Abstract: S207

Title: PHASE 1 STUDY OF ANITOCABTAGENE AUTOLEUCEL FOR THE TREATMENT OF PATIENTS WITH RELAPSED AND/OR REFRACTORY MULTIPLE MYELOMA: RESULTS FROM AT LEAST 1-YEAR FOLLOW-UP IN ALL PATIENTS

Abstract Type: Oral Presentation

Session Title: CAR T cell therapy for the treatment of Multiple Myeloma

Background:

Anitocabtagene autoleucel (anito-cel, previously CART-ddBCMA) is an autologous anti-BCMA chimeric antigen receptor (CAR) T-cell therapy with a synthetic binding domain that is being studied in patients (pts) with relapsed and/or refractory multiple myeloma (RRMM). One-year or more follow-up from all patients are presented in this report.

Aims:

To evaluate the safety & efficacy of anito-cel in pts with RRMM who have received >3 prior lines of therapy.

Methods:

Details of study design have been previously reported (Frigault et al Blood Adv 2023). Briefly, pts with RRMM who had received ≥3 prior lines of therapy received a single infusion of anito-cel following lymphodepletion chemotherapy. Two dose levels (DL1 & DL2, respectively) of 100 & 300 (±20%) × 106 CAR+ cells were evaluated. The primary endpoints were incidence of adverse events (AEs) & dose-limiting toxicities (DLTs). Additional endpoints included quality & duration of clinical response assessed according to the IMWG Uniform Response Criteria for MM, evaluation of minimal residual disease (MRD), progression-free (PFS) & overall survival (OS).

Results:

As of Oct 15, 2023, 40 pts with a median age 66 years (range: 44-76) were enrolled; 38 received anito-cel (32, DL1; 6, DL2) & were evaluable for safety & clinical response. Two pts not dosed had cell product manufactured but were not eligible for infusion due to medical complications. Pts had a median of 4 (range: 3-16) prior lines of therapy. All infused pts (100%) were triple-refractory, 26 (68%) were penta-refractory, 34 (89%) were refractory to last-line of treatment; 9 (24%) had high tumor burden with ≥60% bone marrow plasma cells, 13 (34%) had extramedullary disease, & 11 (29%) pts had high-risk cytogenetics (Del 17p, t(14;16), t(4;14)) at baseline. Median follow-up after anito-cel infusion was 26.5 months (range: 14 - 44 months). CAR+ cells comprised a median 70% of CD3+ T cells & median cell manufacturing yield was 1174 × 106 CAR+ cells (range: 470-1626 × 106). CRS occurred in 36/38 (95%) pts; 1 pt in DL2 had grade (Gr) 3 CRS & all other cases were Gr≤2. ICANS occurred in 7 pts (5, Gr≤2; 2, Gr3), with 1 Gr3 case in each DL. All cases of CRS & ICANS resolved with management and without sequalae. No delayed neurotoxicities, Guillain-Barré syndrome, cranial nerve palsies, or Parkinsonian-like syndromes were observed through the follow-up period. All 38 pts demonstrated investigator-assessed response per 2016 IMWG criteria (ORR, 100%) with 22 sCR & 7 CR (≥CR rate, 76%), 6 VGPR (≥VGPR rate, 92%), & 3 PR. Responses deepened over time & conversion to CR/sCR was observed as late as month 12. Of pts evaluable for MRD testing to date (n=28), 25 (89%) were MRD-neg at 10-5. Median duration of response, PFS, & OS were not reached; Kaplan-Meier estimated PFS rates for 6, 12, 18 & 24 months were 92%, 76%, 64%, and 56%, respectively. Durable responses were observed in patients with high-risk features (EMD, BMPC ≥ 60%, or B2M ≥ 5.5mg/L at baseline), age >65 years, and high-risk cytogenetics, even when inclusive of Chromosome 1q gain (Table). A dose of 115 ± 10 ×106 cells was recommended for the ongoing phase 2 study, iMMagine-1.

Summary/Conclusion:

Adverse events with anito-cel, including CRS & ICANS, were manageable; no off-tumor tissue-targeted toxicity, delayed neurotoxicity or Parkinsonian-like events were observed at time of data-cut. Efficacy analyses demonstrated 100% ORR, including 92% with VGPR or better & 76% with CR/sCR. Clinical responses were durable with an overall estimated 24-mo PFS rate of 56% with comparable responses seen in pts with 'high-risk' disease characteristics.

	PFS Rates
	6-month
All dosed (n=38)	92.1
High Risk Features* (n=24)	91.7
Age ≥65 years (n=20)	95.0
High Risk Cytogenetics** (n=11)	81.8
High Risk Cytogenetics inclusive of 1q gain (n=26)	92.3

*High Risk Features defined as a patient with EMD, ISS Stage III (B2M ≥ 5.5 mg/L), or BMPC ≥ 60%

**High Risk Cytogenetics defined as the presence of Del 17p, t(14;16), t(4;14)

Keywords: B-cell maturation antigen, Plasma cells, Cellular therapy, Multiple myeloma