Abstract: PB2724

Title: IMMAGINE-3: A PHASE 3, RANDOMIZED STUDY TO COMPARE THE EFFICACY AND SAFETY OF ANITOCABTAGENE AUTOLEUCEL (ANITO-CEL) WITH STANDARD OF CARE IN PATIENTS WITH RELAPSED/REFRACTORY MULTIPLE MYELOMA (RRMM)

Abstract Type: Publication Only

Topic: Myeloma and other monoclonal gammopathies - Clinical

Background:

Anito-cel, formerly CART-ddBCMA, is an autologous anti-B-cell maturation antigen (BCMA) chimeric antigen receptor (CAR) T-cell therapy with a novel synthetic D-domain binder that facilitates high CAR transduction efficiency and surface expression with high antitumor activity and low/no tonic signaling (Buonato, et al. *Mol Cancer Ther,* 2022). In a first-in-human, Phase 1 expansion study, anito-cel demonstrated an investigator-assessed overall response rate (ORR) of 100% including a 76% complete response (CR)/stringent CR (sCR) rate in 38 patients (pts) with RRMM who had ≥3 prior lines of therapy. With median follow-up of 26.5 months (range, 14-44), median progression-free survival (PFS) was not reached and estimated 24-month PFS rates were 56% for all dosed (N=38) and 57.5% for pts with extramedullary disease (n=13). At a dose of 100x106 CAR+ T cells (n=32), no pt had ≥Gr 3 CRS, 1 pt (3%) had Gr 3 ICANS, and there were no delayed neurotoxicities (Frigault MJ, et al. ASH, 2023). An ongoing Phase 2 study, iMMagine-1, is investigating anito-cel in pts with RRMM who had ≥3 prior therapies including a proteasome inhibitor, an immunomodulatory drug (IMiD), and an anti-CD38 monoclonal antibody (mAb; NCT05396885).

Aims:

To address the increasing unmet need of pts with MM who have prior anti-CD38 mAb exposure by assessing the efficacy and safety of anito-cel compared with standard of care (SOC) in pts with RRMM who received 1-3 prior lines of therapy and have been exposed to both an IMiD and an anti-CD38 mAb in the randomized, open-label, Phase 3 study, iMMagine-3.

Methods:

iMMagine-3 will enroll approximately 450 adult pts with RRMM 1:1 to 2 arms, anito-cel and SOC. Prior to randomization, the investigator will select one of the following SOC regimens: pomalidomide (P), bortezomib (V), and dexamethasone (d; PVd); daratumumab (D), P, and d (DPd); carfilzomib (K), D, and d (KDd); or K and d (Kd). Pts in the SOC arm will receive the selected SOC regimen (21-day cycles of PVd or 28-day cycles of DPd, KDd, or Kd) until unacceptable toxicity, progression, death, or withdrawal of consent. Pts in the anito-cel arm will undergo leukapheresis and optional bridging therapy (with the selected SOC regimen at discretion of the investigator) followed by lymphodepleting chemotherapy (fludarabine 30 mg/m2/d and cyclophosphamide 300 mg/m2/d for 3 days) and one infusion of anito-cel (115×106 CAR+ T cells) on Day 1.

Additional key inclusion criteria are Eastern Cooperative Oncology Group performance score 0-1, documented evidence of progressive disease within 12 months of the last dose of the last regimen, and measurable disease at screening per the 2016 International Myeloma Working Group (IMWG) criteria. Key exclusion criteria include prior BCMA-targeted therapy, T-cell engager therapy, genetically modified T-cell therapy; prior autologous stem cell transplant (SCT) within 12 weeks before randomization, prior allogeneic SCT, and active or prior history of central nervous system or meningeal involvement of MM.

The primary endpoint is PFS per independent review (time from randomization to disease progression per the 2016 IMWG criteria or death by any cause) with the hypothesis that anito-cel will prolong PFS compared with SOC.

Key secondary endpoints include CR rate (CR/sCR), overall minimal residual disease negativity, overall survival,

and safety.

Results:

The iMMagine-3 study start is expected in 2024 at ~130 study sites across North America, Europe, and rest of world.

Summary/Conclusion:

iMMagine-3 will be enrolling soon.

Keywords: Randomized, Multiple myeloma, Cellular therapy, CAR-T