(PB4073) EARLY TREATMENT WITH BELUMOSUDIL IMPROVES THE CLINICAL OUTCOME OF CGVHD

Topic: 23. Stem cell transplantation - Clinical

Akihisa Hino*[1], Tomoaki Ueda[1], Shinsuke Kusakabe[1], Hidenori Kasahara[1], Keigo Akuta[1], Hiroyuki Takamori[1], Jiro Fujita[1], Kentaro Fukushima[1], Naoki Hosen[1, 2, 3]

[1]The University of Osaka Graduate School of Medicine, Hematology and Oncology, Suita, Japan;[2]The University of Osaka, World Premier International Immunology Frontier Research Centre, Suita, Japan;[3]The University of Osaka, Integrated Frontier Research for Medical Science Division, Institute for Open and Transdisciplinary Research Initiatives (OTRI), Suita, Japan;

Background

Chronic graft-versus-host disease (cGVHD) is a refractory disease, causing tissue inflammation and fibrosis in various organs. In recent years, the advent of novel therapeutic agents has precipitated substantial developments in the management of cGVHD. Belumosudil is one of the novel therapeutic agents for cGVHD. Belumosudil promotes downregulation of inflammatory cytokines and improves fibrosis by inhibiting Rho-associated coiled-coil containing protein kinase 2 (ROCK2). Belumosudil is approved in many countries as the third-line treatment for cGVHD. This drug is permitted for use in earlier lines in a few countries, including Japan.

Aims

We consider that the early inhibition of ROCK2 prevents fibrosis and leads to favorable outcomes in cGVHD. However, there is no clear evidence regarding the impact of prior treatment history or treatment timing on the therapeutic efficacy of Belumosudil. We are permitted to use Belumosudil earlier than many other countries. Based on this background, we examined the impact of early Belumosudil use on cGVHD treatment.

Methods

We retrospectively analyzed 22 patients who received Belumosudil for cGVHD at The University of Osaka Hospital from May 2024 to December 2025. The median duration of cGVHD was 228 days (range: 11-5370 days). There were 17 cases that received early treatment with Belumosudil within one year after cGVHD onset. Thirteen cases received Belumosudil as second-line treatment after steroid therapy. Nine cases received this drug as third-line or beyond treatment. Baseline organ dysfunction was present in the following organs: Eye (n=3), Skin (n=7), Lung (n=4), Gastrointestinal tract (n=5), Mouth (n=3), Liver (n=3), Joint (n=1), Serositis (n=3). Baseline assessment and treatment efficacy evaluation of cGVHD in each organ were performed based on the 2014 National Institutes of Health Consensus Criteria. Treatment efficacy was evaluated at both the short-term (1–3 months) and long-term (6–12 months) time points.

Results

Belumosudil significantly improved cGVHD scores in each organ within 3 months after treatment ($p<0.0001$). Further improvement in the cGVHD score was observed only in the gastrointestinal tract at 6 months and beyond after treatment. Both the early treatment (within 1 year of cGVHD onset) and the late treatment (1 year or later after cGVHD onset) significantly improved cGVHD scores (Figure1 A, B). In particular, the early treatment produced a greater improvement in cGVHD scores compared to the late treatment ($p=0.009$) (Figure1 C). This result demonstrated the effectiveness of early treatment for Belumosudil. No significant difference in treatment efficacy was observed between second-line treatment and third-line or beyond treatment. In organ-specific comparisons, treatment efficacy was low for the lungs in both early and late treatment groups. Complete remission was achieved for serositis in both early and late treatment groups.

Summary/Conclusion

Initiating Belumosudil within one year of cGVHD onset significantly improved cGVHD outcomes. However, the choice of second-line treatment versus third-line or beyond treatment did not affect the results. Regardless of prior treatment, early initiation of Belumosudil after cGVHD onset was shown to deliver effective results.

Figure1