PB1999 ATG-010 PLUS LOW-DOSE DEXAMETHASONE (SD) IN CHINESE RELAPSED/REFRACTORY MULTIPLE MYELOMA (RRMM) PATIENTS PREVIOUSLY RECEIVED CHIMERIC ANTIGEN RECEPTOR T-CELL (CAR-T)

Topic: 14. Myeloma and other monoclonal gammopathies - Clinical

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Background: There are limited treatment options for multiple myeloma (MM) patients who have a disease progression after CAR-T therapy. ATG-010 (selinexor) is a novel, oral selective inhibitor of nuclear export, inhibiting exportin 1. US FDA has approved selinexor plus low dose dexamethasone (SD) to treat patients (pts) with pentarefractory MM. MARCH study, a single arm, phase 2, registrational study evaluating SD in Chinese RRMM pts, achieved an overall response rate (ORR) of 29.3% (95% CI: 19.7, 40.4), rejecting the null hypothesis of the study.

Aims: To evaluate efficacy and safety of SD in Chinese RRMM pts previously treated with CAR-T.

Methods: The study enrolled 82 pts previously exposed and refractory to a proteasome inhibitor (PI), an immunomodulatory agent (IMiD), and last line of therapy. Among them, 10 had received lymphodepleting conditioning followed by CAR-T cell therapy before study screening. ATG-010 (80mg) plus dexamethasone (20mg) was administered orally twice weekly. Response was assessed by an independent review committee.

Results: Among 10 pts, 8 were male and 2 were female. Median age was 58.5 years. Median duration from MM initial diagnosis was 5.2 years. A total of 6 pts (60.0%) had high-risk cytogenetic abnormalities, including 4 pts (40.0%) with del (17p). Three pts had baseline plasmacytoma. Five pts (50%) experienced very rapid disease progression as indicated by a median of 46.2% increase of tumor burden from screening to Cycle 1 Day 1. Patients were heavily pre-treated with a median of 9.5 prior regimens (range: 5-12), with 8 receiving more than 6 regimens. Four pts were exposed to daratumumab (triple-class exposure). ORR was 50% including 1 very good partial response and 4 partial responses. Disease control rate defined as SD and above was 70%. As of 10th Feb 2022, all pts had disease progression, 5 pts are still under survival follow-up. Median duration of response was 1.4 months (mo) (95% CI: 0.96, NE). Median progression free survival was 1.9 mo (95% CI: 0.93, 3.74). Median overall survival was not reached and estimated 12-mo OS rate was 70%. After disease progression (PD) after SD treatment, 4 pts received CD38 antibody based regimen, 4 pts received pomalidomide based regimen, 4 pts had cytotoxic therapy, 1 pt received 2nd CAR-T therapy, and 2 pts had no chance to receive any treatment due to death after rapid PD. Of note,
1 pt received selinexor plus lenalidomide based regimen and obtained a prolonged disease control.

Adverse events were consistent with those events previously reported with Sd regimen in RRMM patients. The most common grade≥3 treatment emergent adverse events (TEAEs) included anemia, thrombocytopenia, neutropenia and nausea. Most events were manageable with appropriate supportive care or dose modification. Four pts (40%) experienced TESAEs, including anemia, pneumonia, neutropenia, and upper gastrointestinal hemorrhage. There were no TEAEs leading to treatment discontinuation or death.

**Summary/Conclusion:** Sd was able to induce an encouraging response with a manageable safety profile for a group of Chinese RRMM patients desperately needing treatment after failing CAR-T therapy. This suggests that selinexor is a highly potent anti-MM therapy and further investigation is warranted, including using selinexor in combination with other anti-MM therapies in earlier lines of treatment.