4. SPECIAL CONDITIONS

TALQUETAMAB INDUCES DEEP RESPONSES IN HEAVILY PRE-TREATED PATIENTS WITH SYSTEMIC LIGHT-CHAIN AMYLOIDOSIS

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Background. Treatment options for relapse/refractory (R/R) light-chain (AL) amyloidosis patients progressing after daratumumab based therapy are scarce, mainly for patients without t11:14 translocation. Talquetamab is a T-cell engager targeting G protein–coupled receptor class C group 5 member D (GPRC5D) with proven efficacy in heavily pretreated MM patients, but also with on-target off tumor toxicity, mainly dysgeusia and weight loss. We report 6 heavily pretreated patients treated with talquetamab for R/R AL amyloidosis.

Methods. This is a retrospective case-series, including all adult patients with biopsy-proven R/R AL amyloidosis and treated with talquetamab in two centers.

Results. Six patients (five males), median age 63 years (range 53–74), were included. Two had concurrent MM. The heart and kidneys were the most commonly involved organs (five patients each). Three patients had ≥3 organs involved at baseline. At talquetamab initiation, 3 patients were mayo stage 3 or 4. All patients had impaired renal function at study entry, including 4 with eGFR<30 ml/min, two them were dialysis dependent. Patients received a median of 7 (range 2–11) prior treatment lines. All were refractory to daratumumab, bortezomib, cyclophosphamide and pomalidomide; 4 were refractory to lenalidomide and belantamab mafodotin; 1 patient with t(11;14) was refractory to venetoclax. Three patients relapsed after academic anti-BCMA CAR-T. Additional therapies included ixazomib (2), carfilzomib (1), elotuzumab (1) and melphalan (1). Talquetamab was initiated for progressive disease in 4 patients and for insufficient response in 2. The median time from diagnosis to talquetamab administration was 71 (range 8-132) months. The median number of cycles was 5.2 (range 1-22). Four patients received talquetamab at a dose of 0.8 mg/kg every other week, and two patients 0.4 mk/kg every week. Five patients (83%) achieved hematologic response, all of whom obtained complete remission (CR). MRD was negative in 3/3 patients tested, including 2 patients with sustained MRD negativity after 6 and 9 months; the third patient was not re-tested for MRD. The median time to documented hematological response was 26 (range 21-63) days. The median follow-up time was 9.6 (range 1-22) months. At data cutoff, 3 patients were alive (all in CR) after 22, 11 and 6 months from talquetamab first dose. Three patients died: 1 relapsed 5 months after talquetamab initiation and died from sepsis, 1 died from cardiac failure despite achieving CR, and 1 who was primary refractory (Figure 1). Two patients with end-stage renal disease were referred to kidney transplantation. Cytokine release syndrome (CRS) occurred in four patients (all grade 1–2). One patient developed grade 2 immune effector-cell associated neurotoxicity syndrome (ICANS). Infectious complications included sepsis (one grade 3, one grade 5). Congestive heart failure exacerbation occurred in two (grades 3 and 4). Additional adverse events included: dysgeusia (grade 2), xerostomia (grade 2) and weight loss (grade 2) in 2 patients each; anemia (grade 3), fever and thrombocytopenia (grade 2) in 1 patient each.

Conclusions. To conclude, talquetamab therapy for heavily pre-treated AL patients with significant end-organ damage resulted in deep responses and clear clinical benefit, with manageable toxicity and without new safety signals. □