Abstract: P1357

Title: LOW-DOSE DEFIBROTIDE TREATMENT FOR HIGH-RISK TRANSPLANT-ASSOCIATED THROMBOTIC MICROANGIOPATHY AFTER ALLOGENEIC HAEMATOPOIETIC STEM CELL TRANSPLANTATION: A PROSPECTIVE OBSERVATIONAL STUDY

Abstract Type: Poster Presentation

Topic: Stem cell transplantation - Clinical

Background:

Transplant-associated microangiopathy (TA-TMA) is a life-threatening complication of allogeneic haematopoietic stem cell transplantation (allo-HSCT) that occurs in approximately 15-30% of allogeneic transplant patients, and the mortality rate reaches 60-90% in severe patients with multiorgan dysfunction. Defibrotide (DF) can act on endothelial cells (ECs) through its antithrombotic, thrombolytic, anti-inflammatory, and anti-ischaemic properties. DF at a dose of 6.25 mg/kg IV every 6 h/25 mg/kg/d for ≥21 days was safe and effective for treating TA-TMA after allo-HSCT. However, the high cost and unpredictable availability of DF may limit its use.

Aims:

This study was to explore the safety and efficacy of low-dose DF in the treatment of TA-TMA after allo-HSCT.

Methods:

This was a prospective observational study. All allo-HSCT recipients with high-risk TA-TMA who received low-dose DF (6.25 mg/kg IV every 12 h) at our institution were included in this study. DF was used until the TA-TMA was resolved. resolved. TA-TMAs were diagnosed in HSCT recipients with histologic evidence of TMA on tissue samples, if available, or the concomitant presence of ≥5 of the diagnostic markers according to Jodele et al. Patients were classified as high-risk TA-TMAs if they met ≥2 of the following 3 criteria at TA-TMA diagnosis: ①random urine protein/creatinine ratio (rUPCR) ≥2 mg/mg; ②elevated sC5b-9 (≥244 ng/mL); and ③clinical evidence of multiorgan dysfunction syndrome (MODS). Patients with severe active bleeding were excluded.

Results:

A total of 32 subjects, including 21 males and 11 females, were included in the study between August 1, 2018, and November 31, 2023. The median age was 36 (range 1-63) years. The majority (n=25, 78.1%) received haploidentical allo-HSCT, 5 patients (15.6%) received matched sibling allo-HSCT, and 2 (6.3%) patients received unrated matched allo-HSCT. Most of the patients (28/32, 87.5%) underwent transplantation for malignancies, and the other 4 (12.5%) underwent transplantation for severe aplastic anaemia. All patients achieved engraftment of neutrophils after a median of 12 days (range 10-20). However, only 21 (65.6%) patients with a median time of 12 (range 7-32) days after allo-HSCT achieved platelet engraftment at TA-TMA diagnosis. Acute GVHD (aGVHD) of any grade was diagnosed before TA-TMA in 17 (53.1%) patients (2 with grade 2, 8 with grade 3, and 7 with grade 4 aGVHD). Five patients (15.6%) developed refractory CMV infection before TA-TMA. At a median of 51 (range 6-397) days after allo-HSCT, patients developed high-rik TA-TMA, and at 8 (0-86) days after high-risk TA-TMA diagnosis, patients received DF treatment. The combined therapy for TA-TMA included withdrawal of CNIs in 18 patients (56.3%), glucocorticoids in all patients, plasma exchange in 7 patients (21.9%) and rituximab in 5 patients (15.6%). Finally, patients received low-dose DF treatment for a median duration of 10 (range, 2-29) days, and high-risk TA-TMA resolved in 16 patients (50%). The other 16 patients had no response to DF or other TA-TMA treatments, and all died from TA-TMA. During DF treatment, only 1 patient experienced severe gastrointestinal bleeding, and DF was discontinued after 2 days of treatment. A total of 20 patients died during the follow-up. For patients who responded to low-dose DF, 4 patients died of severe pneumonia (n=2) or relapse of leukaemia (n=2) during the follow-up.

Summary/Conclusion:

Low-dose DF might be a potential safe and effective treatment for high-risk TA-TMA patients. However, further prospective evaluation in a large cohort of patients with high-risk TA-TMA is warranted.

Keywords: Thrombotic microangiopathy, Defibrotide