Abstract: P1342

Title: REAL-WORLD EXPERIENCE OF BELUMOSUDIL TREATMENT FOR CHRONIC GRAFT-VERSUS-HOST DISEASE AFTER THE FAILURE OF MULTIPLE LINES OF THERAPY: A CANADIAN EXPERIENCE

Abstract Type: Poster Presentation

Topic: Stem cell transplantation - Clinical

Background:

Chronic graft-versus-host disease (cGvHD) remains a challenge in the contemporary management of allogeneic hematopoietic stem cell transplantation (HCT) survivors and contributes to considerable morbidity and mortality. While therapeutic options have expanded with the availability of agents like ruxolitinib and ibrutinib, it is still challenging to manage the patients with irreversible fibrotic or sclerotic cGVHD for which there are few options available. Belumosudil, a selective Rho-associated coiled-coil kinase 2 (ROCK2) inhibitor, has shown promising efficacy in preclinical and early clinical studies based on its immunomodulatory properties. Available in Canada since March 2023 under a compassionate use program, we present here preliminary efficacy data on belumosudil in terms of response rate, patient perceived clinical benefit, and failure-free survival (FFS) for the treatment of cGvHD.

Aims:

To evaluate the efficacy and safety of belumosudil.

Methods:

This retrospective study evaluated the efficacy and safety of belumosudil in a cohort of patients with cGVHD after the failure of multiple lines of therapy. Data were collected retrospectively from medical records at transplant centers in Toronto, Quebec City, Saskatoon, and Calgary between March 2023 and February 2024. Baseline characteristics of the patients and disease, prior treatments received, and details of belumosudil treatment were captured retrospectively in addition to response rates, treatment outcomes, and adverse events. Failure Free Survival (FFS) was defined as the time from starting belumosudil to addition of new GVHD therapy, relapse, or death. Survival outcomes were calculated using Kaplan-Meier survival analysis. Statistical analysis was performed using EZR v1.64.

Results:

Thirty-five patients (N=35) were treated with belumosudil, of whom 25 were evaluable for response with a minimum follow-up of 3 months. All patient had moderate/ severe cGvHD with a median of 3 (range, 2-4) affected organs at the start of belumosudil treatment. Patients had received a median of 5 prior (range, 3.8-6.5) lines of therapy. The median duration from cGvHD onset to commencement of belumosudil was 37.6 months (range, 13.1 – 91.8). Corticosteroids were the most common concurrent treatment with belumosudil (72%), while 44% of the patients were treated with combination therapy of belumosudil with ruxolitinib. With a median follow-up of 4.8 months (3.1-8.4 months) following belumosudil initiation, the overall response rate at 3 and 6 months was 28% (n=7/25) and 31.3% (n=5/16), respectively. Clinical benefit was observed in 16 (64%) and 13 (52%) patients at 3 and 6 months, respectively. In 10 patients (40%), corticosteroid dose was reduced significantly following the initiation of belumosudil. The 6 month FFS rate was 71.9%, while the overall survival rate was 76.6% at 6 months. Notably, no grade ≥ 3 toxicities were noted as of the last follow-up. Treatment was discontinued in 5 patients. This included 2 patients where treatment was stopped due to intolerance (muscle spasm, increased transaminases), 2 patients where additional treatment for cGvHD had to be initiated, and one patient who succumbed to pre-existing infection.

Summary/Conclusion:

Our preliminary findings suggest that belumosudil holds promise as salvage therapy for patients with refractory cGVHD after multiple lines treatment failure. Further studies with larger patient cohorts and extended follow-up durations are strongly warranted to confirm these results and elucidate optimal dosing regimens and long-term outcomes.

Figure 1: Overall Survival

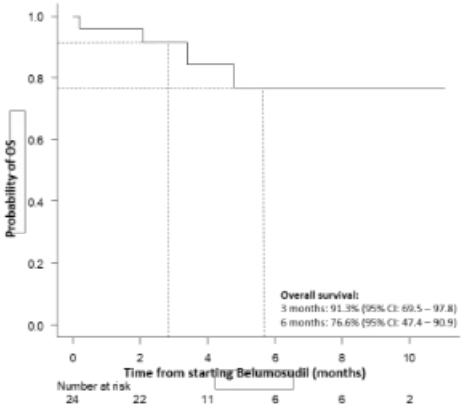
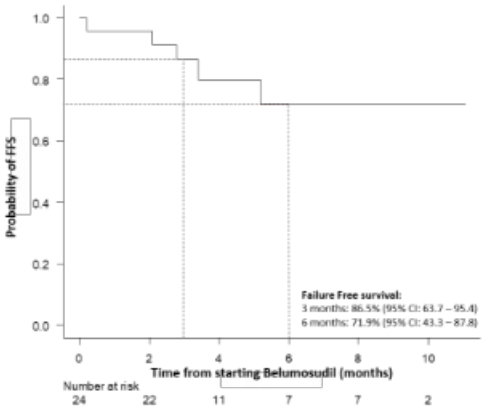


Figure 2: Failure Free Survival



Keywords: Immunomodulation, Allogeneic hematopoietic stem cell transplant, Salvage therapy, Chronic graft-versus-host