NUSURFACE®

ICD-10-PCS Code Request Meniscus Replacement with the NUsurface® Synthetic Meniscus Implant

ICD-10-PCS C&M Meeting – Sept. 14, 2021

Clinical Presenter: Wayne Gersoff, MD, Orthopedic Surgery and Sports Medicine
Advanced Orthopedics & Sports Medicine Specialists, Denver, CO

- **NUsurface SUN Clinical Trial Investigator**
- **Medical Education Consultant – *Active Implants, LLC***

Clinical Presenter: Tom Carter, MD, Orthopedic Surgery and Sports Medicine
Banner University, Professor of Orthopedic Surgery, Phoenix, AZ

- **NUsurface SUN Clinical Trial Investigator**
- **Medical Education Consultant – *Active Implants, LLC***

Company Representative: Erik Harris, MHA, VP Global Market Access & Reimbursement
Active Implants, LLC

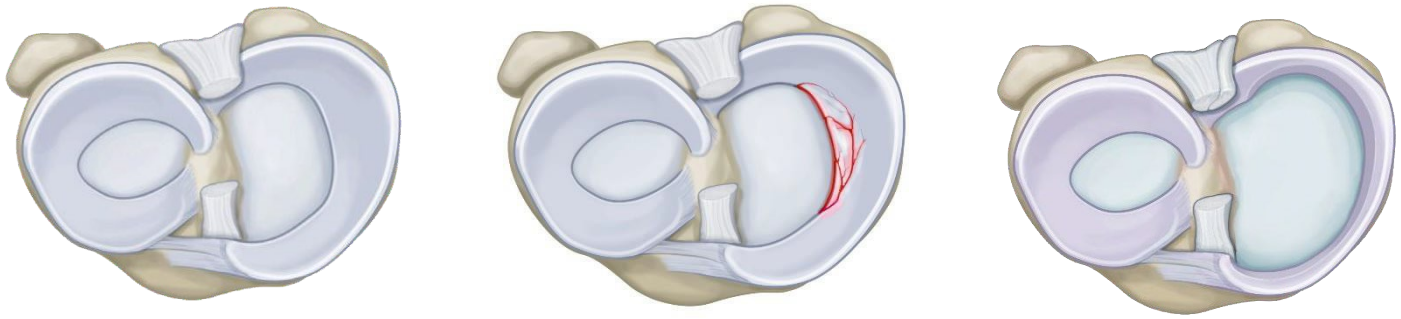
ACTIVE IMPLANTS®

Overview of the Meniscus, Incidence of Injury and Outcomes

- The **meniscus protects the knee by distributing loads** from the femoral condyles to the tibial plateau, absorbing shock during motion, and reducing friction between the articulating bones[1]
- **Meniscus tears** can result at any time from excessive forces caused by **knee trauma** *(acute tears are more common in the 20s-30s age bands)*, or the result of natural, **age-related degeneration**, **resulting in meniscus dysfunction** *(degenerative tears are more common in the 40s-60s age bands)*[2]
  - ❖ *Medial meniscus tears are up to 5x more frequent than lateral meniscus tears*[3]
- **Over 760,000 partial meniscectomies are performed each year**, making it the most common surgical treatment for meniscus-related knee pain and/or loss of knee function[4]
- **25% of patients (190,000)** treated with partial meniscectomy have **persistent symptoms within 2 years after surgery**, and 40% (304,000) within 10-15 years[5-8]
  - ❖ *Partial meniscectomy patients have a 10x higher likelihood for a knee replacement*[9]
- **Non-surgical treatments** of meniscus dysfunction **are ineffective** in the long-term, do not maintain efficacy over repeated procedures, and **do not address the underlying disease state**[10-12]

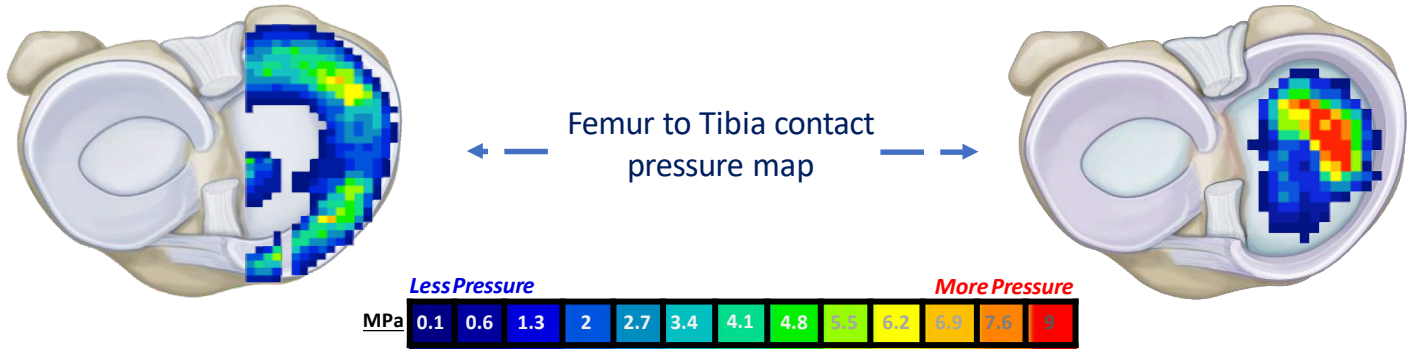
A Damaged / Dysfunctional Meniscus Leads to Increased Femur to Tibia Load Concentration and Eventual Cartilage Loss and Pain

Intact Meniscus | **Torn Meniscus** | **Post Meniscectomy**



Intact Meniscus Pressure Distribution[13]

Concentrated Focal Pressure Distribution[13]



- Partial Meniscectomy Increases Risk of Knee Replacement by **more than 10 times**[9]
- Younger Patient Age for Meniscectomy Increases Risk of Knee Replacement **by Nearly 40 Times**[5-8]
- In a British longitudinal study, by 15 years After Meniscectomy **13.5% of Patients Had Knee Replacements**[14]

Meniscus Dysfunction – Current Treatment Options

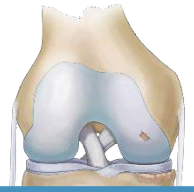
There is a substantial unmet need for a product that can **reduce pain** and **enable function**, thereby bridging the many years between meniscectomy/repair and eventual knee replacement

Increasing Invasiveness of Treatment Options

> 15M Patients/yr

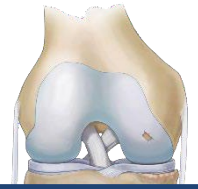
Non-Surgical Interventions

- Physical Therapy
- Weight Loss
- Activity Modification
- Pain Medications
- Unloader Bracing



> 5M Patients/yr

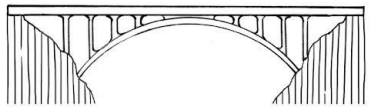
- Corticosteroid Injections
- Hyaluronic Acid Injections

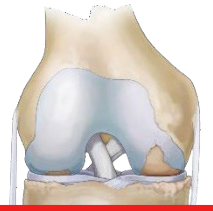


> 1M Patients/yr

- Meniscal Repair
- Meniscectomy
- Meniscus Scaffold
- Meniscus Allograft
- Cartilage Repair
- High Tibial Osteotomy

"Treatment Gap"





> 700K Patients/yr

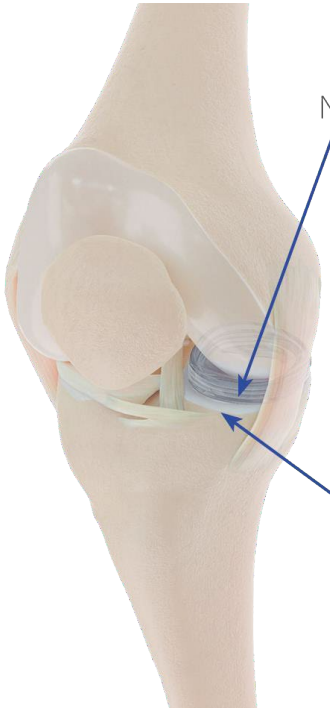
Unicompartmental and Total Knee Replacement

**NUsurface® and Control clinical trial subjects must have failed 1 or more previous meniscectomy(ies) > 6 months prior to enrollment*

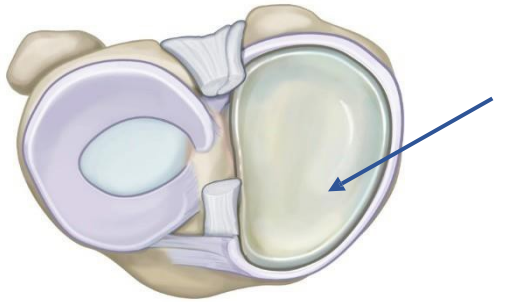
The NUsurface® Meniscus Implant was clinically studied to treat patient pain and function in the "gap" between current meniscus surgical treatment* and an irreversible knee joint replacement

How Does the NUsurface® Implant Work

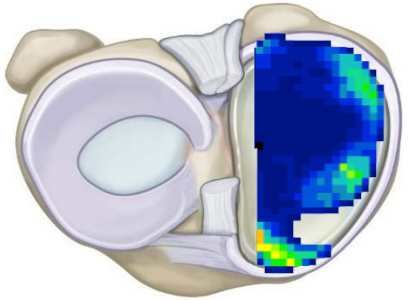
*



Mechanism of Action



NUsurface® Restores Knee Pressure Distribution Similar to an Intact, Articulating Meniscus[13, 15]



***NUsurface® manufactured in 7 sizes in Left and Right configurations**

(Note: final number of sizes TBD per FDA market authorization)

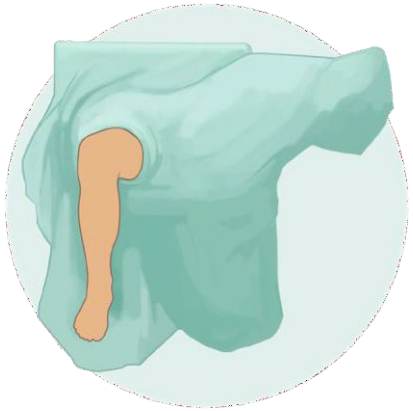
Surgical Technique – ***SIMPLIFIED*** Procedure Overview

Vignette and Procedure Fully Described in the Submitted ICD-10-PCS Code Request

- Pre-operative sizing via MRI assessment *(uses existing patient diagnostic MRI)*
- **Procedure may be completed in approximately 1-1.5 hours** *(per surgeon experience and case complexity)*
- 6 Week Rehab program, weightbearing same day

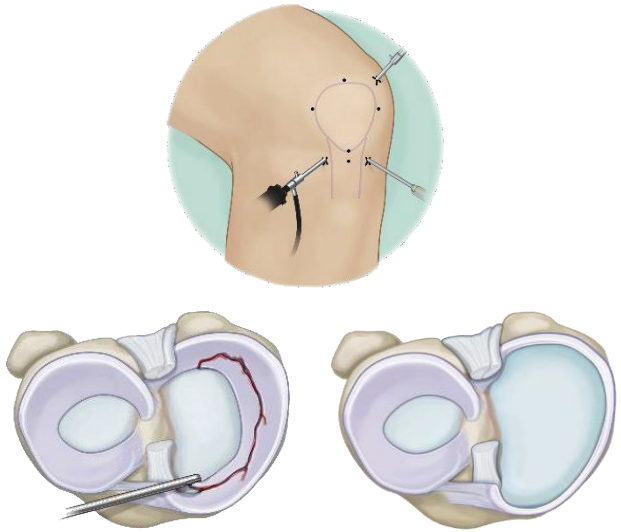
1

Prep & Drape for Procedure



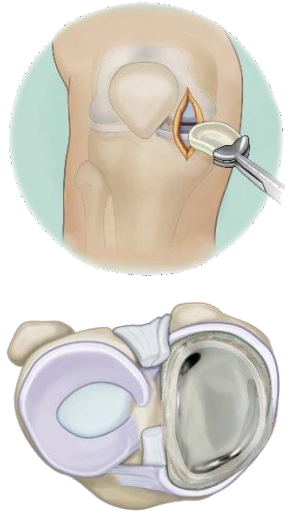
2

Arthroscopic Assisted Joint Preparation



3

Open Arthrotomy NUsurface® Implantation



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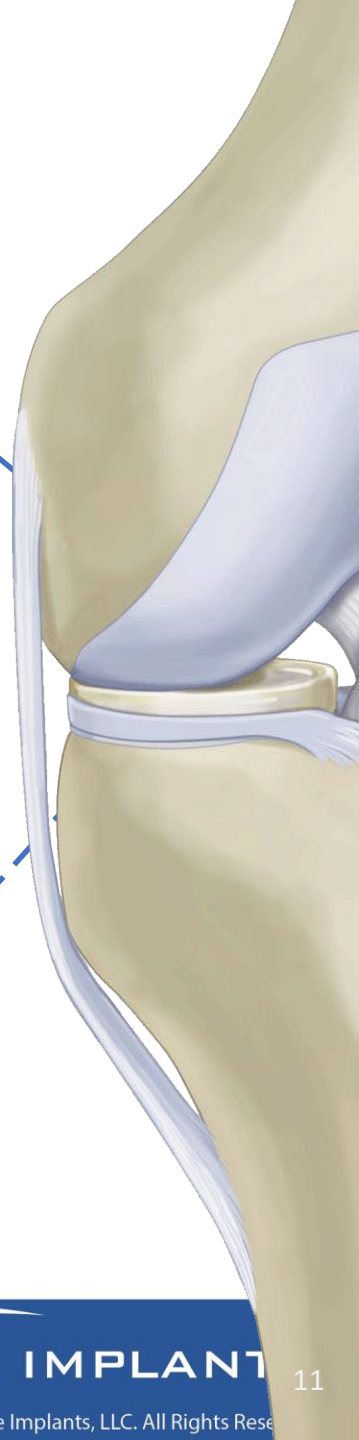
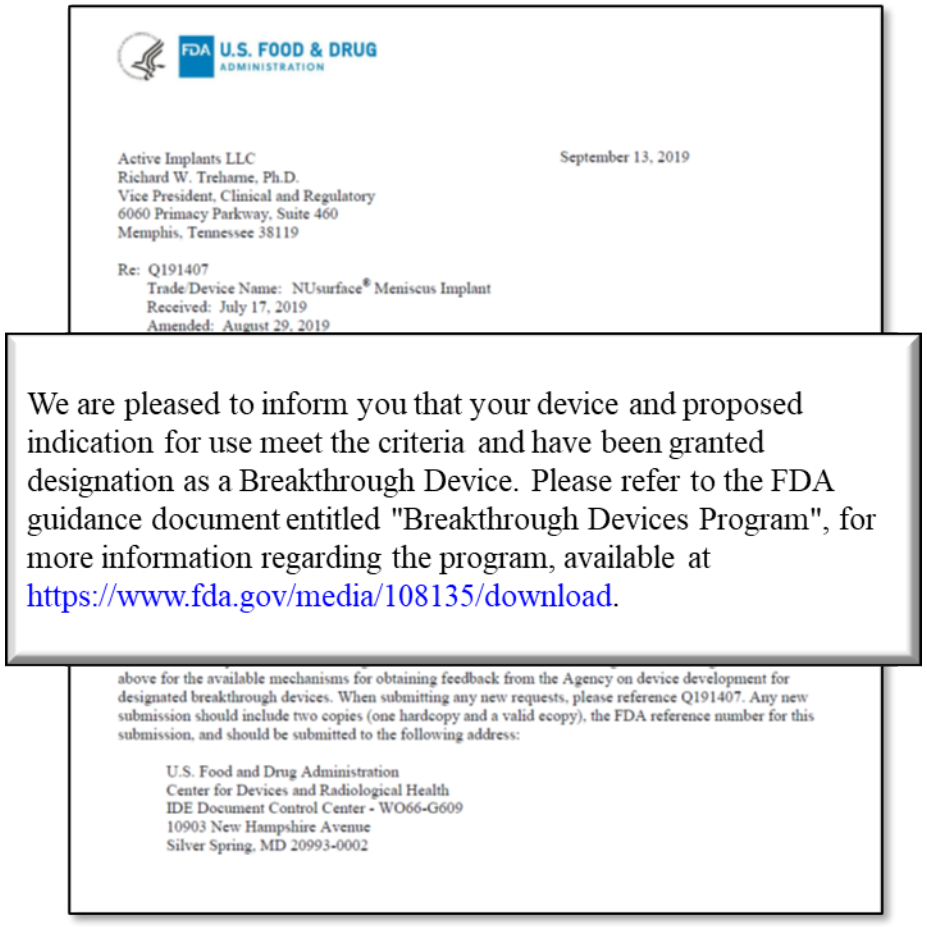
NUsurface® Final Position



- **242 Subject MERCURY Clinical Dataset** is currently Under FDA De Novo 510(k) Evaluation comprising:
  - ✓**VENUS**[16] **= 127 Subject** Randomized Clinical Trial NUsurface (N=61) to Non-Surgical Controls (N=66)
  - ✓**SUN**[17] **= 115 Subject** Prospective Longitudinal Single-Arm Interventional Trial
- Endpoints for **KOOS Pain** and **KOOS Overall** of **20-point improvement at 24 months**
  - ❖ Inclusion/Exclusion criteria identified in the ICD-10-PCS code request
- **FDA Breakthrough Device** Designation – Sept. 13, 2019



U.S. FOOD & DRUG ADMINISTRATION

Active Implants LLC
Richard W. Treharne, Ph.D.
Vice President, Clinical and Regulatory
6060 Primacy Parkway, Suite 460
Memphis, Tennessee 38119

September 13, 2019

Re: Q191407
Trade/Device Name: NUsurface® Meniscus Implant
Received: July 17, 2019
Amended: August 29, 2019

We are pleased to inform you that your device and proposed indication for use meet the criteria and have been granted designation as a Breakthrough Device. Please refer to the FDA guidance document entitled "Breakthrough Devices Program", for more information regarding the program, available at https://www.fda.gov/media/108135/download.

above for the available mechanisms for obtaining feedback from the Agency on device development for designated breakthrough devices. When submitting any new requests, please reference Q191407. Any new submission should include two copies (one hardcopy and a valid ecopy), the FDA reference number for this submission, and should be submitted to the following address:

U.S. Food and Drug Administration
Center for Devices and Radiological Health
IDE Document Control Center - WO66-G609
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002

MERCURY = VENUS RCT + SUN Single-Arm Across 23 Clinical Trial Sites

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Maxwell Alley, MD (Capital Region Orthopedics – Albany, NY)
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William Garrett, MD (Duke University MC – Raleigh, NC)
Thomas Giel, MD (OrthoMemphis – Memphis, TN)
Andreas Gomoll, MD (Hospital for Special Surgery, New York, NY)
Elliott Hershman, MD (North Shore LIJ, Lenox Hill Hospital – New York, NY)
Randall Holcomb, MD (OrthoMemphis – Memphis, TN)
Christopher Kaeding, MD (Wexner Medical Center, OSU – Columbus, OH)
Christian Lattermann, MD (Brigham and Women's Hospital – Boston, MA)
Brian McKeon, MD (New England Baptist Hospital – Boston, MA)
Claude Moorman, MD (Duke University MC – Raleigh, NC)
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Deryk Jones, MD (Ochsner Sports Medicine – New Orleans, LA)
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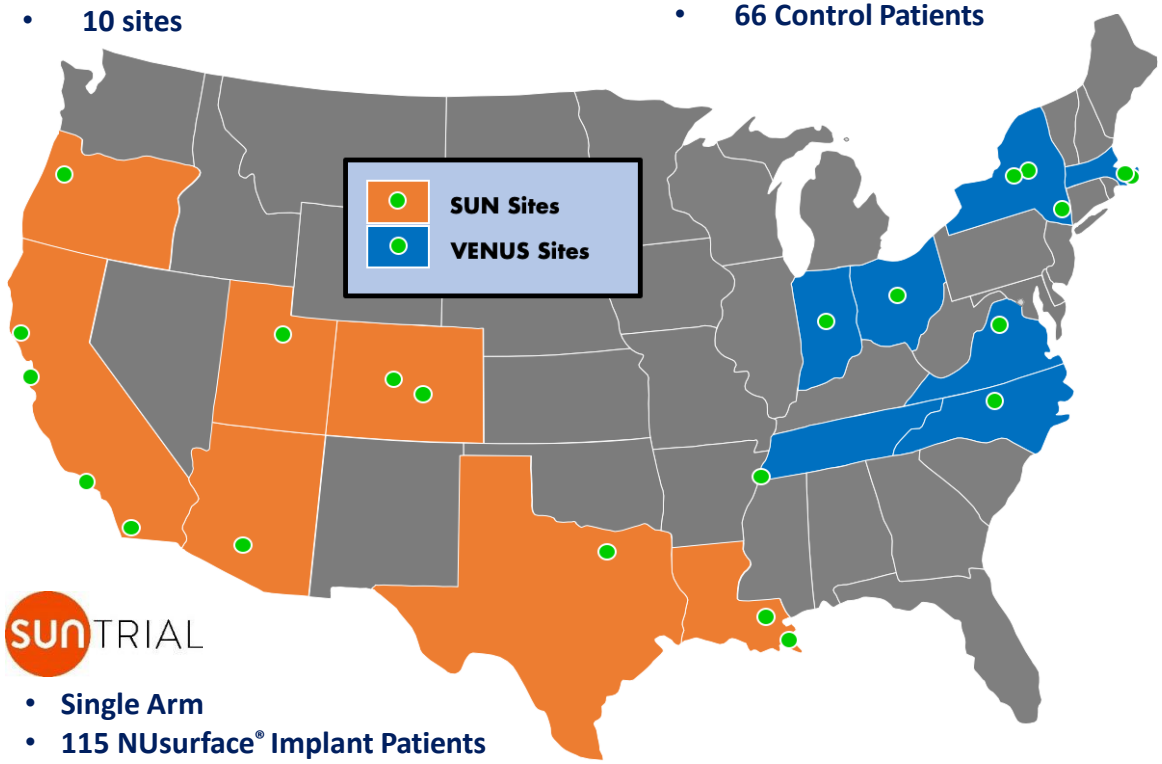
Eric McCarty, MD (CU Sports Medicine -Boulder, CO)
William Montgomery, MD (St. Mary's Medical Center - San Francisco, CA)
Noah Weiss, MD (Weiss Orthopedics, Sonoma, CA)

VENUS TRIAL

- Randomized
- 61 NUsurface® Implant Patients
- 66 Control Patients
- 10 sites

MERCURY

- FDA-Pooled Randomized Data
- 176 NUsurface® Implant Patients
- 66 Control Patients



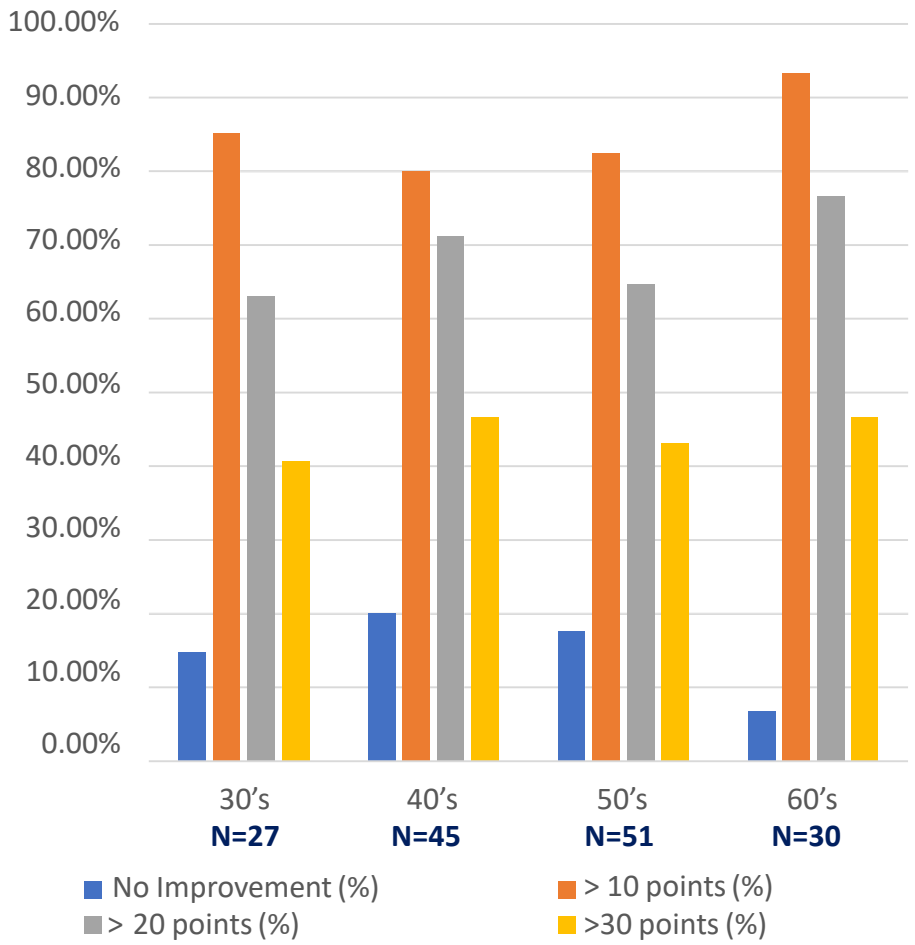
SUN TRIAL

- Single Arm
- 115 NUsurface® Implant Patients
- 13 sites

Clinical Outcomes • NUsurface® KOOS Pain by Stratified Age Bands

Responder Rates at Different Degrees of KOOS Pain Improvement

Baseline Age Range	Total	No Improvement (%)	> 10 points (%)	> 20 points (%)	>30 points (%)
30's	27	14.8%	85.1%	63%	40.7%
40's	45	20%	80%	71.1%	46.6%
50's	51	17.6%	82.4%	64.7%	43.1%
60's	**30**	**6.7%**	**93.3%**	**76.6%**	**46.6%**



NOTE: 12-month trial observations have been published[18, 19] while the 24-month data is currently under FDA review and has not yet been published

Clinical Trial Patient Age Demographics

It's not the Age of the Patient but the "Age" of the Patient's Knee

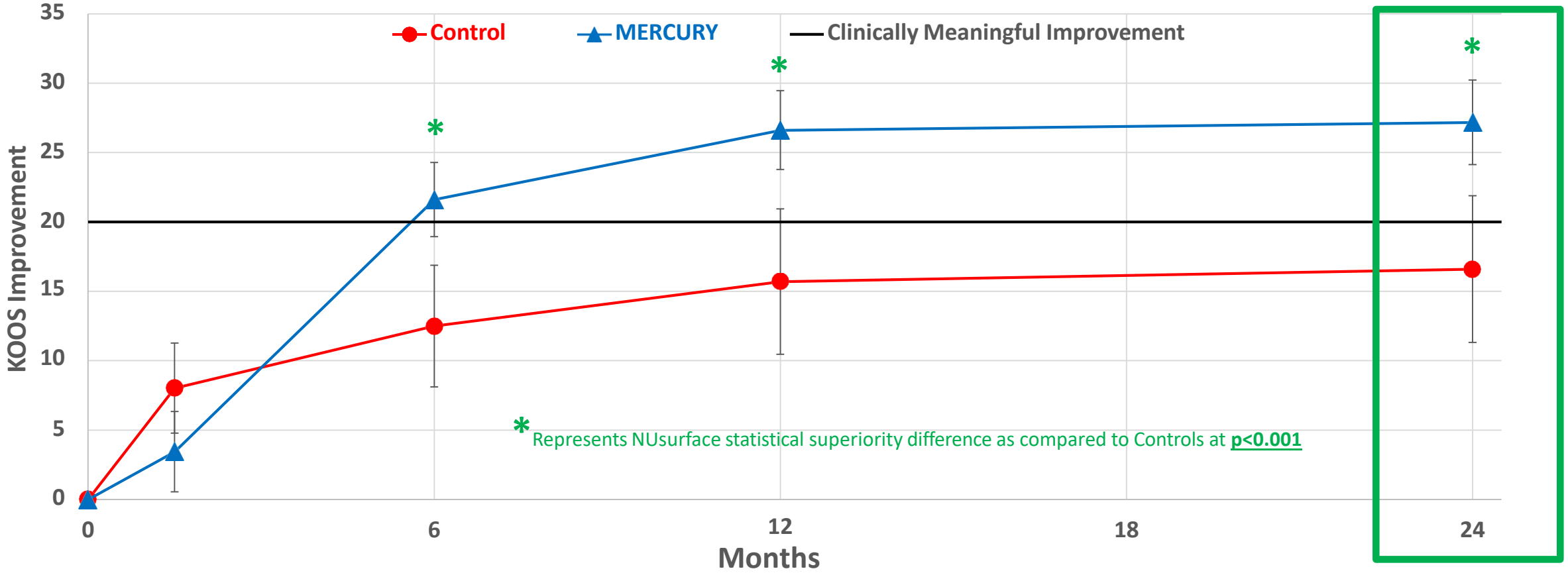
Trial	N Total	Average Age	Standard Deviation	Oldest Treated Patient	Youngest Treated Patient	Total Patients >63 yrs	% >63 yrs at Enrollment	Total Patients ≥65 yrs	% ≥65 yrs at Enrollment
MERCURY	**242**	**49.8**	**10.1**	**69**	**30**	**23**	**9.5%**	**18**	**7.4%**
VENUS	127	50.4	10.7	69	30	14	11%	10	7.9%
SUN	115	49.2	9.4	69	30	9	7.9%	8	7.0%

- Clinical Trial Population Represents a Generalizable Population:
  - Of the **9.5%** treated subjects who were ≥ 65 years old During the 2-year trial
  - **7.4%** were ≥ 65 at the Start of the clinical trial

NOTE: 12-month trial observations have been published[18, 19] while the 24-month data is currently under FDA review and has not yet been published

Clinical Outcomes KOOS Pain • Statistically Superior Efficacy Results

$KOOS_{PAIN}$: Non-Surgical Control vs MERCURY Investigational

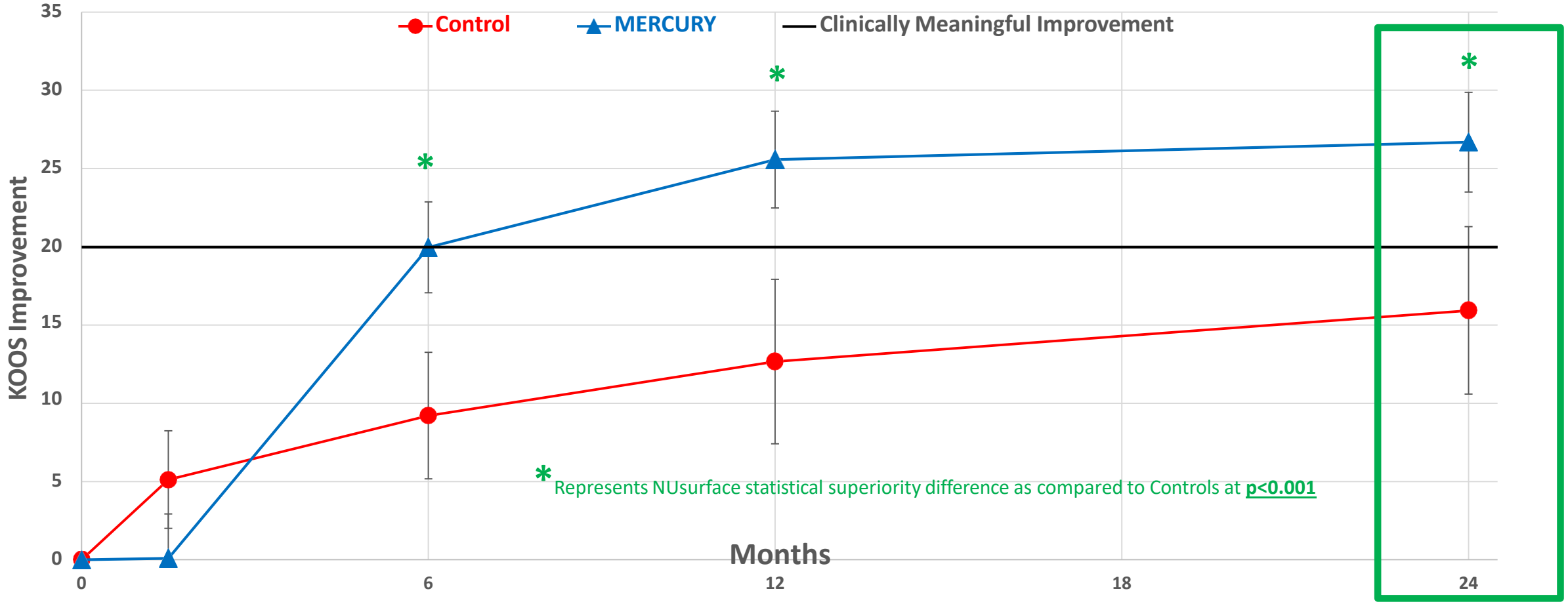


Data Locked 30 June 2020. Error bars represent the 95% CI
Sample size: **MERCURY** (Baseline n=176, 1.5 months n=175, 6 months n=167, 12 months n=165, 24 months n=153)
Sample size: **Control** (Baseline n=66, 1.5 months n=63, 6 months n=56, 12 months n=46, 24 months n=43)

NOTE: 12-month trial observations have been published[18, 19] while the 24-month data is currently under FDA review and represents FDA-submitted data on file (i.e., pre-publication)

Clinical Outcomes KOOS Overall • Statistically Superior Efficacy Results

$KOOS_{OVERALL}$: Non-Surgical Control vs MERCURY Investigational



Data Locked 30 June 2020. Error bars represent the 95% CI
Sample size: **MERCURY** (Baseline n=176, 1.5 months n=166, 6 months n=167, 12 months n=165, 24 months n=153)
Sample size: **Control** (Baseline n=66, 1.5 months n=62, 6 months n=56, 12 months n=46, 24 months n=43)

NOTE: 12-month trial observations have been published[18, 19] while the 24-month data is currently under FDA review and represents FDA-submitted data on file (i.e., pre-publication)

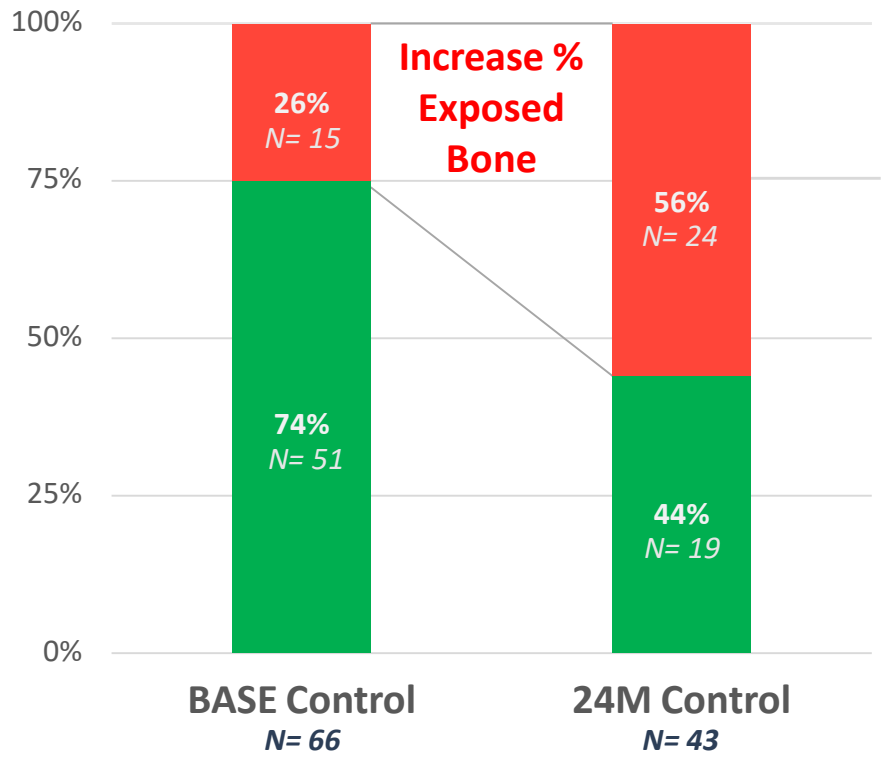
The NUsurface® Implant Maintained Cartilage while Reducing Pain

Measurement of Knee Cartilage Condition in Control Subjects vs. NUsurface® Subjects at Baseline and at 2-Years

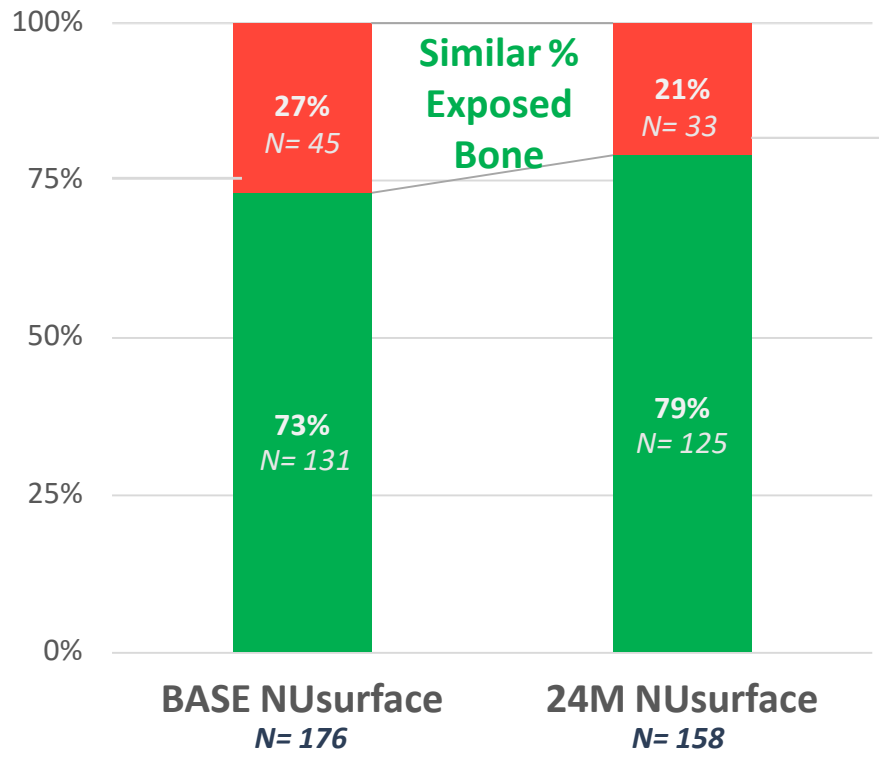
% Full Thickness Cartilage Lesion on Distal Medial Femoral Condyle

Full Thickness Cartilage Lesion Exposing Bone — YES — NO

Cartilage Degeneration in Control Subjects



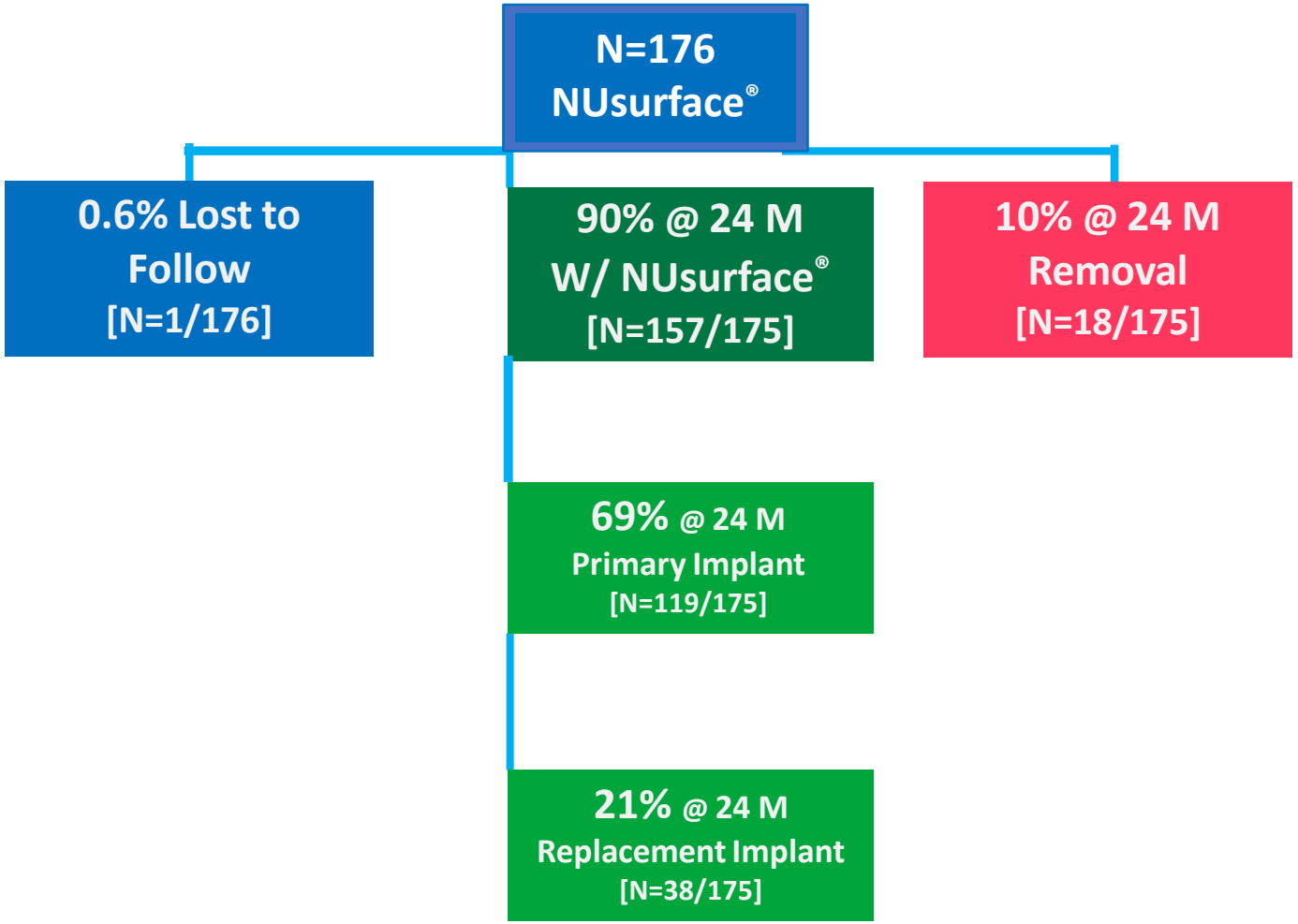
Cartilage Stability in NUsurface® Subjects



NOTE: 12-month trial observations have been published[18, 19] while the 24-month data is currently under FDA review and has not yet been published

Patient Clinical Trial Accountability in the NUsurface® Group

90% of NUsurface® Subjects Completed 24 Months Compared with 65% of Control Subjects



NOTE: 12-month trial observations have been published[18, 19] while the 24-month data is currently under FDA review and has not yet been published

Site of Service

The NUsurface® meniscus implant surgeries in the clinical trials were performed in the outpatient hospital and ASC settings. Because the anticipated NUsurface® patient age range in an anticipated FDA label is likely to be similar to that of the clinical trials (i.e., ages 30-75), it is anticipated that in general use post FDA-decision that surgery in an inpatient setting may be performed dependent on patient comorbidities

Hospital Outpatient Surgery

NUsurface® meniscus implant surgery performed in a hospital outpatient setting or an ASC setting

Outpatient Ambulatory Surgery Center

Inpatient Setting

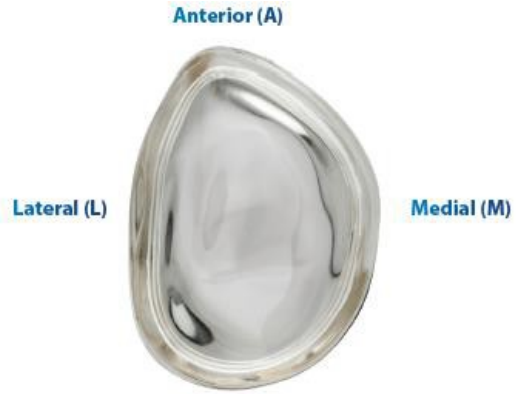
NUsurface® meniscus implant surgery may be performed during an inpatient stay (low incidence), dependent on patient comorbidities

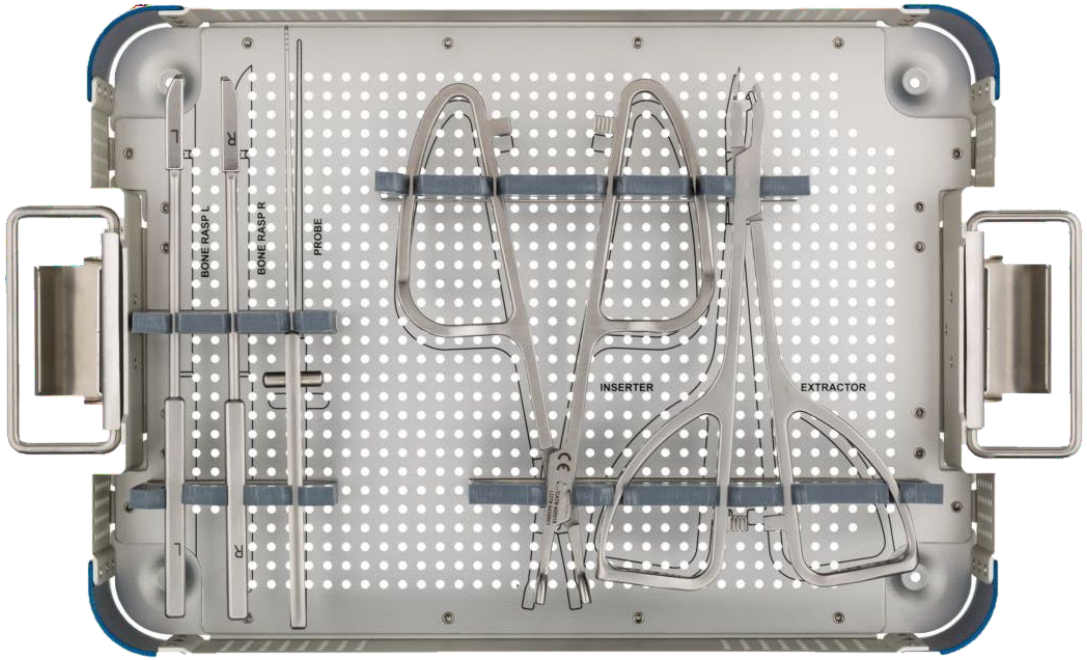
References

1. Fox, A.J., A. Bedi, and S.A. Rodeo, The basic science of human knee menisci: structure, composition, and function. *Sports Health*, 2012. 4(4): p. 340-51.
2. Fox, A.J., et al., The human meniscus: a review of anatomy, function, injury, and advances in treatment. *Clin Anat*, 2015. 28(2): p. 269-87.
3. Lento, P.H. and V. Akuthota, Meniscal injuries: A critical review. *J Back Musculoskelet Rehabil*, 2000. 15(2): p. 55-62.
4. Hall, M.J., et al., Ambulatory Surgery Data From Hospitals and Ambulatory Surgery Centers: United States, 2010, U.S.D.o.H.a.H. Services and C.f.D.C.a. Prevention, Editors. 2017: Natl Heath Stat Report. p. 1-15.
5. Sihvonen, R., et al., Arthroscopic partial meniscectomy versus placebo surgery for a degenerative meniscus tear: a 2-year follow-up of the randomised controlled trial. *Ann Rheum Dis*, 2018. 77(2): p. 188-195.
6. Yim, J.H., et al., A comparative study of meniscectomy and nonoperative treatment for degenerative horizontal tears of the medial meniscus. *Am J Sports Med*, 2013. 41(7): p. 1565-70.
7. Katz, J.N., et al., Surgery versus physical therapy for a meniscal tear and osteoarthritis. *N Engl J Med*, 2013. 368(18): p. 1675-84.
8. Chatain, F., et al., The natural history of the knee following arthroscopic medial meniscectomy. *Knee Surg Sports Traumatol Arthrosc*, 2001. 9(1): p. 15-8.
9. Abram, S.G.F., et al., Long-term rates of knee arthroplasty in a cohort of 834 393 patients with a history of arthroscopic partial meniscectomy. *Bone Joint J*, 2019. 101-B(9): p. 1071-1080.
10. Filardo, G., et al., No Effects of Early Viscosupplementation After Arthroscopic Partial Meniscectomy: A Randomized Controlled Trial. *Am J Sports Med*, 2016. 44(12): p. 3119-3125.

References *(continued)*

11. McAlindon, T.E., et al., Effect of Intra-articular Triamcinolone vs Saline on Knee Cartilage Volume and Pain in Patients With Knee Osteoarthritis: A Randomized Clinical Trial. *JAMA*, 2017. 317(19): p. 1967-1975.
12. Kompel, A.J., et al., Intra-articular Corticosteroid Injections in the Hip and Knee: Perhaps Not as Safe as We Thought? *Radiology*, 2019. 293(3): p. 656-663.
13. Linder-Ganz E, et al,. A novel quantitative approach for evaluating contact mechanics of meniscal replacements. *J Biomech Eng*. 2010 Feb;132(2):024501
14. Abram, S.G.F, et al., Long-term rates of knee arthroplasty in a cohort of 834 393 patients with a history of arthroscopic partial meniscectomy. *Bone Joint J,* 2019; 101-B:1071-1080
15. Shemesh M, Shefy-Peleg A, Levy A, Shabshin N, Condello V, Arbel R, Gefen A. Effects of a Novel Medial Meniscus Implant on the Knee Compartments: Imaging and Biomechanical Aspects. *Biomechanics and Modeling in Mechanobiology*, 2020 March 31
16. ClinicalTrials.gov: NCT02108496
17. ClinicalTrials.gov: NCT02483988
18. McKeon BP et al., Preliminary Results From a US Clinical Trial of a Novel Synthetic Polymer Meniscal Implant. *Orthop J Sports Med*. 2020 Sep 29;8(9).
19. Zaslav K, et al., Treatment of post-meniscectomy knee symptoms with medial meniscus replacement results in greater pain reduction and functional improvement than non-surgical care. *Knee Surg Sports Traumatol Arthrosc*. 2021 Apr 21





1. Meniscus Probe | 2. Universal Insertion Instrument | 3. Extraction Instrument | 4. Bone Rasp, Right + Left

*Ultra-high molecular weight polyethylene

+(Note: final Product & Instruments TBD per FDA market authorization)