3. RELAPSED/REFRACTORY MULTIPLE MYELOMA

EFFICACY AND SAFETY OF TALQUETAMAB + TECLISTAMAB IN PATIENTS WITH RELAPSED/REFRACTORY MULTIPLE MYELOMA AND EXTRAMEDULLARY DISEASE: UPDATED PHASE 2 RESULTS FROM THE REDIRECTT-1 STUDY WITH EXTENDED FOLLOW-UP

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Introduction. Patients (pts) with triple-class exposed (TCE) relapsed/refractory multiple myeloma (RRMM) and true extramedullary disease (EMD) experience poor outcomes with standard therapies. The bispecific combination of talquetamab (Tal; anti-GPRC5D×CD3) and teclistamab (Tec; anti-BCMA×CD3) in TCE RRMM is being assessed in the ongoing RedirecTT-1 trial (NCT04586426); the regimen elicited an ORR of 78.9% and a 12-month progression-free survival (PFS) rate of 61.0% in the primary analysis of the dedicated phase 2 EMD cohort (March 2025 data cut; median follow-up [mFU] 12.6 months). Here, we report updated efficacy and safety results from the EMD population.

Methods. Pts had TCE RRMM and true EMD defined as ≥1 nonradiated soft tissue plasmacytoma noncontiguous with bone ≥2 cm in 1 dimension (with or without paramedullary plasmacytomas). Nonsecretory/oligosecretory disease, prior CAR T, and prior non-BCMA/-GPRC5D BsAb therapies were all permitted. Pts received Tal 0.8 mg/kg + Tec 3.0 mg/kg Q2W, preceded by step-up doses, with a permitted switch to monthly dosing at investigator's discretion after cycle 6 or after cycle 4 with confirmed ≥VGPR. Response was assessed per IMWG; EMD response was assessed by PET-CT or MRI whole-body scans. Tumor burden was assessed by total EMD tumor volume.

Results. As of July 2025, 90 pts received Tal + Tec, with a median follow-up of 16.3 months (range 0.5–23.7). Baseline characteristics were as previously reported. Per investigator assessment, ORR (95% CI) was 77.8% (67.8–85.9); 50.0% had a ≥CR. Median duration of response (DOR) was not estimable (NE; 12-month DOR rate, 60.1%), 12-month PFS was 55.6%, and median overall survival (OS) was NE (12-month OS rate 73.8%). ORR was 90.7% (77.9–97.4; ≥CR 60.5%) in pts with EMD tumor volume <25 cm^2, 66.7% (43.0–85.4; ≥CR 52.4%) for 25–50 cm^2, and 65.4% (44.3–82.8; ≥CR 30.8%) for >50 cm^2. Common adverse events (AEs) included CRS (77.8%; none grade 3/4) and neutropenia (72.2%; grade 3/4 62.2%). Taste changes (78.9%), non-rash skin AEs (68.9%), and nail AEs (55.6%) were all grade 1/2, and rash AEs (30.0%) were mostly grade 1/2. ICANS occurred in 11 (12.2%) pts (grade 3, 1.1%; grade 4, 1.1%). Infections occurred in 72 (80.0%) pts (grade 3/4 40.0%), most commonly upper respiratory tract infection (26.7%; grade 3/4 5.6%); IVIG was highly recommended to prevent and manage hypogammaglobulinemia and infection. Ten (11.1%) pts discontinued Tal + Tec due to treatment-emergent AEs (4 pts due to infections and 6 due to grade 5 AEs), and two pts discontinued Tal only due to AEs. In total, 11 (12.2%) pts had grade 5 AEs (6 due to infections), 6 of which were deemed to be drug related by investigators.

Conclusions. Across extended follow-up in pts with TCE RRMM and EMD, Tal + Tec demonstrated improved efficacy compared with all approved regimens, including T cell redirecting and cellular therapies. Lower total EMD tumor volume was numerically associated with a higher ORR, and the safety profile of Tal + Tec was generally consistent with each monotherapy; AEs were not exacerbated with the combination. These data continue to highlight the clinical benefit of the novel combination of Tal + Tec in pts with true EMD, a population with high disease burden and significant unmet need.