Administration of Treosulfan

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Background

- **Issue:** There is currently no unique ICD-10-PCS code to describe the administration of Treosulfan
- **Background:** Treosulfan is a new chemical entity and novel prodrug of a bifunctional alkylating agent that is used as a preparative regimen for allogenic hematopoietic stem cell transplantation (alloHSCT). Treosulfan received orphan-drug designation from FDA on April 8, 2015
- **New Technology Application Pending:** A New Technology Add-on Payment (NTAP) application for Treosulfan was submitted and presented at the Townhall for federal fiscal year (FY) 2023
- **Food & Drug Administration (FDA) Approval:** Treosulfan is currently under review by the FDA under a New Drug Application (NDA). Medexus hopes to secure FDA approval by June 30, 2022
  - NDA submitted Aug 2020
  - CRL issued Aug 2021
  - Resubmission Apr 2022

Treosulfan Indications, Usage and Documentation

- **If FDA approves as anticipated, indications and usage:**
  - Use in combination with fludarabine as a preparative regimen for allogeneic hematopoietic stem cell transplantation (alloHSCT) in adult and pediatric patients >1 year old with acute myeloid leukemia (AML)
  - Use in combination with fludarabine as a preparative regimen for allogeneic hematopoietic stem cell transplantation in adult and pediatric patients > 1 year old with myelodysplastic syndrome (MDS)
- **Dosage and administration:**
  - Recommended adult dose: 10 g/m² body surface area (BSA) per day as a two-hour intravenous infusion, given on three consecutive days (day -4, -3, -2) in conjunction with fludarabine before hematopoietic stem cell infusion (day 0)
  - Available in 1g and 5g vials
- **Documentation:**
  - Treosulfan is expected to be infused inpatient most of the time
  - Treosulfan is typically documented in a procedure report, MAR (Medication Administration Record), and/or progress note

Disease Trends for Allogeneic Transplants in the US

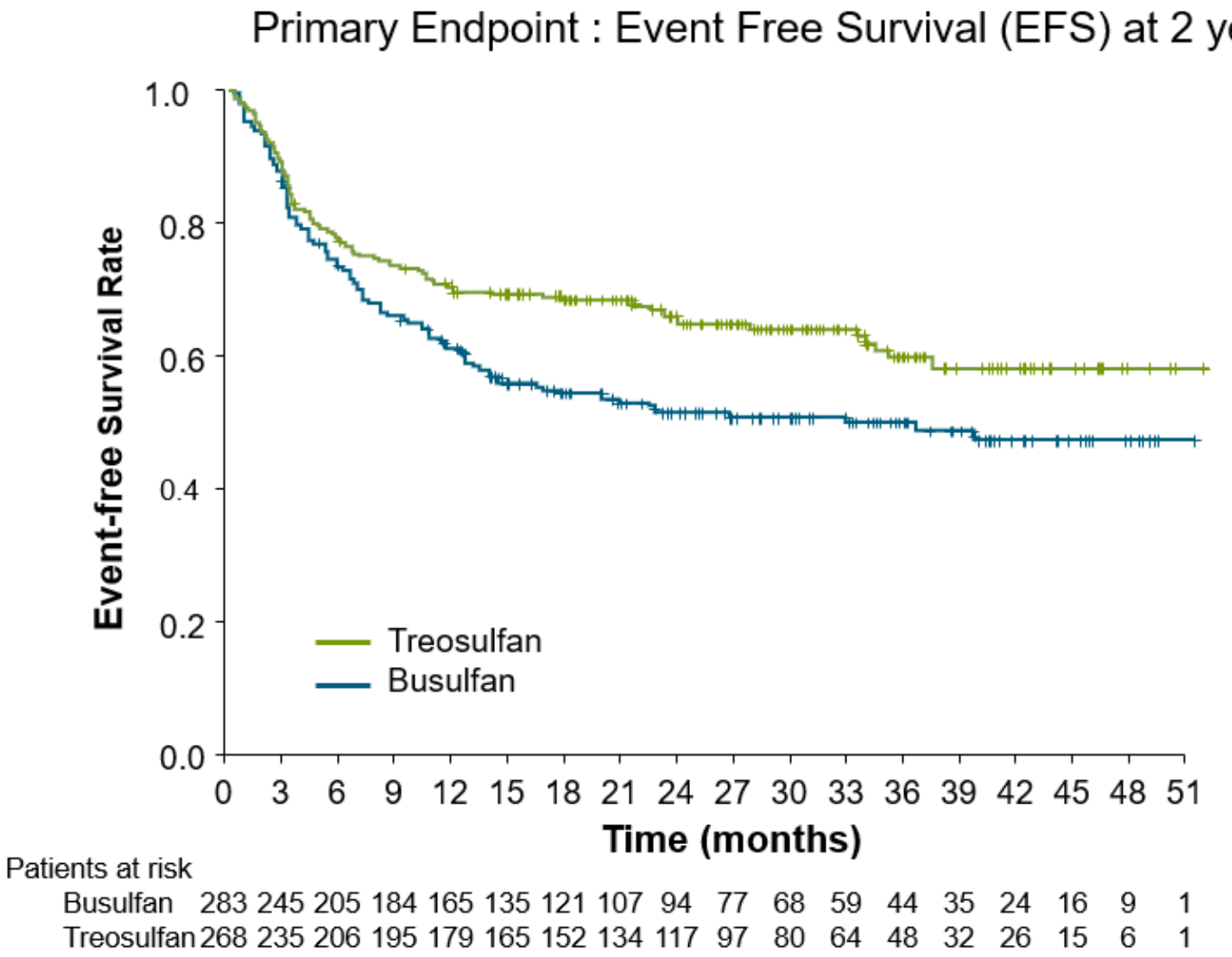
- 30,240 patients are diagnosed with AML and MDS each year[1]
- 9,809 patients received an allogeneic transplant in 2020[2]
- The number of patients receiving allogeneic transplants is increasing
  - 187% increase from 2000 to 2019[2]
  - 28,053 projected in 2029[3]
- AML and MDS impact the Medicare population with a median diagnosis age of 68 and 71 respectively[1]
- Medicare patients represent approximately 30% of allogeneic transplants[4]
- The number of Medicare patients receiving allogeneic transplants is rapidly increasing
  - 3,630% increase from 2000 to 2019[4]

[1] ASCO (American Society of Clinical Oncology) https://www.cancer.net/
[2] Center for International Blood and Marrow Transplant Research (CIBMTR)
[3] Forecast calculated via linear trend based on CIBMTR data (2000-2019)
[4] CIBMTR - Current Uses and Outcomes of Hematopoietic Cell Transplantation (HCT) in US; 2020 Summary Slides
https://www.cibmtr.org/ReferenceCenter/SlidesReports/SummarySlides/pages/index.aspx

Treosulfan is a New, Unique and Transformative Conditioning Agent

- **Treosulfan is a new agent**
  - Will be the first and only FDA-approved allo-HSCT conditioning agent for AML and MDS
  - New chemical entity and novel prodrug
- **Treosulfan demonstrates substantial clinical improvement over existing standard treatments**
  - Event Free Survival (EFS)
  - Overall Survival (OS)
  - Non-Relapse Mortality (NRM)
  - Graft Versus Host Disease (GVHD)
- **Treosulfan fulfills an unmet need by minimizing toxicity while maximizing efficacy**

Treosulfan Demonstrated Substantial Clinical Improvement in Event Free Survival



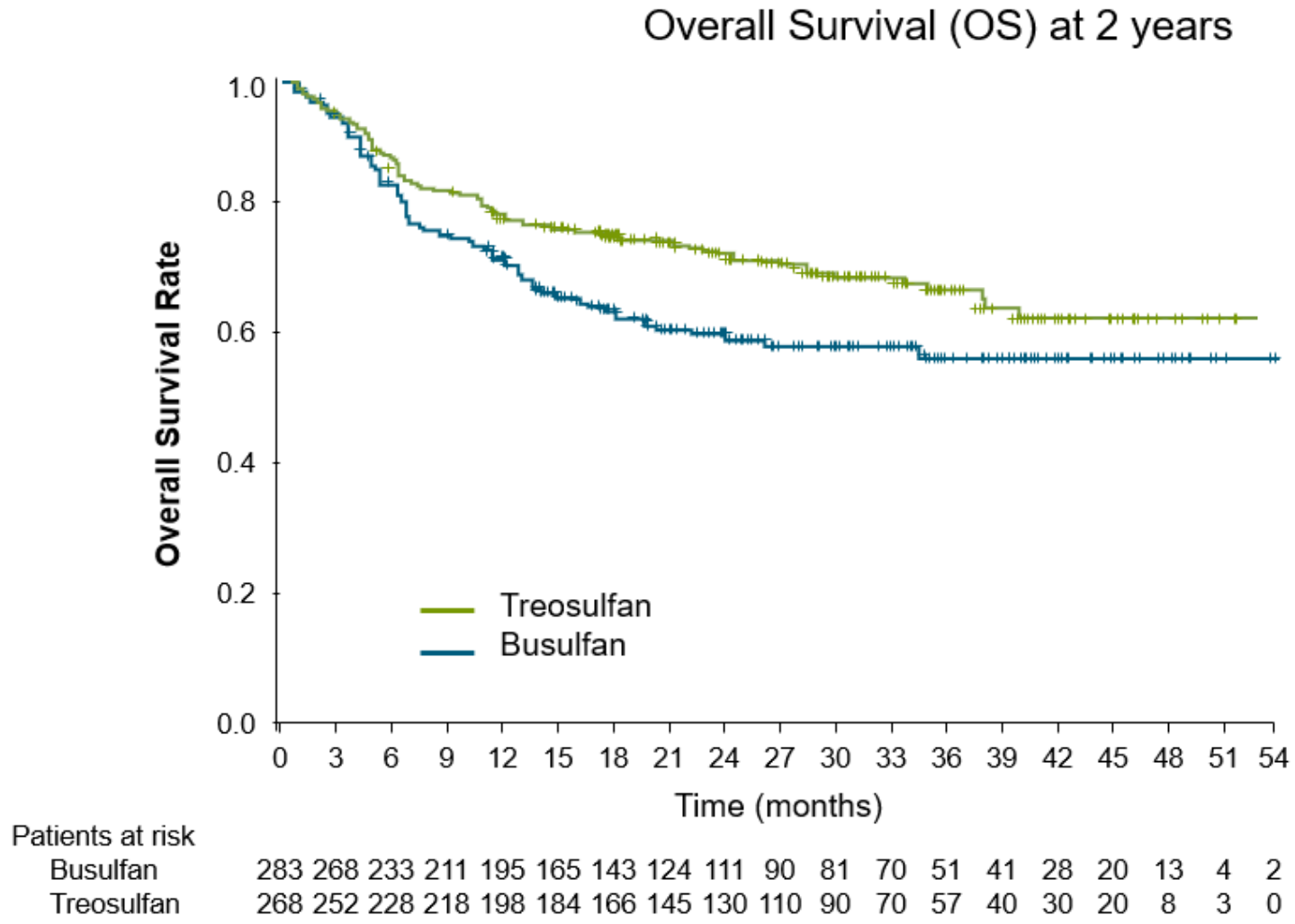
	Busulfan	Treosulfan
Number of patients	283	268
Events n (%)	137 (48.4)	97 (36.2)
Censored (%)	146 (51.6)	171 (63.8)
Rate at 24 months (%)	51.2	65.7
95% CI	(45.0, 57.0)	(59.5, 71.2)
Hazard Ratio	0.64	
95% CI	(0.49, 0.84)	
P value non-inferiority*	0.0000001	
P value superiority*	0.0005787	

*Adjusted for donor type as factor, and risk group and center as strata using Cox regression model. The nominal one-sided significance level resulting from an event-driven O'Brien-Fleming type group-sequential efficacy stopping boundary is 0.001262

CI, confidence interval

Medexus Pharma, data on file.

Treosulfan Demonstrated Substantial Clinical Improvement in Overall Survival



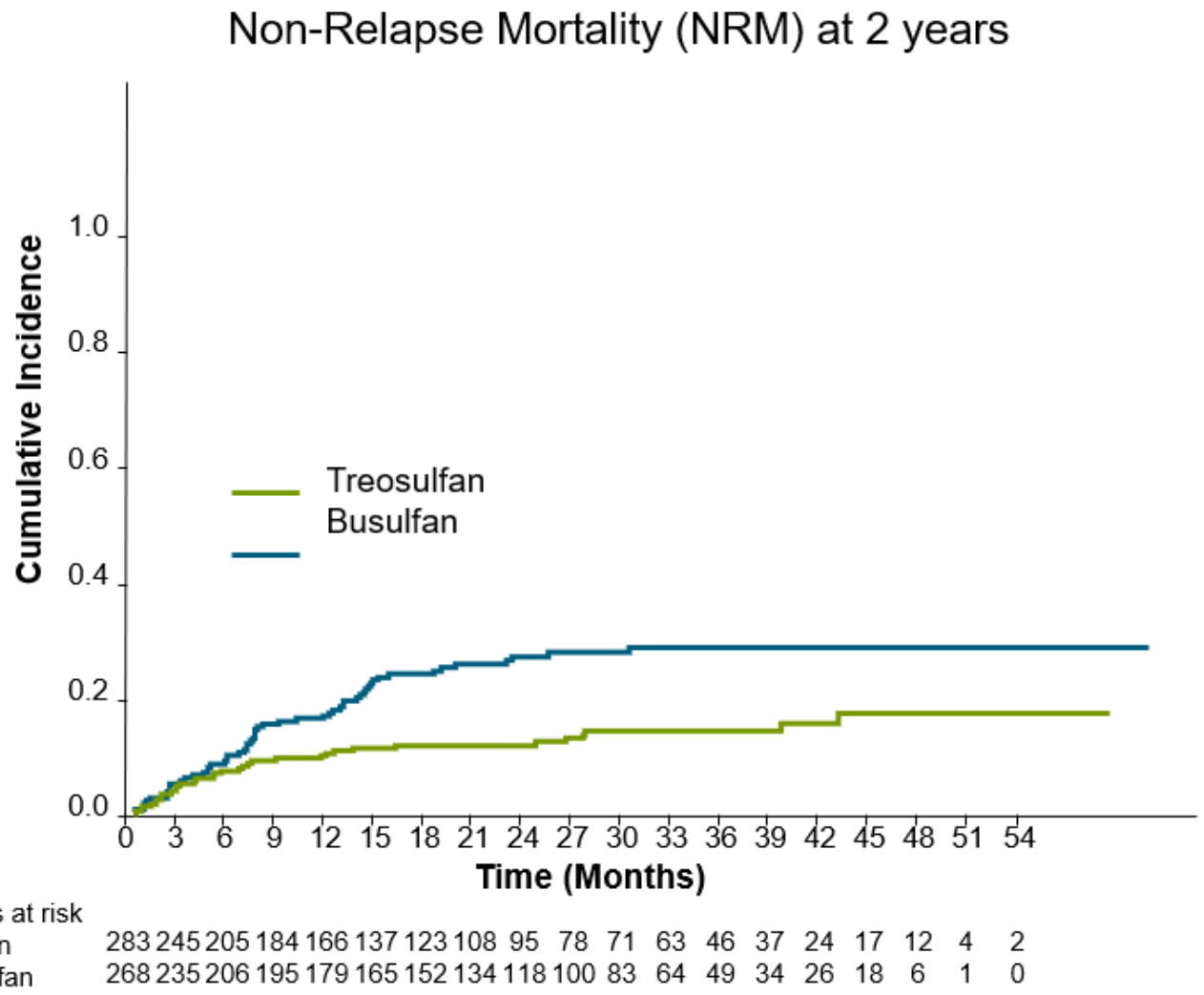
	Busulfan	Treosulfan
Number of patients	283	268
Events n (%)	112 (39.6)	81 (30.2)
Censored n (%)	171 (60.4)	187 (69.8)
Rate at 24 months (%)	60.2	72.7
95% CI	(54.0, 65.8)	(66.8, 77.8)
Hazard Ratio	0.64	
95% CI	(0.48, 0.87)	
P value*	0.0037	

*Adjusted for donor type as factor, and risk group and center as strata using Cox regression model.

CI, confidence interval

Medexus Pharma, data on file.

Treosulfan Demonstrated Substantial Clinical Improvement in Non-Relapse Mortality



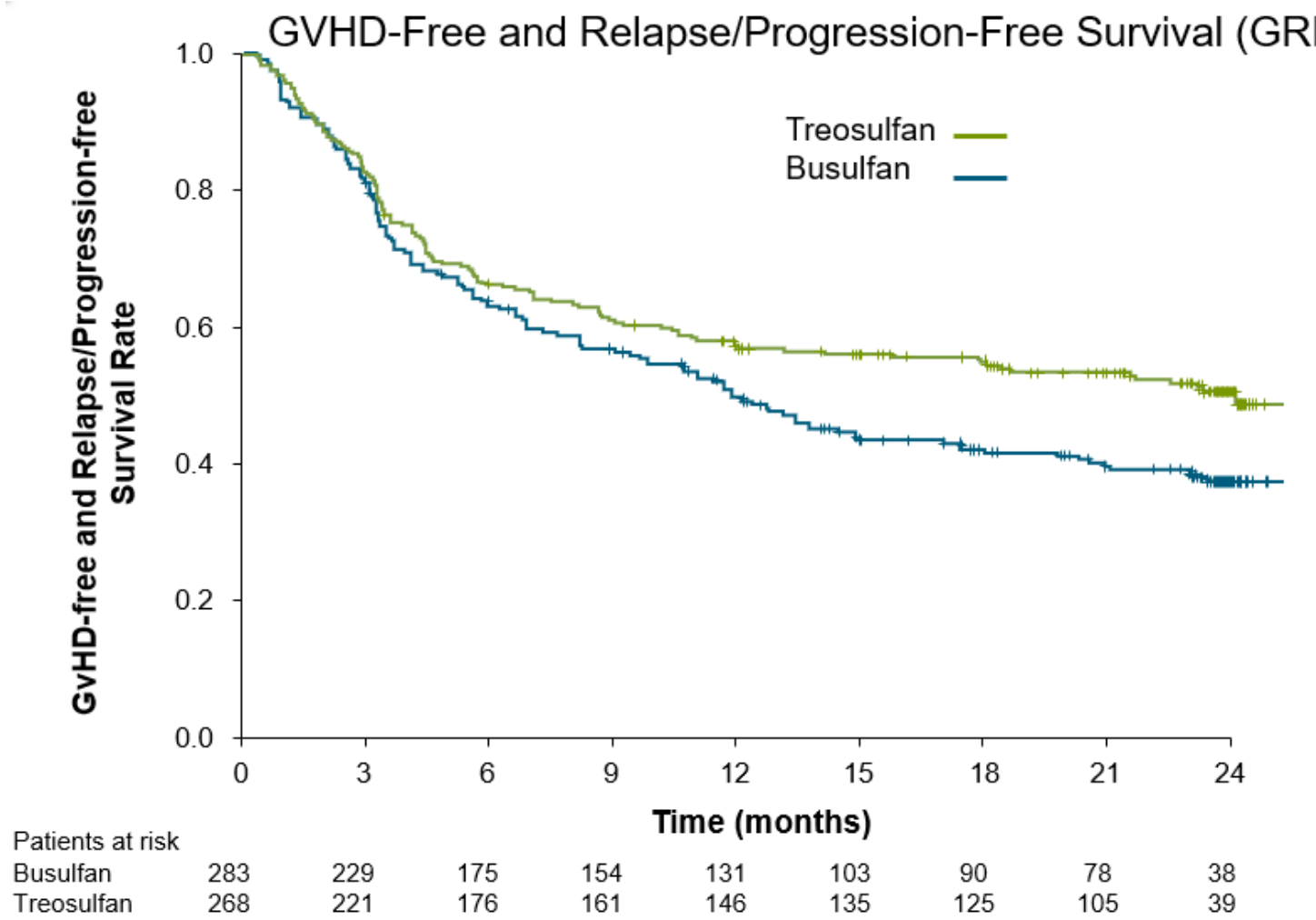
	Busulfan	Treosulfan
Number of patients	283	268
Rate at 24 months (%)	20.4	12.0
95% CI	(15.5, 25.2)	(8.0, 15.9)
Hazard Ratio	0.63	
95% CI	(0.41, 0.97)	
P value*	0.0343	

*Adjusted for donor-type as factor, and risk group as stratum using the Fine and Gray model

CI, confidence interval

Medexus Pharma, data on file.

Treosulfan Demonstrated Substantial Clinical Improvement in Reducing the Impact of GVHD



	Busulfan	Treosulfan
Number of patients	283	268
Events, (n, [%])	169 (59.7)	130 (48.5)
Censored (n, [%])	114 (40.3)	138 (51.5)
Rate at 24 months, (%)	37.1	50.3
95% CI	(31.1, 43.1)	(43.9, 56.3)
Hazard Ratio	0.73	
95% CI	(0.57, 0.92)	
P* value	0.0087	

*Adjusted for donor type as factor, and risk group and center as strata using Cox regression model

CI, confidence interval

Medexus Pharma, data on file.

Treosulfan Demonstrated Substantial Clinical Improvement vs. Current Standard Treatment (Busulfan and Fludarabine)

24-month endpoint	Flu/ Busulfan	Flu/ Treosulfan	Interpretation
24-month Event Free Survival (EFS) (%) (p=0.0005787)	51.2	**65.7**	Treosulfan has higher rate of event free survival
Overall Survival (OS) (%) (p=0.0037)	60.2	**72.7**	Treosulfan has higher rate of overall survival
GVHD-Free and Relapse/Progression-Free Survival (GRFS) (%) (p=0.0087)	37.1	**50.3**	Treosulfan has a higher rate of GVHD-free and relapse/progression-free survival
Graft Failure (n/n for primary/secondary) (p=0.0392)	1/8	**1/0**	Treosulfan has a lower rate of graft failure
Relapse/Progression (%) (p=0.2631)	25.2	**22**	Treosulfan has a similar rate of relapse/progression
Non-Relapse Mortality (NRM) (%) (p=0.0343)	20.4	**12**	Treosulfan has a lower rate of non-relapse mortality
Serious Adverse Events (SAEs) (%)	7.1	**8.5**	Treosulfan has a similar rate of serious adverse events

Medexus Pharma, data on file.

Value of a Treatment Specific Code for Treosulfan

- Various benefits would be realized by having a treatment ICD-10-PCS code for Treosulfan. Specifically, a unique code would facilitate:
  - Value-based analysis of Treosulfan vs. other treatment therapies
  - Research of Treosulfan for potential additional uses
  - Tracking of utilization and outcomes
  - Meeting any post-approval study obligations that may apply
  - Additional studies into dosing regimens, which may vary by provider

Summary

- Treosulfan demonstrates substantial clinical improvement over existing standard treatments (EFS, OS, NRM, GVHD)
- Treosulfan fulfills an unmet need by minimizing toxicity while maximizing efficacy
- The substantial clinical improvements demonstrated by Treosulfan may impact:
  - Length of stay
  - Readmission rates
  - Side effects
  - Total patient encounter costs
  - Medicare system burden
- A unique ICD-10-PCS for Treosulfan has the potential to facilitate research, drug monitoring, tracking patient outcomes, and other important functions

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Questions