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POSTER ABSTRACTS

722.ALLOGENEIC TRANSPLANTATION: ACUTE AND CHRONIC GVHD, IMMUNE RECONSTITUTION

A Novel JAK1 Inhibitor SHR0302 for Treatment of Chronic Graft-Verse-Host Disease: A Phase I Clinical Trial

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Background:
Chronic graft-versus-host disease (cGVHD) is a frequent and potentially life-threatening complication after allogeneic hematopoietic stem cell transplantation (allo-HSCT). Standard steroid first-line treatment could not satisfy therapeutic need due to its limited efficacy. SHR0302 is a highly selective Janus kinase (JAK) 1 inhibitor, which could alleviate symptoms and improve the survival of cGVHD mice in our preclinical study. Herein, we reported updated safety and efficacy results of SHR0302 plus prednisone as first-line treatment for patients with naïve-treatment moderate or severe cGVHD.

Methods:
This was a Phase I open-label study. Patients who were aged 18-70, and confirmedly diagnosed with first-episode moderate/severe cGVHD requiring systemic immunosuppressive therapy after allo-HSCT were included in the study. cGVHD was defined according to national institutes of health (NIH) criteria. A 3+3 design including five dose levels (1mg/2mg/4mg/6mg/8mg once a day) was implemented to define the optimal dose of SHR0302. Meanwhile, prednisone was concurrently administrated with a dose of 1mg/kg/d and then gradually tapered after two weeks. The primary endpoint was safety, and the secondary endpoints were overall response rate (ORR) at day 28 and week 24. Dose-limiting toxicities (DLTs) were defined as grade 4 hematologic toxicity or grade 3 non-hematologic toxicity associated with SHR0302 which occurred in the first 28 days of study treatment.

Results:
From April 2020 to July 2022, 18 patients were enrolled in the trial. Till May 2023, the median follow-up was 17.3 months (range, 1.8-31.7). The median age of the patients was 47 years (range, 31-64). 13 (72.2%) patients had severe cGVHD, and the other 5 had moderate cGVHD. Almost all patients had more than one organ involved, and the most commonly involved organs were skin (66.7%), and mouth (50.0%). In contrast, lung (5.6%) and genital tract (5.6%) involvements were uncommon. Median duration of SHR0302 treatment was 6.3 months (range, 1.5-23.2). Overall, all (100%) patients experienced adverse events (AEs) related to SHR0302 and/or prednisone, and grade 3 or 4 AEs were observed in 7 (38.89%) patients. The most common SHR0302 treatment-related adverse events (TRAEs) included hypercholesterolemia (61.11%, n=11), hypertriglyceridemia (44.44%, n=8), platelet count decreased (38.89%, n=7), and anemia (16.67%, n=3). There were no serious AEs (SAEs) related with SHR0302, and no patient experienced SHR0302 dose reduction / discontinuation or death due to AEs. Only one patient developed DLT (grade≥3 hypercholesterolemia) in the highest dose-level group who had preexisting hypercholesterolemia. The maximum tolerated dose (MTD) was not reached.
The ORR and complete remission (CR) rates were 94.44% and 27.77% at week 4, and were 82.35% and 64.71% at week 24, respectively. Among 18 evaluable patients, only 1 patient treated at dose level 1 showed no response at week 4. The event-free survival (EFS) at 24 months was 72.20% (95% CI, 51.40%-93.00%). Prednisone was discontinued in 8 (44.4%) patients at 24 weeks and all immunosuppressants, including SHR0302, were stopped in 4 (22.2%) patients with CR before the 24-week assessment.

Conclusions:
In summary, SHR0302 in combination with prednisone had a good safety and could achieve a high response for naïve-treatment cGVHD, which suggests that SHR0302 combination might become an optimal choice for naïve-treatment cGVHD.

Disclosures No relevant conflicts of interest to declare.

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