Abstract: P1303

Title: IMPACT OF CONDITIONING INTENSITY ON VENO-OCCLUSIVE DISEASE/SINUSOIDAL OBSTRUCTION SYNDROME SEVERITY AND OUTCOMES IN ADULT HEMATOPOIETIC CELL TRANSPLANT PATIENTS: RESULTS FROM THE DEFIFRANCE REGISTRY

Abstract Type: Poster Presentation

Topic: Stem cell transplantation - Clinical

Background:

Veno-occlusive disease/sinusoidal obstruction syndrome (VOD/SOS) is a serious liver injury caused by damage to sinusoidal endothelial cells and is associated with conditioning regimens preceding hematopoietic cell transplantation (HCT). While reduced-intensity conditioning (RIC) regimens are thought to decrease the likelihood of VOD/SOS, this complication does still occur following RIC and can be severe. Defibrotide is approved for treatment of severe hepatic VOD/SOS post-HCT in patients aged >1 month in the EU and VOD/SOS with renal or pulmonary dysfunction post-HCT in the US.

Aims:

Examine VOD/SOS severity and outcomes following RIC or myeloablative conditioning (MAC) regimens in adult patients who received defibrotide for the treatment of VOD/SOS after HCT in the DEFIFrance registry.

Methods:

DEFIFrance collected retrospective and prospective data on defibrotide-treated patients from 53 HCT centers in France. VOD/SOS diagnosis was at the investigators' discretion and severity was categorized using adult European Society for Blood and Marrow Transplantation criteria. Primary endpoints were Kaplan-Meier (KM)–estimated Day 100 post-HCT survival and complete response (total serum bilirubin <2 mg/dL and multiorgan failure resolution per investigators' assessment). A secondary endpoint was the incidence of serious treatment-emergent adverse events of interest: hemorrhages, coagulopathies, infections, and thromboembolic events.

Results:

In total, data from 247 adult patients were analyzed: 134 received RIC and 113 received MAC. Compared with the MAC subgroup, patients in the RIC subgroup tended to be older (median [range] age 56.4 [18–74] vs 46.6 [18–68] years) and were more likely to have had prior HCTs (≥1 received by 17.2% vs 8.8%, respectively). The most common primary diseases were acute myeloid leukemia (RIC, 35.8% vs MAC, 28.3%), myelodysplastic syndrome (20.9% vs 9.7%), lymphoma (13.4% vs 28.3%), and acute lymphoblastic leukemia (11.2% vs 23.0%). Median time from HCT to VOD/SOS diagnosis was shorter in the RIC subgroup (11.5 days) vs the MAC subgroup (14.0 days). A higher proportion of very severe VOD/SOS (45.0%) was noted in patients receiving RIC vs the MAC subgroup (33.6%), with a corresponding lower proportion of moderate VOD/SOS (13.7% vs 25.7%). Median (interquartile range) duration of defibrotide treatment was similar for both subgroups (RIC: 15.0 [10.0, 22.0] days; MAC: 16.0 [12.0, 22.0] days). KM-estimated Day 100 post-HCT survival was lower in the RIC subgroup (49.3%; 95% confidence interval [CI]: 40.5%, 57.4%) compared with the MAC subgroup (68.1%; 95% CI: 58.7%, 75.9%). Similarly, KM-estimated survival at 1 year post-HCT was lower in the RIC subgroup (33.6% [95% CI: 25.7%, 41.6%]) compared with the MAC subgroup (47.8% [95% CI: 38.3%, 56.6%]). Transplant-related mortality (TRM) was higher in the RIC subgroup vs the MAC subgroup (RIC: 55.2%, n = 74; MAC: 40.7%, n = 46). Serious treatment-emergent adverse events of interest were reported in 33.6% of patients in each subgroup; the most common were hemorrhage (RIC, 17.2% vs MAC, 22.1%) and infection (21.6% vs 12.4%).

Summary/Conclusion:

Adult patients who receive RIC regimens may still be at risk of VOD/SOS due to characteristics such as older

age and previous HCT. In this analysis, VOD/SOS tended to be more severe in patients who received RIC vs MAC, with lower survival rates at Day 100 and 1 year post-HCT along with higher TRM in the RIC subgroup. This highlights the need to maintain vigilance for VOD/SOS signs and symptoms following RIC, as prompt diagnosis and treatment of VOD/SOS may improve patient outcomes.

Keywords: Veno-occlusive disease, Conditioning, Real world data, Hematopoietic cell transplantation