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POSTER ABSTRACTS

626.AGGRESSIVE LYMPHOMAS: PROSPECTIVE THERAPEUTIC TRIALS

Anti-Btla Antibody Tifcemalimab As a Single Agent or in Combination with Toripalimab in Relapsed/Refractory Lymphomas

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Background: The B- and T-lymphocyte attenuator (BTLA) is an inhibitory receptor expressed on B, T and NK cells. Using Peripheral Blood Mononuclear Cell (PBMC) derived from cancer patients, co-blockade of the BTLA and PD-1 pathways improved antigen specific T cell response compared to either blockade alone. Tifcemalimab (JS004 or TAB004) is a humanized IgG4 monoclonal antibody with a hinge mutation (S228P) that binds BTLA and blocks its interaction with its ligand Herpesvirus Entry Mediator (HVEM). Tifcemalimab is the first BTLA antibody to enter the clinical development stage. Here, we report the safety and efficacy of tifcemalimab as a single agent or in combination with toripalimab (anti-PD-1) in patients with relapsed/refractory (R/R) lymphoma after long term follow-up.
Methods: Eligible patients with R/R lymphoma were enrolled in this open-label, multicenter phase 1 study (NCT04477772). Tifcemalimab was administered as a monotherapy at escalating doses of 1, 3 and 10 mg/kg intravenously Q3W, followed by 3 mg/kg and 200 mg monotherapy dose expansion until disease progression or intolerable toxicity. During combination dose escalation, patients received ascending doses of tifcemalimab (100mg and 200mg) plus toripalimab (240mg). Dose-limiting toxicity (DLT) was evaluated by a safety monitoring committee. Study objectives included safety, pharmacokinetics, and efficacy.
Results: By the cutoff date of July 19, 2023, a total of 71 patients were enrolled, including 25 in the monotherapy and 46 in the combination cohorts. The median follow-up time was 57 weeks. The median age was 38 (range 19-70) years with 50 (70%) male patients. The median prior line of therapy was 4 with 54 (76%) progressed upon prior anti-PD-1/L1 therapy. No DLT was observed in either monotherapy or combination dose escalation. Recommended phase 2 dose (RP2D) was determined to be

200 mg tifcemalimab as monotherapy or in combination with toripalimab. Sixty-seven (94%) patients experienced treatment emergent adverse events (TEAEs), 22 (31%) of whom experienced grade 3 or above TEAEs. The most common TEAEs were COVID-19 infection (30%), anemia (30%) and Infusion related reaction (27%). Four treatment-related adverse events led to the discontinuation of the study drug. Among 25 patients receiving monotherapy, 1 PR (follicular lymphoma) and 7 SD were observed with median progression-free survival (PFS) 2.1 months. Among 46 patients receiving combination therapy, 1 CR,16 PR (ORR 37.0%) and 20 SD (DCR 80.4%) were observed and estimated median PFS was 14.7 months. Thirty-four patients with Hodgkin's Lymphoma received RP2D of combination therapy and all of them had received previous chemotherapy and anti-PD-1 or anti-PD-L1 antibody, and 12 PR (ORR 35.3%) and 17 SD (DCR 85.3%) were observed with estimated median progression-free survival was 16.2 months.

Conclusions: Tifcemalimab alone or in combination with toripalimab were well tolerated in all doses evaluated. The combination regimen showed favorable safety and durable efficacy in lymphoma patients with heavily pretreatment, providing evidence for future investigation.

Disclosures Liu: *Shanghai Junshi Biosciences:* Current Employment. **Wang:** *Shanghai Junshi Biosciences:* Current Employment. **Xu:** *Shanghai Junshi Biosciences:* Current Employment. **Wang:** *Shanghai Junshi Biosciences:* Current Employment.

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