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ORAL ABSTRACTS

653.MULTIPLE MYELOMA: PROSPECTIVE THERAPEUTIC TRIALS

Efficacy and Safety of Less Frequent/Lower Intensity Dosing of Talquetamab in Patients with Relapsed/Refractory Multiple Myeloma: Results from the Phase 1/2 MonumenTAL-1 Study

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Introduction: Talquetamab (tal) is an off-the-shelf, T-cell redirecting bispecific antibody targeting G protein-coupled receptor family C group 5 member D (GPRC5D) and CD3. Results from the phase 1/2 MonumenTAL-1 (NCT03399799/NCT04634552) trial showed overall response rates (ORRs) of >71% and a manageable safety profile with the recommended phase 2 doses (RP2Ds) of subcutaneous tal (0.4 mg/kg weekly [QW] or 0.8 mg/kg every other week [Q2W]) in patients (pts) with relapsed/refractory multiple myeloma (RRMM). The impact of reducing dose intensity with bispecifics on safety and efficacy is an area of clinical interest. We report safety and efficacy in pts from MonumenTAL-1 who switched to less frequent or reduced dosing with tal.
Methods: In phase 1, pts were intolerant to or progressed on established therapies and had an Eastern Cooperative Oncology Group performance status (ECOG PS) of 0 or 1. In phase 2, pts had received ≥3 prior lines of therapy, including ≥1 proteasome inhibitor, ≥1 immunomodulatory drug, and ≥1 anti-CD38 monoclonal antibody, and had an ECOG PS of 0-2. Phase 1 included 2 prospectively designed cohorts: (A) a reduced dosing cohort in which pts treated with tal 0.8 mg/kg Q2W were permitted to switch to 0.4 mg/kg Q2W at the next cycle following a confirmed partial response or better (≥PR), and (B) a less frequent dosing cohort in which pts treated with tal 0.8 mg/kg Q2W were permitted to switch to 0.8 mg/kg monthly (Q4W) at the next cycle following a confirmed ≥PR. Results for these phase 1 prospective cohorts are pooled. Supportive analyses were also performed based on pts in phases 1/2 who received the RP2Ds and switched to reduced dosing based on meeting response criteria or to mitigate treatment-emergent adverse events (TEAEs). Dose reduction could be achieved by reducing dose frequency or by reducing dose. ORRs were assessed per IMWG criteria. TEAEs were graded per CTCAE v4.03.
Results: In total, 45 pts switched to reduced intensity dosing. As of June 20, 2023, 24 pts were included in the prospective cohorts, with a median follow-up of 9.7 months. In total, 9/12 pts achieved a ≥PR and switched from 0.8 mg/kg Q2W to 0.4 mg/kg Q2W dosing, and 10/12 pts achieved a ≥PR and switched from Q2W to 0.8 mg/kg Q4W dosing. Generally, pts switched to reduced intensity dosing during cycles 3-5. Following the change in dosing, responses deepened in 11/19 pts and were maintained in 5/19 pts; 3/19 pts had disease progression. At 6 months post switch, an estimated 88.9% of responders maintained a response. Oral-related TEAEs, reported in 16/19 (84.2%) pts, improved or resolved in 4 pts 1-6 months after switching to reduced intensity dosing. Nail-related TEAEs, reported in 7/19 (36.8%) pts, improved or resolved in 2 pts after 3-4 months. Skin-related TEAEs, reported in 8/19 (42.1%) pts, resolved in 3 pts after 1-3 months. Overall, improvement or resolution of oral-, nail-, and skin-related TEAEs was observed over time in some pts in the prospective reduced and less

frequent dosing cohorts. No pts discontinued tal due to these TEAEs. As of January 17, 2023, supportive phase 1/2 analyses included 20 pts who switched from tal 0.4 mg/kg QW to a reduced dose (TEAE mitigation, n=16; response, n=3; both, n=1), and 6 pts who switched from tal 0.8 mg/kg Q2W to a reduced dose (TEAE mitigation, n=4; response, n=2). In pts who switched from tal 0.4 mg/kg to a reduced dose, an estimated 84.2% and 78.9% of responders maintained a response at 9 and 12 months, respectively. In pts who switched from tal 0.8 mg/kg Q2W to a reduced dose, an estimated 100% and 80.0% of responders maintained a response at 9 and 12 months, respectively.
Conclusions: Most pts who switched to reduced intensity dosing in MonumenTAL-1 deepened or maintained responses to tal. GPRC5D-associated TEAEs generally improved over time in the prospectively design cohorts. Overall, reduced or less frequent tal dosing may help to mitigate these TEAEs while maintaining response. Further analyses on the impact of reduced or less frequent tal dosing on clinical outcomes are warranted.

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