:02.449
Dr. Johnny John: in in in in our trial that patients could have prior therapy in terms of complete response. It was seven point seven percent observed for the focus trial versus zero. The partial response. Of twenty, eight point six versus nine. Your comparison is thirty, six point, three percent versus nine percent

956
02:31:02.460 --> 02:31:13.729
Dr. Johnny John: and in terms of disease control rate seventy-three point six versus forty-six, and then the overall Kfs medium Fs: nine point zero three months versus three point three months

957
02:31:13.740 --> 02:31:38.680
Dr. Johnny John: um and a and a duration of fourteen months versus nine point nine months, an immediate over of survival. Twenty point five, three months versus twenty, one point six months. We also provide a six-month bfs and a one-year Os comparison with sixty six patients that we're alive six months and eighty patients in one year or less for them. Ah, for the focus trial, using the soda kit versus thirty, one patients for

958
02:31:38.690 --> 02:31:45.710
Dr. Johnny John: for the Kim track, where to van a fest in six months and seventy three patients in the one-year-old was so far

959
02:31:45.720 --> 02:31:55.610
Dr. Johnny John: so. We do feel that this meets the criteria of a

clinical significant political benefit for this on that need for this fiction population.

960
02:31:55.960 --> 02:31:58.029
Dr. Johnny John: I'm happy to take any questions.

961
02:32:01.480 --> 02:32:04.820
Drew Kasper: Thank you very much for your presentation.

962
02:32:04.830 --> 02:32:08.240
Drew Kasper: Are there any questions from the public

963
02:32:09.200 --> 02:32:10.999
Drew Kasper: or Cms

964
02:32:12.140 --> 02:32:21.560
Drew Kasper: as a reminder? Please use the Q. And a function or the raised hand function in zoom, or if you're called in, only you can email us at

965
02:32:21.930 --> 02:32:26.320
Drew Kasper: New Tech at Cms. Hhs. Gov. The

966
02:32:28.440 --> 02:32:31.349
Drew Kasper: and I could start us out with a question. Here.

967
02:32:32.640 --> 02:32:43.230
Drew Kasper: Is there an established population of patients ineligible for a surgical oversection and systemic chemotherapy that could be treated with hepato kits.

968
02:32:45.070 --> 02:33:00.859
Dr. Johnny John: Yes, it it so happens with metastatic killer melanoma, the the the the presentation of the disease in the liver is diffuse or with micrometastatic presentation what we call a milling representation.

969
02:33:00.870 --> 02:33:15.859
Dr. Johnny John: So there is a very small percent of patients that would be eligible for surgical dissection. The majority of patients

would not be eligible, and would have to seek either liver, directive, therapy, or systemic.

970
02:33:18.260 --> 02:33:20.619
Drew Kasper: Okay, and for those that are

971
02:33:20.810 --> 02:33:26.870
Drew Kasper: ineligible or aren't good candidates for systemic therapy. But would you

972
02:33:27.060 --> 02:33:40.050
Drew Kasper: um be expected to tolerate or respond well to hepsato Kit? Is that population a a known or established or quantified population?

973
02:33:40.410 --> 02:34:08.949
Dr. Johnny John: Well, um In the In the trial we did not limit um the the the patients who had prior systemic therapy. So um! It would be the same population that is eligible for societal therapy. We allowed all prior therapies, whether it's just a make or a liver directed. Um! Ah, you know patients to um to enroll and have ah Abs out of kit treat as long as there was a wash out period, so that they will recover from the toxins from the prior there.

974
02:34:08.960 --> 02:34:24.260
Dr. Johnny John: Um! And the excluded, and this included immunotherapy as well. So the you know the answer to your question is, you know the same population that is, um, you know, has a availability of receiving system for a new therapy. Can we see how that? Okay?

975
02:34:31.460 --> 02:34:35.590
Drew Kasper: Are there other questions from the public or from

976
02:34:39.040 --> 02:34:42.790
Drew Kasper: I use the raise hand feature. Um, go ahead, Edena.

977
02:34:43.940 --> 02:34:51.129
Adina Hersko: This is a follow up set question So to clarify all patients could be eligible for systemic chemotherapy.

978
02:34:52.790 --> 02:35:00.990

Dr. Johnny John: All patients could be that that had systemic therapy are eligible for heads out of fifty. Yes,

979
02:35:02.430 --> 02:35:06.319
Adina Hersko: So the question i'm asking is a little bit different from that um

980
02:35:06.570 --> 02:35:17.659
Adina Hersko: Are their patients with medicine at oxy or melanoma will deliver burden, all eligible for the first prim of chemotherapy, or the coroner anywhere that's contrindicated.

981
02:35:18.100 --> 02:35:30.889
Dr. Johnny John: Well, and I hope I understand your question. No. So the tumor burden in the liver we restricted to a maximum of fifty percent.

982
02:35:31.010 --> 02:35:45.000
Dr. Johnny John: So if patients have a tumor burden that supersedes fifty percent of total liver volume. They would not be eligible for a heps out of treatment. They could still be eligible for systemic therapy, but not, for example.

983
02:35:46.450 --> 02:35:47.499
Adina Hersko: Thank you.

984
02:35:53.270 --> 02:36:12.089
Drew Kasper: I i'm sorry I just want to make sure. I understand now as a follow-on question to that. So there are folks who wouldn't be eligible for hipsado kit, but could still receive systemic therapy. But the the opposite is not true. Is that what you're saying, where there are,

985
02:36:12.690 --> 02:36:27.010
Drew Kasper: there wouldn't be a group of patients who are ineligible or not good candidates for systemic therapy, but yet could be good candidates for hepsado,

986
02:36:27.580 --> 02:36:47.400
Dr. Johnny John: and my point was that um you know any patient um, you know whether the patient is eligible for so semi- therapy or not. Our criteria is that with the tumor burden. Um, Any Any candidate for

hebsato kid um must have a tumor bringing less than fifty percent.

987
02:36:47.410 --> 02:36:54.620
Dr. Johnny John: So any person over to a fifty percent tumor burden would not be a candidate for

988
02:36:59.850 --> 02:37:03.739
Drew Kasper: any other questions from the public, or from Cms.

989
02:37:05.240 --> 02:37:07.399
Drew Kasper: Iing for raised hands.

990
02:37:08.430 --> 02:37:10.130
Drew Kasper: I don't see any

991
02:37:11.100 --> 02:37:14.039
Drew Kasper: general attendees. I don't see any with panelists,

992
02:37:14.700 --> 02:37:21.069
Drew Kasper: and I don't see any new questions in the new Tech mailbox or the Q. And A.

993
02:37:21.650 --> 02:37:22.760
Drew Kasper: Okay

994
02:37:23.300 --> 02:37:28.399
Drew Kasper: right? Well again, Thank you very much,

995
02:37:28.450 --> 02:37:34.669
Drew Kasper: and we will now hear from presenters from Al Renatomab

996
02:37:36.070 --> 02:37:39.959
Drew Kasper: technology application, and you may now unmute your phone.

997
02:37:40.690 --> 02:37:49.000
Dr. Caroline Hoang: Thank you. Good afternoon. My name is Caroline Hong, and I am employed and compensated by Pfizer as a Us. Medical affairs hematology, team lead

998
02:37:49.010 --> 02:38:00.780
Dr. Caroline Hoang: in the next ten minutes I will provide an overview of the applications submitted in support of elder and atomat in the setting of relapsed refractory multi-p myeloma. Please note that Lor anatomab is not yet Fda approved. Next slide, please.

999
02:38:01.650 --> 02:38:12.240
Dr. Caroline Hoang: Albern Atomab, which i'll refer to as Ellra is an investigational humanized by a specific antibody targeting Bcma and Cd. Three personalized manufacturing is not required to produce. Lra.

1000
02:38:12.270 --> 02:38:22.340
Dr. Caroline Hoang: The mechanism of action is shown on the right. Briefly, Ellra engages cd three on t-cells and bcma on myeloma cells, to induce selective t cell, mediated cytolysis

1001
02:38:22.350 --> 02:38:34.640
Dr. Caroline Hoang: to reiterate. Elrea is not yet approved by the Fda. It's worth noting. That early last month the Fda granted breakthrough therapy designation to Ellra for relapse refractory, multiple Dalai Lama after four prior lines of therapy.

1002
02:38:34.650 --> 02:38:47.720
Dr. Caroline Hoang: This highlights the potential of Ellra as a therapeutic option in this treatment setting, and it also highlights the high, unmet need for patients with multiple myeloma whose disease has progressed through multiple lines of therapy. And i'll talk about that more on the next slide, please.

1003
02:38:48.670 --> 02:39:06.270
Dr. Caroline Hoang: Multiple myeloma is a disease characterized by the build up of polygonic plasma cells or myeloma cells of the bone marrow. It's the second most common blood cancer in adults in the Us. More often diagnosed in men than women, and it's also a disease of older adults with the median age at diagnosis being sixty eight years.

1004
02:39:06.280 --> 02:39:17.870
Dr. Caroline Hoang: It's important to call out that multiple dilemma is the most common blood cancer in black Americans who are twice as likely to be diagnosed with, and twice as likely to die for multiple dilemma compared with their non-black counterparts

1005
02:39:17.880 --> 02:39:39.869
Dr. Caroline Hoang: for most patients with multiple dilemma, the disease is considered incurable with inevitable relapse, and the challenge in treating this disease is shown below. The vertical access represents the level of M. Protein, the biochemical hallmark of myeloma, where high circulating levels are associated with symptomatic active disease, while the horizontal access depicts the number of lines of therapy used to treat active disease.

1006
02:39:39.880 --> 02:39:52.940
Dr. Caroline Hoang: The main takeaway here is that as patients progress through multiple lines of therapy collapsed, disease is less likely to respond, and the duration of response becomes shorter until eventually the disease is refractory to further treatment. Next slide, please

1007
02:39:54.130 --> 02:40:22.370
Dr. Caroline Hoang: Shown on this slide are claims made in the application that support. Why elbow represents a substantial cynical improvement over existing treatment. The bulk of my remaining time will be focused on the most recent Elmer data. But before that i'll touch briefly on existing therapies. That, said the presentation will be limited to therapies available at the time of our N. Tap submission, and it's worth noting that the therapeutic landscape and the setting of relapsed, refractory, multiple myeloma has since changed, but will not be covered here. Next slide, please,

1008
02:40:24.140 --> 02:40:38.519
Dr. Caroline Hoang: as mentioned. Earlier, achieving response to subsequent therapy is challenging in patients with disease that is, triple-class refractory, meaning. It no longer responds to three main classes of drug, a proteasome inhibitor, an immunomodulatory drug and an anti-cd thirty, eight,

1009
02:40:38.560 --> 02:40:51.380
Dr. Caroline Hoang: and this is shown in the table on the right, which summarizes the design and results from separate studies evaluating philanthropy selenixor or conventional chemo for patients with heavily pre-treated tripleclass refractory disease

1010
02:40:51.390 --> 02:41:01.740
Dr. Caroline Hoang: focusing in on the data within the red box. The objective response rates range from twenty five percent to thirty one with complete response rates ranging from zero point. Four to three

next slide, please.

1011
02:41:03.390 --> 02:41:20.800
Dr. Caroline Hoang: Vcma-car t therapies have provided substantial clinical improvement over targeted therapies and conventional chemo in the study and overlapsed refractory disease with objective response rates of at least seventy percent and stringent cr rates of at least twenty nine percent carte therapies, however, are largely unveiled.

1012
02:41:20.810 --> 02:41:39.869
Dr. Caroline Hoang: First, access is limited to select authorized medical centers specializing in the administration of cellular therapies. Second, most patients waiting for car T. Do not receive it, because the personalized manufacturing process typically requires weeks, and most patients with heavily pre treated, relaxed, refractory disease, experience, relapse or death. During the week.

1013
02:41:40.040 --> 02:41:58.360
Dr. Caroline Hoang: Third patients with inadequate renal function, a common complication of multiple myeloma require careful consideration, as they are at higher risk for toxicity with lympho depleting regimens that must precede carbon therapy. And one final point there is limited data evaluating carte in patients at least sixty five years of age,

1014
02:41:58.370 --> 02:42:06.080
Dr. Caroline Hoang: approximately a third of patients in the Id cell and silica cell registrational studies respectively, where age sixty five are older. Next, like, please.

1015
02:42:07.270 --> 02:42:13.529
Dr. Caroline Hoang: The rest of the presentation will focus on the aroad data presented this past weekend at the Ash annual meeting next slide, Please

1016
02:42:14.640 --> 02:42:27.200
Dr. Caroline Hoang: shown Here is a study design for our registration enabling magnetism. Three study referred to as Mm. Three, an open label, multi-center non-randomized phase, two trial and patients with triple-class refractory seeds,

1017
02:42:27.210 --> 02:42:39.350
Dr. Caroline Hoang: The study consists of two independent cohorts cohort a enrolled Bcma. Naive patients and cohort be enrolled prior

Bcma exposed patients. The data recorded here is from cohort A. Only

1018
02:42:39.360 --> 02:42:51.530
Dr. Caroline Hoang: in this study. The full dose of Ellra is a seventy six milligram fixed, dose administered, subcue once weekly, after a step up regiment of twelve milligrams on day, one and thirty, two milligrams on day four

1019
02:42:51.540 --> 02:43:08.029
Dr. Caroline Hoang: per protocol. Patients were hospitalized for the first forty, eight hours after step up dose one and the first twenty four hours after step up dose two. No hospitalization was required with the full dose. The primary endpoint is objective response rate by blinded, independent central review. Next slide, please

1020
02:43:09.090 --> 02:43:25.259
Dr. Caroline Hoang: shown here are patient demographics and baseline disease characteristics. To the left. The Median age of patients in cohort A was sixty eight years. It's not shown on the slide, but I want to call out that eighty of the one hundred and twenty three patients for sixty, four percent, or at least sixty, five years old

1021
02:43:25.270 --> 02:43:36.559
Dr. Caroline Hoang: in cohort, a overall. Seven percent of patients were black or African, American, and in cohort a patients enrolled in the Us. Only seventeen percent of patients were black or African American

1022
02:43:36.570 --> 02:44:04.879
Dr. Caroline Hoang: multiple core prognostic features were present in the baseline disease characteristics most notable. A quarter of patients had high-risk cytogenetics a third of patients had extraditionary disease, and there was heavy pre-treatment captured in the prior lines of therapy, in which there were a median of five exposure status, in which all patients were triple-class, exposed and refractory status, in which nearly all patients were triple-class refractory. And all Nearly all patients were refractory to the last line of therapy.

1023
02:44:05.360 --> 02:44:06.889
Dr. Caroline Hoang: Next slide please.

1024
02:44:08.320 --> 02:44:23.360

Dr. Caroline Hoang: Efficacy Data from cohort. A of Mm. Three are shown here with a medium duration of follow up of ten point four months. The bar graph on the left summarizes the objective response rate, which was sixty, one, twenty, seven point, six percent of patients achieved a complete response, or, better,

1025
02:44:23.370 --> 02:44:33.939
Dr. Caroline Hoang: in the subset of patients at least sixty, five years or older, and as a reminder that was eight hundred and twenty three patients, the objective response rate is consistent with the overall population,

1026
02:44:33.990 --> 02:44:49.780
Brenda Hudson: as shown on the Kaplan Meyer Curve to the right. The median duration of response in patients who achieved a partial response are better, has not been reached. Responses are durable with the probability of maintaining response at nine months being eighty, four percent next slide, please share our three-minute remaining.

1027
02:44:49.790 --> 02:45:10.919
Dr. Caroline Hoang: The safety profile is shown here for cohort a the most common grade, three four treatment, emergent adverse events for chemical logic the majority of non-heem treatment. Emergent events for grade one or two with cytokine release, syndrome or crs being the most common, and i'll talk about that A little more later infection was observed in two thirds of patients with thirty, five percent of infection, events being rate three, four,

1028
02:45:10.930 --> 02:45:20.389
Dr. Caroline Hoang: fifteen percent of patients with treatment. Emergent adverse events permanently discontinued. Elro please note this discontinuation rate does not reflect treatment related.

1029
02:45:20.400 --> 02:45:30.040
Dr. Caroline Hoang: Dads were reported in twenty, one patients with eleven of those deaths being due to progressive disease, and of those deaths two or considered treatment related for investigator. Next slide, please.

1030
02:45:31.100 --> 02:45:38.590
Dr. Caroline Hoang: Immuno oncology therapies that harness, t-cell activation are associated with crs and immune cell associated neurotoxicity

1031
02:45:38.600 --> 02:45:44.669
Dr. Caroline Hoang: no more toxicity syndrome, or I cans the slide here characterizes these events from Mm. Three

1032
02:45:44.750 --> 02:45:59.359
Dr. Caroline Hoang: again one hundred and twenty-three patients, or in the safety population. But note that the first four patients in Mm. Three received a single forty, four milligram, step up dose of all the one hundred, while the remaining one hundred and nineteen received the twelve milligram, thirty, two milligrams step up regiment,

1033
02:45:59.370 --> 02:46:19.690
Dr. Caroline Hoang: and the data shown shown here, and the first four patients were excluded. The table to the left summarizes the rates and management of Crs and icons. Please note that there were no grade, three, four crs or icons events. I won't go through the data in detail, but focusing on Ics. First we see that four patients experienced icons and three of those cases were grade. Two

1034
02:46:19.700 --> 02:46:28.090
Dr. Caroline Hoang: icans was managed with tocy and steroids, and none of the patients permanently discontinued aroad due to Ics. In addition, there were no fatal neurotoxicity events

1035
02:46:28.100 --> 02:46:45.389
Brenda Hudson: focusing on crs. We see the majority of crs, events for grade, one with grade, two events reported in fourteen percent of patients. Fifteen percent of patients experience more than grade more than one Crs event patients who manage with toasti or steroids, and no patients permanently discontinued aroad due to Crs on the right hand side

1036
02:46:45.400 --> 02:46:51.440
Brenda Hudson: that visualizes the timing of Crs events for Elro, for each patient

1037
02:46:51.450 --> 02:47:20.440
Dr. Caroline Hoang: going from left to right on the horizontal axis. The first and second hash hash marks represents double dose. One and step up does two respectively. The third hash mark is the third nose, which is the first full dose of era, and the fourth hash part represents doses for and beyond the majority of Crs events occurred with step up dosing. The rate of crs was forty, five percent after

dose, one, twenty percent after dose, two and six percent after dose, three and less than one percent after dose for and beyond the main takeaway. Here is a crs profile that aura is predicted.

1038
02:47:20.460 --> 02:47:28.300
Dr. Caroline Hoang: Crs events are early and manageable with supportive care. And again, no patients permanently discontinued Elro, due to Crs next slide, please.

1039
02:47:29.730 --> 02:47:42.470
Dr. Caroline Hoang: In summary. There is currently high unmet need implications for the real astro factory, multiple nyloma after multiple lines of therapy, and this is due largely to either inadequate response rates or challenges in broad immediate access with available treatments.

1040
02:47:42.480 --> 02:47:49.769
Dr. Caroline Hoang: Ellra is expected to provide substantial clinical improvement in this treatment setting, and it is well studied in patients sixty five years of age and older.

1041
02:47:50.240 --> 02:47:58.989
Dr. Caroline Hoang: The potential of Elro to demonstrate significant improvement over existing therapies was recognized by the Fda with the breakthrough therapy designation granted in early November.

1042
02:47:59.000 --> 02:47:59.869
Dr. Caroline Hoang: Thank you.

1043
02:48:06.260 --> 02:48:09.790
Drew Kasper: Okay. Thank you for your presentation.

1044
02:48:10.560 --> 02:48:14.880
Drew Kasper: Are there any questions from the public or from Cms.

1045
02:48:16.960 --> 02:48:20.180
Drew Kasper: Now enter your questions in the Q. And A.

1046
02:48:20.310 --> 02:48:22.110
Drew Kasper: Raise a hand,

1047
02:48:23.140 --> 02:48:30.619
Drew Kasper: or if you're on telephone only, and don't have access to those features, you can email us at N. Ew. Tvch,

1048
02:48:30.750 --> 02:48:33.650
Drew Kasper: at B. M. S. Dot A. H. S. Gov.

1049
02:48:37.570 --> 02:48:46.280
Drew Kasper: No questions in the Q. And A. I do see a raised hands about Dr. Alexei.

1050
02:48:47.250 --> 02:48:49.690
Perry Alexion: Good afternoon. Thank you for your presentation.

1051
02:48:49.700 --> 02:49:01.699
Perry Alexion: There's some evidence to suggest that parties therapies may be amendable to patients with real and sufficiently insufficiency, at least in the in the lymphoma setting.

1052
02:49:01.710 --> 02:49:11.350
Perry Alexion: Do you find that as being a significant portion of the of the reasons for in availability of Car t in your second bullet

1053
02:49:14.730 --> 02:49:32.330
Dr. Caroline Hoang: um from the the publications. Um! And what is out there in to-reviewed journals? It is not I. I don't believe that renal ah inadequate renal function is the reason for that. There I believe that it's a manufacturing process, and the availability of slots for patients

1054
02:49:32.340 --> 02:49:34.930
Dr. Caroline Hoang: that limit the access to the treatment.

1055
02:49:38.830 --> 02:49:39.989
Okay, thank you.

1056
02:49:45.450 --> 02:49:48.549
Drew Kasper: Any follow up questions or

1057

02:49:49.220 --> 02:49:54.050
Drew Kasper: for their questions. I do see Adena and her scope. Please proceed.

1058
02:49:55.120 --> 02:50:07.489
Adina Hersko: Thank you. And will the data from cohort be that you mentioned with where patients were tested with Prior, Bcme, therapy, c. Provided to Cms one won't be available.

1059
02:50:09.400 --> 02:50:20.949
Dr. Caroline Hoang: The data from cohort B um has not been presented or published yet. Um, we are waiting for a longer follow up to to present that data when it is available, we will make it available to Cms:

1060
02:50:23.150 --> 02:50:24.220
Adina Hersko: Thank you.

1061
02:50:31.680 --> 02:50:32.930
Drew Kasper: A.

1062
02:50:33.150 --> 02:50:36.819
Drew Kasper: I don't see any new questions in the new tech mailbox.

1063
02:50:37.570 --> 02:50:39.869
Drew Kasper: No new questions in the Q. A

1064
02:50:40.350 --> 02:50:44.949
Drew Kasper: last call for follow up questions from attendees or panelists,

1065
02:50:49.400 --> 02:50:51.159
Drew Kasper: Adina, Is that a following

1066
02:51:04.650 --> 02:51:07.960
Adina Hersko: any of the evidence here, or any thoughts about that.

1067
02:51:08.550 --> 02:51:38.129
Dr. Caroline Hoang: Yes, um so ah! Between the ah submission of our application and the presentation today another vcm a by-specific

cluster. Math was approved for relapse. Your factory multiple myeloma after four prior lines of therapy. In addition to that the latomap the pcma antibody drug conjugate has made public that they've ah initiated plans to withdraw the the U. S. Indication, because of a

1068
02:51:38.140 --> 02:51:55.750
Dr. Caroline Hoang: three study that that did not meet the the primary endpoint, I think, in terms of the the application. There is no evidence at this time to suggest that Elvin Asom app is or is not substantially different from tquista map.

1069
02:51:55.760 --> 02:52:07.510
Dr. Caroline Hoang: Um! It's our position that these two therapies should be considered as a class against other therapies, and not against each other in terms of the in-tap submission.

1070
02:52:09.980 --> 02:52:11.020
Adina Hersko: Thank you.

1071
02:52:15.950 --> 02:52:18.300
Drew Kasper: And last call for any other questions.

1072
02:52:20.400 --> 02:52:26.630
Drew Kasper: There are no hands raised, nothing new in the Q. And A. And no new emails at the new tech mailbox.

1073
02:52:27.320 --> 02:52:40.879
Drew Kasper: So with that, thank you again. We will now hear from presenters for the Soviet Union technology application, and you may Now unmute your phone.

1074
02:52:41.920 --> 02:52:51.610
Dr. Arash Mostaghimi: Good afternoon. I'm a Raj mah sugimi. And today i'm excited to talk to you about Sp. Viggo and generalize Buster's rises where for adults next slide, please,

1075
02:52:52.550 --> 02:53:22.140
Dr. Arash Mostaghimi: so as to Viggo, is a first and class humanized monochronal antibody against il thirty six is part of the innate immune pathway as part of the I. One family of cytokines that includes three isoforms, A, B and and Gamma, and also an antagonist, and when the aisle thirty six pathway is activated. It leads to downstream

information, including neutrophilic information which is the core of partial,

1076
02:53:22.150 --> 02:53:44.190
Dr. Arash Mostaghimi: ah generalized questionlosis. So aisle thirty. Six. Our pathway is distinct from the Tnf and aisle twenty three pathways that we are familiar with for Psoriasis and I'll go a little bit into the details of this momentarily, and we're excited that the Viggo, as of September of this year, is actually approved for the treatment of generalized question which rises, flares and adults

1077
02:53:44.200 --> 02:53:45.230
Dr. Arash Mostaghimi: next slide.

1078
02:53:47.440 --> 02:54:12.440
Dr. Arash Mostaghimi: So unlike psoriasis, which has a more indolent course. Generalized butular psoriasis is a multi-systemic disease with a relapsing and remaining clinical course acute generosis is notable for flares where you get scattered sterile pustules occurring all over the body, although the word psoriasis is in the name Gpp. This can occur with or without psoriasis,

1079
02:54:12.450 --> 02:54:20.969
Dr. Arash Mostaghimi: and when people get these spots. They have distinct skin symptoms, including pain and

1080
02:54:20.980 --> 02:54:34.239
Dr. Arash Mostaghimi: and peritis, but they also get systemic symptoms, including fever, which i'll go into into the next slide. There are also systemic signs of inflammation, which again we'll review it more closely on the next slide. Next slide, please.

1081
02:54:35.930 --> 02:55:04.710
Dr. Arash Mostaghimi: So to draw the distinction between Gpp and plaques. For is this a little bit more clearly? So? As I said, the primary skin finding and Gpp is the partial. So you get these little studded white dots over the body, and in addition to the skin findings, you have substantial morbidity, including fever. Malays pain increased inflammatory markers and organ involvement, including hepatic, renal, respiratory, and cardiovascular systems.

1082
02:55:04.720 --> 02:55:16.390
Dr. Arash Mostaghimi: The mortality from this affair can be up to

sixteen percent, as reported in some studies. Gpp can occur in patients who have a history of plaques, viruses, or can occur independently without five psoriasis

1083
02:55:16.400 --> 02:55:35.969
Dr. Arash Mostaghimi: in contract plaques rises which we are a bit more familiar with in general is a chronic inflammatory condition with sharp boundaries. It may have some cluster of this that's not the primary ah endpoint, and although it may flare, it has a much more ah indolent Ah! And chronic component to it.

1084
02:55:35.980 --> 02:55:41.179
Dr. Arash Mostaghimi: When it does flare it does not have the systemic symptoms typically next slide, please.

1085
02:55:42.230 --> 02:56:12.180
Dr. Arash Mostaghimi: As a result of these flares, which are associated with both skin conditions and substantial systemic comorbidity comparing ah ah gpp with other inflammatory conditions, such as homo-lantaros rises atopic dermatitis and general plaques rises. It shows worst outcomes in physical functioning, vitality and mental health, as measured by the Ss. Thirty six scale on the red bar on the left is Gdp, and a lower score is,

1086
02:56:12.190 --> 02:56:19.919
Dr. Arash Mostaghimi: and you can see that across all three domains it is lower or very similar to the comparison. Cohorts next slide, please.

1087
02:56:23.800 --> 02:56:25.339
Dr. Arash Mostaghimi: Next slide, please.

1088
02:56:28.000 --> 02:56:57.770
Dr. Arash Mostaghimi: So, as I mentioned, the flares are the key component of Ah generized bustal poriasis that's the Viggo treats at present. Ah! Flares can come in. An unpredictable fashion can be triggered by many different things. One of the most common things we see is medications, so either new medications, like banner blockers or lithiums, but also withdrawal of temporary immunosuppressive medication. For example, if somebody takes a short course of steroids for an as a flare or an exim of flare that they can

1089
02:56:57.780 --> 02:57:27.639

Dr. Arash Mostaghimi: results in uh, that the cessation of steroids can result in a gpp flair. Environmental triggers upon traveling or changes in season with sunlight can do it. We've seen a range of respiratory illnesses, including, uh, Coronavirus, Rsv. And other retroviral infections that can cause these triggers. There are no genetic mutations which are associated with increased risk of of Gpp. Pregnancy itself is a risk factor, and it can be particularly dangerous for both the mother and the fetus of those conditions,

1090
02:57:27.650 --> 02:57:37.769
Dr. Arash Mostaghimi: and simply stress, emotional or physical stress can cause this many times. We cannot identify a clear trigger for somebody's flair next slide, please.

1091
02:57:40.970 --> 02:58:07.649
Dr. Arash Mostaghimi: In addition to having more systemic conditions when they have a flare, the patients with Gpp have a worse comorbidity profile than plaques for Isis patients. You can see that twenty one percent of patients have arthritis versus six, with psoriasis, hyperlipidemia type, two diabetes and mental health conditions such as anxiety and depression are more highly expressed in Gdp patients than blacks rises. Patients next slide, please.

1092
02:58:09.990 --> 02:58:39.390
Dr. Arash Mostaghimi: As I mentioned there is some cross-talk, and we'll go and a little bit more detail with this on the next slide between Gpp and psoriasis. So, prior to the approval of Sp Viggo, other Psoriasis medications and biologics were typically used for the treatment of Gpp. The The challenge with these treatments is that although on some occasions they may help partially a survey in two thousand and twenty one prior to the approvals to Viggo demonstrated that eighty three percent of dermatologists reported that patients

1093
02:58:39.400 --> 02:58:45.219
Dr. Arash Mostaghimi: still have continued flares despite and residual disease. Despite these treatments. Next slide.

1094
02:58:47.860 --> 02:59:17.829
Dr. Arash Mostaghimi: Let's dive a little bit more into the aisle Thirty, six pathway, and how it differentiates Gdp from facts for Isis. So on the right you have plaques for Isis driven by I twenty, three. I'll seventeen in it alpha leading to epidermal hyperproliferation. On the left you see gpp which is defined by custules and neutrophilic drive disease driven by ile thirty, six idle six, I one, and although there's a different phenotype of disease in

the middle, you can see. There's crosstock between these two differences

1095
02:59:17.840 --> 02:59:32.480
Dr. Arash Mostaghimi: systems with some interplay between the aisle six, i'll seventeen ah pathways. So while there's some connection, and that's why some of the flax. Horiasis medications are thought to help Tpp. You can see why a more targeted is key next slide, please.

1096
02:59:34.880 --> 02:59:47.290
Dr. Arash Mostaghimi: So Slavico blocks the Io thirty, six receptor, and when it blocks a receptor it does not allow the binding of endogenous agonists. When those agonists do not bind, you do not have it

1097
02:59:47.300 --> 02:59:49.190
Campbell, Kimberly A. (CMS/CM): three minutes for a meeting

1098
02:59:49.200 --> 02:59:57.040
Dr. Arash Mostaghimi: for Io. Thirty, six to dimerize with I one, and as a result you have attenuated aisle thirty, six inflammatory signaling.

1099
02:59:57.470 --> 02:59:58.910
Dr. Arash Mostaghimi: Next slide, please.

1100
03:00:00.720 --> 03:00:09.360
Dr. Arash Mostaghimi: I'll quickly go through a proof of concept phase, one trial. This is of seven patients getting a single dose of Suvigo at ten milligrams per kilogram. Iv. Next slide.

1101
03:00:10.550 --> 03:00:19.890
Dr. Arash Mostaghimi: You can see that as soon as week one patients had substantial improvement in their postular score, with many patients clearing next slide.

1102
03:00:20.690 --> 03:00:34.299
Dr. Arash Mostaghimi: The key thing here is really in the pictures. You can see the tremendous difference between the baseline clusterlysis in both patients here at week one you had improvement of the posture, with computed improvement in Eroshema by week. Four next slide

1103
03:00:35.610 --> 03:00:59.619
Dr. Arash Mostaghimi: our pivotal trial. The Fsl. One trial design recruited fifty three patients from all across the world. They were randomized either to a single dose of nine hundred milligrams of Savigo or Placebo at on day. One at day eight patients who did not respond completely to the initial dose, or who were in the placebo, or given a second dose of Suvigo. Next slide, please.

1104
03:01:01.200 --> 03:01:22.170
Dr. Arash Mostaghimi: You can see here on the left postulation of the score. So at a week we had fifty, three, and fifty. Four percent of patients were clear from a pussular ah standpoint versus only five percent of placebo D. T. To get a plust of arithmetic and scaling forty, two percent clear at a week versus eleven percent in placebo, showing the tremendous response of this medication. Next slide, please.

1105
03:01:23.170 --> 03:01:43.189
Dr. Arash Mostaghimi: Here again you see the pictures with the resolution Ah! Of the partial beginning at day, three and completely by week, one ah! With improvements through week, twelve sustained on the bottom. You have a patient that's the same at baseline and week one post placebo res resolution of crust rules at week, two and complete clearing by week. Twelve next slide, please.

1106
03:01:45.030 --> 03:01:55.510
Dr. Arash Mostaghimi: In addition to having the improvements in their physical condition, patients report a substantial improvement in patient-reported outcomes, including pain, fatigue, and quality of life. Next slide

1107
03:01:57.360 --> 03:02:09.439
Dr. Arash Mostaghimi: the side-effect profiles were mild and included. Ah nausea and vomiting and headache Ah! Some ah for uncles and influenza were reported at a slightly higher rate than placebo next slide.

1108
03:02:11.720 --> 03:02:26.690
Dr. Arash Mostaghimi: Two areas that were identified in the trial were asidely, were two reported cases addressed in three reported cases of yamboree syndrome. These were adjudicated and found to not be true cases or not likely not caused by Svigo next slide.

1109
03:02:27.360 --> 03:02:56.629
Dr. Arash Mostaghimi: So, in conclusion, Fsl: one was a pivotal trial for Sp Viggo, which is the first in class medication uh approved for uh by the fda for treatment of pestular uh generalized clusterlosis in adults, with presenting with flares to Viggo rapidly treated their skin and improve their both skin condition and patient-reported Outcomes the most common adverse effects for a Sydney and fatigue Nige and vomiting with a no clear signal for elevated risk of infection.

1110
03:02:56.640 --> 03:03:08.759
Dr. Arash Mostaghimi: The present long-term administration of to Viggo is being evaluated in a subcutaneous formulation, and an ongoing five-year open label extension for prevention of flares. Thank you very much for your time. I'm happy to take any questions.

1111
03:03:12.290 --> 03:03:14.290
Drew Kasper: Thank you for your presentation.

1112
03:03:14.300 --> 03:03:17.770
Drew Kasper: Are there any questions from the public, or Cms

1113
03:03:22.980 --> 03:03:25.640
Drew Kasper: and Dina if you get it started?

1114
03:03:27.120 --> 03:03:36.050
Adina Hersko: So in this trial there was the availability of escape treatment offered for position, discretion. Can you talk about what the standard to care treatments that were offered? Were:

1115
03:03:36.750 --> 03:04:03.530
Dr. Arash Mostaghimi: Yeah. So per uh physician discretion. They had the option to uh do the traditional treatments for Gpp. If patients either did not respond or had not responded completely. Um! About seventeen percent of patients received this with six patients overall. They included topical steroids. Ah, two patients receive cyclone or methotrexate, which are conventional treatments, and one each received uh exekism at an influx of that.

1116
03:04:09.890 --> 03:04:16.630
Adina Hersko: Thank you. Is there any clinical evidence available comparing those treatment to the use of the Viggo?

1117
03:04:16.850 --> 03:04:24.389
Dr. Arash Mostaghimi: No, there haven't been randomized control trials or Fda approval for any of those treatments based on the

1118
03:04:24.400 --> 03:04:37.780
Dr. Arash Mostaghimi: overlap of the pathways that I presented to you. They have been ah used. But, as I said, even in in the studies, their efficacy has been very limited. They may reduce disease, but do not result in clearance, generally speaking.

1119
03:04:51.440 --> 03:04:57.320
Drew Kasper: Okay, Do we have any follow-up questions or any questions from others?

1120
03:05:02.240 --> 03:05:11.049
Drew Kasper: One here i'll ask for cms could you describe or clarify the inpatient or outpatient administration of the medication.

1121
03:05:11.480 --> 03:05:27.919
Dr. Arash Mostaghimi: Ah! This medication is an Iv medication. It can be administered in either. Setting Often it is given in an in-patient setting just because the patients are very ill when they are ah receiving the treatment. But it is also been given in outpatient settings at normal and fusion centers.

1122
03:05:35.280 --> 03:05:41.720
Drew Kasper: And Adina, I you have a raised hand. Is that from before? Do you have an additional question?

1123
03:05:44.590 --> 03:05:46.560
Adina Hersko: Sorry that was from before?

1124
03:05:49.170 --> 03:05:51.739
Drew Kasper: Um great. How about uh, Cindy ache.

1125
03:05:52.920 --> 03:06:10.380
Cindy Hake: I appreciate your presentation. The um, the outpatient treatments. Are they explicitly done in Id centers? Or have you had patients with the treatment at their home.

1126

03:06:11.350 --> 03:06:21.010
Dr. Arash Mostaghimi: My understanding to date is that the majority of patients have received treatment in fusion centers. There has been one patient who has received therapy at home.

1127
03:06:21.760 --> 03:06:27.970
Dr. Arash Mostaghimi: It's only been available since September, so the true treatment patterns haven't been clarified, yet

1128
03:06:32.950 --> 03:06:39.609
Cindy Hake: there's no Fda recommendations or restrictions on setting of care.

1129
03:06:40.240 --> 03:06:47.619
Dr. Arash Mostaghimi: I do not think so? No, it's based on where the where the patient is comfortable and where they have the nursing,

1130
03:07:11.920 --> 03:07:15.920
Dr. Arash Mostaghimi: you know I see your hand raise. I'm not sure if you have a question again.

1131
03:07:17.810 --> 03:07:33.819
Adina Hersko: Yes, so it's in the study. From what I understand, two of the patients treated were over sixty five. Can you explain whether the results being here can demonstrate whether

1132
03:07:34.510 --> 03:07:36.920
respond differently. Given the numbers

1133
03:07:39.200 --> 03:07:43.470
Dr. Arash Mostaghimi: so which patients who had What if I missed the first part?

1134
03:07:45.010 --> 03:07:46.790
Adina Hersko: Patients over sixty, five,

1135
03:07:46.800 --> 03:07:48.289
Dr. Arash Mostaghimi: a patient over sixty, five.

1136
03:07:48.300 --> 03:08:14.999

Dr. Arash Mostaghimi: Yes, yes, there are two patients over there. I I don't I don't have the the details separating them from from the rest of the patients. Um, so I I don't have those specifically. Um! This is a condition that affects a range of patients. Ah! Of all different ages it is very rare. Ah, so an orphan disease, which is why we only have those two, those two patients. Um. The sample size, I think, is too small to make specific conclusions. But, um! My understanding is that they talk

1137
03:08:15.010 --> 03:08:18.590
Dr. Arash Mostaghimi: it, that the study drug appropriately.

1138
03:08:29.970 --> 03:08:36.620
Adina Hersko: Another question is where any skin bikes is done to confirm diagnosis or in follow-up assessment.

1139
03:08:37.510 --> 03:09:04.360
Dr. Arash Mostaghimi: So biases are not required for confirmation of this disease. Histologically, there's a lot of overlap between um just psoriasis ah acute, generalized ex andematics bustulosis, and this condition, so it's a combination of clinical assessment. And uh, and in the context of where the disease is occurring, so uh, there's not bias, is not required for inclusion. And the following biases: We're not we're not done as part of this trial.

1140
03:09:08.080 --> 03:09:09.240
Adina Hersko: Thank you.

1141
03:09:16.230 --> 03:09:32.819
Dr. Arash Mostaghimi: Yeah. So there's three different sub-scores. There's an error theme. They're scaling, and there's by oscillosis, and there's a specific. There's specific guidelines for how you categorize each subscore individually and then you combine them into a total score.

1142
03:09:37.270 --> 03:09:40.049
Dr. Arash Mostaghimi: I'm not sure if that answered your your question.

1143
03:09:43.380 --> 03:09:44.810
Adina Hersko: Yeah, that's all. Thank you.

1144

03:09:45.850 --> 03:09:47.149
Dr. Arash Mostaghimi: You are our constituents.

1145
03:09:49.930 --> 03:09:52.139
Drew Kasper: Are there any last questions,

1146
03:09:54.650 --> 03:10:00.030
Drew Kasper: any questions in the Q. And A. There are currently no raised hands, and there are

1147
03:10:00.180 --> 03:10:03.449
Drew Kasper: no new questions in the new tech box.

1148
03:10:03.940 --> 03:10:07.250
Drew Kasper: Okay? Well again, Thank you.

1149
03:10:07.300 --> 03:10:17.189
Dr. Arash Mostaghimi: And we will now hear from presenters for the Sabbath Zabulin technology application. You may now unmute your phone.

1150
03:10:26.340 --> 03:10:28.400
Oh, again.

1151
03:10:33.670 --> 03:10:49.589
Fangting Yu: And Dr. Ginfallis, you may. Yeah, you're still muted. I'll say thank you to your throne or i'm still in a question for us this past two weeks. Oh, that's That's great. It's good. Yeah, it's very complimentary of both of you and and sterling to that.

1152
03:10:49.600 --> 03:10:50.990
Fangting Yu: That's good.

1153
03:10:51.000 --> 03:10:55.589
Fangting Yu: Okay, that's great. Yeah, that's been a year. I have an army. I Haven't really had to say

1154
03:10:55.600 --> 03:10:57.480
Fangting Yu: that a two of your phone.

1155

03:10:59.010 --> 03:11:02.559
Fangting Yu: We're getting there. That's exciting.

1156
03:11:04.130 --> 03:11:06.470
Drew Kasper: Okay? And Dr. Gonzalez, Are you ready?

1157
03:11:11.350 --> 03:11:14.709
Drew Kasper: I think you were unmuted for a moment. There, and

1158
03:11:15.030 --> 03:11:16.120
there we go.

1159
03:11:20.510 --> 03:11:21.830
Drew Kasper: Here, Gonzales,

1160
03:11:22.160 --> 03:11:27.339
you may be double-needed. If you have a mute on your phone as well. It looks like you're unmuted in Zoom.

1161
03:11:29.420 --> 03:11:33.119
Drew Kasper: Okay, now, i'm unmuted in both. The Ra will be all right.

1162
03:11:33.180 --> 03:11:35.500
Drew Kasper: Thank you. Yeah, Please proceed.

1163
03:11:35.660 --> 03:11:38.690
Dr. Tara L. Gonzales: Is there an echo? Because i'm unmuted in both, and I don't want to

1164
03:11:38.700 --> 03:11:39.590
echo.

1165
03:11:40.480 --> 03:11:42.250
Drew Kasper: I do not hear an echo.

1166
03:11:50.740 --> 03:12:02.170
Dr. Tara L. Gonzales: I'm going to quickly go over the Covid nineteen overview and unmet need, as it relates to mortality. Then I will introduce the visibility and go over our clinical trial data. So next

slide, please,

1167
03:12:03.900 --> 03:12:05.020
Dr. Tara L. Gonzales: next slide.

1168
03:12:06.890 --> 03:12:24.259
Dr. Tara L. Gonzales: So I think we all can recognize. There still is an unmet need, as it relates to Covid, nineteen mortality. This slide looks at her historical trends since March twenty twenty, and it shows that there are recurring sites throughout up to this point, and the spikes may continue

1169
03:12:24.270 --> 03:12:41.500
Dr. Tara L. Gonzales: looking at the weekly total of of Covid mortality out to November fourteenth of this year we are seeing numbers as high as one thousand nine hundred and seventy two. When I checked this morning on the Cdc. Site, even up as high as two thousand nine hundred and eighty one.

1170
03:12:42.850 --> 03:12:55.310
Dr. Tara L. Gonzales: This just underscores what it looks like from a monthly standpoint, looking at the last three to four months. We are seeing thousands of deaths that are occurring monthly, as it relates to Covid. Nineteen disease next slide, please,

1171
03:12:56.800 --> 03:13:14.630
Dr. Tara L. Gonzales: and this is even in light of available pharmacologic agents, that both function in an antiviral and anti-inflammatory manner. We're still seeing large numbers of deaths that are occurring that are averaging out to between four and five hundred per day next slide, please.

1172
03:13:17.000 --> 03:13:26.800
Dr. Tara L. Gonzales: So one of the key indicators that lead to morbidity and mortality associated with Covid. Nineteen disease is, of course, acute respiratory distress, syndrome, or ards.

1173
03:13:26.910 --> 03:13:39.900
Dr. Tara L. Gonzales: In terms of prevalence, thirty, three percent of hospitalized Covid. Nineteen patients may develop a Rds while hospitalized seventy five percent of Covid, nineteen patients who have been minutes who have been admitted to the Icu have a Rdf.

1174
03:13:39.990 --> 03:13:48.550
So preventing disease. Progression is paramount to reducing mobility and mortality. Seen with Kovat nineteen early diagnosis is

1175
03:13:48.560 --> 03:14:02.119
Dr. Tara L. Gonzales: clearly important, but also safe and effective mechanisms for treatment from an antiviral and anti-inflammatory standpoint are also important, because studies do show. Reducing inflammation can reduce progression to Ards

1176
03:14:02.140 --> 03:14:03.310
next slide, please

1177
03:14:04.780 --> 03:14:06.000
Dr. Tara L. Gonzales: next slide.

1178
03:14:07.730 --> 03:14:28.090
Dr. Tara L. Gonzales: So let me first start off by saying that the Zealand is not a Us. Fda-approved product at this time, and so the Zealand has not been granted Fda emergency use authorization in clinical trials to visibility or in West Studies for the treatment of Sars. Cov. Two Infections in hospitalizable patients with moderately severe Covid. Nineteen infection we're at high risk for

1179
03:14:28.100 --> 03:14:43.160
Dr. Tara L. Gonzales: Yes, this positive results of direct stars could be two viral testing who are hospitalized, and we're at high risk for developing ards, and for whom alternative covid. Nineteen treatment options authorized by the Fda are not accessible or not clinically appropriate.

1180
03:14:43.510 --> 03:14:51.889
Dr. Tara L. Gonzales: The visibility is dose in nine milligrams, capsules given daily orally, or can be opened and administered via the navigatric tube

1181
03:14:52.130 --> 03:14:57.679
Dr. Tara L. Gonzales: Viru ink has requested emergency use, authorization for the visa eulen next slide.

1182
03:14:59.770 --> 03:15:13.100

Dr. Tara L. Gonzales: So the visibility is a unique agent. It has both antiviral and anti-inflammatory processes. It is a microtubule of disruptor which functions by the inhibiting polymerization and inducing depolarization of the microtubules

1183
03:15:13.190 --> 03:15:28.980
Dr. Tara L. Gonzales: from an an antiviral standpoint to the Zebulin is believed to interrupt the transport of Sars cov two into and out of the cell thereby disrupting the sars. So we two viral life cycles from an anti-inflammatory standpoint. The visibility is believed to suppress inflammatory

1184
03:15:29.530 --> 03:15:40.360
Dr. Tara L. Gonzales: thereby reducing the cytokine storm triggered by sars. Clearly two infections specifically tnf alpha I one alpha I. O one beta I l six and ilh next slide, please.

1185
03:15:44.440 --> 03:16:02.699
Dr. Tara L. Gonzales: So let's look at the antiviral action. We are aware that microtubule, traffic and networks play a critical role in viral infection replication, and spread. Sars Cov. Two uses microtubules for viral entry, transport to the endoplasm for endoplasmic reticulum for replication

1186
03:16:02.710 --> 03:16:15.480
Dr. Tara L. Gonzales: and transferred to the endoplasmic reticulum golgi intermediate compartment to the golgi apparatus assembly, and finally outbound trafficking to address the infected viral particles from the south

1187
03:16:15.800 --> 03:16:27.449
Dr. Tara L. Gonzales: the visibulin targets binds and cross-link Alpha and Beta-tubulin subunits to inhibit polymerization and induce deep polymerization of the microtubules by doing this it disrupts the

1188
03:16:27.460 --> 03:16:36.000
margaret two group microtubule trafficking network, which makes them unusable for the virus, thereby disrupting and suppressing the Sars Cov. Two viral life cycle

1189
03:16:36.740 --> 03:16:37.760
slide, please,

1190
03:16:41.450 --> 03:17:00.579
Dr. Tara L. Gonzales: from an anti-inflammatory standpoint. We also know that microtubules play a key role in transporting proteins necessary for inflammation, assembly and activation to the microtubule organizing center, waiting for the release of hydrogen in the cytokines. Microtubules are also necessary for the transport of cytokines from the neutral field.

1191
03:17:00.700 --> 03:17:13.830
Dr. Tara L. Gonzales: So, by inhibiting microtubulinization and inducing deep polymerization the vibrant may inhibit the release of pyrogens or cytokines known to be involved in the in the Covid nineteen cytokine store next slide, please.

1192
03:17:16.370 --> 03:17:19.159
Dr. Tara L. Gonzales: So let's look at our phase. Three clinical study.

1193
03:17:19.220 --> 03:17:36.120
Dr. Tara L. Gonzales: So this was a randomized, double-controlled trial of Covid, nineteen patients. These were a hospitalized basis with modern to Severe Covid, nineteen at high risk for Ards, and death, and they had to be adults greater than or equal to eighteen years of age. Patients patients were randomly assigned to

1194
03:17:36.230 --> 03:17:48.219
Dr. Tara L. Gonzales: randomly signed, two to one to receive either nine milligrams of oral to visibility, or a placebo plus standard of care up to twenty, one days, or discharge whichever came first. Next slide, please.

1195
03:17:50.940 --> 03:17:53.719
Dr. Tara L. Gonzales: So i'm going to discuss our interim analysis.

1196
03:17:53.730 --> 03:17:59.019
Analysis, population that we will be discussing will be of one hundred and fifty subjects.

1197
03:17:59.150 --> 03:18:18.720
Dr. Tara L. Gonzales: Patients were included in the study. If they were greater than April to eighteen years of age, they had laboratory confirmed sars Go v. Two infection had a baseline S. C. O. Two of less

than or equal to ninety. Four patients were then categorized, based on A. W. H. O. Nine point ordinal scale for clinical improvement.

1198
03:18:18.730 --> 03:18:20.690
Dr. Tara L. Gonzales: Patients were categorized as oh,

1199
03:18:20.700 --> 03:18:35.869
Dr. Tara L. Gonzales: for if they were receiving oxygen via mass or naval prone, but they also had to have a document of comorbidity, such as asthma, crime, lung disease, diabetes, hypertension, severe obesity. They had to be greater than, or equal to sixty. Five years of age

1200
03:18:35.880 --> 03:18:49.690
Dr. Tara L. Gonzales: they had to primarily reside in a heresy home or a long-term care, facility, or were in their compromise. Patients were classified as wh Oh, five if they were receiving oxygen via noninvasive ventilation, or high school

1201
03:18:49.700 --> 03:18:50.800
three minutes,

1202
03:18:51.240 --> 03:19:08.899
Dr. Tara L. Gonzales: and patients who would. W. H. Six, were intubated in our mechanical ventilation. Patients were exclusive; they were pregnant of breastfeeding required mechanical ventilation, and other supportive care they were excluded. If they had hepatic insufficiency or realist efficiency, hepatic insufficiency

1203
03:19:08.910 --> 03:19:26.569
Dr. Tara L. Gonzales: was was determined by the refrunction studies that were greater than eight or three times the upper upper limit of normal, and a toability with this level that was above the upper limit of normal renal insufficiency was determined by a creative experience of less than sixty milliliters per minute. Next slide, please.

1204
03:19:28.500 --> 03:19:32.310
Dr. Tara L. Gonzales: Standard of care What's similar in both groups next slide, please.

1205
03:19:34.600 --> 03:19:50.000
Dr. Tara L. Gonzales: So, looking at the primary Fsb. Endpoint the

Zealand demonstrated a twenty, four point, nine percent absolute reduction in mortality versus the evil and standards of care that translated into a fifty five point two percent relative reduction in all all cause mortality

1206
03:19:50.010 --> 03:20:04.319
Dr. Tara L. Gonzales: um by the sixty versus standard of care, and which gave a p-value of zero point zero zero four one. The mortality rate in the of the bulin arm was twenty point two. The mortality rate in the plus c. One was forty, five point, one, six, five, please.

1207
03:20:07.240 --> 03:20:19.829
Dr. Tara L. Gonzales: And looking at the subgroup analysis, the relative existing death was consistent with overall study, results favoring for disabilities, treatment, regardless of the subgroup that they were grouped into next slide, please.

1208
03:20:21.390 --> 03:20:39.429
Dr. Tara L. Gonzales: T-secondary endpoints were as follows: For visual and treatment resulted in a forty, three percent relative reduction in ipu days a forty, nine percent relative reduction in mechanical ventilation days and a twenty, six percent reduction in hospitaling the same versus Perceval of standard of care. These were all statistically significant and exciting

1209
03:20:44.320 --> 03:21:01.190
Campbell, Kimberly A. (CMS/CM): in terms of safety. Ah! The proportion of patients who experienced any antibiotics in the vibrant treatment group was lower at sixty one point five percent compared to conceivable to seventy, eight point, three percent. And in terms of the serious adverse events there there were a lower proportion of patients who experienced

1210
03:21:01.200 --> 03:21:08.919
serious adversity of instance, the Dol and Treatment Group at twenty nine point two compared to the Placebo group at forty six point four next by planes.

1211
03:21:10.830 --> 03:21:24.439
Dr. Tara L. Gonzales: So in summary vis-bulent, has a unique mechanism of action. It functions as both an antiviral and anti-inflammatory agent in clinical clinical trials There was a fifty five point two reduction in death versus disabling

1212
03:21:24.530 --> 03:21:38.279
person's Death versus the C. One standard of care. And there was a twenty, four point, nine percent absolute reduction in mortality rate which translates to another needed to treat of four. There was reduction in Hospital Bay's, Ic. Days in the Council ventilation.

1213
03:21:38.540 --> 03:21:43.790
Peru again has requested emergencies authorization for the Zealand. Thank you very much,

1214
03:21:44.200 --> 03:21:46.060
Dr. Tara L. Gonzales: and i'm happy to answer any questions.

1215
03:21:51.300 --> 03:21:53.860
Drew Kasper: Thank you very much for your presentation.

1216
03:21:54.010 --> 03:21:57.790
Drew Kasper: I will now take questions from the public or Cms.

1217
03:21:58.290 --> 03:22:02.719
Drew Kasper: I see we do have a question in the Q. And A.

1218
03:22:03.340 --> 03:22:11.590
Drew Kasper: When does Veru expect the Fda to grant an Eu A. For Sabbath, and thank you.

1219
03:22:12.480 --> 03:22:25.770
Dr. Tara L. Gonzales: So we are waiting as well because we are applying for emergency use. There is no peduce a date, so we have. We continue to have conversations with them, but we are waiting

1220
03:22:26.670 --> 03:22:28.869
for them to come up with their decision.

1221
03:22:31.340 --> 03:22:34.680
Drew Kasper: Yeah, and uh, Adina, please go ahead and unmute.

1222
03:22:35.350 --> 03:22:48.719
Adina Hersko: Thank you. Um! You had a slide that talked about Um,

said Visibility, being tested in patients who for whom other treatments are not accessible or clinically appropriate. Can you talk more about that fusion population.

1223
03:22:49.630 --> 03:22:54.169
Dr. Tara L. Gonzales: So that is actually the Eua verbiage.

1224
03:22:54.210 --> 03:23:01.069
Dr. Tara L. Gonzales: So that's why we were able to use. That's why we included standard of care in both arms of the study,

1225
03:23:01.760 --> 03:23:03.300
Dr. Tara L. Gonzales: because we,

1226
03:23:03.430 --> 03:23:22.440
Dr. Tara L. Gonzales: in in order for us to meet meet that language, we had to be able to say, You know, use the standard of care that was available for people to use to use that study. So the patients that we that we looked at with faces that were included in the study those who required oxygen at a baseline o two, that of less than or equal to ninety, four,

1227
03:23:22.450 --> 03:23:27.399
Dr. Tara L. Gonzales: and we're adults; and if we're considered to be at a high risk for a Rdf.

1228
03:23:31.600 --> 03:23:38.739
Adina Hersko: So to clarify the study tested patient for whom those standard of care treatments were accessible.

1229
03:23:43.780 --> 03:23:46.369
Dr. Tara L. Gonzales: I know it's confusing it conceives me as well.

1230
03:23:47.930 --> 03:23:50.290
Adina Hersko: So is there a patient population

1231
03:23:50.740 --> 03:23:57.139
Adina Hersko: for whom this would be eligible as a treatment option, that Don't have access to other options.

1232

03:23:58.240 --> 03:24:06.040
Dr. Tara L. Gonzales: So yes, it could be used in patients that that also did not have these other standard of care. Standards of care use as well,

1233
03:24:07.740 --> 03:24:12.420
Dr. Tara L. Gonzales: so it's not looked at as an add on it could be used in solo as well

1234
03:24:15.350 --> 03:24:20.469
Adina Hersko: for those standard of care. Treatments stratified to determine differences in outcome.

1235
03:24:21.240 --> 03:24:22.810
Dr. Tara L. Gonzales: No, they were not.

1236
03:24:23.830 --> 03:24:24.869
Adina Hersko: Thank you.

1237
03:24:29.700 --> 03:24:46.019
Dr. Tara L. Gonzales: So just as a follow. Up to that the majority of patients in both arms in the study were given Dexter messes, but only about thirty percent of the patients received Rem Dezevir in both arms of the study, and in terms of they're sitting in to legitimate

1238
03:24:46.030 --> 03:24:50.560
and other Jack inhibitors, they were less than five percent in both arms of the study.

1239
03:24:55.170 --> 03:25:06.870
Adina Hersko: Is there Is there any clinical evidence comparing the outcomes between patients treated with that did not have those prior treatment, and those treated with only the prior treatment.

1240
03:25:07.120 --> 03:25:22.860
Dr. Tara L. Gonzales: So yes, actually so looking. Um! What we did. And I I apologize because I guess it was stratified when we look at the subgroup analysis, i'm looking at that fourth button. I'm sorry I didn't have enough time to go through it. But these data are published in New or in Journal of Medicine Evidence

1241

03:25:22.870 --> 03:25:41.480
There is there's it's it's. It's still favor to the the dealing with either with or without either of these, so we look at it with decks without decks, with, from disappear with the Jack inhibitors without the deck and interest as well. So I apologize. Yes, we did. We did stratify that. I I missed.

1242
03:25:41.490 --> 03:25:43.769
I misspoke. I misunderstood your question.

1243
03:25:45.900 --> 03:25:47.219
Adina Hersko: Okay, Thank you.

1244
03:25:52.740 --> 03:25:57.289
Drew Kasper: Are there any other questions from the public or from Cms:

1245
03:26:06.060 --> 03:26:07.240
Drew Kasper: Okay?

1246
03:26:07.820 --> 03:26:15.880
Drew Kasper: Well, thank you again, and at this point we will move into a brief break.

1247
03:26:16.690 --> 03:26:21.999
Drew Kasper: We will rejoin in ten minutes and one hundred and forty five.

1248
03:35:21.290 --> 03:35:36.259
Drew Kasper: We will begin again in just a minute here as a reminder for folks. Please do make sure that if you are in charge of your own new functions that you make sure you aren't indeed muted when you are not presenting you appreciate it

1249
03:35:38.180 --> 03:35:43.059
Drew Kasper: day we could begin re-recording it. It looks like we are all right.

1250
03:35:46.560 --> 03:35:48.609
Drew Kasper: We'll start again in just a minute Here,

1251
03:35:54.490 --> 03:35:56.129
Drew Kasper: all right. So

1252
03:35:56.370 --> 03:36:04.390
Drew Kasper: we will now hear from presenters for the tech bailey or to quest of lab technology application.

1253
03:36:04.650 --> 03:36:06.649
Drew Kasper: You may now unmute your phone.

1254
03:36:06.820 --> 03:36:09.169
Dr. Jessica Fowler: Good afternoon. Can you hear me? Okay,

1255
03:36:10.360 --> 03:36:19.040
Dr. Jessica Fowler: we can thank you. Okay, This is Jessica Fowler. I'm. The Us. Met affairs, Lee, for the by specifics program at Jansen next slide.

1256
03:36:20.290 --> 03:36:43.579
Dr. Jessica Fowler: So my almost as we've already seen, is characterized by the stereotypical cycling of relapse and permission which is represented by the Graphic below. That shows M. Protein that's indicative of tumor burden. And you can see that patients have these recurring cycles of relapse, and about two-thirds of patients in the us database study shows that

1257
03:36:43.590 --> 03:36:48.889
Dr. Jessica Fowler: that two-thirds of the patients received at least three or more prior lines of

1258
03:36:48.900 --> 03:37:04.249
Dr. Jessica Fowler: treatments. Um, since their initial myeloma diagnosis, and we know that my aluma primarily affects the elderly, patient population and patient comorbidities typically increase with each line of therapy as well

1259
03:37:04.410 --> 03:37:05.690
Dr. Jessica Fowler: next line

1260
03:37:05.700 --> 03:37:06.670

Dr. Jessica Fowler: slide.

1261
03:37:07.510 --> 03:37:36.379
Dr. Jessica Fowler: So with this cycling of relapse and remission, we know that that that time to progression also shortens with each subsequent line of therapy, and that the duration of these responses really diminishes over time. And typically, you know, patients that have a media prior for power lines of therapy and that are triple-class refractory biological patients. Um have really aggression free survival only around three months and overall survival around nine months. This is

1262
03:37:36.390 --> 03:37:57.150
Dr. Jessica Fowler: obviously outside of the carte clinical trial data. Uh, but um current treatment there. The options for these patients that are in this triple class refractory disease are really limited by toxicities and accessibility, which is the case in carte therapy as a further elaborate and subsequent slides.

1263
03:37:57.270 --> 03:37:58.740
Dr. Jessica Fowler: Next slide.

1264
03:37:59.630 --> 03:38:18.190
Dr. Jessica Fowler: So T. Vailey is the the first and only by specific. That is, a Btm. A directed Cd. Three T-cell Engagement that's indicated for a treatment of myeloma patients with relapsed refractory disease that have received at least four prior lines of therapy that include ah

1265
03:38:18.700 --> 03:38:24.659
Dr. Jessica Fowler: Proteasome, inhibitor enamid as well as an anti-sev thirty eight monochronal antibodies,

1266
03:38:24.670 --> 03:38:37.020
Dr. Jessica Fowler: and we received approval at the end of October, based on an early phase trial that will be further validated in subsequent confirmatory trials. Next slide.

1267
03:38:38.050 --> 03:38:57.229
Dr. Jessica Fowler: So Tech Vale is based on this dual body platform of t cell directing therapies, and it really provides an off-the-shelf ah therapy that doesn't require the same manufacturing delays and utilizes the patient's own. So to target the myeloma cells

1268
03:38:57.240 --> 03:38:58.390
Dr. Jessica Fowler: next slide

1269
03:39:00.840 --> 03:39:02.900
Dr. Jessica Fowler: next. Okay, Thank you.

1270
03:39:02.910 --> 03:39:23.270
Dr. Jessica Fowler: So um in ah tequila's mechanism of action. Like I already mentioned, it real. It activates the patient's immune system by binding the Cd. Three receptor that's expressed on the surface of T cells to the b cell Maturation Antigen that's expressed on the multiple myeloma cells, as well as some healthy B cell lineage cells

1271
03:39:23.280 --> 03:39:24.440
Dr. Jessica Fowler: next slide.

1272
03:39:26.020 --> 03:39:42.059
Dr. Jessica Fowler: So the Fda accelerated approval was based on the majestic one cohort a study, and in this study there were a total of one hundred and sixty five patients that were treated with Tech as part of this phase one and two

1273
03:39:42.070 --> 03:40:04.190
Dr. Jessica Fowler: um, and then, just for clarity's sake, that there the safety analysis was based on the total one hundred and sixty-five patients, and the efficacy analysis was based on one hundred and ten patients, which included only the patients in the phase two uh portion that have received the first treatment dose by that march um eighteenth data cut off,

1274
03:40:04.200 --> 03:40:12.419
Dr. Jessica Fowler: and the Median Ah! Treatment duration was around was eight point five months in terms of this data cut off that was used

1275
03:40:13.190 --> 03:40:14.730
Dr. Jessica Fowler: next slide.

1276
03:40:16.100 --> 03:40:43.699
Dr. Jessica Fowler: So in terms of Ah key patient characteristics,

We're part of this. Ah, follow up but the the seven point four months, the the age. The Median age was sixty six years of age, but the range was thirty, three to to eighty, two years of age. Also key to point out is that the end of prior line therapy was close to eighty percent

1277
03:40:44.300 --> 03:40:45.730
Dr. Jessica Fowler: next slide.

1278
03:40:47.020 --> 03:41:10.829
Dr. Jessica Fowler: So in terms of the efficacy data or this I already mentioned, you'll see in the the Graphic. In the middle is the efficacy patient population. That's part of the the Us. Prescribing information that consisted of the one hundred and ten patients you'll see. The overall response rate was close to sixty two, but the the deeper responses of Cr. Greater at twenty, eight percent.

1279
03:41:10.840 --> 03:41:21.880
Dr. Jessica Fowler: The responses were relatively quick for the median time to first response being one point, two months, and median time to best response being three point eight months.

1280
03:41:21.940 --> 03:41:36.489
Dr. Jessica Fowler: And these these responses are typically viewed as being durable, and they deepened over time where we had a data cut off. Seventy of the one hundred and four patients responders that had maintained their response

1281
03:41:36.500 --> 03:41:38.409
Dr. Jessica Fowler: next slide.

1282
03:41:40.360 --> 03:41:43.789
Dr. Jessica Fowler: So, as I already mentioned on the previous presentation there,

1283
03:41:43.800 --> 03:42:08.359
Dr. Jessica Fowler: our have been recent changes to the treatment landscape so primarily focused your attention on Selenex, or when uh has been uh currently removed as only used uh through a compassionate use program. So selenex or uh it's the other therapy that's found in the same treatment population, and relapsed for fractured patients with four more prior lines of therapy

1284

03:42:08.370 --> 03:42:21.470
Dr. Jessica Fowler: to note the overall response rate in the their pivotal study that the label was based on in this patient population was twenty five percent compared to the sixty. One point, eight percent of

1285
03:42:21.480 --> 03:42:46.679
Dr. Jessica Fowler: an overall response rate that was found in the majestic. One study, also important to note is that the the number of patients, the percentage of patients that result in discontinuation of of tech daily due to adverse events was only one point, two percent uh in comparison to the twenty-seven percent of selenex or patients that had to discontinue therapy due to toxicity

1286
03:42:47.140 --> 03:42:48.640
next slide,

1287
03:42:49.730 --> 03:43:17.590
Dr. Jessica Fowler: and, as I mentioned in the Introduction um accessibility not only toxicity but excess. Accessibility is a problem with some of the carte therapies, and this is due to a a number of complexities. Um, you know, one of which, being manufacturing constraints, and and also the the complex logistics that are required for Rt. Directed therapy. There are multiple steps, including a pheresis, t cell activation.

1288
03:43:17.600 --> 03:43:23.589
Dr. Jessica Fowler: The introduction of the therapy is quality controlled, etc. And so patients are not

1289
03:43:23.600 --> 03:43:24.690
Dr. Jessica Fowler: all right,

1290
03:43:24.700 --> 03:43:46.969
Dr. Jessica Fowler: and not all patients that are intended to receive the carte therapies end up receiving the therapy due to them, expiring or having a product that is not able to be given, as well as the wait lists that have already been mentioned in previous presentation, and the carte therapies also require a specialized trained staff, and

1291
03:43:46.980 --> 03:43:52.969
Dr. Jessica Fowler: at certain centers that are in fact certified to be able to deliver these therapies as well.

1292
03:43:53.840 --> 03:43:55.559
Dr. Jessica Fowler: So next slide.

1293
03:43:56.210 --> 03:44:07.360
Dr. Jessica Fowler: So, in conclusion of tech vale, or to cluster map, um. Efficacy results in this first ah approval is based on the digestive one study,

1294
03:44:07.370 --> 03:44:35.479
Dr. Jessica Fowler: and we have demonstrated that this does provide a substantial clinical benefit over approved therapies, and even more so. Now the other blend rep has been removed off of the market. This therapy does not require the manipulation of complex manufacturing, such as carte therapies, and in comparison to car t therapies that crs rates are relatively low and manageable compared to carbon therapy

1295
03:44:35.490 --> 03:44:50.420
Dr. Jessica Fowler: Response Rates are, you know, at close to sixty, two percent in comparison to the current other off the shelf therapy that sell an Xor that is, is less than thirty percent.

1296
03:44:50.430 --> 03:45:12.739
Dr. Jessica Fowler: So really overall the the efficacy results as well as the lower toxicity profile that's seen in comparison to cardi therapy, and the the um therapy being off the shelf readily available, really make this um really support this as a substantial clinical benefit, and for currently available therapies,

1297
03:45:22.210 --> 03:45:24.420
Dr. Jessica Fowler: and i'll take any questions.

1298
03:46:02.840 --> 03:46:05.530
Dr. Jessica Fowler: Hello! Can you still hear me?

1299
03:46:07.050 --> 03:46:13.729
Dr. Jessica Fowler: I'm sorry I fell victim to the double mute myself. Okay,

1300
03:46:13.740 --> 03:46:20.849
Drew Kasper: So thank you very much for your presentation. Are there

any questions from the public, or Cms

1301
03:46:21.740 --> 03:46:39.639
Drew Kasper: as a recap for those of you that weren't around for earlier announcements? You both have recently joined. You can use the Q. And a function within the zoom toolbar to type in your questions for presenters, or you can read the hand, and we will undo you, or you can unmute yourself. Of course, if you're a panelist,

1302
03:46:39.650 --> 03:46:42.589
Drew Kasper: that is a participant or a presenter,

1303
03:46:44.550 --> 03:46:46.510
Drew Kasper: any questions

1304
03:46:46.520 --> 03:46:52.799
Drew Kasper: don't see any questions in the Q. And A. And there are no new questions in the new tech

1305
03:46:52.990 --> 03:47:00.129
Drew Kasper: email box, which is an Ew. Tech at Cms. Hhs. Gov:

1306
03:47:00.260 --> 03:47:08.559
Drew Kasper: you have that email box. If folks are only on the telephone and don't have access to the Q. And A. Or the raised Hand features in zoom

1307
03:47:08.890 --> 03:47:15.390
Drew Kasper: there, Aren't. Questions there, though there are no questions in the Q. And A. And there are no raised hands, so i'll make a last call.

1308
03:47:19.460 --> 03:47:22.390
Drew Kasper: Great? Well,

1309
03:47:22.450 --> 03:47:28.569
Drew Kasper: Thank you again, and we will now hear from presenters,

1310
03:47:30.300 --> 03:47:37.159
Drew Kasper: from the nexar Grid or an extra bride technology

application.

1311
03:47:37.350 --> 03:47:39.480
Drew Kasper: You may proceed and unmute.

1312
03:47:40.200 --> 03:47:42.019
Dr. James Boron: Thank you, Drew. Can you hear me?

1313
03:47:43.240 --> 03:47:45.819
Drew Kasper: I can. Okay, Wonderful.

1314
03:47:46.210 --> 03:47:56.180
Dr. James Boron: Good afternoon, everybody, and thank you for joining us. I'm. Dr. James Boron and I'm. The medical director for Burned products at Arizona, and today we'll be discussing next of it

1315
03:47:56.490 --> 03:47:59.839
a new enzymatic agreement agent for a thermal birds.

1316
03:48:00.040 --> 03:48:01.190
Dr. James Boron: Next slide

1317
03:48:04.290 --> 03:48:11.320
Dr. James Boron: Nex bread, or inaccurate is currently pending The Fda Review with an anticipated padua day of January. The first

1318
03:48:11.790 --> 03:48:17.650
Dr. James Boron: It is an enzymatic non-surgical option for escal removal and hospitalized burn patients

1319
03:48:17.820 --> 03:48:24.820
Dr. James Boron: the proposed indication for Mexico is escal removal, and adults with deep, partial, and faultless thermal groups

1320
03:48:25.080 --> 03:48:32.139
Dr. James Boron: I've heard of the American Burn Association. More than forty thousand patients are hospitalized, annually following a burning

1321

03:48:32.900 --> 03:48:40.379
Dr. James Boron: after a burn to the skin occurs. Non-fiable ascar is formed in the area of in Theascar contains dead tissue

1322
03:48:40.630 --> 03:48:43.499
Dr. James Boron: that skin along with dried secretion.

1323
03:48:43.660 --> 03:48:46.349
Dr. James Boron: The removal of this ascar is important for properties.

1324
03:48:47.690 --> 03:48:53.870
Dr. James Boron: An exhibit is a biologic product derived from pineapple stems that is delivered in two components

1325
03:48:54.160 --> 03:49:05.040
Dr. James Boron: The first is an expert powder, which contains proteolytic enzymes. In the rich and brumbling. The second component is the ched vehicle. The two components are mixed prior to application on me.

1326
03:49:05.480 --> 03:49:10.539
Dr. James Boron: An expert has been used in Europe since his approval by the Ema in two thousand and twelve.

1327
03:49:10.860 --> 03:49:25.389
Dr. James Boron: Next to bread can be used on up to fifteen percent. Tbsa, during one application, once applied to clean burnskin is left on the barn, wound s car under an inclusive dressing for four hours, and then removed the gentle stream,

1328
03:49:25.500 --> 03:49:27.880
Dr. James Boron: revealing viable healthy tissue.

1329
03:49:28.320 --> 03:49:29.460
Dr. James Boron: Next slide.

1330
03:49:31.950 --> 03:49:38.940
Dr. James Boron: The current standard of of care and burn wounds involves timely removal of wood, of Bernoulli Ascar.

1331
03:49:39.040 --> 03:49:45.640
Dr. James Boron: Often by search folk. City surgical excision involves general anesthesia in an operating theory.

1332
03:49:45.850 --> 03:49:52.679
Dr. James Boron: During the procedure the patient may experience blood loss heat loss along with sacrifice of healthy viable tissues.

1333
03:49:52.830 --> 03:50:05.449
Dr. James Boron: The timely removal of escar usually accomplished within the first two to three days after Burgundry is essential to stop local inflammation that can constrict adjacent blood vessels further extending the zone of.

1334
03:50:06.260 --> 03:50:11.890
Dr. James Boron: In addition, the dead non-violent tissue contained in the esper can become a source of profession

1335
03:50:12.000 --> 03:50:20.969
Dr. James Boron: may lead to Systemic sepsis, burn-u, and infection and sepsis are one major cause of morbidity. Mortality falling Burning

1336
03:50:21.170 --> 03:50:29.030
Dr. James Boron: nexa bread may be applied outside of the operating room theater in the patient's bed bedside with appropriate pain control.

1337
03:50:29.440 --> 03:50:34.660
Dr. James Boron: It was developed to selectively target only teenager collagen. While sparing healthy tissue.

1338
03:50:34.820 --> 03:50:42.770
Dr. James Boron: This may reduce the amount of tissue that is removed. And thus we've reduced the need for skin graphs to close the loop

1339
03:50:43.140 --> 03:50:50.890
Dr. James Boron: limited single-center retrospective studies have also demonstrated clinical benefit of necks of bread when used on difficult to excise areas

1340

03:50:50.900 --> 03:50:56.589
Dr. James Boron: including hands and face, while shield in sensitive areas such as eyes and proposal services

1341
03:50:56.760 --> 03:51:03.010
Dr. James Boron: next to it has been identified by the Us. Biomedical advance, research and development of Dorothea authority,

1342
03:51:03.540 --> 03:51:08.039
Dr. James Boron: a critical countermeasure for public health emergence emergencies. The

1343
03:51:08.050 --> 03:51:11.849
Dr. James Boron: has procured an exhibit stockpile for emergency response.

1344
03:51:12.170 --> 03:51:13.320
Dr. James Boron: Next slide

1345
03:51:15.270 --> 03:51:20.260
Dr. James Boron: two phase, three studies have been completed. Studying. Next to

1346
03:51:20.360 --> 03:51:28.930
Dr. James Boron: that a check trial was a multi-center-winded, randomized, controlled, free-armed phase three study that included multiple uss.

1347
03:51:29.520 --> 03:51:38.610
Dr. James Boron: The study compared an exorbit to the standard of care. And Jel vehicle and deep, partial and full thing is Burns raging from three to thirty percent in adults.

1348
03:51:38.620 --> 03:51:44.290
Dr. James Boron: A total of one hundred and seventy five patients were studied, randomized, the three to three to one ratio.

1349
03:51:44.580 --> 03:52:00.850
Dr. James Boron: Mw. Two thousand and four trial was a multi-center, open-layable, randomized, two-arm phase, Three study completed outside of the United States the study compared an exhibit to the standard of

care and one hundred and fifty, six patients, aged as four through fifty five.

1350
03:52:00.930 --> 03:52:05.589
Dr. James Boron: The patients had deep, partial, and fol thickness. Burns ranging from five to thirty percent

1351
03:52:05.980 --> 03:52:15.340
Dr. James Boron: standard of care patients were treated with a combination of both surgical and non-surgical esper removal procedures based on the investigator's judgment and post-

1352
03:52:16.640 --> 03:52:17.799
Dr. James Boron: Next, slide

1353
03:52:20.060 --> 03:52:23.809
Dr. James Boron: the results of the text study are demonstrated on this slide.

1354
03:52:23.910 --> 03:52:30.740
Dr. James Boron: Nexuberg completely removed Bernoulli, Nascar, and ninety three percent of patients compared to four percent in the gel vehicle.

1355
03:52:31.100 --> 03:52:34.649
Dr. James Boron: The other incidents of patients require a surgical excision.

1356
03:52:34.860 --> 03:52:38.380
Dr. James Boron: Their Bernoulli's was just four percent in the next

1357
03:52:39.120 --> 03:52:42.060
Dr. James Boron: to seventy, two percent in the standard of care.

1358
03:52:42.450 --> 03:52:52.669
Dr. James Boron: In addition, an exhibit demonstrated a short shortened time to complete escar removal and less blood loss associated with escar removal compared to the standard of care,

1359
03:52:54.190 --> 03:52:55.369

Dr. James Boron: looks like

1360
03:52:57.860 --> 03:53:00.969
Dr. James Boron: Mw. Two thousand and four is outlined up here.

1361
03:53:02.660 --> 03:53:19.270
Dr. James Boron: The surgical escar removal was performed in only twenty-five percent of next grid patients, while seventy percent of the standard of care patients had their s car surgically removed. In addition, a statistically significant smaller version of the wounds were excised in the next retreat

1362
03:53:20.070 --> 03:53:28.009
Dr. James Boron: in patients with deep partial thickness wounds a decrease need for skin grafting was demonstrated in the next big group. Compared to the standard of care.

1363
03:53:28.040 --> 03:53:34.719
Dr. James Boron: Only eighteen percent of the wounds autographed to the next big group compared to thirty four percent in the standard of care.

1364
03:53:35.310 --> 03:53:46.560
Dr. James Boron: In addition, the next word group wounds has statistically smaller percentage of the wounds autographed in compared to standard of care, eight point, four percent versus twenty, one point, five percent.

1365
03:53:47.700 --> 03:53:55.420
Dr. James Boron: When autographed or skin grafting is performed, a new wound is created, and this skin is often harvested from

1366
03:53:55.610 --> 03:53:59.109
Dr. James Boron: the patient's own skin. This is referred to as a donor site,

1367
03:53:59.240 --> 03:54:09.220
Dr. James Boron: a reduction in the number of burns in the burn area. Auto crafted may translate to decreased need for donor-site tissue and decrease donor-site-related morbid

1368

03:54:10.270 --> 03:54:11.530
Dr. James Boron: next slide

1369
03:54:16.200 --> 03:54:18.749
Dr. James Boron: the next of bread was well tolerant.

1370
03:54:18.900 --> 03:54:26.090
Dr. James Boron: The slide demonstrates adverse reactions that occur even greater than five percent of patients treated with an expert based on

1371
03:54:26.100 --> 03:54:27.999
Dr. James Boron: who will face three studies.

1372
03:54:28.220 --> 03:54:34.099
Dr. James Boron: The most common adverse reactions for patients with necks and bread were paritis and pyroxy

1373
03:54:34.450 --> 03:54:35.869
Dr. James Boron: The frequency of

1374
03:54:36.150 --> 03:54:38.489
Dr. James Boron: treatment emergent events

1375
03:54:38.500 --> 03:54:48.370
Dr. James Boron: has indicated as any pain, any fever wound-related infections for any sepsis were similar between the next orbital and the standard of care.

1376
03:54:51.410 --> 03:54:52.490
Dr. James Boron: Next slide,

1377
03:54:56.430 --> 03:55:07.769
Dr. James Boron: therefore, in summary next to bread encules is indicated for the escar removal or agreement in adults with deep partial thickness and full thickness; thermal,

1378
03:55:08.460 --> 03:55:13.300
Dr. James Boron: that bedside and provides a non-surgical option for complete escar remove the

1379
03:55:13.600 --> 03:55:21.009
Dr. James Boron: the next of bread was developed to targets. Selective removal of ascar or teenager collagen. Well-spared healthy tissue

1380
03:55:21.400 --> 03:55:39.669
Dr. James Boron: in phase three randomized controlled trials An exorbit was shown to decrease the time needed to achieve complete escalating, reduce the incidence of surgical exhibition, decrease the need for autographs in deep, partial fitness, rooms to reduce actual blood loss related to Ascard

1381
03:55:40.530 --> 03:55:41.619
Dr. James Boron: next slide.

1382
03:55:43.480 --> 03:55:49.020
Dr. James Boron: Thank you very much for your time, and i'm happy to answer any questions that any of anyone may ask.

1383
03:55:52.060 --> 03:55:54.179
Drew Kasper: Thank you for your presentation

1384
03:55:54.830 --> 03:55:58.379
Drew Kasper: there any questions from the public or from Cms.

1385
03:56:01.990 --> 03:56:06.859
Drew Kasper: I see a hand raised, Please unmute and proceed, Valerie.

1386
03:56:08.900 --> 03:56:15.710
Valerie Favela: Thank you. Is there any available clinical data demonstrating comparisons between Mexal grid and collagen. A.

1387
03:56:16.670 --> 03:56:17.949
Dr. James Boron: Currently no.

1388
03:56:18.350 --> 03:56:23.750
Dr. James Boron: The two products have a much different

1389
03:56:23.820 --> 03:56:37.339

Dr. James Boron: indicate, or much different usage case. Um, with the time needed to use a collagenase, being days to weeks, and the time needed to use next for it being minutes to

1390
03:56:40.630 --> 03:56:42.039
thank you for that.

1391
03:56:46.280 --> 03:56:47.539
Drew Kasper: And Theina.

1392
03:56:49.020 --> 03:56:58.909
Adina Hersko: Thank you. Can you explain a little bit more about what you mean? Are you saying that cloud units cannot be used immediately in the same time, frame, or that it takes longer to be effective,

1393
03:56:59.470 --> 03:57:13.350
Dr. James Boron: it generally takes longer to be effective. Ah! Patients who generally receive Pelagenase Ah! Will receive it for longer than a day. Where an exhibit is used in a timeframe of four hours.

1394
03:57:18.060 --> 03:57:25.280
Adina Hersko: Thank you. Were any of these products included in a standard of care arms for the non-surgical methods you mentioned.

1395
03:57:26.380 --> 03:57:28.209
Dr. James Boron: Ah, I boo!

1396
03:57:28.840 --> 03:57:30.530
The use of Santal would have been

1397
03:57:31.470 --> 03:57:35.170
Dr. James Boron: some patients in both trials. Yes,

1398
03:57:36.960 --> 03:57:39.619
Adina Hersko: so is there any stratification of those outcome?

1399
03:57:40.400 --> 03:57:42.920
Dr. James Boron: Uh, not in the published item.

1400
03:57:44.420 --> 03:57:45.480
Adina Hersko: Thank you.

1401
03:57:54.310 --> 03:57:58.070
Drew Kasper: Are there any other questions from the public

1402
03:57:58.200 --> 03:58:00.060
Drew Kasper: for Cms.

1403
03:58:00.690 --> 03:58:09.540
Drew Kasper: There are no new questions in the new tech mailbox which there are only a couple of people who are on phone only. But if you don't have access to

1404
03:58:09.760 --> 03:58:11.480
Drew Kasper: the Um.

1405
03:58:11.700 --> 03:58:16.060
Q. And a function or the radiation function in zoom.

1406
03:58:16.480 --> 03:58:30.469
Drew Kasper: You can use the speed new heck at Cms. Ah, Ah, go to the email box to submit your questions, and we'll be sure to ask them for you. There are no questions in the Q. And A. And there are no new raised hands.

1407
03:58:31.030 --> 03:58:33.860
Drew Kasper: So with that we thank you again,

1408
03:58:34.530 --> 03:58:40.499
Drew Kasper: and we will now hear from presenters for the duration of technology. Applications

1409
03:58:41.090 --> 03:58:43.460
may now unmute your phone.

1410
03:58:44.010 --> 03:58:46.309
Dr. Steve Brooks: Okay, thank you. Everyone

1411
03:58:46.320 --> 03:59:01.410
Dr. Steve Brooks: Hi. My name is Steve Brooks. I'm. The chief Medical Officer Marrazine. We'll speak today about duragraph a solution for the preservation of vascular conduits during bypass surgery. My disclosures are that i'm an employee of stockholder. Mar the next slide, please.

1412
03:59:01.470 --> 03:59:06.189
Dr. Steve Brooks: There are over four hundred thousand bypass surgeries in the United States. Every year

1413
03:59:06.200 --> 03:59:35.640
Dr. Steve Brooks: Multiple studies have documented its clinical value, and it has a class. One indication of the latest ech and guidelines. Studies have shown the cabbage surgery of truce, survival on symptoms of patients with advanced and complex coronary disease next libraries. Unfortunately, over the past sixty years there has been little innovation, innovation to address the major issue of being graph failure. Bing graph disease from addressing to being rest. Failure remains the major cause of long term failure of bypass surgery.

1414
03:59:35.650 --> 03:59:37.410
Dr. Steve Brooks: Next slide, please.

1415
03:59:37.440 --> 03:59:56.710
Dr. Steve Brooks: Eighty five percent of surgeries employed. Beans as conduits. This slide shows the findings of a bit analysis looking to Stephen as being graph failure rates at different time points the failure rate of individual graphs known as graph level failure rate is approximately thirty percent in the first year, increasingly greater than forty percent between five to ten years

1416
03:59:56.720 --> 04:00:07.790
Dr. Steve Brooks: since most patients have more than one graph. The patient level graph failure rate is fifty percent meaning that fifty percent experience at least the failure of one graph within twelve months

1417
04:00:07.800 --> 04:00:22.839
Dr. Steve Brooks: Multivariate analysis from the prevent four trial looked at causative factors of ingrat failure. One of the most important was the beam graph storage solution used with a p-value of p less than zero point zero one next slide, please.

1418
04:00:22.870 --> 04:00:40.720
Dr. Steve Brooks: Um. This slide depicts the path of physiology of being grab disease bypass graphs. Experience stress resulting from the physical trauma of harvesting, inhaling, post-harvesty ischemia oxidative stress rate, profusion, industry, and adaptive stress in the new post-rafting environment

1419
04:00:40.730 --> 04:01:10.439
Dr. Steve Brooks: the occurrence of staphonous being graft disease after my certificate can be divided into three temporally distinct but at the physiologically-related mechanisms, the first is thrombosis which occurs within hours to less than a month. The second intimal hyperplasia, which occurs within months, and the last atherosclerosis, which occurs within twelve hours, which occurs greater than twelve months. This process is depicted. Here, again, with the accumulation of platelets, inflammatory cells, and from fly this trigger, smooth muscle cell proliferation,

1420
04:01:10.450 --> 04:01:31.160
Dr. Steve Brooks: which manifest is wall thickening this progresses to atheron formation. This damage of the endothelia on which comprises the structural and functional integrity of the graphs, is identified as the mean trigger for these path of logic processes within the conduits, and is the target of bangrap preservation with to our rep next slide, please,

1421
04:01:31.170 --> 04:01:35.159
Dr. Steve Brooks: and actually let's skip this next slide and move on to the next one. So

1422
04:01:35.490 --> 04:01:36.090
Dr. Steve Brooks: you

1423
04:01:36.100 --> 04:01:37.420
Dr. Steve Brooks: perfect.

1424
04:01:37.430 --> 04:01:56.269
Dr. Steve Brooks: These are the important clinical impacts of vagraph, disease and Bangladesh failure being ref failure, can lead to microcardial infarction. We Pedro Vascularization Hospital readmission itself an important cause of morbidity and mortality, as well as a great cost to the health care system. The poor quality of life. Next

slide, please

1425
04:01:57.690 --> 04:02:26.849
Dr. Steve Brooks: to target this problem, Mirrorzzyme has developed Dur a raft, a solution for the flushing and storage of vascular conduits used one of the harvesting and grafting interval of bypass surgery is prepared by pouring the two containers into a bowl on the or back table during preparation for the bypass surgery. This is similar to how ceiling or alpha buffered, say alien, would be poured into the same role. The surgeon harvest the Venus, or arterial conduits flushes to a ref down the conduit, and then stores the conduit in the roll until it is ready to be signed

1426
04:02:26.860 --> 04:02:35.519
Dr. Steve Brooks: of the patient. The preparation and use of derelict, therefore, does not disrupt or modify the natural course of the circle. Procedure Next slide, please.

1427
04:02:35.610 --> 04:02:46.829
Dr. Steve Brooks: Derelict is composed of inorganics, components, and salts, All components, including the organic components at their respective concentrations, are normal constituents of blood,

1428
04:02:46.840 --> 04:03:05.739
Dr. Steve Brooks: and they are included for their roles in preserving and maintaining the extracellular environment of vascular conduit together. The components impart ph balance and buffering Ionic balance and isotonicity and a reducing environment to reduce prevent risk for oxidative damage during scheming storage. Next slide, please.

1429
04:03:06.510 --> 04:03:24.219
Dr. Steve Brooks: Multiple Creek clinical studies demonstrate the path of physiology, of deregraph's, Effects on beans, including reduction of oxidative damage and stress decreased hypoxic damage and increased antioxidant reserves, and the maintenance of the structural and functional integrity of the vascular andphelium at

1430
04:03:24.230 --> 04:03:53.329
Dr. Steve Brooks: three clinical studies demonstrate the path ofizi anthropology of durograph's use and important clinical outcomes. The first is a randomized clinical trial of one hundred and twenty five patients undergoing first-time bypass surgery. The trials have placed at seven Sites, in Canada and Europe, between two thousand and fourteen, and two thousand and sixteen having libraries. The design

was a within-patient randomized double lion, a study to compare the impact of durograph treated graphs against a standard of care. Sailing tree graphs.

1431
04:03:53.340 --> 04:04:11.889
Dr. Steve Brooks: One hundred and twenty five patients had at least two staff in his vein graphs of their surgery. One was randomized to durograph treatment, the other to staling treatment. Ct. Scanning was performed at one, three and twelve months to measure wall, thickness, lum and diameter, and maximal focal lum and narrowing of the grass next slide, please.

1432
04:04:11.900 --> 04:04:27.259
Dr. Steve Brooks: This ah, unfortunately complicated slide depicts the outcomes of the study at three months there were no mace events. At twelve months there was no death or re-puber vascarization in either. Arm. One. Stephen's name was occluded causing an Mi in a salient treated graph

1433
04:04:27.490 --> 04:04:47.069
Dr. Steve Brooks: for the primary effectiveness, endpoint, wall thickness at three months. Ct. Analysis real. But there was no statistically significant difference between Dur and the ceiling room for the mean of all thickness. There was numerical thickness difference, however. At twelve months this difference had increased, and the durigraph treated Stefan as Vegas

1434
04:04:47.080 --> 04:05:16.090
Dr. Steve Brooks: has a significantly smaller. Meanwhile thickness versus their sailing-treated counterparts point one two millimeters compared to point two millimeters almost half total vessel diameter was also significantly lower in the durable affluence group at three to twelve months, indicating less negative remodeling of the being graphs. These images and grass here show duragraph-treated veins in blue and ceiling and red. On the left. The maximum little narrowing in the whole graph is seen to be decreased,

1435
04:05:16.100 --> 04:05:34.969
Dr. Steve Brooks: but it does not reach statistical significance with a P. Of one zero eight in the proximal five centimeters of the graphs where the maximum sheep, pure forces are, and studies have shown the highest rate of bread, narrowing the difference in maximal focal thickening, narrowing, Sorry is significant. Next slide, please.

1436

04:05:35.510 --> 04:05:52.449
Dr. Steve Brooks: A second study was a retrospective cohort study performed at the Ba. Medical Center in Boston, comparing the performance of Gala, a direct precursor, Derek to ceiling. Heal and durographs have identical components. The only difference is La Gayla is compounded.

1437
04:05:52.690 --> 04:05:53.930
Dr. Steve Brooks: I'm: sorry.

1438
04:05:56.110 --> 04:05:58.989
Campbell, Kimberly A. (CMS/CM): Three minutes. Oh, okay, Sorry

1439
04:05:59.000 --> 04:06:25.549
Dr. Steve Brooks: is compounded by the hospital pharmacy that sent to the aerop for use, whereby Dur Raft is manufactured and shifted to keen containers, which are mixed in the or at the time of use. Two thousand four hundred and thirty six patients were studied, underwent first time bypass surgery. The control group of one thousand four hundred patients had standard care treatment between one thousand nine hundred and ninety, six and one thousand nine hundred and ninety nine. The treatment group of one thousand and thirty six patients had a surface vagraph street of a durable

1440
04:06:25.560 --> 04:06:45.710
Dr. Steve Brooks: between two thousand and one and two thousand and four. The results demonstrated a benefit of Derek at one thousand days follow up with a forty five percent reduction in Mi, thirty five percent reduction in repeated vascularization and percent reduction of mace, driven primarily by improvement in Mi and repeat riskquisition. Next slide, please.

1441
04:06:46.150 --> 04:06:57.700
Dr. Steve Brooks: The final study was performed after an observation of the principal investigator of our Ce Marc Bruce approval. Study that patients, and who we used aircraft had lower elevations of tone and post-operatively

1442
04:06:57.910 --> 04:07:17.660
Dr. Steve Brooks: troponin is a biomarker, indicating mycardial cell death that is used to detect post-op Emmon in addition to flesh and and storing the grass with dagraph Dr. Winkler willrew a flesh-turgraph down the graft and into the vascular bed to perform leak Testing of the grass after sewing in the distal an estimosis to

investigate This analysis was performed,

1443
04:07:17.670 --> 04:07:44.989
Dr. Steve Brooks: was recently published in the frontiers of cardiovascular medicine. Dr. Winkler compared patients who wonder what by? Passed from July two thousand and nineteen to march twenty twenty, using either dirt, aircraft, or a combination of sailing. At the second the seco is a commercially available hem plasma derivative indicated for interbascular volume, expansion and protein replacement. Mix with ceiling. That's also been used as a graph storage solution during cabbage surgery to bring the ph of ceiling to physiologic levels.

1444
04:07:45.000 --> 04:07:55.890
Dr. Steve Brooks: Next slide, please Two hundred and seventy. Two patients were identified, who, under my bypass surgery. During this interval they were divided into two propensity match groups of eighty three patients. Each one was remaining.

1445
04:07:55.900 --> 04:07:58.649
Dr. Steve Brooks: Okay, uh, next slide, please.

1446
04:07:58.660 --> 04:08:28.489
Dr. Steve Brooks: This table demonstrates the measurements of a sensitivity chapone in the two groups. The second column is the directory to patients. The third is the ceiling of the Eco, and the fourth is the p-value You can see that you're probably in Rose quickly, peaking at three to six hours, twelve to twenty, four hours one day, two day, and four days next slide, please. This table is similar, showing the Cdk levels. These were not statistically significant. Going to the non specific nature of C.

1447
04:08:28.500 --> 04:08:45.960
Dr. Steve Brooks: Okay, our next slide, please. In conclusion, Ah! Repeated Flushing, the distal anastymosis with the aircraft was associated with significantly lower toprono levels. Post cabbage. Um suggest the enhanced monochrome protection when compared to you. Don't see any less live, please.

1448
04:08:45.970 --> 04:09:15.959
Dr. Steve Brooks: In conclusion, Dur a graft is a solution for preservation, of rescue, of conduits during a bypass surgery which targets the path of physiology, of being raft disease being graph failure by preventing damage to the end of healing from iskemia,

reprofusion, injury. Three studies validate the mechanism of actually path physiology, including the randomized trials showing reductions in wall, thickness and vocalulum, and narrowing the Ba. Study showing reduction in mi repeat or vascarization and bease, and finally, the sulkwood study showing a reduction

1449
04:09:15.970 --> 04:09:24.399
Dr. Steve Brooks: and high-sensitive in with durograph use, demonstrating a protective effect of derelict and cabbage surgery. Thank you very much,

1450
04:09:28.790 --> 04:09:31.850
Drew Kasper: and thank you very much for your presentation.

1451
04:09:31.870 --> 04:09:35.110
Are there any questions from the public

1452
04:09:35.510 --> 04:09:37.000
Drew Kasper: for Cms.

1453
04:09:42.950 --> 04:09:47.999
That's so. Be a chance. I have a question here, and nobody from the

1454
04:09:48.320 --> 04:09:52.720
it has caught in and asked questions that

1455
04:09:53.510 --> 04:09:55.480
Dr. Steve Brooks: Yes, please.

1456
04:09:56.130 --> 04:10:00.430
SOPHIA CHAN: Ah, thank you so much, Dr. Brooks. For your presentation.

1457
04:10:01.260 --> 04:10:09.449
SOPHIA CHAN: You clarify how the components of gala are different from those of

1458
04:10:10.010 --> 04:10:16.690
Dr. Steve Brooks: Yeah. That's the great question. So the components are identical, and the concentration in the final product is identical.

1459
04:10:16.700 --> 04:10:46.689
Dr. Steve Brooks: The only difference is the method of manufacturers. So gala was manufactured in a compounding pharmacy of the hospital brought up to the operating room. It was captive at that time for a period of up to two weeks. We know now that ah, after approximately four to six hours, the the activity starts to decline the buffering capacity. So you know, you can see the forty five percent mi reduction thirty, five percent return to vascarization.

1460
04:10:46.700 --> 04:10:58.739
Dr. Steve Brooks: So it's the current manufacturing. Is It's manufactured in two different and stored in two bottles, and these are combined in the operating room at the time of the surgery stirred up.

1461
04:10:58.750 --> 04:11:17.829
Dr. Steve Brooks: And then you have the same final product, the same concentrations, because of the nature of the manufacturing um, the activity, the buffering, the reduction of the oxidative Ah! Reduction that lasts much longer. So, in fact, had this been deregred and not ah gala.

1462
04:11:17.840 --> 04:11:24.429
Dr. Steve Brooks: The effects may have been even larger, so we hope to see that in in some upcoming studies which we have going on,

1463
04:11:32.500 --> 04:11:40.910
Drew Kasper: Sophia, if you have additional questions. You can continue on on your questioning before we solicit more broadly.

1464
04:11:43.110 --> 04:11:56.249
SOPHIA CHAN: Yes. Are you aware of any study or studies that look at the effects of dereograph on us Medicare population.

1465
04:11:57.790 --> 04:12:26.329
Dr. Steve Brooks: Um, so um The The va study, which was the gala study had about two-thirds of the patients were back your age. Um! We are not, you know, cleared in the United States yet. We are starting a prospective, randomized trial to look at biomarkers. If all the outcomes out for a year pending clearance, and our denot will be hopefully cleared by the deadline

1466

04:12:26.340 --> 04:12:39.930
Dr. Steve Brooks: we expect to, and some us ah patients that said as part of our Ce mark. We were. We were See you marked in two thousand and fifteen. We have a nearly three thousand patient post approval, Study in Europe,

1467
04:12:39.940 --> 04:13:09.649
Dr. Steve Brooks: forty, five sites, and eight countries. Of those again two-thirds are older than age sixty, five. Um! We've performed a propensity match analysis from the Us. Sts database that's a Us database of about ninety seven percent of the United States patients undergoing bypass surgery, and we compared ours. We did a propensity match group. We matched two thousand four hundred patients that received isolated cabbage. That's ninety five percent of our

1468
04:13:09.660 --> 04:13:38.830
Dr. Steve Brooks: cohort very close match. We looked at mortality compared to the Sts, which was us database, and ah! The mortality was identical. Um, that Ah, that data is going to be hopefully published soon. Ah, two-thirds of those patients in the Sts database and our database were sixty, five and older Medicare age, and we're hoping to take the next step with Sts, and can again draw from the Dcr controls the

1469
04:13:38.870 --> 04:13:51.419
Dr. Steve Brooks: um, the Medicare. Ah, database we're hoping to do a cohort match looking at M. I'm repeated. So we we hope to have that data. But we do not have that it today. Hopefully, in the next year we have more of that data.

1470
04:13:52.370 --> 04:13:53.989
Okay, thank you.

1471
04:14:00.460 --> 04:14:05.219
Drew Kasper: Do we have any other questions from the public or from Cms.

1472
04:14:10.670 --> 04:14:12.940
Drew Kasper: Adina. Please go ahead and unmute it.

1473
04:14:13.250 --> 04:14:24.139
Adina Hersko: Thank you. I'm sorry i'm not sure if i'm a first one to clarify something I heard earlier. Were you saying that in some of

these studies it was, in fact, gala that was used and not

1474
04:14:24.230 --> 04:14:26.640
Dr. Steve Brooks: It was only the Va. Study.

1475
04:14:26.650 --> 04:14:54.340
Dr. Steve Brooks: And since that's that was that. That's the one to depict it in the middle of the page. Here the the randomized study was telegraphed. The silkwood study on the right. That was also derelict, you know, and in our development of the product we approved the manufacturing process. So it is always fresh and and most active. That's the only difference in the in the difference between gala and

1476
04:14:54.350 --> 04:14:58.200
Dr. Steve Brooks: and dereographed, and that's the one. Study the Va: study.

1477
04:14:59.260 --> 04:15:00.529
Adina Hersko: Okay, Thank you.

1478
04:15:01.300 --> 04:15:02.510
Yes.

1479
04:15:06.250 --> 04:15:09.549
Drew Kasper: Are there any other questions from anyone?

1480
04:15:14.080 --> 04:15:20.709
Dr. Steve Brooks: Also, to add that last question. Our post-approval study was also nearly three thousand patients. With the

1481
04:15:20.790 --> 04:15:21.840
So

1482
04:15:28.210 --> 04:15:30.190
Drew Kasper: Thanks. Last call for questions.

1483
04:15:36.210 --> 04:15:38.390
Drew Kasper: Okay? Well, thanks again.

1484

04:15:38.540 --> 04:15:40.039
Dr. Steve Brooks: Thank you. Everyone.

1485
04:15:41.010 --> 04:15:46.820
Drew Kasper: We'll now hear from presenters for the Van flydo or quizzart lid

1486
04:15:47.000 --> 04:15:49.180
Drew Kasper: technology application.

1487
04:15:49.390 --> 04:15:52.330
You may now unmute your phones

1488
04:15:52.340 --> 04:16:04.210
Dr. Albert Fliss: great. Ah, thank you for allowing me to present today. My name is Alphliss. I'm an employee of Daiji. Thank you. Working on this particular um inhibitor of Ah flip three next slide

1489
04:16:06.220 --> 04:16:08.810
Dr. Albert Fliss: a little bit about next slide, please.

1490
04:16:10.080 --> 04:16:26.980
Dr. Albert Fliss: A little bit about. Aml Aml is a highly aggressive and acute disease. That accounts for the the largest block of patients um of acute leukemia and the highest mortality for acute leukemia Of these patients that have aml,

1491
04:16:26.990 --> 04:16:33.469
Dr. Albert Fliss: about thirty percent have a particular mutation as a group of mutations in a gene called Flip three

1492
04:16:33.540 --> 04:16:51.380
Dr. Albert Fliss: um. Some of these mutations in the gene called Flip three cause a very, very poor outcomes. Generally the outcomes in Aml are poor in general, with A. With a five-year survival of about thirty um, and about forty. Eight percent of the deaths related to leukemia are associated with aml.

1493
04:16:51.390 --> 04:16:55.700
Dr. Albert Fliss: There's about twenty thousand new cases of aml every year. Next slide, please.

1494
04:16:58.030 --> 04:17:11.910
Dr. Albert Fliss: Very relevant is is that aml is a disease of generally of the elderly. The mean age of diagnosis is well within the Medicare Age bracket of sixty, eight years old next slide,

1495
04:17:14.700 --> 04:17:32.799
Dr. Albert Fliss: and, as I mentioned earlier, one of the one of the primary drivers of of poor outcomes in this primarily elderly, patient population is the presence of a particular mutation in a gene called Flip three itd that pretends a very, very poor outcome Next slide, please.

1496
04:17:34.840 --> 04:17:47.080
Dr. Albert Fliss: And as you can see in this slide, this is so retrospective analysis of looking at the particular flip-three, itd mutation in comparison to other flip-three mutations and flickering wild type patients

1497
04:17:47.090 --> 04:18:00.100
Dr. Albert Fliss: the itd mutation actually poor tends a very poor outcome with about a twenty percent overall survival rate compared to your standard flip. Three wild type patient, which is about, you know, between thirty and forty percent

1498
04:18:00.620 --> 04:18:02.099
Dr. Albert Fliss: next slide, please.

1499
04:18:03.570 --> 04:18:20.199
Dr. Albert Fliss: What one of the primary drivers of of poor prognosis in this particular variety of aml is the the reoccurrence of relapse essentially after treatment with intensive chemotherapy,

1500
04:18:20.300 --> 04:18:31.560
Dr. Albert Fliss: about forty percent of the patients will relapse by the the second year of therapy with the existing therapeutic options that exist in this space.

1501
04:18:31.820 --> 04:18:33.329
Dr. Albert Fliss: Next slide, please.

1502

04:18:34.720 --> 04:18:38.639
Dr. Albert Fliss: And now i'll talk about quizzart and him again. Quizzart nib next slide,

1503
04:18:40.150 --> 04:18:57.719
Dr. Albert Fliss: Juzartin. It is a a targeted and Ah Tyrosine kindness inhibitor that is highly potent, and targets a particular mutation, the flip three itd mutation. This slide shows the pivotal trial that is currently with the Fda for review.

1504
04:18:57.730 --> 04:19:10.380
Dr. Albert Fliss: In this patient population Um Cruzartnid was added to Standard seven plus three chemotherapy, and compared to um the standard of care, which is a seven plus three chemotherapy alone.

1505
04:19:10.530 --> 04:19:32.759
Dr. Albert Fliss: It was it was Um. It was treated through the induction phase um, which is primary um utilized to debug the disease followed by the consolidation phase, which is Um. The goal of this is to um reduce the disease, burden and follow. And then followed by the maintenance phase and the goal of this stage is to actually prevent relapse.

1506
04:19:32.770 --> 04:19:39.870
Dr. Albert Fliss: This particular clinical study, looked at an age range from eighteen years old to seventy five years old.

1507
04:19:39.880 --> 04:19:56.290
Dr. Albert Fliss: Previous clinical innovations in this particular. Um Disease State pivotal studies looked at only from eighteen to fifty-nine years old, making this particular study much more relevant to the Medicare population next slide, please,

1508
04:19:57.990 --> 04:20:07.850
Dr. Albert Fliss: and it is here. These are the inclusion criteria for the pivotal study again at eighteen years old, to seventy, five newly diagnosed acute myeloid leukemia.

1509
04:20:07.860 --> 04:20:33.519
Dr. Albert Fliss: Ah! In these patient populations are the patients that are eligible for what we call intensive chemotherapy or standard seven plus three. The patient had to have a flip. Three Itd Mutation. Previous innovations in this space looked at a broad group of flip,

three mutations, including the flip, three T Kd. Mutations that do not pretend a a particularly poor outcome.

1510
04:20:33.530 --> 04:20:35.089
Dr. Albert Fliss: Next slide, please.

1511
04:20:36.540 --> 04:21:06.090
Dr. Albert Fliss: And and again, the the the Median age in this particular study that will hopefully lead to the approval of Cresar, and in this space is is, and in the in the upper fifty S. In comparison to the the um. The The previous innovator in this space, for the the Median age of the the Median age of diagnosis was in the mid forty S. In this particular study about forty percent of the patient's population was over sixty, and about twenty. Five percent of the population was over. Sixty. Five

1512
04:21:06.120 --> 04:21:07.590
Dr. Albert Fliss: next slide, please.

1513
04:21:09.010 --> 04:21:19.280
Dr. Albert Fliss: And again, this is this is a a very well-balanced study when comparing the quizzart nip seven plus three arm versus the seven plus three next slide please

1514
04:21:21.040 --> 04:21:44.090
Dr. Albert Fliss: um. In this this slide represents the Kaplan Meyer curve, showing the overall survival benefit of quizzart nip added to standard seven plus three, and this population, ranging from eighteen to seventy five years old, with approximately a twenty, two percent reduction in the risk of death and overall um and overall doubling the overall survival.

1515
04:21:44.230 --> 04:21:45.780
Dr. Albert Fliss: Next slide, please.

1516
04:21:47.780 --> 04:21:59.890
Dr. Albert Fliss: Um. This this slide represents a look at um Comparing patients that went through a stem cell transplant versus patients who did not go through stem, cell transplant

1517
04:21:59.900 --> 04:22:19.979
Dr. Albert Fliss: and quizartin was able to show substantial clinical

benefit in both of these patient populations. I think it's important to note that the the elderly patients are less likely to go through a stem cell transplant because of the rigorous and aggressive treatment, you know, based on the age.

1518
04:22:20.480 --> 04:22:34.500
Dr. Albert Fliss: Um, and again, the the you know, the the clinical benefit with transplant or without transplant, is relatively the same, and again showing a a significant improvement over the comparison.

1519
04:22:34.510 --> 04:22:35.610
Dr. Albert Fliss: Next slide.

1520
04:22:38.120 --> 04:23:05.119
Dr. Albert Fliss: And, as I mentioned earlier, the other major issue as as far as a female leukemia that drives very, very poor outcomes. Um. And again, in this patient population and overall survival rate of about twenty percent is relapse. And as you can see on this slide when comparing the quizarnip arm to the standard seven plus three arm, you have A. You have a more than threefold difference in the relapse, free survival

1521
04:23:05.130 --> 04:23:15.240
Dr. Albert Fliss: from like, I believe it's thirty, nine months compared to a little bit over a year again showing substantial clinical benefit Here, next slide, please.

1522
04:23:17.570 --> 04:23:36.770
Dr. Albert Fliss: In addition, this is another way to look at this. This is actually looking at the the rate of of of cumulative relapse and and quizzart, and have had about a about eleven percent better cumulative relapse rate here. So

1523
04:23:36.780 --> 04:23:43.989
Dr. Albert Fliss: I believe it was. It was thirty, one percent to about the lower forty percent, showing that quizzart n

1524
04:23:44.120 --> 04:23:55.770
Dr. Albert Fliss: decrease the rate of cumulative relapse. And again, this is the major driver of poor outcomes in this, you know heavily Medicare eligible population

1525

04:23:55.790 --> 04:23:57.080
Dr. Albert Fliss: next slide,

1526
04:23:59.690 --> 04:24:03.149
Dr. Albert Fliss: and I and I thank you for for your time.

1527
04:24:10.670 --> 04:24:13.119
Drew Kasper: Thank you very much for your presentation.

1528
04:24:13.910 --> 04:24:17.680
Drew Kasper: Are there any questions from the public or from Cms.

1529
04:24:21.630 --> 04:24:24.750
Drew Kasper: Kelsey? Marie? Go ahead and unmute, please.

1530
04:24:27.630 --> 04:24:33.519
Kelcymarie Bye: Hi, Thank you. So the one question that I had was,

1531
04:24:33.540 --> 04:24:40.949
I know a couple of times you mentioned another therapy, and you were mentioning the age group of the population.

1532
04:24:40.980 --> 04:24:47.389
Kelcymarie Bye: Um, do you have any other kind of comparison between that other therapy in terms of clinical outcomes.

1533
04:24:48.410 --> 04:25:17.709
Dr. Albert Fliss: Um! Nothing, nothing, nothing that would be apples to apples, because the the the particular a particular clinical study that I I was kind of all alluding to, looked at a a mixed population of Flip three mutations, and and I remember there there's the flippery. It d mutation. That port turns a very poor prognosis, and and in poor patient outcomes, whereas the the the other innovator that is currently on the market

1534
04:25:17.720 --> 04:25:30.239
Dr. Albert Fliss: had a mixture of the flip three, itd as well as the Tkd population, so it's It's very. It's very hard to compare those two directly.

1535

04:25:32.420 --> 04:25:43.920
Kelcymarie Bye: Thank you. Thank you for that. Um. And just one of our questions. Can you just clarify what the dose that you're submitting? Um for approval is?

1536
04:25:44.520 --> 04:26:02.740
Dr. Albert Fliss: Um, I mean it is as far as there. There, there, there, there, there's There's multiple dosage forms there, there, there's actually two dosage forms, and and each level of therapy from induction to consolidation to maintenance, has its own, its own dosage.

1537
04:26:04.090 --> 04:26:10.609
Dr. Albert Fliss: It's it's, it's, it's a it's a rather complicated um, you know, flow as far as dosage is concerned.

1538
04:26:11.540 --> 04:26:15.570
Kelcymarie Bye: So it's a hard question. It's a hard question to answer.

1539
04:26:16.020 --> 04:26:20.690
Kelcymarie Bye: Yeah, but would it be similar to what the trial the thing was?

1540
04:26:20.700 --> 04:26:25.449
Dr. Albert Fliss: It's it's it's it's it's it's it's It's exactly as what the trial is. Yes,

1541
04:26:26.850 --> 04:26:27.910
Kelcymarie Bye: okay.

1542
04:26:37.640 --> 04:26:46.290
Drew Kasper: And Dr. Deb. Could you go ahead and unmute? Sure. Thank you. For the presentation. Can you hear me?

1543
04:26:46.300 --> 04:26:49.690
Arkaprava Deb: Yes, I can hear you absolutely thank you for a presentation

1544
04:26:49.700 --> 04:27:12.619
Arkaprava Deb: and um and you're working down on um, Let's say, for

the for the first study since we're looking at it. Um, we realized that um some pay issues, or what the some patients got stem cell transportation set up transplantation someday for that protocol. Yes, I did. Did the results. Um adjust for this

1545
04:27:12.630 --> 04:27:23.989
Arkaprava Deb: and um, and was stem cell. Transplantation also was part of the protocol. Who can? Um! Who can tolerate stem cell transportation at the time? Is that part of the protocol?

1546
04:27:24.000 --> 04:27:38.440
Dr. Albert Fliss: Yeah, I mean, I mean all all ultimately, you know, and in the in the you know, the the protocol, you know. Definition of of whether a patient could get to stem cell transplant was was based on whether they had a a composite complete remission.

1547
04:27:38.450 --> 04:27:50.159
Dr. Albert Fliss: Um, but ultimately them getting stem cell transplant is is going to be a a a discussion between the you know the patient and the Hcp. In this situation, because

1548
04:27:50.570 --> 04:28:09.749
Dr. Albert Fliss: stem cell transplant itself, you know, has a, you know, anywhere from a ten to a twenty percent risk of mortality. So it it. It really depends on on where they were at the end of of standard seven plus three, and in standard um high deck consolidation to whether they would actually go through a transplant.

1549
04:28:11.630 --> 04:28:22.369
Arkaprava Deb: But but but but the bar, the bar here was they. They would They would have to have a a some level of a complete remission. So what we would call a crc event

1550
04:28:24.130 --> 04:28:40.700
Arkaprava Deb: sure uh, is that shown? And I guess the only thing I have to look at is your um sort of the slide deck from the presentation at one point is that still adjusted for it all in the data or in your findings, or is there any?

1551
04:28:40.710 --> 04:28:45.080
Arkaprava Deb: Yeah, is that? That's my my question. Is there an adjustment in your findings for that?

1552
04:28:45.190 --> 04:28:51.009
Dr. Albert Fliss: An adjustment for for for for that kind of decision, whether to go to transplant or not,

1553
04:28:51.210 --> 04:28:59.399
Arkaprava Deb: even even just the finding of who got transplant amongst the people in one arm another who got transplanted. Who didn't?

1554
04:28:59.410 --> 04:29:28.819
Dr. Albert Fliss: I mean that that that that was accounted for in in the in the one figure in that I believe in the slide that you had um, actually. Maybe it wasn't in the site we we have looked at that where we've actually censored the patient at time of transplant and looked at that to you know again, you know. Try to take that transplant out of it, and and the clinical, the clinical benefit. When the patients were centered at the time of transplant. The the reduction in the risk of death was about twenty five percent,

1555
04:29:28.830 --> 04:29:45.620
Dr. Albert Fliss: and in the in the whole study the rust. The The reduction in the risk of death was between twenty two and twenty-three percent. So again, it's pretty consistent between the two. Whether we extract transplant from the entire study.

1556
04:29:46.350 --> 04:29:48.050
Dr. Albert Fliss: I hope I hope that helps.

1557
04:29:49.090 --> 04:30:07.549
Arkaprava Deb: I appreciate the attempt. I i'll indulge myself with another question. Can you let him speak on comparing this to a ride that is, Is there any studies that compare this to

1558
04:30:07.560 --> 04:30:10.500
Arkaprava Deb: the the first generation? Um tkis

1559
04:30:10.640 --> 04:30:29.120
Dr. Albert Fliss: um No, no, there there there, there is, There is no current study that is, is walking at that at this point in time with Cuzart, and it has not been compared directly to riot app, because when the original, when the the quantum first study was initiated, ride app wasn't approved.

1560
04:30:29.130 --> 04:30:45.690
Dr. Albert Fliss: So so we used a comparative of of standard, so seven plus three. In this particular situation. There there there will be in the future some um, you know, future innovators, comparative studies that that are looking ahead to head at right now.

1561
04:30:47.390 --> 04:31:05.290
Arkaprava Deb: This will be my last one. I promised. Yeah, it's okay for, and I I guess I also want to make space for my colleagues. Is there a role for the other sort of second generation more specific? I felt t three inhibitors, The ones we found were the alternative.

1562
04:31:05.300 --> 04:31:10.990
Arkaprava Deb: Good, Yeah, guilty, you guilty. It's their role for them in this illness.

1563
04:31:11.000 --> 04:31:17.990
Dr. Albert Fliss: There, there's there's I mean, guilty guilt or rhythm is is currently approved for

1564
04:31:18.140 --> 04:31:25.429
Dr. Albert Fliss: either flip three itd or flip three Tkd patient population in the refractory relapse setting at this point in time.

1565
04:31:26.100 --> 04:31:43.400
Dr. Matthew Matasar: There, there, there are future studies. I mean. There are studies that are ongoing that are currently enrolling there. There's a couple of studies, one's the pre-cogged study, and one's the Hov on study that are looking at guilty written in this this upfront.

1566
04:31:43.410 --> 04:31:49.599
Dr. Albert Fliss: But there's no data from those studies to this point in time. So it's it's it's difficult to judge that.

1567
04:31:50.010 --> 04:31:54.560
Arkaprava Deb: Thank you very much i'll i'll I'll see my time. Thanks, everyone, sure. Sure. Pleasure.

1568
04:31:58.480 --> 04:32:03.369
Drew Kasper: Do we have any other questions from the public or Cms

1569
04:32:07.360 --> 04:32:11.010
Drew Kasper: any new tech mailbox? There are no new questions there.

1570
04:32:11.360 --> 04:32:13.620
Drew Kasper: There are no questions in the Q. A.

1571
04:32:14.520 --> 04:32:17.499
Drew Kasper: And there are no raised hands.

1572
04:32:17.520 --> 04:32:19.530
Drew Kasper: Let's call for questions.

1573
04:32:24.500 --> 04:32:35.780
Drew Kasper: Okay, Then at this point we will move into a break until three o'clock. Thanks for the opportunity to see.

1574
04:32:36.630 --> 04:32:38.089
Drew Kasper: Yes, thank you.

1575
04:32:39.330 --> 04:32:45.589
Drew Kasper: At which time, at three o'clock, we will enter our last block of presentations, we

1576
04:32:46.070 --> 04:32:48.460
Drew Kasper: starting with Mos and the twos man.

1577
04:32:48.850 --> 04:32:52.170
Drew Kasper: We will see you at three o'clock,

1578
04:33:06.189 --> 04:33:11.920
Drew Kasper: and Jay, if you want to pause the recording. We've got about eighteen minutes till we go live again.

1579
04:33:35.250 --> 04:33:37.359
Drew Kasper: Right? So um

1580
04:33:37.660 --> 04:33:47.959

Drew Kasper: welcome back everyone from that break. We're entering the last block of presentations now, and we'll now hear from presenters for the

1581
04:33:48.279 --> 04:33:49.420
Drew Kasper: um.

1582
04:33:49.970 --> 04:33:56.929
Drew Kasper: I was in Rosa to choose an app technology application. He may now unmute your phone.

1583
04:34:06.080 --> 04:34:12.330
Dr. Matthew Matasar: Thank you so much for the opportunity to present today. Will I be controlling the slides.

1584
04:34:14.119 --> 04:34:20.189
Dr. Matthew Matasar: We will advance the slides if you just give us a queue such as the using slide

1585
04:34:20.200 --> 04:34:31.289
Dr. Matthew Matasar: perfect. So my name is Dr. Matthew Madison. I'm. The chief of blood disorders at the Rutgers, Kansas Vitamin, New Jersey. It's my pleasure to be presenting to you today on the subject of Mos on a Tuesday

1586
04:34:31.300 --> 04:34:32.190
next slide.

1587
04:34:33.869 --> 04:34:49.429
Dr. Matthew Matasar: So, by way of brief introduction, we'll on a two-sab is a novel t-cell engaging by specific antibody targeting Cd. Twenty and Cd. Three that offers patients the opportunity to achieve a deep and durable response. And this is with with manageable safety profile,

1588
04:34:49.590 --> 04:34:59.430
Dr. Matthew Matasar: it's being evaluated in the treatment of patients with relapse, or refracted for lymphoma, for patients who have received two or more prior lines of therapy next slide.

1589
04:35:00.990 --> 04:35:08.580

Dr. Matthew Matasar: So to set the stage for you. Follicular lymphoma is the most common, indolent B. Seldom foam in America and other Western countries.

1590
04:35:08.900 --> 04:35:18.980
Dr. Matthew Matasar: As such, it is considered an incurable disease, and is usually managed as a chronic illness, and thus patients are expected to experience multiple relapses over the course of their illness.

1591
04:35:19.450 --> 04:35:29.549
Dr. Matthew Matasar: This is a common illness and a common illness of older patients, with a medium age of diagnosis of sixty four years, making it particularly relevant to the Medicare population.

1592
04:35:30.230 --> 04:35:44.350
Dr. Matthew Matasar: Unfortunately, when patients experience readouts of this disease, this is typically associated with worst disease status, meaning that patients are expected to achieve lower response rates and less durable response when they do respond with each subsequent line of therapy,

1593
04:35:44.849 --> 04:35:58.190
Dr. Matthew Matasar: the most common cause of death for patients diagnosed with silicon lymphoma. Unfortunately, is the lymphoma itself. Although treatment-related morbidity is an important cause of mortality in this patient population as well highlighting the need for safe treatments,

1594
04:35:58.810 --> 04:36:10.360
Dr. Matthew Matasar: unfortunately as patients go through subsequent lines of therapy. Outcomes do indeed worse, and and patients are less and less likely to achieve deep responses as measured by complete response or durability.

1595
04:36:10.369 --> 04:36:24.190
Dr. Matthew Matasar: Furthermore, as it is a disease largely of older patients, it's important to note that older patients with liquid or diploma do indeed experience greater toxicities with the subsequent line of therapy. In addition to this pattern I've described, of, of course, outcomes

1596
04:36:24.200 --> 04:36:25.200

Dr. Matthew Matasar: next slide

1597
04:36:28.400 --> 04:36:39.560
Dr. Matthew Matasar: so given this multi-breeding nature of molecular lymphoma it's important to understand that this does really lead to a high societal burden resulting from this.

1598
04:36:39.570 --> 04:37:05.369
Dr. Matthew Matasar: This is all the more true in patients who have higher risk disease, and we understand that there are certain clinical characteristics associated with higher-risk disease, including a higher score on the so-called flippy or follicular diploma international prognostic index further more patients who are refractory to prior Cd twenty antibody therapy by itself, or that in combination with alternative chemotherapy, so-called double refractory disease, is known to be high risk and lastly

1599
04:37:05.700 --> 04:37:17.679
Dr. Matthew Matasar: patients who experience Congressional disease within twenty four months of initiation of initial chemotherapy or so-called od twenty four failures are known to portendoorse prognosis

1600
04:37:17.869 --> 04:37:39.979
Dr. Matthew Matasar: The outcome of this is that the disease does indeed impose a significant economic burden on our society with annualized health care costs high across all lines of therapy, but going up, as we need to give treatments for subsequent lines of therapy, starting at approximately ninety-seven thousand dollars for first-line therapy, going to as high as over four hundred and twenty-four thousand dollars, or

1601
04:37:41.220 --> 04:37:58.009
Dr. Matthew Matasar: it's not just a financial burden. There certainly is a quality of life for not patients living with footage of a phenomenon, and it's well recognized that patients who experience relapse disease tend to score much more unfavorably on folded life indices than newly diagnosed. Patients will have.

1602
04:37:58.029 --> 04:38:06.700
Dr. Matthew Matasar: This is due to overall quality of life, negative impact, as well as the experience of anxiety and depression associated with the disease and impacts on work, productivity.

1603

04:38:06.939 --> 04:38:08.300
Dr. Matthew Matasar: Next slide

1604
04:38:09.930 --> 04:38:24.989
Dr. Matthew Matasar: for patients. With multiply we left molecular development as third line and beyond setting. While there are treatments that have currently been Fda approved, there is certainly no single standard of care for this patient population, and this is due to limitations associated with our currently available treatments.

1605
04:38:25.000 --> 04:38:32.640
Dr. Matthew Matasar: Two such treatments include the pi three T inhibitor in Copenhagen, and the orally administered Zh, two inhibitor tasimatostat

1606
04:38:32.650 --> 04:38:46.519
Dr. Matthew Matasar: panelists, and is associated with modest clinical activity with an overall response rate of approximately sixty percent and a complete response rate of approximately twenty percent Durability, however, is suboptimal with only a twelve month Median duration of response.

1607
04:38:46.529 --> 04:38:57.809
Dr. Matthew Matasar: This treatment is further limited by a challenging treatment schedule with an intravenous administration three weeks on and one week off, with an intention of treatment and to progression or intolerance

1608
04:38:58.570 --> 04:39:16.609
Dr. Matthew Matasar: casimetostat has activity, although this activity is differential between whether or not the disease harbors a mutation, in the ezh? Two gene in both so-called mutant and wild type. Disease, However, durability also is suboptimal with durations of response only approximately one year in both groups.

1609
04:39:17.169 --> 04:39:30.539
Dr. Matthew Matasar: This, too, is limited by treatment until progression or intolerance formats, as well as the observation that only a minority of patients disease harbors this mutation, though we believe, sensitizes to best effects of test medicine.

1610
04:39:30.660 --> 04:39:31.980
Dr. Matthew Matasar: Next slide.

1611
04:39:34.279 --> 04:39:51.380
Dr. Matthew Matasar: Certainly we also have access to car t-cell therapy for patients with multiple relapse molecular lymphoma including both axi, cell and tease a cell. These drugs are both very highly active in its patient population, with high rates of complete response and excellent durability of response.

1612
04:39:51.770 --> 04:40:19.290
Dr. Matthew Matasar: These agents are limited, however, by toxicity, with unfortunately high rates of cytokine, ready syndrome, and neurological adverse events, as well as challenges regarding limitations of access. Understanding that relatively few patients have the ability to receive this treatment given geographic variability and access. Long wait times for aphoresis slots and the social impacts of hospitalization and post hospital care.

1613
04:40:20.580 --> 04:40:32.150
Dr. Matthew Matasar: In this context we recognize that there remains on mended in this patient population, and thus we sought to pursue an evaluation of the role form of Santa two's and map in the treatment of patients with malls that relapse molecular phone.

1614
04:40:32.210 --> 04:40:33.350
Dr. Matthew Matasar: Next slide.

1615
04:40:35.900 --> 04:40:56.860
Dr. Matthew Matasar: This molecule, again, is what we call a bicycific antibody, and I know that this group is now familiar with by specific antibodies. This is a constructed antibody with an epidel binding Cd. Twenty on the malignant beam cell, and Cd. Three on healthy native t cells, creating this immune synapse alone for t cell activation expansion, antisl mediated cell

1616
04:40:57.060 --> 04:41:03.610
Dr. Matthew Matasar: Well, son of two's map was granted breakthrough designation in two thousand and twenty for patients with multi-year-olds, molecular And

1617
04:41:03.780 --> 04:41:04.850
Dr. Matthew Matasar: next slide

1618

04:41:07.240 --> 04:41:29.780
Dr. Matthew Matasar: we've conducted our single arm pivotal phase to study of most unitudes in that monotherapy in patients with follicular involvement having received two or one prior treatment. This medicine is given intravenously in a step up format, with a small dose given cycle one day, one then day eight, and then step up dosing on cycle one day fifteen, and then it goes to every three week intravenous treatment.

1619
04:41:30.230 --> 04:41:41.190
Dr. Matthew Matasar: This is a fixed duration and treatment with eight cycles administered, followed by a response assessment for patients who have achieved a complete response. At that time treatment is discontinued

1620
04:41:41.200 --> 04:41:53.069
Dr. Matthew Matasar: for patients who have drive clinical benefit, but have not yet achieved a complete response. Treatment may be continued up to seventeen cycles in total, after which responses are again assessed, and treatment is discontinued.

1621
04:41:53.780 --> 04:42:20.150
Dr. Matthew Matasar: Inclusion, exclusion, criteria, are shown for you here, and the patients that we treated were largely in all our patient population in keeping with the demographics of this disease, with the Median age of sixty patients, largely had a band-stage disease. Patients had a median of three prior lines of therapeutic treatment, and this population was enriched for adverse factors, such as refract readiness to the last line of therapy, double refractory status, and ped twenty, four fifty

1622
04:42:20.430 --> 04:42:26.899
Dr. Matthew Matasar: primary objective was to measure the complete response rate, and we will see these results on in subsequent slides.

1623
04:42:26.910 --> 04:42:27.730
It's like

1624
04:42:29.290 --> 04:42:45.769
Allison Pompey: it's it's primary, unplugged, met it's primary, unplugged with an overall response rate of eighty percent and a complete response rate of sixty percent when we reported the same Median font of eighteen point three months, certainly far in excess of what we would have anticipated with historical controls in this

patient population.

1625
04:42:45.780 --> 04:42:46.780
Dr. Matthew Matasar: Next slide.

1626
04:42:49.160 --> 04:42:59.039
Dr. Matthew Matasar: In looking at sub-group analyses, we see that there is no subgroup of patients which did not derive clinical benefit from Jeremiah Bilson and touse me, including the risk factors that I've outlined for you already

1627
04:42:59.050 --> 04:43:09.490
Dr. Matthew Matasar: certainly of note is the fact that patients over the age of sixty five seem to derive, if anything, numerically superior, results from treatment. Mos on a Tuesday's map compared to the younger patients

1628
04:43:09.700 --> 04:43:10.850
Dr. Matthew Matasar: next slide.

1629
04:43:13.360 --> 04:43:28.939
Dr. Matthew Matasar: Not only is this drug active in terms of achieving response, but we are seeing durability of response at this earlier cut off. We estimate a duration and response of almost two years in duration of a complete response. Also almost two years, with an overall. Pfs originally estimated in eighteen months.

1630
04:43:29.130 --> 04:43:30.420
Dr. Matthew Matasar: Next slide

1631
04:43:32.300 --> 04:43:56.070
Dr. Matthew Matasar: balancing against that activity is the toxicity profile. And i'm saying that this toxicity profile is indeed manageable with low rates of treatment, discontinuation due to adverse events which I feel is a very nice summit of statistic to look at. The tolerability of treatment to only four percent of patients discontinuing treatment due to any adverse events attributed by investigators to most lemon shoes.

1632
04:43:56.550 --> 04:43:57.840
Dr. Matthew Matasar: Next slide.

1633
04:43:58.340 --> 04:44:09.490
Dr. Matthew Matasar: In looking more carefully at the key toxicity of the cited kind, release Syndrome Crs was seen in this patient population, but with largely low rate in severity grades one and two, and was self-limited

1634
04:44:09.500 --> 04:44:16.110
Allison Pompey: It typically occurred during the step up first cycle dosing, and was uncommon in subsequent a minute

1635
04:44:16.740 --> 04:44:20.700
Dr. Matthew Matasar: postalism and cortico steroid use was rare. Next slide

1636
04:44:21.910 --> 04:44:33.670
Dr. Matthew Matasar: we've offered updated results out of the recent ash meeting, and we see that durability estimates have indeed persisted, as our data have matured encouraging progress. Next slide,

1637
04:44:34.990 --> 04:44:51.159
Dr. Matthew Matasar: in some remote sanitary's about it is a highly active and tolerable treatment that meets unmet need in this patient population and multi-trade s mole it offers high overall and committed response rates and is well tolerated offering a readily available off-the-shelf therapy that can be accessed to cross-treatment. Settings

1638
04:44:51.170 --> 04:45:00.820
Dr. Matthew Matasar: fixed duration treatment is an additional advantage to this treatment, and really does represent a significant advance in the treatment of patients with multi-grade labs for liquid on.

1639
04:45:01.020 --> 04:45:03.639
Dr. Matthew Matasar: Thank you for your attention and I welcome your questions.

1640
04:45:08.830 --> 04:45:10.919
Drew Kasper: Thank you for your presentation.

1641
04:45:11.390 --> 04:45:18.610
Drew Kasper: Are there any questions from the public or Cms, and I see

a hand up

1642
04:45:18.650 --> 04:45:22.839
Drew Kasper: from Lang. Let's start with you, Lane. Go ahead and unmute, please.

1643
04:45:23.940 --> 04:45:28.629
Lang Le: Hi Drew. Thanks. I just have a few questions. You're going to be on

1644
04:45:28.890 --> 04:45:44.920
Lang Le: a study that was submitted as part of the application. Um, and i'm trying to just wrap my head around the um how the drug is administered! And now, in the in-patient setting, I did see you know in in the

1645
04:45:44.930 --> 04:46:04.679
Lang Le: towards the bomb um where I was describing some simple mental materials. Where um you know where you guys describe how the drug is administered. Uh, we will then intervene in this in the inefficient setting. It's like to confirm that, and when or not it can also be done in the location serving.

1646
04:46:04.810 --> 04:46:21.519
Dr. Matthew Matasar: Thank you for your question. So. Yes, mo sanitism that is being developed as an intravenous administration For this submission it is being co-developed in separate efforts as a subcutaneous treatment. But here we are discussing its use intravenously administered, it can be administered in the outpatient setting,

1647
04:46:21.530 --> 04:46:26.749
Dr. Matthew Matasar: particularly during this step up period of time. Given that there is a risk of cytokine release syndrome.

1648
04:46:27.020 --> 04:46:44.460
Dr. Matthew Matasar: We will typically leave it to physician discretion, whether patients need to be admitted for observation and management of potential risk of such a kind release. Once treatment has been stepped up and tolerated, treatment typically reverts to the outpatient setting for subsequent cycles.

1649

04:46:45.010 --> 04:46:46.489
Lang Le: Okay, thank you for that.

1650
04:46:46.500 --> 04:46:54.689
Lang Le: And um. Just to um just to um to go over here. So when the when the drug is in the in the in the in-patient setting

1651
04:46:54.700 --> 04:47:11.010
Lang Le: I think um the protocol had mentioned. Um during the first bills. The picture may require at least seventy two hours of um Patient modeling is that is, that where the patient stays in the inpatient setting for the first seventy two hours.

1652
04:47:11.020 --> 04:47:19.269
Dr. Matthew Matasar: That's right. So So to to remind you of the step up dosing it's cycle one day one day eight, and then a full step up on day. Fifteen

1653
04:47:19.280 --> 04:47:26.780
Dr. Matthew Matasar: cytokine, really syndrome can be seen during any of these treatments, as well as a little bit of a lower rate, but still seeing it cycle to day one,

1654
04:47:27.020 --> 04:47:33.400
Dr. Matthew Matasar: the majority of the Crs seemed does happen at that full step up dose. So the cycle one day fifteen dose.

1655
04:47:33.460 --> 04:47:50.030
Dr. Matthew Matasar: But whenever a physician feels that it's in the patient's safety and best interests to receive hospital-based care during this step of dosing time. It would typically be monitoring for forty, eight to seventy, two hours. Given the kinetics of cytokine and syndrome that we've seen in this.

1656
04:47:51.180 --> 04:48:03.050
Lang Le: And um. Are there any planned trials or ongoing trials where you compare? Does this enjoy that? The The drug to the same um, the end of care or current stand up here.

1657
04:48:03.060 --> 04:48:26.840
Dr. Matthew Matasar: It's a good question, and there is certainly multiple studies that are currently ongoing to further evaluate how

best the leverage most undertes that it's being compared. Um! It's being studied as a single agent in earlier lines of therapy, it's being studied as monotherapy compared to other treatments, and we're evaluating its combination with other agents, all with the attempt of trying to best understand how best to deploy this effectiveness,

1658
04:48:27.700 --> 04:48:30.170
Lang Le: and the last question drew um

1659
04:48:30.230 --> 04:48:43.469
Lang Le: um for the the phase two trial. I believe that's not um. Is there any survival data on the ninety patients or so?

1660
04:48:44.090 --> 04:49:08.889
Dr. Matthew Matasar: So? We actually just at this last Ash, two days ago offered our updated outcomes data. Now we have a Median and a Median follow up of twenty-seven months At that time. We now have improved estimates of durability and response. And we see that the Median progression-free survival has not yet been reached at a Median in the following twenty-seven months. And those that do respond in chief

1661
04:49:08.900 --> 04:49:14.289
Dr. Matthew Matasar: response we see durability of complete response. That is really quite extraordinary in this data set as well

1662
04:49:14.300 --> 04:49:23.809
Dr. Matthew Matasar: overall survival is very high as we would expect, given the activity by the more stringent measures of pfs and duration and response.

1663
04:49:25.340 --> 04:49:29.369
Lang Le: Thank you, Dr. Matthews. Sorry I'm. Drew um and Vina, I don't have any additional questions.

1664
04:49:31.540 --> 04:49:32.830
Thanks.

1665
04:49:32.950 --> 04:49:40.489
Drew Kasper: There is a question that dovetails nicely into what the two of you were just talking about with

1666
04:49:41.150 --> 04:49:52.650
Drew Kasper: requirements for hospitalization there was a question and type. How often does that happen that Mosaitus and Abdoses require hospitalization for administration?

1667
04:49:53.930 --> 04:50:02.820
Dr. Matthew Matasar: So good question. I don't have the statistic off the top of my head in terms of the percent of patients that underwent elective admission during the trial.

1668
04:50:02.940 --> 04:50:22.209
Dr. Matthew Matasar: It would be fair to ask whether that estimate would be representative of what would be experienced in the real world after It's anticipated approval and deployment in community-based settings. My personal anticipation is that particularly earlier on, as physicians who may not yet have experience with the administration of I of the antibodies

1669
04:50:22.270 --> 04:50:35.190
Dr. Matthew Matasar: may be expected to take a more conservative approach, and perhaps use hospitalization during step of dosing more frequently in order to make sure that they are keeping patient safety centered in their practice.

1670
04:50:38.090 --> 04:50:42.370
Drew Kasper: Thank you. And Adina. Can you go ahead and unmute?

1671
04:50:43.660 --> 04:50:52.479
Adina Hersko: Yes, thank you. So just to confirm what you were talking about previously. It's it's possible that this would require multiple admissions

1672
04:50:52.980 --> 04:50:55.070
Adina Hersko: for the multiple devices.

1673
04:50:55.840 --> 04:51:04.869
Dr. Matthew Matasar: It is possible, you know, as we have conducted the work that has been left to position discretion. My anticipation is that it it would not be

1674
04:51:04.880 --> 04:51:34.260

Adina Hersko: many admissions when we are worried about a patient given their disease, kinetics, their disease, burden the factors that we believe may be associated with higher risk of cytokine release. We will often do an elective admission um for that. Step up dose to the foldos that's like a one-day fifteen dose, and if that is tolerated without significant side of time release, then we would typically return such treatments to outpatient therapy. If Crs were seen. During that admission

1675
04:51:34.270 --> 04:51:39.759
Dr. Matthew Matasar: you may again elect to treat the cycle two day, one a patient as well

1676
04:51:39.820 --> 04:51:55.200
Dr. Matthew Matasar: out of a measure of caution. So is there a chance that there could be multiple missions as a chance, but it's not intended to be sequentially and indefinitely administered in a patient setting. That's not my anticipation for how the medicine would be used.

1677
04:51:56.040 --> 04:52:14.219
Adina Hersko: Thank you. Um. You had noted that before the proposed invocation was for molecular lymphoma. Um. I noted that the trial tested patients with popular lymphoma upgrade um for one through three A. Can you confirm that the indication wouldn't include a patient for a bulk of simple Must be.

1678
04:52:14.700 --> 04:52:27.239
Dr. Matthew Matasar: That's my understanding. Correct. We we group phillip it on the following grade: one two and three under the rubric of low-grade molecular lymphoma Grade Iii. B foricular lymphoma is probably best understood and certainly recognized by

1679
04:52:27.250 --> 04:52:38.769
Dr. Matthew Matasar: one of the film of physicians as a more aggressive form of peace on a hodgkin Loma, and would typically follow treatment practice patterns more aligned with that of its congen or diffuse large B cell.

1680
04:52:39.640 --> 04:52:40.770
Adina Hersko: Thank you.

1681
04:52:40.870 --> 04:52:42.890

Adina Hersko: An additional question

1682
04:52:42.900 --> 04:52:53.940
Adina Hersko: in the base. Two trial. How many patients that we're receiving with Matthews and maps had previously a failed treatment with at least three of the other currently available airline plus lego. And

1683
04:52:54.550 --> 04:53:14.220
Dr. Matthew Matasar: so in the ninety patients that we report in the pivotal study. Um, who are eligible for molecular environment. Indeed, the median number of prior lines of therapy was three. I don't know the exact percentage, but with a meeting of free that tells you that the majority of patients were indeed pre-treated to this degree.

1684
04:53:21.850 --> 04:53:24.940
Dr. Matthew Matasar: Perhaps I don't understand your question could ask you to clarify

1685
04:53:25.910 --> 04:53:36.099
Adina Hersko: so of the of the drugs that you had listed, as indicated for third line, plus treatment for those previously treated with those particular drugs.

1686
04:53:36.440 --> 04:53:49.580
Dr. Matthew Matasar: I do not know that we have collected all of the prior. Ah! The the components of the prior lines of therapy that patients received prior to enrolment On go two hundred and seventy.

1687
04:53:52.880 --> 04:54:00.750
Adina Hersko: Thank you. How many patients were treated at centers that were approved to administer the carte treatment

1688
04:54:01.660 --> 04:54:03.000
Adina Hersko: in this condition.

1689
04:54:04.390 --> 04:54:16.979
Dr. Matthew Matasar: That's a good question. I do not know the full list on the daft on my head, which were all the participating centers in this trial. Um, i'm sure that we can get that information for you.

1690

04:54:18.550 --> 04:54:19.630
Adina Hersko: Thank you.

1691
04:54:26.040 --> 04:54:32.819
Drew Kasper: Are there any more questions? Laying? Is that a new hand up, or is that from before.

1692
04:54:34.120 --> 04:54:35.490
Lang Le: Sorry your goes home

1693
04:54:35.500 --> 04:54:36.430
Lang Le: before.

1694
04:54:47.690 --> 04:54:57.880
Drew Kasper: Okay. I don't see any additional hands up, and there are no questions in the Q. And A. There are no new questions in the and mailbox.

1695
04:54:59.070 --> 04:55:01.820
Drew Kasper: Okay? Well, again, Thank you.

1696
04:55:01.950 --> 04:55:03.560
Dr. Matthew Matasar: Thank you for the opportunity.

1697
04:55:05.250 --> 04:55:14.779
Drew Kasper: We'll now hear from presenters for the Lova cell technology application, and you may now unmute your phone.

1698
04:55:17.250 --> 04:55:19.989
Dr. Jennifer Leiding: Let me pick my camera real quick. Thanks, guys.

1699
04:55:23.950 --> 04:55:25.580
Dr. Jennifer Leiding: Can I get started?

1700
04:55:29.800 --> 04:55:31.620
Dr. Jennifer Leiding: Would not be okay to hear you.

1701
04:55:31.860 --> 04:55:33.480
Dr. Jennifer Leiding: Okay, perfect.

1702
04:55:33.660 --> 04:55:49.010
Dr. Jennifer Leiding: Um. My name is Dr. Jennifer Lighting, and I am a medical director at Bluebird Bio, and today i'm going to speak to you about Lovo T. Beglaging auto tempal, which I will now refer to as lovo cell for treatment of sickle cell disease. Next slide,

1703
04:55:50.640 --> 04:56:01.809
Dr. Jennifer Leiding: so sickle cell disease is a severe, progressive, and facilitating disease that begins with a point mutation in the beta globe and gene which is depicted in the the picture on the right.

1704
04:56:02.550 --> 04:56:14.180
Dr. Jennifer Leiding: This abnormality in the boat beta-globin gene leads to high levels of sickled hemoglobin that leads to subsequent polymerization of red blood cells under low oxygen conditions

1705
04:56:14.190 --> 04:56:24.540
Dr. Jennifer Leiding: causing red blood cells to become sickled, sticky, and rigid, that ultimately lead to painful and unpredictable episodes of ves occlusion, which are the hallmark of sickle, cell disease,

1706
04:56:24.550 --> 04:56:32.959
Dr. Jennifer Leiding: current management, of sickle cell disease relies on lifelong use of acute and chronic therapies which have sub-optimal clinical benefits

1707
04:56:32.970 --> 04:56:40.490
Dr. Jennifer Leiding: to date. The only potentially curative treatment for sickle cell disease is allogenic stem cell transplant with a match sibling sona.

1708
04:56:40.580 --> 04:56:44.540
Dr. Jennifer Leiding: But significant risk is associated with that next slide

1709
04:56:46.260 --> 04:56:55.750
Dr. Jennifer Leiding: so lova cell is an investigational personalized one-time administered autologist and therapy that's under evaluation for the treatment of sickle cell disease

1710
04:56:55.890 --> 04:57:07.849
Dr. Jennifer Leiding: as of December, two thousand and twenty one. The Fda has placed a partial clinical hold on our program for patients under the age of eighteen. Um. In this particular treatment,

1711
04:57:07.930 --> 04:57:24.420
Dr. Jennifer Leiding: that being said, Lovo cell is still a one-time administration gene therapy product that results in durable production of an antisycling adult hemoglobin. Hb. A. T. Eighty, seven, two that reduces red blood cell cycling by intervening at the genetic level a hallmark

1712
04:57:24.430 --> 04:57:36.069
Dr. Jennifer Leiding: of hemoglobin. T. Eighty sevenq is that it substantially reduces sickling with a goal of reducing hemoglobin S. Homolysis and other complications.

1713
04:57:36.080 --> 04:57:52.609
Dr. Jennifer Leiding: We are expecting to submit our biologic license. Application by Q. One of twenty twenty, three, with a request for priority review. But other earlier regulatory designations for Lova style include fast-track orpan drugs, rare pediatric disease and regenerative medicine advanced therapy.

1714
04:57:53.650 --> 04:57:54.720
Dr. Jennifer Leiding: Thanks. Bye

1715
04:57:56.330 --> 04:58:07.960
Dr. Jennifer Leiding: so on this slide i'm going to walk you through the process of our x-vo gene therapy with loomo cell for patients enrolled in our clinical trials, and what would be expected in the real world setting as well.

1716
04:58:07.970 --> 04:58:23.470
Dr. Jennifer Leiding: So initially, patients are admitted to the hospital where they undergo stem cell collection. Um! This part of the procedure typically occurs in the hospital, but could theoretically occur in the fusion center, but within our clinical trial setting has been in the hospital

1717
04:58:23.480 --> 04:58:33.200
Dr. Jennifer Leiding: patients. Then those cells are then sent to our

manufacturing facility, where they undergo transduction of the Bb. Three hundred and five lent viral. Vector

1718
04:58:33.210 --> 04:58:53.009
Dr. Jennifer Leiding: Once um that has been successful, the cells are then sent back to the treating facility. The patient is readmitted to undergo myelobulative conditioning. They remain in the hospital during this time, where they receive the drug product infusion with a hospitalization of approximately five weeks within our study.

1719
04:58:53.020 --> 04:59:09.960
Dr. Jennifer Leiding: During this time we are anticipating and waiting for engraftment and repopulation. Of these modified hematophobic control. Patients are then followed for a two year follow, and are eligible for a thirteen year long. Term follow up study next slide,

1720
04:59:11.490 --> 04:59:20.970
Dr. Jennifer Leiding: So, if approved by the Fda Lovo cells expected to provide a much-needed treatment option that's with potentially durable effects for people with sickle cell disease.

1721
04:59:20.980 --> 04:59:42.230
Dr. Jennifer Leiding: So, as I mentioned already, allogenic transplant is the only temporal restorative treatment option for a circle protected. At this time, however, it's broad utility is significantly limited by the age of the patient being treated. Limited Availability of Hla match donors, and the rarity of hla haplotypes specifically in patients of African or black assass.

1722
04:59:42.240 --> 04:59:57.049
Dr. Jennifer Leiding: Um, patients that use or sickle cell disease. Patients that do undergo allergenic transplant using an unrelated or mismatched donor have increased risk of serious, potentially fatal complications, such as graffiti and graph rejection

1723
04:59:57.060 --> 05:00:07.170
Dr. Jennifer Leiding: in comparison. Low a cell utilizes the stem cells from the patient themselves with the fulfill diseases and starting material, thereby relieving the need for a matched donor

1724
05:00:07.230 --> 05:00:08.460
Dr. Jennifer Leiding: next slide.

1725
05:00:09.610 --> 05:00:26.840
Dr. Jennifer Leiding: So our study, H. T. V. Two S. Six, is an ongoing phase one, two non-randomized open, labeled a study that's being conducted at eleven sites across the United States. I'm going to present data from our most recent data cut of February twenty, twenty, one which were recently published in the Ring on Journal of Madison.

1726
05:00:26.850 --> 05:00:37.489
Dr. Jennifer Leiding: So Group c. Was Ah. Was established for the pivotal evaluation of Lovo Sal, and as of February, two thousand and twenty, one, thirty, five patients in group, c. Had received logo cell infusion.

1727
05:00:37.530 --> 05:00:57.139
Dr. Jennifer Leiding: Our primary efficacy Endpoint has been the assessment or our determining proportion of patients. Um. Achieving complete resolution of severe voe's between six months and eighteen months after drug products in fusion. We did assess many other endpoints, including the proportion of patients achieving a gorb and response.

1728
05:00:57.150 --> 05:01:07.349
Dr. Jennifer Leiding: Other voe and svoe endpoints an assessment of multiple humans logic, clinical and disease endpoints as well as pharmac dynamic assessment.

1729
05:01:07.820 --> 05:01:19.730
Dr. Jennifer Leiding: I will say that not all patients who are valuable for severe voes as they had to meet certain criteria which are listed here, including a force for their abilities in the twenty four months before, and

1730
05:01:19.740 --> 05:01:23.799
Dr. Jennifer Leiding: and reaching the minimum follow-up time of six months for the analysis,

1731
05:01:23.910 --> 05:01:25.020
Dr. Jennifer Leiding: but fine.

1732
05:01:26.430 --> 05:01:55.150
Dr. Jennifer Leiding: So, as you can see in this slide patients with sickle cell disease, experience, complete remission of serious phase

of inclusive events. After the one-time treatment of love of cell with an overall meeting rate of viewe at zero per year. So again, just reminding you, this is data from our group C Beta cut off of February two thousand and twenty one. This particular graphic, those swim lanes of individual patients with the blue dots indicating

1733
05:01:55.160 --> 05:02:06.650
Dr. Jennifer Leiding: um voe's pre-treatment, and then post-lobo solemn fusion in the yellow which is on the right side so on the left there was a Median of three point five severe voes

1734
05:02:06.660 --> 05:02:15.339
Dr. Jennifer Leiding: pre pre-lower cell treatment, and then following love of cell treatment has been complete resolution of the oes in the

1735
05:02:15.740 --> 05:02:16.940
Dr. Jennifer Leiding: next slide.

1736
05:02:17.960 --> 05:02:32.290
Dr. Jennifer Leiding: Additionally, we assess the quantity of hemoglobin, T. Eighty, seven. Q. That was produced amongst patients, and again each line represents an individual patient over time with months, post-lobo cell infusion,

1737
05:02:32.300 --> 05:02:35.970
Allison Pompey: three minutes on the bottom.

1738
05:02:35.980 --> 05:03:01.040
Dr. Jennifer Leiding: So what you can see is that um with treatment with lova cell Um, there's an increase in total hemoglobin concentration and overall decreased concentration of humor than s in the blood. And with this increased concentration of hemoglobin a we expect halting of sickle cell disease in the halting of sickle cell disease, progression through lifelong production of hemoglobin, A. T. Eighty, seven. Q.

1739
05:03:01.510 --> 05:03:02.750
Dr. Jennifer Leiding: That's fine.

1740
05:03:03.800 --> 05:03:21.589
Dr. Jennifer Leiding: So our safety data from Study Hgv To a sex um group, c. Does appear to present an acceptable benefit. Risk profile

for patients with chemical properties. In the left panel are treatment related aes, and then in the smaller right panel is serious treatment emergent aes.

1741
05:03:21.600 --> 05:03:33.470
Dr. Jennifer Leiding: The majority of these, especially those on the left, are consistent with the effects of Myelobi of conditioning that we would expect than any individual who received that conditioning prior to cellular therapy.

1742
05:03:33.480 --> 05:04:02.899
Dr. Jennifer Leiding: I should also mention that in ah an earlier cohort of our groups of group A. And just to remind you I've been presenting data for mercy. But from group a two patients treated with globe cell did develop a amount Um, after investigation as to the cause of aml. Ah! We believe that the underlying risk of human's, logical lignancy and sickle cell disease, combined with the transplant procedure and associate of proliferative stress and continued hemataquatic stress due to mental clinical benefit in these two patients,

1743
05:04:03.040 --> 05:04:10.919
Dr. Jennifer Leiding: the cause of their Aml. The data regarding these investigations has been published with with references listed here.

1744
05:04:11.330 --> 05:04:12.520
Dr. Jennifer Leiding: That's fine.

1745
05:04:13.370 --> 05:04:23.530
Dr. Jennifer Leiding: So in summary, if approved by the Fda Bovo so provide a much-needed one-time potentially curative treatment for patients with sickle cell disease.

1746
05:04:23.540 --> 05:04:51.469
Allison Pompey: Um, In summary our http to a six routine data, Ah demonstrate that lovo cell uniquely impacts the have the physiology of sickle cell disease at the genetic level. It offers seven minutes stable, durable and light bulk production of anticycling hemoglobin, H. B. A. T. Eighty seven, two. The normalization or near a normalization of hemoglobin and hemollytic markers. We resolution that seriously,

1747
05:04:51.480 --> 05:04:53.890

Dr. Jennifer Leiding: fifty-four point eight patient here's a follow up

1748
05:04:54.240 --> 05:05:06.190
Dr. Jennifer Leiding: the sustained results support the potential for long-term durability from this one-time treatment, and represent a paradigm shift in the treatment of sickle cell disease which can be transformational benefit for patients and society

1749
05:05:06.400 --> 05:05:07.649
Dr. Jennifer Leiding: looks fine.

1750
05:05:09.220 --> 05:05:12.159
Dr. Jennifer Leiding: Thank you for your attention, and I welcome any questions.

1751
05:05:15.840 --> 05:05:18.050
Drew Kasper: Thank you very much for your presentation.

1752
05:05:18.560 --> 05:05:22.229
Drew Kasper: Are there any questions from the public or from Cms?

1753
05:05:25.310 --> 05:05:29.630
Drew Kasper: Let's start with with Cindy. Go ahead and unmute Cindy.

1754
05:05:30.510 --> 05:05:44.249
Cindy Hake: Thanks, Jay. Thank you, Dr. Lining, for your presentation. Do you have a Kadufa or other date from the Fda by which you anticipate authorization for marketing.

1755
05:05:44.260 --> 05:05:55.259
Dr. Jennifer Leiding: Yeah, we can't speak to the Fda Timelines. We're still on schedule to submit in our Bla in Q. One two thousand and twenty three, and then the Fda will determine that timeframe for us.

1756
05:06:03.960 --> 05:06:05.190
Cindy Hake: Thank you.

1757
05:06:09.140 --> 05:06:10.960
Drew Kasper: You have any other questions

1758
05:06:11.030 --> 05:06:13.469
Um. Public or Cms

1759
05:06:16.170 --> 05:06:21.349
Drew Kasper: checking the new tech mailbox. I don't see any new questions. There.

1760
05:06:22.500 --> 05:06:24.870
Drew Kasper: There are no questions in the Q. A.

1761
05:06:29.520 --> 05:06:31.519
Drew Kasper: Um last call

1762
05:06:31.600 --> 05:06:33.470
Drew Kasper: for any questions.

1763
05:06:39.100 --> 05:06:40.380
Drew Kasper: Okay,

1764
05:06:40.660 --> 05:06:42.720
Drew Kasper: All right. Well, thanks again.

1765
05:06:43.110 --> 05:06:44.150
Dr. Jennifer Leiding: Thank you.

1766
05:06:45.670 --> 05:06:55.250
Drew Kasper: This next presentation is actually going to be. It's. It's two presentations combined. Two applications combined.

1767
05:06:55.520 --> 05:07:00.930
Drew Kasper: So we have a lot of twenty minutes for this and ten minutes to Q. And A. To follow the.

1768
05:07:01.210 --> 05:07:05.700
Drew Kasper: We will now hear from the presenters for sidelocks

1769
05:07:05.820 --> 05:07:07.710

Drew Kasper: otherwise known as

1770
05:07:08.270 --> 05:07:10.050
Drew Kasper: Ephol the See, a name

1771
05:07:10.870 --> 05:07:12.629
Drew Kasper: we Now unmute your phone.

1772
05:07:13.300 --> 05:07:28.479
Dr. Bert Slade: Great. Thank you very much. So i'm Dr. Burke's slate. I'm serving as the chief medical officer for on target laboratories, and I'm going to give the first part of the talk, introduce you to the problem and what it is that Cyidlocks does.

1773
05:07:28.540 --> 05:07:32.789
Dr. Bert Slade: It's new and novel and quite elegant. It literally allows surgeons to

1774
05:07:33.200 --> 05:07:34.380
see cancer

1775
05:07:34.580 --> 05:07:40.760
Dr. Bert Slade: intra-operatively, the goal being to remove more cancer than they would otherwise be able to remove the

1776
05:07:40.810 --> 05:07:42.680
Dr. Bert Slade: and potentially remove all of the cancer,

1777
05:07:43.050 --> 05:07:44.249
the next one,

1778
05:07:45.990 --> 05:07:50.119
Dr. Bert Slade: the surgery of the first one therapy ovarian cancer, lung cancer.

1779
05:08:00.840 --> 05:08:04.190
Dr. Bert Slade: The problem is recurrence is the

1780
05:08:04.400 --> 05:08:08.209

this is unable to find all of the cancer station in the movement the

1781
05:08:09.910 --> 05:08:15.670
Dr. Bert Slade: seventy percent of patients with ovarian will have a recurrence, and up to half of patients

1782
05:08:15.820 --> 05:08:17.780
I want to go surgery for

1783
05:08:23.450 --> 05:08:24.650
indicating that

1784
05:08:26.220 --> 05:08:29.840
operative field, and it just wasn't found by the sergeant

1785
05:08:31.410 --> 05:08:32.510
Dr. Bert Slade: next one.

1786
05:08:34.070 --> 05:08:37.060
Dr. Bert Slade: So would it be better to get more of the cancer

1787
05:08:37.080 --> 05:08:39.320
out of the data suggests.

1788
05:08:39.340 --> 05:08:40.520
The answer is Yes,

1789
05:08:40.720 --> 05:08:54.390
Dr. Bert Slade: for ovarian cancer on the left, five-year overall survival if you look at the blue line, that's the survival with no cytone reduction, and the orange line on the top is cases where the surgeon believed that all of them

1790
05:08:54.490 --> 05:08:56.800
Dr. Bert Slade: the cancer system has been removed. The

1791
05:08:57.580 --> 05:08:58.969
Dr. Bert Slade: so in R. Zero

1792
05:09:01.850 --> 05:09:05.710
is looking at margins of respected tissue,

1793
05:09:05.730 --> 05:09:08.470
and so you can take the tissue out and look at

1794
05:09:23.390 --> 05:09:26.210
Dr. Bert Slade: so Cylinder looks. Um

1795
05:09:27.810 --> 05:09:29.620
Dr. Bert Slade: Many, most

1796
05:09:29.740 --> 05:09:33.830
of ovarian and lung cancers over express full-legged receptors.

1797
05:09:33.990 --> 05:09:37.359
Dr. Bert Slade: These are receptors on the cell that will bind to foamic acid

1798
05:09:37.420 --> 05:09:38.740
cytlux is

1799
05:09:39.010 --> 05:09:40.320
some analog

1800
05:09:41.140 --> 05:09:53.710
Dr. Bert Slade: there's an analog of folding N. So the then it's linked to a floor of four. And so what does that mean when it's excited with the proper wavelength of light? It fluoresces, and so literally the cancer

1801
05:09:54.140 --> 05:09:57.890
Dr. Bert Slade: glows when it's exposed to near infrared light.

1802
05:09:57.990 --> 05:10:03.630
Dr. Bert Slade: And so this is given intravenously for one to nine hours with prior to surgery.

1803

05:10:03.720 --> 05:10:05.150
It's a one hour. Infusion.

1804
05:10:05.400 --> 05:10:07.849
Um. The drug is

1805
05:10:07.950 --> 05:10:09.080
distributed

1806
05:10:10.900 --> 05:10:16.359
in the body, and it's taken up by the cancer cells, and it's amber cycl. So it concentrates.

1807
05:10:26.310 --> 05:10:27.809
Dr. Bert Slade: So it's a nice,

1808
05:10:32.430 --> 05:10:33.580
Dr. Bert Slade: the next,

1809
05:10:41.340 --> 05:10:43.210
and the agency designated that

1810
05:10:43.380 --> 05:10:48.130
Dr. Bert Slade: fast track and priority review on the business of the data

1811
05:10:48.350 --> 05:10:51.049
presented to them. They recognize that this is

1812
05:10:52.230 --> 05:10:54.160
Dr. Bert Slade: a substantial input.

1813
05:10:55.180 --> 05:10:58.899
Dr. Bert Slade: So it's ah described as an optical imaging, A

1814
05:11:00.000 --> 05:11:05.290
Dr. Bert Slade: for adult patients with a variant cancer as an adjunct for interoperative identification

1815
05:11:05.730 --> 05:11:07.000
living in patients.

1816
05:11:10.870 --> 05:11:13.730
Dr. Bert Slade: So everybody is going to look on the right side, even if it's

1817
05:11:19.050 --> 05:11:20.580
of source tissue between the

1818
05:11:22.060 --> 05:11:24.459
Dr. Bert Slade: it doesn't look any different from the rest of the tissue

1819
05:11:24.650 --> 05:11:25.789
can feel a different

1820
05:11:26.330 --> 05:11:41.610
Dr. Bert Slade: Ah, but you know you don't necessarily see that it looks like cancer. So this patient has been accused of someone else, and when the their infrared light source is turned on, you can now see this issue that has taken up

1821
05:11:42.910 --> 05:11:49.200
Dr. Bert Slade: literally are able to visualize where that cancer tissue is, and the

1822
05:11:49.870 --> 05:11:50.990
Dr. Bert Slade: potentially not,

1823
05:11:51.750 --> 05:11:54.790
then you would be able to otherwise.

1824
05:11:54.840 --> 05:11:55.900
Um.

1825
05:11:56.080 --> 05:11:59.010
Dr. Bert Slade: So let's come over to the left and read it from the bottom up. So it's

1826
05:11:59.160 --> 05:12:01.829
the use of visual inspection and palpation.

1827
05:12:08.240 --> 05:12:20.569
Dr. Bert Slade: If if you can get most of all of it out you have better progression-free survival and overall survival, and the amount of residual tissue is an independent and diagnostic benefactor

1828
05:12:20.750 --> 05:12:21.859
of survival.

1829
05:12:24.700 --> 05:12:33.330
Dr. Bert Slade: So here's the phase: Three study. One hundred and fifty patients were infused, and then they all underwent the examination under white light and calpation.

1830
05:12:33.420 --> 05:12:43.960
Dr. Bert Slade: An envelope was open, and one hundred and thirty. I'm: Sorry. Yeah. One hundred and thirty. Four of them had been randomized to have to turn on their infrared. So then the surgeon was able to make it

1831
05:12:45.060 --> 05:12:47.210
um and visualize.

1832
05:12:49.820 --> 05:12:57.220
Dr. Bert Slade: The surgery took place, Susan was able to come back and look again under ar to see if I missed anything to take additional.

1833
05:12:57.750 --> 05:13:01.690
Dr. Bert Slade: All of the issues were sent for pathologic evaluation.

1834
05:13:01.700 --> 05:13:02.380
This.

1835
05:13:05.270 --> 05:13:19.289
Dr. Bert Slade: So who was in the study that among the one hundred and fifty they were mostly white and eighty five percent, mostly post

menopausal, eighty, five, and among one hundred and nine, Ah C. Fifty, who had confirmed cancer and coming in

1836
05:13:19.300 --> 05:13:25.949
Dr. Bert Slade: about eighty, five percent head stage, three or four, and it was mostly Sara and the person

1837
05:13:29.800 --> 05:13:35.839
Dr. Bert Slade: the safety profiles. So these are adverse events reported as to

1838
05:13:37.040 --> 05:13:44.020
Dr. Bert Slade: possibly they were mild and moderate. The only severe was, and a Nieman Anenia, which

1839
05:13:57.850 --> 05:14:05.280
Dr. Bert Slade: So here's what happens if I'm one hundred and thirty, four, the bar on the left, twenty, seven percent of them had tissue removed

1840
05:14:05.630 --> 05:14:06.860
that proof

1841
05:14:07.040 --> 05:14:09.160
the cancer, and would not have been removed,

1842
05:14:09.340 --> 05:14:11.429
and it not been visualized. With this,

1843
05:14:11.510 --> 05:14:12.540
the cytoplasm

1844
05:14:12.630 --> 05:14:15.740
Dr. Bert Slade: among his one hundred and night cancer, patients, thirty, three percent

1845
05:14:23.610 --> 05:14:25.869
Dr. Bert Slade: among patients coming in for cyto reduction mate

1846

05:14:26.200 --> 05:14:27.839
to have additional tissue boots,

1847
05:14:28.120 --> 05:14:31.240
Dr. Bert Slade: and those who were in for interval people and forty percent

1848
05:14:40.350 --> 05:14:44.199
Dr. Bert Slade: detective using slid locks and not detective using

1849
05:14:44.340 --> 05:14:47.190
Dr. Bert Slade: It's a standard, you know. White lighted palpation alone.

1850
05:14:50.570 --> 05:14:55.699
Dr. Bert Slade: So my last slide, the investigators reported to us that

1851
05:14:55.750 --> 05:14:57.460
fifty six percent of patients

1852
05:15:02.930 --> 05:15:05.200
side of being able to visualize tissue

1853
05:15:05.400 --> 05:15:06.489
the with us,

1854
05:15:08.610 --> 05:15:10.550
Dr. Bert Slade: fifty, one percent of patients

1855
05:15:15.040 --> 05:15:16.720
Dr. Bert Slade: and sixty-two percent that she,

1856
05:15:17.110 --> 05:15:20.039
section or zero, In the opinion the

1857
05:15:22.400 --> 05:15:24.090
normally be in the ranch, and

1858
05:15:24.120 --> 05:15:25.460
twenty to seventy percent.

1859
05:15:27.110 --> 05:15:29.119
It's a wide way to tell patient alone.

1860
05:15:29.540 --> 05:15:33.129
Dr. Bert Slade: Those are my slides. I'm going to turn it over to Dr. Eva.

1861
05:15:33.200 --> 05:15:35.599
Dr. Bert Slade: Talk about the the lung study.

1862
05:15:36.180 --> 05:15:47.249
Dr. Michael Ebright: Hello! Thank you for giving us the opportunity to present today. My name is Michael Ebr. Right? I'm. A thoracic surgeon at Stanford Hospital in Connecticut, at Columbia University, New York.

1863
05:15:47.260 --> 05:15:57.959
Dr. Michael Ebright: I'll be speaking about the use of sidelines during Lung Cancer Surgery and please. Forgive me. I'm getting over some kind of respiratory thing like half the population. So forgive my voice.

1864
05:15:58.080 --> 05:15:59.770
Dr. Michael Ebright: Next slide.

1865
05:16:00.190 --> 05:16:03.410
Dr. Michael Ebright: Those are my disclosures. Next slide.

1866
05:16:04.040 --> 05:16:19.709
Dr. Michael Ebright: So sidelocks is currently under review by the Fda for the proposed indication as an optical imaging agent for patients with known or suspected lung cancer. It's received fast track and Priority review designations demonstrating a significant unmet need

1867
05:16:20.010 --> 05:16:21.410
Dr. Michael Ebright: next slide.

1868

05:16:24.120 --> 05:16:40.419
Dr. Michael Ebright: So Sidelock's address is an important unmet clinical need in the surgical treatment of Lung Cancer five year. Survival for lung cancer, even at early stage, remains poor at just over sixty percent for localized disease, and about only one in three for regional disease.

1869
05:16:40.430 --> 05:16:49.590
Dr. Michael Ebright: A high percentage of patients end up with a recurrence after surgery, with a quarter of them recurring locally, meaning near a suture liner within the same lobe of the lung,

1870
05:16:49.690 --> 05:17:00.799
Dr. Michael Ebright: and what's really important to note is that the average survival after a local recurrence is less than one year. This is when you start off with early stage disease potentially curable.

1871
05:17:01.060 --> 05:17:11.800
Dr. Michael Ebright: We know that a significant number of patients have synchronous malignant lesions undetected by pre-operative imaging. In fact, one study showed this number to be eight to nine percent.

1872
05:17:11.850 --> 05:17:18.820
Dr. Michael Ebright: We know we are occasionally and unknowingly leaving disease behind in patients after surgery.

1873
05:17:18.830 --> 05:17:38.590
Dr. Michael Ebright: We also know that obtaining an adequate surgical margin is critical In lung cancer surgery, for instance, a ten millimeter margin from the edge of the tumor to the staple line has about a forty-five percent lower risk of recurrence than if the margin were half done. And so we need to know that i've obtained an adequate march at the time of surgery.

1874
05:17:38.660 --> 05:17:47.330
Dr. Michael Ebright: And very importantly, as we're proporting more and more of our operations thoroughoscopically more robotically meaning, we're not spreading the ribs to get into the chest

1875
05:17:47.340 --> 05:18:00.729
Dr. Michael Ebright: it's very difficult to perform deportation with your own fingers during imaging it. You can um during the surgery, as

you can imagine, to feel, and and and obviously a lot of these lesions are below the surface of the bung. You can't actually see them.

1876
05:18:00.740 --> 05:18:09.800
Dr. Michael Ebright: And currently, we have no foolproof techniques for this, although minimally invasive surgery has become, or it's quickly becoming, the standard of care for lung cancer.

1877
05:18:09.810 --> 05:18:34.979
Dr. Michael Ebright: And if your eyes haven't already moved to the right of this slide, you see, or maybe you don't see in the upper panel. Ah, that's the upper lobe of the lung, and there's a tumor there. You can't see the tumor, because it's below the plural surface. By using side locks you can clearly see where it is, and you know where to perform the reception, and I don't think you need to be a thoracic surgeon to see how amazing this technology is. Next slide

1878
05:18:37.080 --> 05:18:52.789
Dr. Michael Ebright: a prospective, randomized, clinical trial was performed in order to assess the utility of cytos for the surgical treatment of lung cancer. This was a phase Iii. Randomized, controlled surge of trial cases with a known or suspected lung cancer undergoing minimally invasive thoracic surgery.

1879
05:18:52.800 --> 05:19:11.740
Dr. Michael Ebright: We're given sidelux infusion within twenty-four hours pre-operatively all patients underwent standard of care white light examination you know with your scope in the chest and paltation of the lung, to the best of a certain ability to detect the primary tumor or any other suspicious abnormalities. When looking around the store,

1880
05:19:11.820 --> 05:19:28.719
Dr. Michael Ebright: ten to one. Randomization was performed, and those who are randomized to sidelocks underwent near-impreted imaging pre-operative just like dr slade sent for ovarian um lesions, seen by white light and through mirror and thread imaging, were documented, and then reception was performed,

1881
05:19:28.730 --> 05:19:39.590
Dr. Michael Ebright: all sessions were evaluated with post-section near infrared imaging, and to evaluate to valued margins, and of course all specimens were ultimately sent for a pathological valuation.

1882
05:19:40.180 --> 05:19:41.470
Dr. Michael Ebright: Next slide.

1883
05:19:44.070 --> 05:19:56.340
Dr. Michael Ebright: The demographics were fairly uninteresting. You can see the mean age of a cohort with sixty six years. This is actually younger than most, since the average age of diagnosis of lung cancer is aged seventy.

1884
05:19:56.410 --> 05:20:14.370
Dr. Michael Ebright: Ah! Smoking history was as expected, for this population. Most cases were Adenal carcinoma, as expected. Initial procedures were mostly sublimari sections, taking out less and low like a wedge or a sect, and all cases were basically evenly split between

1885
05:20:14.380 --> 05:20:17.860
Dr. Michael Ebright: plain, handheld camera, throatoscopic and robotic circuit.

1886
05:20:18.570 --> 05:20:19.750
Dr. Michael Ebright: Next slide.

1887
05:20:21.160 --> 05:20:31.940
Dr. Michael Ebright: Thank you, the infusion was found to be safe. The most common effect was nausea. Ninety Three percent of the adverse effects were considered mild to moderate, and there were no essays.

1888
05:20:32.130 --> 05:20:33.320
Dr. Michael Ebright: Next slide.

1889
05:20:36.430 --> 05:20:46.870
Dr. Michael Ebright: The primary endpoint was what was defined as a clinically significant event. These were defined as three specific scenarios where the use of sidelocks allowed the surgeon to detect cancer

1890
05:20:47.070 --> 05:20:55.429
Dr. Michael Ebright: which was not visualized during standard methods. So where was there an advantage? In nineteen percent of cases the

primary tumor

1891
05:20:55.440 --> 05:21:08.570
Dr. Michael Ebright: was unable to be visualized or detected interoperatively using the standard white light and paltation that was only able to be localized after near image, near infrared dimension was performed similar to the picture I showed you on the prior slide

1892
05:21:08.910 --> 05:21:20.690
Dr. Michael Ebright: in eight percent of cases in a cult malignant lesion not seen on pre-operative imaging and not detected by standard visualization was discovered only after the use of side locks in the Arctic red image.

1893
05:21:20.930 --> 05:21:38.529
Dr. Michael Ebright: Finally, in thirty-eight percent of cases, a close Martian was identified, using sidelines by God, too close marshal with identification sidelocks which ordinarily mandated, seeking a more aggressive margin. All in all, fifty three percent of cases had one or more clinically significant events

1894
05:21:38.670 --> 05:21:39.850
Dr. Michael Ebright: next slide.

1895
05:21:41.530 --> 05:21:49.540
Dr. Michael Ebright: So to reach that there are three important ways that Sidelux imparts a substantial clinical improvement to the way we operate on lung cancer today.

1896
05:21:49.550 --> 05:21:56.600
Dr. Michael Ebright: In fact, this may proof to be one of the most important advances in throughout the rest of social ecology. In recent years Number one

1897
05:21:56.620 --> 05:22:13.209
Dr. Michael Ebright: it helps us localize tumors. When we want to remove a tumor in the long it should be emphasized that the tumor is often beneath the surface of the plura, and you cannot see it. So we're dependent on being able to feel it with a finger between the ribs, which is not so easy and sometimes impossible,

1898
05:22:13.220 --> 05:22:20.340

Dr. Michael Ebright: with side locks, the tumor just close right in front of you, like you can see on these pictures, even if it's three centimeters beneath the surface

1899
05:22:20.350 --> 05:22:31.800
Dr. Michael Ebright: without cycle. Observation has to go through an additional invasive procedure for preactive localization. That may be an interventional radiology procedure, such as a wire localization in a different department,

1900
05:22:31.810 --> 05:22:43.119
Dr. Michael Ebright: or potentially navigational bronchoscopy, which often requires an additional Ct stand. Both are associated with their own complications and their own costs, and neither of those methods for food.

1901
05:22:43.190 --> 05:22:57.319
Dr. Michael Ebright: You need to have aporary knowledge of where the tumor is in order for both of those techniques to work. You don't need it for cytos. So logistically sunlocks is easy on the patient. It's easier on the surgeon, and it's more reliable.

1902
05:22:57.850 --> 05:23:07.890
Dr. Michael Ebright: Number two. It helps us find cancer where we didn't know it existed. We have a pre-operative Ct. And we have a pre-operative pet for most patients but they're far from perfect.

1903
05:23:07.900 --> 05:23:23.449
Dr. Michael Ebright: You need to. They have a limited sensitivity. So, for instance, here's a personal example. I had a patient with the tumor in the left upper low, who who agreed to be on the trial we use the sidelux I use near infrared image Gene. I found that tumor with no difficulty.

1904
05:23:23.500 --> 05:23:45.569
Dr. Michael Ebright: The Ct. Scan was otherwise clear when I flipped on the nearest red light, I actually saw a very tiny area in the lower, low along the plural service, which I initially completely would have written off as a small focus of star, basically less than two millimeters, and I never would have taken it out. But we were on trial. My level of fish was a little higher because it glowed. I removed it, and lo and behold, it was actually

1905

05:23:45.580 --> 05:24:04.019
Dr. Michael Ebright: ah cancer and a culture cancer that I absolutely absolutely would have left behind. Had I not used the cytos? The patient is so happy. She signed up for this trial. It changed our discussion in tumor board. We discussed the need for agent therapy office much closer. Ah, luckily, today she is still disease-free.

1906
05:24:05.200 --> 05:24:12.950
Dr. Michael Ebright: We also know that if you leave the seas behind, there's a local recurrence, as I mentioned before, survival is less than one year.

1907
05:24:13.860 --> 05:24:15.170
Dr. Michael Ebright: Number three

1908
05:24:15.180 --> 05:24:31.559
Allison Pompey: three minutes. Bidalux allows us to visually see the distance from the tumor edge to the margin of our stable, so this may ultimately allow us to plan our reception margins with greater accuracy. So, for instance, when i'm performing an operation, and I see the tumor goal

1909
05:24:33.700 --> 05:24:37.510
Dr. Michael Ebright: to take my margin to make sure it's adequate on the first shot,

1910
05:24:37.640 --> 05:24:55.020
Dr. Michael Ebright: and the first shot is usually the best shot. All in all satellites may change the way we perform selassic surgery, and it allows the surgeon to approach the disease with much greater confidence. In fact, surgeons indicated a change in slope of their procedure due to sidewalks for twenty nine percent of their case patients in the study

1911
05:24:55.900 --> 05:24:57.800
Dr. Michael Ebright: last slide next one for me.

1912
05:24:58.190 --> 05:25:13.650
Dr. Michael Ebright: So just to sum up um in ovarian cancer. Patient survival is greater among patients who receive complete set of reduction satellites identified additional cancer not otherwise plan for re-section in twenty, seven percent of the Mitch patients,

1913
05:25:13.960 --> 05:25:20.490
Dr. Michael Ebright: ovarian cancer patients receiving interval defaulting sidelines identified additional cancer, and forty percent of patients

1914
05:25:20.610 --> 05:25:33.120
Dr. Michael Ebright: students indicated achieving a complete reception. In sixty-two percent of cases with the use of sidewalks in lung cancer, thirty to Fifty five percent of patients have recurrence following lung cancer surgery

1915
05:25:33.130 --> 05:25:45.700
Dr. Michael Ebright: fifty-three percent of cases in the Iucidite trial had a clinically significant event. Using satellites in percent of patients. The surgeon localized the primary lesion where they otherwise would not have been able to localize it with,

1916
05:25:45.710 --> 05:26:00.850
Dr. Michael Ebright: and eight percent of patients that surgeon identified occult, synchronous lesions that would not have been identified were not recycled, and in thirty eight percent of patients a close reception margin was identified from each of the sidelines. So basically it indicated that surgeons use in sidelines,

1917
05:26:01.370 --> 05:26:05.089
Dr. Michael Ebright: their operative scope in twenty nine percent of taxes.

1918
05:26:05.910 --> 05:26:10.880
Dr. Michael Ebright: That's all I have. Thank you very much for allowing us to present this very exciting technology,

1919
05:26:14.880 --> 05:26:17.519
Drew Kasper: and thank you very much for your presentation.

1920
05:26:17.690 --> 05:26:21.879
Drew Kasper: Are there any questions from the public or from Cms.

1921
05:26:23.330 --> 05:26:26.239
Drew Kasper: And we start with Jane? Go ahead and unmute, please, Jane.

1922
05:26:27.080 --> 05:26:44.430
Jing Xu: Hi, and thank you for this, your presentation and I have one question for the oaring cancer, and we noticed that in the phase three trial you reported that the sensitivity to detect the overeign cancer was eighty, three percent, and the patient fought positive rate

1923
05:26:44.460 --> 05:26:52.870
Jing Xu: was twenty, four point eight percent. And could you discuss the impact of that false, positive rate in terms of patient outcome.

1924
05:26:53.140 --> 05:26:54.240
Jing Xu: Thank you.

1925
05:26:54.800 --> 05:26:56.520
Dr. Bert Slade: Yes, thank you

1926
05:27:03.400 --> 05:27:06.469
Dr. Bert Slade: has been done removing Fisher, but

1927
05:27:06.560 --> 05:27:08.079
turned out not to be cancer, and

1928
05:27:08.270 --> 05:27:15.389
Dr. Bert Slade: and did it affect morbidity in in any substantial way? And it did not.

1929
05:27:15.430 --> 05:27:19.250
Dr. Bert Slade: I have an adverse effect on the patient to have those additional

1930
05:27:31.020 --> 05:27:37.580
Drew Kasper: okay? Do we have additional questions from the public or Cms. Adina? Please go ahead and unmute.

1931
05:27:38.240 --> 05:27:39.190
Adina Hersko: Thank you.

1932
05:27:39.200 --> 05:27:48.809

Adina Hersko: The sixty two percent recorded for a complete reception with the ovarian. Would that only the use of title? Or is that in the total of

1933
05:27:51.400 --> 05:27:54.010
Dr. Bert Slade: um that was only with sidelines?

1934
05:27:56.570 --> 05:28:04.729
Adina Hersko: Thank you. Can you also talk about how much more extra tissue was taken when you're in the sidelines. On average,

1935
05:28:06.020 --> 05:28:08.010
Dr. Bert Slade: I don't have the answer to that. But

1936
05:28:08.170 --> 05:28:09.240
you get a for you.

1937
05:28:10.570 --> 05:28:11.770
Adina Hersko: Thank you.

1938
05:28:20.490 --> 05:28:23.019
Jim Rollins: This is Jim Rowland's.

1939
05:28:24.250 --> 05:28:27.320
Jim Rollins: Can you please go ahead, Dr. Wrongs? Yes.

1940
05:28:27.330 --> 05:28:30.760
Jim Rollins: Can you explain why a false positive might occur?

1941
05:28:34.470 --> 05:28:36.450
Dr. Bert Slade: Um,

1942
05:28:36.820 --> 05:28:40.240
Dr. Bert Slade: you know One possibility is that macrophations

1943
05:28:40.410 --> 05:28:43.190
Dr. Bert Slade: um fully receptor beta,

1944

05:28:43.680 --> 05:28:47.179
and so they can't.

1945
05:28:49.180 --> 05:28:51.700
And

1946
05:28:53.230 --> 05:28:54.860
Dr. Bert Slade: if some,

1947
05:28:55.300 --> 05:28:57.379
Dr. Bert Slade: if there are enough of them to download,

1948
05:28:57.650 --> 05:29:01.160
Dr. Bert Slade: that would be a good thing, because if they are tumor invading macrophations,

1949
05:29:08.280 --> 05:29:10.300
Dr. Bert Slade: I tell you, when the cancer was gone.

1950
05:29:10.340 --> 05:29:13.489
Dr. Bert Slade: But you know other than that,

1951
05:29:14.690 --> 05:29:16.210
Dr. Bert Slade: i'll tell you

1952
05:29:16.260 --> 05:29:17.489
Dr. Bert Slade: what are the other tissues,

1953
05:29:24.010 --> 05:29:27.810
Dr. Bert Slade: you know, interoperatively.

1954
05:29:28.850 --> 05:29:32.130
Dr. Bert Slade: It may not always be quite so clear whether

1955
05:29:32.770 --> 05:29:33.990
false coloration is

1956
05:29:35.500 --> 05:29:38.550

Make you believe that, he said. You should take that tissue out,

1957
05:29:38.860 --> 05:29:40.290
Dr. Bert Slade: and so I think

1958
05:29:40.590 --> 05:29:44.319
Dr. Bert Slade: experience and practice. The false policy in the rate will certainly go down.

1959
05:29:46.300 --> 05:29:48.689
Dr. Michael Ebright: I I agree with that wholeheartedly. Yes,

1960
05:29:48.700 --> 05:30:13.300
Tim Biro, RPh: not. This is Timberl and i'm cheap oper an obst for Ontario laboratories. In the case of lung cancer surgery I can verify this. These patients are the known lung cancer, or are they suspicious for lung cancer? So there are cases where it's suspicious, based on Ct. And ah, if the doctor could not, the surgeon could not find it, which found on her side of lots. Only several of those lesions were not cancer.

1961
05:30:13.310 --> 05:30:19.159
Tim Biro, RPh: They were, you know, they could have been ground glass capacities or other small areas of interest, but

1962
05:30:19.770 --> 05:30:32.389
Tim Biro, RPh: did not have cancer in those cases. So that would be another source of the false positives, even though the side of it was exactly what it was meant to do which has helped to identify cancer. They might have missed otherwise, or even non-cancerization.

1963
05:30:32.420 --> 05:30:34.400
They're not. Only

1964
05:30:35.370 --> 05:30:37.150
Jim Rollins: thank you, Thank you.

1965
05:30:40.140 --> 05:30:45.420
Jim Rollins: One more question. And speaking of lymph nodes

1966

05:30:45.490 --> 05:30:51.630
Jim Rollins: during the examination, were there any left notes positive, based on ciderlux?

1967
05:30:52.070 --> 05:30:54.540
Dr. Michael Ebright: I can answer that in the long.

1968
05:30:54.550 --> 05:31:18.870
Dr. Michael Ebright: Um! So just for the same reasons, Dr. Slade. Ah, ah! Mentioned the lymph. Nodes can often light up. Ah, because there are macro pages in the lymphatic system. So it's. It's very clear to the thoracic surgeon where the lymph nodes lie, and where they don't in any of these receptions, it's standard of care to reset a generous amount of lymph nodes. So they're coming out, anyway, and they're all being evaluated.

1969
05:31:18.880 --> 05:31:35.960
Dr. Michael Ebright: That's part of the learning curve, as when you're looking at the lung of something within the long lights up we're much more concerned. But if something within a a regional dream lymphatic station lights up, we're less concerned. But those areas are coming out anyway. So it's less of a problem.

1970
05:31:36.790 --> 05:31:38.539
Jim Rollins: Thank you. Thank you.

1971
05:31:38.640 --> 05:31:45.679
Dr. Bert Slade: Covariant study there. There were a few links, those they were removed only because they were positive of satellites.

1972
05:31:46.880 --> 05:31:48.020
Jim Rollins: Thank you.

1973
05:31:53.140 --> 05:31:58.210
Drew Kasper: And I see Dean also has a hand up who i'm unmuted enough.

1974
05:31:59.180 --> 05:32:11.520
Adina Hersko: Thank you. Um. Going back to my question previously about the sixty two percent with complete reception, you had an answer that was just in the side of look. Were you able to determine how many had complete reflection without sidelines.

1975
05:32:13.990 --> 05:32:16.629
Dr. Bert Slade: I don't have that answer. Maybe

1976
05:32:19.820 --> 05:32:23.460
Tim Biro, RPh: no. We don't we don't have that information readily available.

1977
05:32:24.840 --> 05:32:34.150
Adina Hersko: Thank you Is there any longer-term data on the outcomes comparing Sedalu to no sidelock Or is that kind of

1978
05:32:34.180 --> 05:32:38.710
Adina Hersko: are you able to kind of demonstrate the change in outcomes

1979
05:32:38.930 --> 05:32:44.610
Adina Hersko: without side of locks, and how it might have changed. Having looked at it with the side of

1980
05:32:45.470 --> 05:32:55.100
Dr. Michael Ebright: we do not in lung cancer, it's it's very difficult to use the early endpoints and the studies, you know

1981
05:32:55.120 --> 05:32:59.400
Dr. Michael Ebright: not old enough to figure that out and wasn't powered for it. But

1982
05:32:59.900 --> 05:33:14.289
Dr. Michael Ebright: what we do know historically, is that leaving cancer behind is a bad thing, and we know that without the sidelux, in a good number patiently it was eight. We would have left cancer behind. How do we not use it?

1983
05:33:14.300 --> 05:33:15.990
Dr. Michael Ebright: Including one of my cases?

1984
05:33:19.910 --> 05:33:23.519
Adina Hersko: But the impact of that was not directly demonstrated. Is that right?

1985
05:33:23.600 --> 05:33:26.560
Dr. Michael Ebright: No, no, the study was not designed to look at that.

1986
05:33:27.140 --> 05:33:28.249
Thank you.

1987
05:33:38.130 --> 05:33:45.039
Drew Kasper: I don't see any questions in the intoat mailbox, or in the Q. And A.

1988
05:33:45.700 --> 05:33:47.420
Drew Kasper: Do we have any

1989
05:33:47.530 --> 05:33:51.179
Drew Kasper: additional questions from the public or Cms.

1990
05:33:59.060 --> 05:34:03.099
Drew Kasper: And Dr. Wrongs. I think your hands just up from the previous question. Is that right?

1991
05:34:06.360 --> 05:34:08.760
Jim Rollins: Yeah, I think That's from the previous question.

1992
05:34:09.550 --> 05:34:10.920
Drew Kasper: Okay, thanks.

1993
05:34:13.310 --> 05:34:15.450
Adina Hersko: One additional question.

1994
05:34:17.390 --> 05:34:18.980
Drew Kasper: Please proceed. Adena.

1995
05:34:20.210 --> 05:34:30.209
Adina Hersko: Um. One additional question without sidelock is the determination of clear surgical margins determined by pathology by local recurrence at follow-up, or both

1996

05:34:31.820 --> 05:34:32.970
Dr. Bert Slade: orthropology

1997
05:34:34.780 --> 05:34:36.140
Dr. Michael Ebright: by mythology.

1998
05:34:37.390 --> 05:34:41.159
Adina Hersko: Thank you. And how long was the follow up in the trial.

1999
05:34:44.320 --> 05:34:46.609
Dr. Michael Ebright: There were no survival studies done.

2000
05:34:47.070 --> 05:34:49.649
Dr. Bert Slade: Yeah, but they didn't incorporate long-term follow up.

2001
05:34:50.960 --> 05:34:53.400
Adina Hersko: So it was just that at the time of the surgery

2002
05:34:53.990 --> 05:34:54.790
Adina Hersko: right

2003
05:34:54.800 --> 05:35:02.040
Dr. Michael Ebright: looking at the difference between white light and sidelux, and looking at the the pathologic metrics.

2004
05:35:03.280 --> 05:35:06.530
But we have regarding margins in the lung study of the surgeon.

2005
05:35:07.120 --> 05:35:08.460
We removed

2006
05:35:08.760 --> 05:35:15.210
Dr. Bert Slade: you to a back table and illuminate it with the new infrared, and and measure the

2007
05:35:16.120 --> 05:35:18.820
the staple line to the edge of the fluorescence,

2008

05:35:19.420 --> 05:35:23.290
Dr. Bert Slade: allows them the opportunity to go back in and take for an issue of it

2009
05:35:24.020 --> 05:35:26.520
that the fluorescence was too close

2010
05:35:27.140 --> 05:35:28.480
than ten millimeters.

2011
05:35:31.300 --> 05:35:39.409
Dr. Michael Ebright: Just a quick correction to that. There was twenty eight. They follow up just for safety in the trial, but nothing for survival or recurrence

2012
05:35:41.690 --> 05:35:44.490
Adina Hersko: for for uh re operation for margin.

2013
05:35:44.500 --> 05:35:49.869
Dr. Michael Ebright: No, not for me. It was well, yes, exactly for any serious adverse events

2014
05:35:49.920 --> 05:35:53.360
Dr. Michael Ebright: based on the surgery or on the the infusion.

2015
05:36:00.170 --> 05:36:01.240
Thank you.

2016
05:36:08.800 --> 05:36:12.840
Drew Kasper: Okay. No new questions have come up in the Q. A.

2017
05:36:13.570 --> 05:36:17.469
Drew Kasper: No new questions have come up in the mailbox,

2018
05:36:18.250 --> 05:36:26.769
Drew Kasper: but we'll take a last call for questions. I don't see any hands at the moment, any last questions from the public or from Cms:

2019
05:36:31.530 --> 05:36:34.609

Drew Kasper: Okay, Great. Well, again, Thank you.

2020
05:36:35.150 --> 05:36:36.789
Dr. Michael Ebright: Thank you for the opportunity,

2021
05:36:38.590 --> 05:36:45.039
Drew Kasper: and we'll now hear from presenters for the Xeno View hyperpolarize Gen. On one hundred and twenty nine

2022
05:36:45.200 --> 05:36:49.720
Drew Kasper: technology application. You may now unmute your phones.

2023
05:36:50.650 --> 05:37:03.609
Dr. Bastiaan Driehuys: Okay, thank you very much for the opportunity to present Xeno view is a method of enabling Mri to be used to image pulmonary function three dimensionally and regionally. This patented agent

2024
05:37:03.620 --> 05:37:18.790
Dr. Bastiaan Driehuys: helps us identify treatment for diseases like idiopathic pulmonary fibrosis has unique sensitivity to abnormalities in long Covid and can quantify ventilation abnormalities in obstructive lung diseases. Next slide please

2025
05:37:20.560 --> 05:37:39.099
Dr. Bastiaan Driehuys: the fundamental technology platform is that with the conventional Mri scan. The addition of Xeno view allows patients to inhale the gas, and we are able to produce a three-dimensional image of the distribution of that gas in a ten second breathful without using ionizing radiation.

2026
05:37:39.130 --> 05:37:52.659
Dr. Bastiaan Driehuys: The technology is supported by positive results from two phase, three trials that were completed, and they are currently under review by Fda with action Expected December thirtieth of this year. Next slide, please.

2027
05:37:54.180 --> 05:37:59.950
Dr. Bastiaan Driehuys: The workflow, for Xeno view is depicted here. Xenon is a stable,

2028

05:37:59.960 --> 05:38:18.209
Dr. Bastiaan Driehuys: an inert gas isotope that comes from the atmosphere. It is activated by aligning the nuclear magnetic moments in the hyperpolarization system during dose production, and that is measured and dispensed into a dose delivery device that's highlighted in the blue Box. There

2029
05:38:18.220 --> 05:38:35.689
Dr. Bastiaan Driehuys: it's, then transported to the mri suite, where the patient has been positioned on the table in a radio frequency coil that can be used to detect Xenon signals. A very rapid scan is then acquired in the ten second breathful, and it can be interpreted by just radiologists.

2030
05:38:35.700 --> 05:38:39.239
Dr. Bastiaan Driehuys: Xeno View is considered a new chemical entity.

2031
05:38:39.570 --> 05:38:41.450
Dr. Bastiaan Driehuys: Next slide, please,

2032
05:38:42.790 --> 05:38:51.269
Dr. Bastiaan Driehuys: as compared to other means of evaluating lung function. You're of course, aware that conventional lung function, testing such as spirometry

2033
05:38:51.280 --> 05:39:10.359
Dr. Bastiaan Driehuys: is not able to visualize function regionally is relatively effort-dependent and therefore relatively insensitive function is possible to image spatially, using gamma centigraphy. But this is a low resolution scan that takes a long time to acquire and administers radiation.

2034
05:39:10.370 --> 05:39:26.670
Dr. Bastiaan Driehuys: Ct, Scanning, of course, does an exquisite job of imaging long anatomy, but not function. It delivers ionizing radiation. Xenon and Mri, as you can see, overcomes each of these obstacles by achieving functional imaging

2035
05:39:26.680 --> 05:39:30.479
Dr. Bastiaan Driehuys: without ionizing radiation and effort. Dependence Next slide please.

2036

05:39:32.620 --> 05:40:02.030
Dr. Bastiaan Driehuys: A particularly unique aspect of Xenon that we'll highlight in this presentation is that when it is inhaled, it enters the album and airspace. It fuses freely across the blood gas barrier and into the pulmonary capillary red blood cells. In each of these three compartments the Xenon can be imaged and distinguished separately from the others, and what that lets us do is essentially decompose each of the aspects of pulmonary gas exchange that are conventionally measured by

2037
05:40:02.040 --> 05:40:19.480
Dr. Bastiaan Driehuys: the diffusing capacity of carbon monoxide dlco But of course, we're able to resolve it three-dimensional and identify the contributions of each of these compartments to pathophysiology, and the next slide I'll ask my colleague, Joe Monopoly, to walk you through. What these images look like,

2038
05:40:20.230 --> 05:40:38.049
Dr. Joe Mammarappallil: hey? Everyone! Thank you for the opportunity to present I'm. Just radiologists at Duke and I'm going to talk to you about the diverse cardiaculary. Some of the signatures we see with different type of diseases in the long, so i'll draw your attention to the left, where you're looking at your healthy patient with the three different signatures that we

2039
05:40:38.180 --> 05:40:47.230
Dr. Joe Mammarappallil: just talked about. We're able to actually image the gas in a ventilatory aspect that you can see here in our healthy

2040
05:40:47.360 --> 05:41:09.770
Dr. Joe Mammarappallil: controlled here. What are the healthy appearances indicated by the green. We can also in, as it transits from the airspaces to the membrane tissue, and this is a normal appearance here to the left, with our normal patient, with our green barrier tissue signal there, and ultimately we can see the gas being imaged in a gas exchange transit to the Rbc. In an old patient we have normally

2041
05:41:09.780 --> 05:41:15.610
Dr. Joe Mammarappallil: transferred to the Rbc. Indicated by Green. So we have some specific signatures with our three different.

2042
05:41:15.620 --> 05:41:45.170

Dr. Joe Mammarappallil: So we're showing you here, and the first one i'll draw your attention to is our Co. Pd. Group. So what do we see with specific types of beta type with Cpd. Obviously ventilation defects, and you can see that indicating here by a decrease in multifocal areas of red. Seeing here with coronal imaging here we indicate a defect percentage of ventilation of fifty six percent. Now, we're going to move to a signature which I love to talk about, which is our Ips

2043
05:41:45.180 --> 05:41:46.090
patient.

2044
05:41:46.360 --> 05:42:07.279
Dr. Joe Mammarappallil: And what is the classic we willow, we see with a lot of I Pm. Patients. Well, in most patients. I draw your attention here to the barrier tissue and a lot of those patients with the stick in areas of fibrootic membrane. What we see is an elevated barrier signal, and you can see in this situation, in this particular patient in eighty to seven percent

2045
05:42:07.290 --> 05:42:25.889
Dr. Joe Mammarappallil: high barrier percentage. And then ultimately, as we talked about, we can image gas exchange where we're imaging the gas. All that we get all the way to the Rbc. And i'll draw your attention to the third column, where we're looking at pulmonary or hypertension. We've imagined many groups of image, these patients, and what we see here is a low

2046
05:42:25.900 --> 05:42:40.849
Dr. Joe Mammarappallil: transition to the Rbc. We're, indicating here for forty-seven percent, and that's indicated where we saw green with our healthy patient. We have got decreased areas of Rbc. Transfer, particularly here at the lung basis and the next slide, please.

2047
05:42:42.700 --> 05:42:48.910
Dr. Joe Mammarappallil: So some examples of the clinical applications of hyper polarizing on Mri

2048
05:42:49.110 --> 05:43:02.040
Dr. Joe Mammarappallil: to draw your attention here to the left, looking at this patient with asthma and the tier on the left lower lobe here in criminal imaging. And if we look at the pre treatment image, you can see that there's a ventilation team

2049
05:43:02.050 --> 05:43:19.470
Dr. Joe Mammarappallil: ventilation, percentage defects here indicated by ten percent most notable here at the lung bases And this is pre-treatment. Now, post treatment you can see that this area almost completely resolves, and that Bdp percentage has dropped as well. So a nice way to see how post biologic, positive response in an asthma patient.

2050
05:43:19.480 --> 05:43:35.780
Dr. Joe Mammarappallil: Another thing we're really excited about is looking at barrier tissue particularly. We talked about it with our pulmonary fibrosis patients. And if you look at this pulmonary Fibrosis patient. This is now just barriers. That was ventilation that we looked at with the asthma patient

2051
05:43:35.790 --> 05:43:55.789
Dr. Joe Mammarappallil: the various signal in this patient pre-treatment is elevated indicated by the purple, and we can see post-treatment scans. That That barrier tissue is actually we think shrunk in because the gas is now no longer elevated in this area of tissue. Another aspect we're really excited about as well, which is Rbc. Transfer defects. And you can see that nicely evidenced here

2052
05:43:55.800 --> 05:43:58.490
Dr. Joe Mammarappallil: by this long haul Kovat patients, which we'll get into

2053
05:43:58.500 --> 05:43:59.810
Allison Pompey: three minutes.

2054
05:44:00.010 --> 05:44:05.569
Dr. Joe Mammarappallil: You can see normal patient here, and our abnormal Covid patient here. Next slide.

2055
05:44:07.470 --> 05:44:14.259
Dr. Joe Mammarappallil: Also, there is we all focus on Ct: If you look at this Ct image here, what can we see with with

2056
05:44:14.270 --> 05:44:33.970
Dr. Joe Mammarappallil: with hyperpolarized Gen. On imaging? Well, we can see abnormalities that we wouldn't see in Ct. And if you look at the the bottom image, this patient's relatively neural normal, there

is some permanent fibrosis going on. But i'll draw your attention to the barrier tissue. Much more abnormal, very tissue than we would see with abnormalities in Ct. Next slide, and i'll hear this off.

2057
05:44:37.050 --> 05:45:07.040
Dr. Chase S. Hall: I get up here and Chase Hall here. Hominologist, University of Kansas, one of the most uh unique things that we're seeing in interstitial Lyme disease is that this Um, as previously alluded to, a barrier signal is elevated in the setting interstitial lung disease, and we're seeing this in all sorts of interstitial lung disease, where it's ipf or nsip um. But what the remarkable feature about it is that it signifies um long tissue that is, at risk of progression. Um! And here you can see that we can actually, on an individual patients, see

2058
05:45:07.050 --> 05:45:36.539
Dr. Chase S. Hall: the the change in the barrier signal after only three months of treatment with op-ed Um! If you think about the clinical trials. Looking at Opec to see a response, it's taken hundreds of patients over a year to demonstrate a change in course vital capacity, which is our typical um endpoint in clinical trials. But here you can see that there, within three months in an individual patient, we can see response to treatment, and then, when the treatment is withdrawn, you can also see that that barrier signal begins to increase again over time. Next to our next step

2059
05:45:36.550 --> 05:45:37.760
side, please

2060
05:45:39.430 --> 05:46:05.699
Dr. Chase S. Hall: in this study here. Um! Ah, that was performed. Looking at ipf patients, they compared um progressors to non-progressors. So the definition of progressors was a decline in forced by a capacity of ten percent or greater over a year or a Dlco decline of fifteen percent over a year or ah transitioned into the life, care of death. And what was unique about this was that

2061
05:46:05.710 --> 05:46:33.749
Dr. Chase S. Hall: Ct. Imaging areas of fibrosis? Obviously, if there's more fibrosis that can predict that progression. But what was interesting here was that in areas where there was not progression or ah fibrosis on Ct. Imaging. But yet there was a low Rvc. To barrier, meaning that the Xenon was not getting to the Rvcs, or was increased in the barrier. These were the patients that demonstrated progression. So you could predict who was going to have decline at one year's time

based on this imaging signal. Next slide

2062
05:46:36.440 --> 05:46:39.240
Dr. Chase S. Hall: i'll pass off to Dr. Gleason.

2063
05:46:47.240 --> 05:46:53.689
Dr. Chase S. Hall: You may be inadvertently in the attendee room, so he looks to be trapped in the attendees room.

2064
05:46:53.700 --> 05:47:16.629
Dr. Chase S. Hall: What would you like to finish it off? Yeah, I can go ahead and talk about these slides here. So um one of the uh newest problems, obviously that um pulmonologists, and everyone has really been seeing in the clinical world. Here is this long Covid. So patients who are having uh persistent symptoms after a a diagnosis of Covid Um, and finding out what is causing those symptoms, has been quite challenging.

2065
05:47:16.640 --> 05:47:21.290
Dr. Chase S. Hall: Um! So we've often obtained Pfts echo.

2066
05:47:21.300 --> 05:47:47.370
Dr. Chase S. Hall: I I think I can speak now so oh, perfect! So i'm sorry about that folks. Clinton here in Austin, in my attic in North Oxford. We know that we know that Covid is a big problem. Long Covid affects about two hundred thousand people in the Uk. And probably about eighteen million in the States. They have normal lung function, normal Ct: but a shorter breath. And what we've shown in a couple of hundred patients is that Zen, or despite

2067
05:47:47.380 --> 05:48:16.159
FERGUS gleeson: having normal cts, can identify patients who have abnormal abnormalities within their lungs, functional abnormalities, and in a study with a couple of hundred patients. We've shown that that persists in around about half of the patients, one to two years after they have had their covid inflation, we can separate them out from those that are disnick. But don't have functional lung damage from those using Xenon,

2068
05:48:16.170 --> 05:48:24.989
FERGUS gleeson: and we're repeating them at three, six and twelve months, and we've shown that a significant proportion about half of those patients Don't, get better. So

2069
05:48:25.000 --> 05:48:40.350
FERGUS gleeson: at the moment it looks like Xenon is the only way of actually identifying an abnormality of patients with Long Covid cannot be seen in any other, any other form of imaging or testing next slide, please.

2070
05:48:41.580 --> 05:48:54.150
FERGUS gleeson: And What this study shows is that we've identified where it's. Actually I'm. I'm. I'm sorry we we gave you an extra minute here, because the second launch is always few, but we do need to keep to

2071
05:48:54.250 --> 05:48:58.400
Drew Kasper: for ten minutes to be fair to all other presenters.

2072
05:48:59.930 --> 05:49:04.160
Drew Kasper: So if you have just a sentence and closing it. That would be helpful.

2073
05:49:04.170 --> 05:49:18.739
Dr. Bastiaan Driehuys: Okay. So, Bastion, I'll hand back to you back to you to close if I made him. Thank you, Fergus. No, thank you. All for the opportunity, and you can have a look at this data. But we understand we've gone over time. So happy to answer questions.

2074
05:49:21.040 --> 05:49:27.259
Drew Kasper: Okay, and thanks very much for your presentation. Are there any questions from the public or from Cms?

2075
05:49:28.530 --> 05:49:31.230
Start with Lily. Go ahead and on, mute, please, Lily.

2076
05:49:31.650 --> 05:49:45.969
Lily Yuan: This is clearly for Cms. May you discuss how the use of Zemo view, such as the visualized therapy response, or to identify gas sheet exchange abnormalities that are undetectable with Ct. Has effective management of patients.

2077
05:49:47.790 --> 05:49:50.790
Dr. Bastiaan Driehuys: Can I ask Dr. Gleason to comment on that?

2078
05:49:50.800 --> 05:50:02.100
FERGUS gleeson: Thanks, bass. So the answer is at the moment it hasn't, because we have to confirm, as we are confirming that it's a real finding, and then

2079
05:50:02.110 --> 05:50:15.520
FERGUS gleeson: the patients that there is no proven therapy for long, Covid Yet so what you need to do is establish that you can identify an abnormality and then trial different therapies to see if they are work.

2080
05:50:15.530 --> 05:50:23.689
FERGUS gleeson: So at the moment there isn't a proven therapy, so we can't confirm that Xenon will identify that it is working,

2081
05:50:32.350 --> 05:50:37.030
Drew Kasper: and Dr. Jim Rollins, please go ahead and unmute.

2082
05:50:37.380 --> 05:50:54.420
Jim Rollins: Yes, thanks. Um. If you have a patient population that has ads and a Copd cystic fibrosis as well as idiopathic pulmonary fibrosis Can this technology differentiate between all four of them. I know you showed a previous slide,

2083
05:50:54.430 --> 05:51:01.490
Jim Rollins: which seemed to indicate things was sort of different. But can you differentiate? Especially if I know it's impossible.

2084
05:51:01.500 --> 05:51:11.410
Jim Rollins: If it were to occur in a single patient, would you be able to tell which of those diseases are present?

2085
05:51:11.770 --> 05:51:14.630
Dr. Bastiaan Driehuys: I'm going to ask Dr. Hall to take that one.

2086
05:51:15.600 --> 05:51:44.800
Dr. Chase S. Hall: Oh, I was hoping you. And it's now to yeah, he's being bashful. But uh, actually they've kind of developed an algorithm that looks at these different signatures from from Xenon. So, looking at the ventilation, um barrier or membrane uptake and um Rvc. Uptake

as well as something, we didn't talk about looking at um the red blood cell oscillations, and can actually look at that imaging profile, and independent of knowing anything about the patient.

2087
05:51:44.810 --> 05:52:14.269
Dr. Chase S. Hall: Um, take a pretty good guess at what the disease is that's causing them So for um many of these diseases, it's it's pretty easy to separate out, so you know. Uh, say, asthma compared to Ipf. You can absolutely tell the difference based on Xenon imaging, because the imaging profiles are so different. Um Ipf patients will not have a lot of ventilation abnormalities, although they'll have this elevated barrier signal as well as reduced. Rvc. Uptake, whereas the asthma patients are going to

2088
05:52:14.280 --> 05:52:39.820
Dr. Chase S. Hall: have the ventilation. Defects. But otherwise we'll have, you know, preserved um gas exchange um metrics. Um! It could get a little bit more complicated in Co. Pd. And asthma. However, again you'll be able to see those Rbc. Uh. Defects are going to be much higher uh in the Covid patient. So yes, you can tell the difference. If you were in a in a vacuum, and didn't have any other clinical information the difference between these diseases.

2089
05:52:43.290 --> 05:52:44.429
Thank you.

2090
05:52:50.230 --> 05:52:54.209
Drew Kasper: We We have a question from Medina herscow. You go ahead and unmute.

2091
05:52:54.830 --> 05:53:06.080
Adina Hersko: Thank you. It sounds like you were mostly referring to in the the case of Long Covid before, when you're talking about change of management. Has there been any studies showing a change of management, and the other disease that you're talking about

2092
05:53:06.390 --> 05:53:08.329
Adina Hersko: for any change in outcome?

2093
05:53:10.610 --> 05:53:17.190
Dr. Bastiaan Driehuys: It's early days for those chase. Are you? Are you willing to take a stab at that one as well?

2094
05:53:17.200 --> 05:53:40.379
Dr. Chase S. Hall: Yeah, I mean, i'll definitely I can give an example where it was. Um absolutely change management, although it's just not been uh studied yet. So in the case of I showed you the study looking at Ipf showing progression of Ipf. Um. You know it's fairly standard that most patients wants to diagnose with Ipf for being placed on an antibiotic treatment. What's not so clear is

2095
05:53:40.390 --> 05:54:05.930
Dr. Chase S. Hall: patients with interstitial lung abnormalities. So these early changes that are um increasingly being seen on Ct. Scan, where a subset of those patients are going to progress into a full-fledged and interstitial lung disease. That's going to be progressive in identifying who would benefit from early treatment, and that situation is challenging at this point in time, uh which requires frequent follow up in the clinic with tfts and

2096
05:54:06.020 --> 05:54:07.890
Dr. Chase S. Hall: Ct scans and um.

2097
05:54:07.900 --> 05:54:23.250
Dr. Chase S. Hall: So in that regards, if we had an imaging modality that can show. Who's more likely to progress? Um, Then that makes it much easier to decide who we're going to treat early before the disease is already progressed in the full, full-fledged dial. D

2098
05:54:24.050 --> 05:54:29.290
Dr. Bastiaan Driehuys: That question may I add for long of hope? It please do. Yes,

2099
05:54:29.300 --> 05:54:32.250
FERGUS gleeson: thank you just to say, although we haven't altered

2100
05:54:32.260 --> 05:54:58.720
FERGUS gleeson: um in terms of new treatments. When the patients are referred to us, and their lungs are entirely normal. On Xenon and on Ct. And on lung function. They then get um sent to um the physiotherapist for um treatment of what's called breathing passion disorders, so it doesn't lead to a drug, though it does lead to reassurance of patients and concentrating on helping them get getting back to the

2101

05:54:59.330 --> 05:55:00.450
FERGUS gleeson: Thank you.

2102
05:55:03.190 --> 05:55:06.190
Dr. Bastiaan Driehuys: Thank you and commute. Sorry. Go ahead.

2103
05:55:06.200 --> 05:55:08.440
Dr. Bastiaan Driehuys: No, go ahead. I'm sorry, please.

2104
05:55:09.290 --> 05:55:25.460
Adina Hersko: Um, I had just one more question. Um! Would this be used when When exactly would this be use? Would it be um when a follow up for a patient that has a known disease. But no currents have done, or to diagnose something

2105
05:55:25.560 --> 05:55:27.150
Adina Hersko: for the first time.

2106
05:55:33.970 --> 05:55:37.259
Dr. Bastiaan Driehuys: Right, Fergus, would you. Would you take that one?

2107
05:55:37.880 --> 05:55:53.149
FERGUS gleeson: Well, in in Long Covid? We we we do it. When the patients have got a normal Ct: normal lung function, We're doing it as part of the study. But that's when we're doing it in in Long Covid. In that patient,

2108
05:55:53.190 --> 05:55:58.950
FERGUS gleeson: you know clinical practice. But now we've converted into a trial practice to confirm our findings,

2109
05:55:59.220 --> 05:56:01.600
Dr. Bastiaan Driehuys: and and maybe Dr. Hall can.

2110
05:56:01.610 --> 05:56:30.650
Dr. Chase S. Hall: I would like to take a stab at this as well. So this is pretty versatile, I mean, when we're going to use it, It's going to be on the situation. So um a lot of diseases we're not going to be using this necessarily to make the diagnosis right? A lot of diseases can be made. Um diagnoses can be made based on the clinical

history, and maybe spirometry um, and Ct. Scan is is definitely not going anywhere. Um. So a lot of diagnoses are going to made in that regards, however,

2111
05:56:30.660 --> 05:57:00.540
Dr. Chase S. Hall: um treatment decisions, as I mentioned with ilas or interstitial lyme disease, for that matter. Um is Ah, it's an extremely evolving field, whether to use immunosuppressants or antibiotics patients need escalation of therapy. Um, seeing areas that are at risk would be very helpful in making that decision. And as of right now, we have no way to know for our patients to know if they're responding to treatment. So you start a preach on the antibiotic. All you can tell them is that yes, you're going to have symptoms of side effects. Your lung function is still going to decline, but

2112
05:57:00.550 --> 05:57:09.239
Dr. Chase S. Hall: the study suggests that you're declining slower than you would if you're not on this treatment. Here we have a way to actual visualize response to therapy.

2113
05:57:09.250 --> 05:57:38.249
Dr. Chase S. Hall: The other thing is, um. There are other situations, interstitial lung disease where this may be helpful in diagnosing, so we're currently undergoing a study. Um in school or derma, so patients are younger. Um, they're getting frequent ct scans um to screen for interstitial one disease at an early stage. Um, And we're doing a study using this to actually diagnose um interstitial one disease at an early stage without ionizing mediation, so that they can get repeated studies over time

2114
05:57:38.260 --> 05:57:44.850
Dr. Chase S. Hall: without having concerns about long-term issues from the ct scans, since it's beginning at such an early age.

2115
05:57:48.820 --> 05:57:51.070
Drew Kasper: Now. Um I see. Uh,

2116
05:57:51.080 --> 05:58:02.890
Drew Kasper: Dr. Ron and the Adena Hesco. Both have had hands up there. If either of you have something follow on to um to to this. But let's do that first before any new questions.

2117
05:58:02.900 --> 05:58:04.590

Yes, this is Jim. Um.

2118
05:58:04.600 --> 05:58:11.200
Jim Rollins: Would this test ever be used as a screening test in patients who had had previous lung transplants.

2119
05:58:14.620 --> 05:58:33.330
Dr. Bastiaan Driehuys: That's an excellent question. We we have a study ongoing at following patients with lung transplants, and that's in its early stages, but we're able to see abnormalities quite early on, really much before spirometric decreases

2120
05:58:33.370 --> 05:58:46.759
Dr. Bastiaan Driehuys: currently used. So we're in the process of looking at outcomes on those patients. But yes, certainly we are able to see abnormalities Actually, in all three of these compartments in patients who have undergone lyme transplant.

2121
05:58:50.870 --> 05:58:53.039
Jim Rollins: Thank you. Thank you.

2122
05:58:56.380 --> 05:58:59.369
Drew Kasper: Are there any other questions from the public or thems?

2123
05:59:03.580 --> 05:59:13.599
Drew Kasper: And taking one last look at our antenna mailbox? There are no new questions. There are no questions in the Q. And A. And there are no new raised hands.

2124
05:59:14.150 --> 05:59:18.460
Drew Kasper: Okay. So with that, thank you again for your presentation.

2125
05:59:18.950 --> 05:59:21.080
Dr. Bastiaan Driehuys: Thank you for the opportunity. I'm.

2126
05:59:22.640 --> 05:59:43.460
FERGUS gleeson: And as a reminder for cms of consideration in the Ips proposed rule, public comments must be submitted to Pms. In writing via comments via email Excuse me to New Tech at Cms. Dot hs I go at N. E. W. T. V. C. H. C. Ms. Dot H. S. Gov.

2127
05:59:43.470 --> 05:59:50.329
Drew Kasper: With the subject line Town Hall comment, and then we'd appreciate it If you'd insert the technology name that it pertains to.

2128
05:59:50.340 --> 06:00:03.970
Drew Kasper: All comments must be received by five Pm Eastern standards time on Thursday, December twenty second, two thousand and twenty two. So even if you raised a verbal comment during the Channel today, you must send the written comment to ensure a consideration in the post rule.

2129
06:00:04.070 --> 06:00:16.930
Drew Kasper: We'd also appreciate any feedback on the Town Hall, whether it's about what you think worked well or what didn't work well or how we might improve the process. We welcome any input that you have about the Town Hall sincerely.

2130
06:00:16.940 --> 06:00:26.859
Drew Kasper: So any feedback can be sent to us via email as well at that new tech and a Pms. Ah, ehs gov email box with the subject line Town Hall.

2131
06:00:28.390 --> 06:00:33.570
Drew Kasper: Thanks again to all the presenters all the panelists and all the attendees,

2132
06:00:34.390 --> 06:00:38.099
Drew Kasper: and concludes our day's, events, happy holidays to you all.

2133
06:00:38.500 --> 06:00:40.599
Allison Pompey: Thank you, Drew. Good job.