Comparative Outcomes and Toxicities of Tresulfan Vs Busulfan-Based Myeloablative Conditioning in Allogeneic Hematopoietic Stem Cell Transplantation

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Introduction

Busulfan is a widely used agent in myeloablative conditioning regimens for allogeneic hematopoietic stem cell transplantation (allo-HSCT), but its toxicity profile—including hepatic sinusoidal obstruction syndrome (SOS) and graft-versus-host disease (GVHD)—has led to the investigation of alternative agents such as treosulfan. Treosulfan may offer similar efficacy with improved tolerability, but comparative real-world data remain limited.

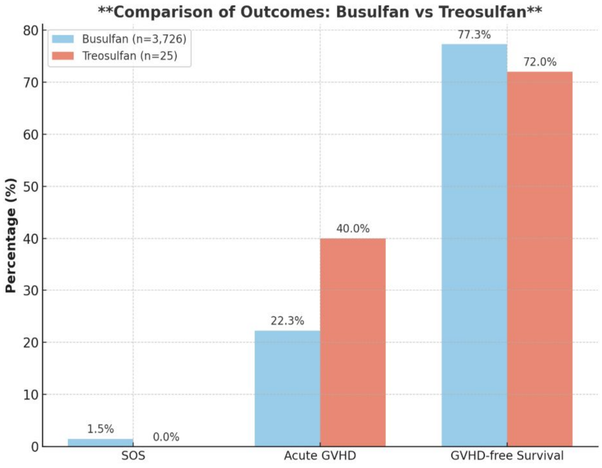
Objectives

To compare the incidence of SOS and acute GVHD in patients undergoing myeloablative allo-HSCT with busulfan- versus treosulfan-based conditioning regimens using real-world clinical data.

Methods

- Retrospective cohort study utilizing real-world data from the **TriNetX Global Health Research Network.**
- Multi-institutional analysis across **67 U.S. healthcare organizations** using federated electronic health record data.
- **Adults (≥18 years) undergoing allo-HSCT between 2005 and 2024 were identified**. Myeloablative conditioning was defined by drug regimen: busulfan-based regimens were considered myeloablative if they included ≥4 doses (e.g., FluBu4), while treosulfan regimens were presumed myeloablative based on standard practice. **Inclusion required exposure to treosulfan or busulfan within 30 days prior to transplant**. Data on GVHD grade, relapse, progression-free survival (PFS), and overall survival (OS) were not available in structured EHR fields.
- Patients were grouped by conditioning regimen—busulfan vs. treosulfan—and outcomes were evaluated from the transplant index date. Propensity score matching was not performed due to the small treosulfan sample size (n=25).
- Incidence of hepatic SOS within 60 days and acute GVHD within 100 days post-transplant was the main outcome measure.

Results



Among 3,726 busulfan-treated and 25 treosulfan-treated patients, SOS occurred in 1.5% vs. 0%, respectively (risk difference −1.5%, p=0.542).

- Acute GVHD occurred in 22.3% of busulfan patients and 40.0% of treosulfan patients (risk difference 17.7%, p=0.034).
- GVHD-free survival was 77.3% for busulfan vs. 72.0% for treosulfan.

Summary

Busulfan is a standard conditioning agent in allogeneic stem cell transplantation but carries risks of hepatic sinusoidal obstruction syndrome (SOS) and graft-versus-host disease (GVHD). Treosulfan has emerged as a potential alternative with a more favorable toxicity profile, though real-world comparisons remain limited.

Using the TriNetX Global Health Research Network, we conducted a retrospective analysis of adults undergoing myeloablative allo-HSCT between 2005–2024. Patients were grouped by conditioning regimen: busulfan (n=3,726) and treosulfan (n=25). Outcomes included SOS within 60 days and acute GVHD within 100 days post-transplant.

SOS occurred in 1.5% of busulfan-treated patients and 0% of treosulfan-treated patients. Acute GVHD was observed more frequently with treosulfan (40.0%) compared to busulfan (22.3%, p=0.034). GVHD-free survival was similar between groups (77.3% vs. 72.0%).

These findings suggest that treosulfan may reduce hepatic toxicity relative to busulfan but could carry a higher risk of acute GVHD. Interpretation is limited by the small treosulfan cohort and lack of structured GVHD severity data. Prospective studies are warranted to confirm these observations.

Discussion

Treosulfan may reduce hepatic toxicity relative to busulfan but may be associated with increased acute GVHD. Interpretation is limited by cohort imbalance and lack of GVHD grading.

Limitations

Retrospective design, small treosulfan cohort, and lack of structured data on GVHD severity, relapse, PFS, and OS.