

Cost Savings With Treosulfan and Fludarabine (Flu/Treo) vs. Busulfan and Fludarabine (Flu/Bu2) Conditioning Regimen in Patients Undergoing Allogeneic HSCT for Acute Myeloid Leukemia (AML) or Myelodysplastic Syndrome (MDS)

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Objective

To compare cost savings from avoided complications with treosulfan + fludarabine (Flu/Treo) vs. busulfan + fludarabine (Flu/Bu2) conditioning regimens in patients undergoing allogeneic haematopoietic stem cell transplantation (allo-HSCT) for acute myeloid leukemia (AML) or myelodysplastic syndrome (MDS).

Methods

The Phase III trial¹ comparing Flu/Treo vs. Flu/Bu2 conditioning regimen was used to gather outcomes data: event free survival (EFS), overall survival (OS), non-relapse mortality (NRM), and rate of key complications: acute and chronic graft vs. host disease (aGVHD/cGVHD), relapse, graft failure, severe veno-occlusive disease (VOD) and mucositis (Table 1).

Table 1: Rate of key survival outcomes and key complications: Flu/Bu2 vs Flu/Treo

Rate of key survival outcomes ¹	Flu/Treo	Flu/Bu2	Difference
Event Free Survival (EFS) (%)	65.7%	51.2%	14.5%
Overall Survival (OS) (%)	72.7%	60.2%	12.5%
Non-Relapse Mortality (NRM) (%)	12.0%	20.4%	-8.4%
Rate of key complications ¹	Flu/Treo	Flu/Bu2	Difference
aGvHD	52.8%	57.2%	-4.4%
Extensive cGvHD	19.8%	28.6%	-8.8%
Relapse	22.0%	25.2%	-3.2%
Graft failure	0.4%	3.2%	-2.8%
Severe VOD	0.0%	0.4%	-0.4%
Grades 3-4 Mucositis	5.9%	7.4%	-1.5%

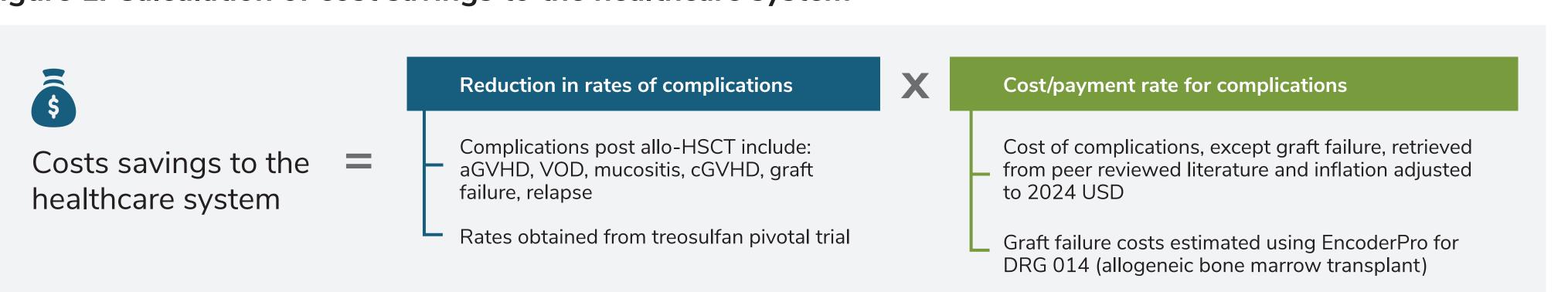
Cost of key complications except graft failure retrieved from peer reviewed literature and inflation adjusted to 2024 (Table 2). Graft failure costs estimated using EncoderPro "adjusted total" payment rates for allo-HSCT (DRG 014) for 30 hospitals (excluding PPS exempt hospitals) based on total number of allogeneic transplants as reported by National Marrow Donor Program. Patients with graft failure often receive second HSCT therefore DRG payment for allo-HSCT used to calculate costs assuming ~38.5% patients undergo second allo-HSCT following graft failure².

Table 2: Cost of complications

Severe VOD ³	Mucositis ⁴ (Grades 3-4)	aGvHD ^{5,6}	cGvHD ^{7,8}	Graft failure ⁹	Relapse ¹⁰
\$172,323	\$173,747	\$108,222	\$379,874	\$144,802	\$547,354

Costs associated with complications of allo-HSCT calculated by multiplying costs/payment rates by rate of complications with Flu/Treo vs. Flu/Bu2 regimens from a health system perspective (Figure 1).

Figure 1: Calculation of cost savings to the healthcare system



Results

Flu/Treo demonstrated a significant improvement in EFS (\triangle 14.5%), OS (\triangle 12.5%), and NRM (\triangle -8.4%), vs. Flu/Bu2. Rate of key complications were lower with Flu/Treo vs. Flu/Bu2 (Figure 2). Estimating cost implications of fewer complications suggests a reduction in inflation adjusted costs of ~\$6.1M over 2 years to the healthcare system for every 100 patients treated with the Flu/Treo relative to Flu/Bu2 agnostic of costs of conditioning regimens (Figure 3). Cost savings were driven primarily by reduction in cGvHD followed by relapse and aGvHD.

Figure 2: Rate of complications- Flu/Treo vs Flu/Bu2

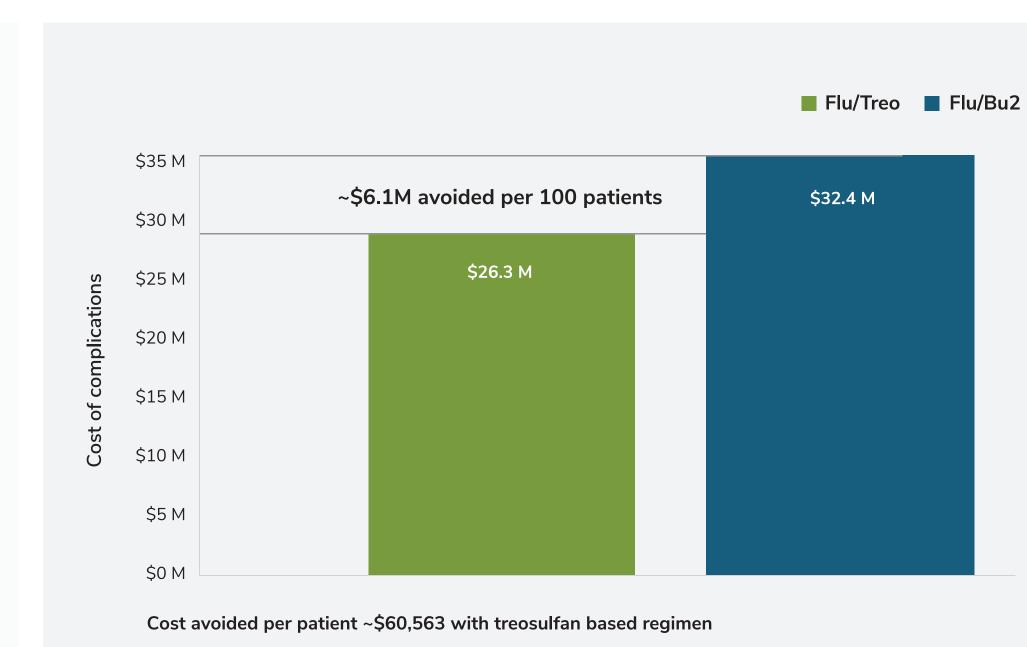
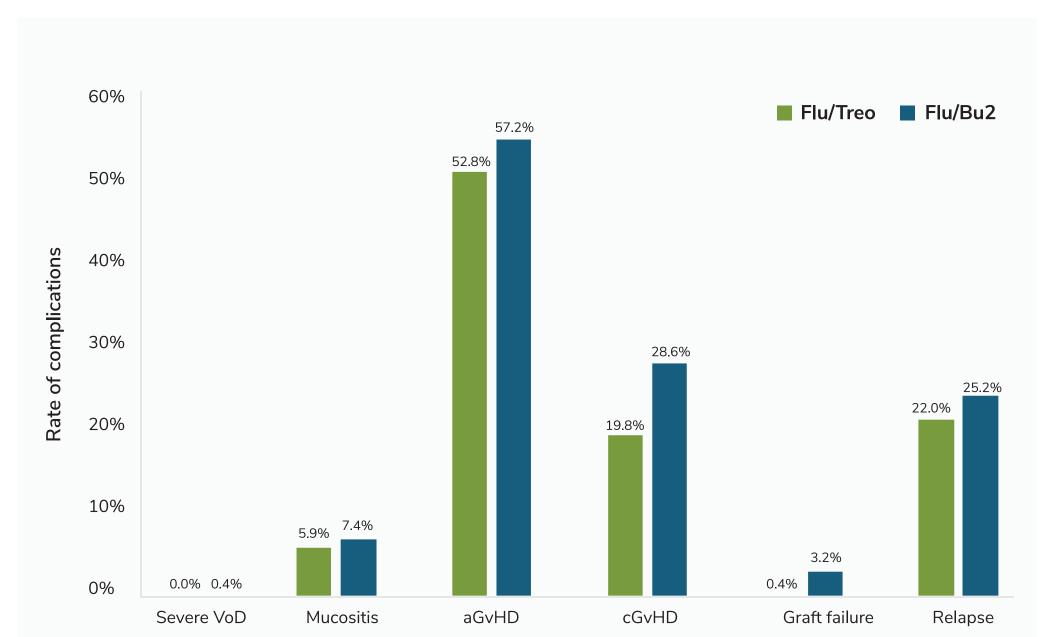


Figure 3: Cost of complications- Flu/Treo vs Flu/Bu2



Conclusion

- Flu/Treo conditioning regimen results in a substantial reduction in total cost of care from avoided complications vs. Flu/Bu2
- This is likely a conservative estimate of the value of Flu/Treo given this analysis does not include QALY gains from improved OS and EFS

Limitations

- Cost for cGvHD could be an underestimate if recently launched novel therapies are considered
- In many facilities, case rates are applied which could be substantially different from the payment rates DRG 014 used to estimate the cost of graft failure in this analysis
- Furthermore the range of costs for mucositis reported in the meta-analysis was large depending on the need for total parenteral nutrition (TPN) which could skew the average costs away from typical values

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