TPS7564 Poster Session

QUINTESSENTIAL-2: A phase 3 study comparing efficacy and safety of arlocabtagene autoleucel (arlo-cel) versus standard regimens in adult patients with relapsed or refractory multiple myeloma (RRMM) refractory to lenalidomide.

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Background: Despite advances in MM treatment, nearly all patients (pts) will relapse, highlighting the need for new drug classes to improve outcomes in RRMM. Further, MM refractory to lenalidomide, an immunomodulatory drug (IMiD) used in frontline and maintenance therapies, poses an additional challenge as the disease is less likely to respond to subsequent treatment. G protein-coupled receptor class C group 5 member D (GPRC5D) is a promising therapeutic target for MM as the receptor is highly expressed on malignant plasma cells; it has little to no expression on non-plasma immune cells and limited expression elsewhere. Arlo-cel is a GPRC5D-directed autologous CAR T-cell therapy that has demonstrated safety and efficacy in patients with RRMM in a first-in-human ph1 study. Following a single infusion of arlo-cel at the recommended ph2 dose (RP2D) of 150×10^6 CAR T cells, overall response rate (ORR) was 96% (23/24) and 91% (21/23) in those with 1-3 and ≥3 prior lines of therapy (pLOT), respectively (Bal S, et al. ASH 2024. Abstracts 2069 and 922). Here we present the design of the QUINTESSENTIAL-2 study. **Methods:** QUINTESSENTIAL-2 (NCT06615479) is a randomized, open-label, multicenter, ph3 confirmatory study comparing the efficacy and safety of arlo-cel versus standard of care (SOC) in adults with RRMM. Pts aged ≥18 y must have received 1-3 pLOT (may include a proteasome inhibitor, IMiD, and anti-CD38 monoclonal antibody) and be refractory to lenalidomide (progression on or within 60 days of completing therapy). Additional inclusion criteria include confirmed MM diagnosis per International Myeloma Working Group criteria, measurable disease during screening, and Eastern Cooperative Oncology Group performance status 0 or 1. Eligible pts will be randomized 1:1 to one of 2 treatment arms. Arm A: single infusion of arlo-cel (RP2D of 150×10^6 CAR T cells), including leukapheresis within 3 days of randomization, bridging therapy of DPd (daratumumab, pomalidomide, dexamethasone) or Kd (carfilzomib, dexamethasone) per Investigator within 3 days of leukapheresis, and lymphodepleting chemotherapy prior to arlo-cel infusion. Arm B: SOC of DPd or Kd per Investigator, dosed per labeling. Primary endpoints are progression-free survival and minimal residual disease (MRD) negativity in complete response. Secondary endpoints include overall survival, ORR, MRD negative status, complete response rate, time to response, duration of response, pharmacokinetics, patient-reported quality of life outcomes, and safety. Pts will be followed for ≤5 years after the last patient is randomized, with a subsequent long-term follow-up study (≤15 years post infusion) for pts receiving arlo-cel. The trial is expected to enroll 440 pts across 111 sites globally, with first patient enrollment planned for Feb 2025. Clinical trial information: NCT06615479. Research Sponsor: Juno Therapeutics, Inc., a Bristol-Myers Squibb Company.