Abstract: P951

Title: SAFETY AND PRELIMINARY EFFICACY OF BMS-986393, A GPRC5D CAR T CELL THERAPY, IN PATIENTS WITH RELAPSED/REFRACTORY (RR) MULTIPLE MYELOMA (MM) AND 1–3 PRIOR REGIMENS: FIRST RESULTS FROM A PHASE 1 STUDY

Abstract Type: Poster Presentation

Topic: Myeloma and other monoclonal gammopathies - Clinical

Background:

With the increased use of quadruplet induction regimens and maintenance therapies, MM often becomes refractory early in its course and patients (pts) have an unmet need for novel therapies. BMS-986393, a potential first-in-class autologous CAR T cell therapy targeting G protein-coupled receptor, class C, group 5, member D (GPRC5D), has been granted FDA Regenerative Medicine Advanced Therapy designation for RRMM. Data from the phase 1 CC95266MM001 study (NCT04674813) suggest BMS-986393 is safe and efficacious in heavily pretreated pts with RRMM (median 5 prior regimens) regardless of prior B-cell maturation antigen (BCMA)-targeted therapy. At a dose of 150 × 106 CAR T cells, the overall response rate (ORR) was 91% and complete response rate was 48% (Bal et al, ASH 2023).

Aims:

To report the first results of BMS-986393 in pts with RRMM and 1–3 prior antimyeloma regimens from the CC-95266-MM-001 study.

Methods:

Pts had 1–3 prior antimyeloma regimens including a proteasome inhibitor and an immunomodulatory agent. After leukapheresis, pts received lymphodepleting chemotherapy (fludarabine/cyclophosphamide) followed by a single infusion of BMS986393 150 × 106 CAR T cells. The primary objective was safety. Secondary objectives included clinical activity per IMWG Uniform Response Criteria and pharmacokinetics (PK).

Results:

As of Jan 15, 2024, 30 pts had received BMS-986393. Median age was 62 yr (range 31–78), and 20% were Black or African American. 27% had high-risk cytogenetics (del[17p], t[4;14], and/or t[14;16]), 63% had 1q21 amp, and 27% had extramedullary disease. Pts had received a median of 2 prior regimens; 33% had received 3 prior regimens. 53% of pts had prior stem cell transplantation; 70% had received an anti-CD38 antibody; 90% were lenalidomide-refractory and 57% were triple-class refractory; 93% had myeloma refractory to the last regimen. One pt (3%) had a prior BCMA-targeted therapy (belantamab mafodotin).

Median follow-up was 3.2 mo (range 0.5–5.8); 29 pts (97%) had ≥29 d of follow-up. Treatment-emergent adverse events (TEAEs) occurred in 28 (93%) of 30 treated pts; 23 (77%) experienced a grade (G) 3/4 TEAE. Treatment-related AEs (TRAEs) occurred in 27 pts (90%); 12 (40%) had a G3/4 TRAE. Cytokine release syndrome occurred in 24 pts (80%); all were G1/2. No pts had macrophage activation syndrome/hemophagocytic lymphohistiocytosis. Two pts (7%) experienced lowgrade (G1/2) immune effector cell-associated neurotoxicity syndrome. To date, 11 pts (37%) had an on-target/off-tumor TRAE of the mouth, nails, or skin; all were G1/2. Updated safety will be presented.

Among 20 pts evaluable for efficacy who had complete data entry at data cutoff, 19 achieved a response for an ORR of 95% (the rate of very good partial response or better was 75%). 18 of 19 responses (95%) were ongoing.

PK analyses revealed fast and robust cellular expansion with a median time to peak transgene level (Tmax) of 10 d and a peak transgene level (Cmax) comparable to that seen in heavily pretreated pts. Pharmacodynamic

longitudinal assessment of soluble BCMA indicated BMS-986393 led to deep tumor clearance post-infusion.

Summary/Conclusion:

Initial results suggest a single infusion of BMS-986393 is safe and demonstrates promising preliminary efficacy in pts with MM and 1–3 prior regimens. While follow-up is limited, the safety profile of BMS-986393 at 150 x 106 CAR T cells was favorable with no new safety signals. High response rates were achieved. Early data support GPRC5D-directed CAR T cell therapy by BMS-986393 as a potential early-line treatment in RRMM. The trial is ongoing and updated data will be presented.

Keywords: CAR-T, Clinical trial, Multiple myeloma, Phase I