Abstract: S193

Title: BMS-986393 (CC-95266), A G PROTEIN–COUPLED RECEPTOR CLASS C GROUP 5 MEMBER D (GPRC5D)–TARGETED CAR T-CELL THERAPY FOR RELAPSED/REFRACTORY MULTIPLE MYELOMA (RRMM): RESULTS FROM A PHASE 1 STUDY

Abstract Type: Oral Presentation

Session Title: MM Clinical: New combinations and novel targets

Background:

While chimeric antigen receptor (CAR) T-cell therapies targeting B-cell maturation antigen (BCMA) have shown deep and durable responses in RRMM, new targets are needed as most patients (pts) relapse. GPRC5D, an orphan receptor expressed on MM cells with limited expression in other tissues, is a promising therapeutic target for MM.

Aims:

To present safety and efficacy from the Part A dose escalation of CC-95266-MM-001 (NCT04674813), a phase 1, first-in-human, multicenter, open-label study of BMS-986393 (CC-95266), a GPRC5D-targeted autologous CAR T-cell therapy, in pts with RRMM.

Methods:

Part A includes pts with ≥ 3 prior lines of therapy, including a proteasome inhibitor, an immunomodulatory agent, an anti-CD38 therapy, and autologous stem cell transplant (if eligible). Prior BCMA-directed and CAR T-cell therapies were allowed. After screening and leukapheresis, pts underwent lymphodepletion followed by a single infusion of BMS-986393. Safety and determination of maximum tolerated dose (MTD) and/or recommended phase 2 dose of BMS-986393 were primary objectives.

Results:

As of September 7, 2022, 40 pts enrolled and 33 pts received BMS-986393 at doses of 25 (n = 6), 75 (n = 9), 150 (n = 11), 300 (n = 6), and 450 (n = 1) × 10^6 CAR T cells. Among treated pts, 16 (48%) had high-risk cytogenetics (del[17p], t[4;14], and/or t[14;16]) and 15 (45%) had extramedullary plasmacytomas. Eighteen (55%) pts had received prior BCMA-targeted therapies, including BCMA-directed CAR T-cell therapy in 13 (39%) pts. Eight (24%) pts had penta-refractory MM.

Grade (G) 3/4 treatment-emergent adverse events (TEAEs) were reported in 24/33 (73%) pts; the most frequent were neutropenia (61%), anemia (21%), and thrombocytopenia (21%). On-target off-tumor TEAEs, including skin TEAEs (30%), dysgeusia (15%), nail TEAEs (9%), and dysphagia (3%), were all G1.

Dose-limiting toxicities of prolonged (out to day 42) G4 neutropenia and/or thrombocytopenia were reported in 2 pts; MTD was not exceeded. Cytokine release syndrome (CRS) occurred in 21/33 (64%) pts (G1/2, 19; G3, 2). Immune effector cell-associated neurotoxicity syndrome (ICANS)–type neurotoxicity occurred in 2/33 (6%) pts and was low-grade and reversible with steroid treatment.

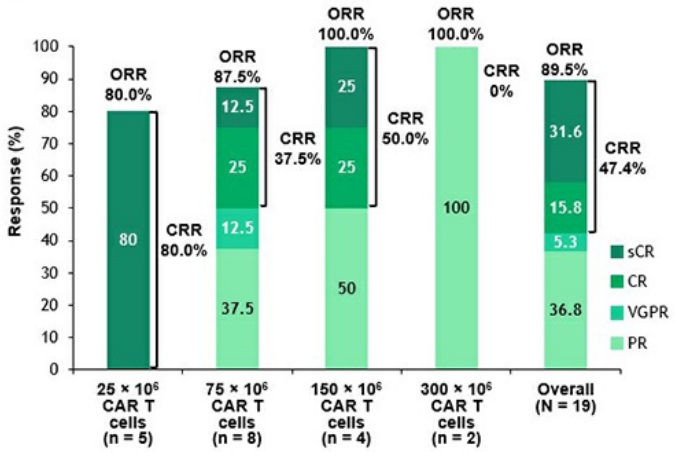
Overall response rate was 89% (17/19) in efficacy-evaluable pts, including responses in 7/9 pts treated with prior BCMA-directed therapies, including CAR T cells. Median follow-up for all treated pts was 3.1 mo (range, 0.1–15.5). At the time of analysis, 15/17 pts with at least partial response were ongoing.

All 4 pts with available minimal residual disease (MRD) data and a best overall response of complete response (CR) were MRD-negative (10^{-5} depth) at month 3. BMS-986393 reduced soluble BCMA levels (indicative of tumor burden reduction) across all dose levels in preliminary pharmacodynamic analyses. Preliminary cellular pharmacokinetics showed a dose-dependent increase in BMS-986393 exposure.

Summary/Conclusion:

Dose escalation of BMS-986393 from 25 through 450 × 10^6 CAR T cells has not exceeded the MTD at the time of data cutoff. Observed CRS was mostly G1/2. ICANS-type neurotoxicity was infrequent, low-grade, and reversible. On-target off-tumor TEAEs occurred in a minority of patients and were G1. BMS-986393 showed durable responses and promising efficacy at all tested dose levels, including MRD-negative CRs and in pts previously exposed to BCMA-directed therapies. These preliminary data support GPRC5D-directed CAR T-cell therapy with BMS-986393 for treating RRMM, irrespective of prior BCMA-directed therapy. Enrollment in the Part B dose expansion is underway. Updated data will be presented.

Figure. Best overall response in the efficacy-evaluable analysis set[a]



[a]Includes all patients who received conforming BMS-986393 cell product, had measurable disease at the last disease assessment prior to BMS-986393 infusion, and had ≥ 1 post-infusion disease-response assessment. The patient in the 450 x 10^6 CAR T-cell group was not included in the set. CAR, chimeric antigen receptor; CR, complete response; CRR, complete response rate; ORR, overall response rate; PR, partial response; sCR, stringent complete response; VGPR, very good partial response.

Keywords: Clinical trial, CAR-T, B-cell maturation antigen, Multiple myeloma