3. RELAPSED/REFRACTORY MULTIPLE MYELOMA

SAFETY AND EFFICACY OF TALQUETAMAB + TECLISTAMAB IN PATIENTS WITH RELAPSED/REFRACTORY MULTIPLE MYELOMA FROM PHASE 1B OF REDIRECTT-1: RESULTS WITH AN EXTENDED MEDIAN FOLLOW-UP OF 3 YEARS

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Introduction. In previous results from the phase 1b stage of RedirecTT-1 (NCT04586426; median follow-up [mFU] 20.3 mo), Tal (anti-GPRC5D×CD3) + Tec (Tec, anti-BCMA×CD3) elicited deep, durable responses in pts with triple-class exposed (TCE) RRMM and demonstrated a safety profile generally consistent with each monotherapy across all dose levels (DLs), including the recommended phase 2 regimen (RP2R) of Tal 0.8 mg/kg + Tec 3.0 mg/kg Q2W and in true extramedullary disease (EMD). We report efficacy and ongoing safety from phase 1b of RedirecTT-1 at an extended mFU of 36.2 mo.

Methods. Pts had TCE RRMM and were refractory, relapsed, or intolerant to the last line of therapy. True EMD was defined as ≥1 nonradiated soft tissue plasmacytoma noncontiguous with bone ≥2 cm in 1 dimension. Primary objectives were to evaluate safety and identify a RP2R. Investigator-assessed confirmed response per IMWG criteria was reported in all treated pts; EMD response was assessed by CT, PET-CT, or MRI whole-body scans.

Results. As of July 2025, 94 pts received Tal + Tec (44 pts at the RP2R), with an mFU of 36.2 mo. Baseline characteristics were as previously reported. Dose-limiting toxicities occurred in 3 pts across non-RP2R DLs (all grade [gr] 3) and in 1 pt at the RP2R (gr 4 thrombocytopenia). The most common adverse events (AEs) were infections (gr 3/4, 68.1% [54.5% at the RP2R]), with COVID-19 (40.4%; gr 3/4, 17.0%) the predominant infection type; likely a reflection of pt enrolment between 2020-2023, concurrent with the COVID-19 pandemic. Other frequent adverse AEs included CRS (80.9%; gr 3, 2.1%; no gr 4/5), neutropenia (74.5%; gr 3/4, 70.2%), taste changes (66.0%; all gr 1/2), and non-rash skin AEs (62.8%; gr 3, 2.1%). ICANS occurred in 3.2% of pts (gr 3/4, 1.1%). Overall, drug-related AEs were associated with 9 Tal + Tec discontinuations (6 at the RP2R) and 9 deaths (2 at the RP2R). 12 discontinuations were due to infections (5 at the RP2R). At the RP2R, overall response rate (ORR) was 79.5%, with a ≥CR rate of 61.4%; ORR was 61.1% (≥CR, 44.4%) in pts with EMD and 92.3% (≥CR, 73.1%) in pts without EMD. Across all DLs, ORR was 77.7% (≥CR, 52.1%). Responses continued to be durable at the RP2R and across all DLs, including in pts with EMD. The median duration of response (DOR) was non-estimable (NE) at the RP2R (NE with and without EMD), as well as across all DLs, with 36-mo DOR rates of 71.1% at the RP2R (61.4% with EMD, 76.4% without EMD) and 58.5% across all DLs. Median PFS was NE at the RP2R (21.6 mo with EMD, NE without EMD) and 38.6 mo across all DLs, with 36-mo PFS rates of 57.9% at the RP2R (39.7% with EMD, 70.5% without EMD) and 52.6% across all DLs. Median OS was NE at the RP2R (NE with and without EMD), as well as across all DLs, with 36-mo OS rates of 73.9% at the RP2R (57.0% with EMD, 83.2% without EMD) and 65.8% across all DLs.

Conclusions. At an extended mFU of ~3 yrs, Tal + Tec continued to exhibit a safety profile generally consistent with each monotherapy, with no exacerbation of AEs in combination. A high ORR was achieved, and responses across all pts were both deep and durable, including at the RP2R and in those with true EMD, contributing to the extended PFS observed. DOR and survival in pts with and without EMD exceeded all other regimens in this therapy area. These data continue to highlight the clinical benefit of Tal + Tec in pts with TCE RRMM.