TPS7563 Poster Session

QUINTESSENTIAL: A multicenter phase 2 study evaluating the efficacy and safety of arlocabtagene autoleucel (arlo-cel) in triple- and quad-class exposed patients with relapsed or refractory multiple myeloma (RRMM).

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Background: There are limited treatment options for patients (pts) with RRMM who are triple-class exposed (TCEx: immunomodulatory drugs [IMiD], anti-CD38 antibodies [aCD38], and proteasome inhibitors [PI]) and quad-class exposed (QCEx: IMiD, aCD38, PI, and B-cell maturation antigen [BCMA]-targeted therapy). To address this unmet need, new treatment options are needed for late-line populations, which will continue to grow with more QCEx pts due to the approval of BCMA-targeted therapies in earlier lines. G protein-coupled receptor class C group 5 member D (GPRC5D) is an orphan receptor expressed on plasma cells, with limited expression elsewhere, making it a promising therapeutic target for MM. Data from a phase 1 first-in-human study (NCT04674813) suggested that arlo-cel, a GPRC5D-directed autologous chimeric antigen receptor (CAR) T-cell therapy, is safe and efficacious in pts with TCEx RRMM, including pts who received prior BCMA-targeted therapy. At the recommended phase 2 dose (RP2D) of 150×10^6 CAR T cells, overall response rate (ORR) was 91% (21/23), median progression-free survival (PFS) was 18.3 months, and median overall survival (OS) was not reached in those with ≥3 prior lines of therapy (LOT) (Bal S et al. ASH 2024. Abstract 922). Here, we present the study design of QUINTESSENTIAL, an open-label, multicenter, phase 2 study (NCT06297226) evaluating arlo-cel in pts with TCEx and QCEx RRMM. **Methods:** For analyses, enrollment is planned at ~138 pts with ~125 pts receiving therapy. Key inclusion criteria include age ≥18 years, confirmed diagnosis of MM as per IMWG criteria, ≥3 classes of MM treatment (including IMiD, PI, and anti-CD38), and ≥3 prior LOT. Pts must also have documented disease progression (PD) during or after the most recent regimen as per IMWG, measurable disease, and an ECOG performance status of 0 or 1. Pts who previously received a GPRC5D-targeted therapy are excluded. After screening, pts will undergo leukapheresis followed by bridging therapy. Pts will then receive lymphodepleting chemotherapy followed by a single infusion of arlo-cel at the RP2D of 150×10^6 CAR T cells (range: $120–180 \times 10^6$). The primary endpoint is ORR by IMWG response criteria per an independent review committee in pts who are QCEx and received ≥4 prior LOT. Key secondary endpoints are ORR and complete response rate in all pts. Other secondary and exploratory endpoints include time to response, duration of response, PFS, OS, minimal residual disease-negative status, and safety. Pts will be followed for ≤5 years after the last pt receives arlo-cel, with a subsequent long-term follow-up study continuing for ≤15 years. This study will recruit at 47 centers across the USA, Canada, and Japan. The first pt first visit was achieved on March 21, 2024. Clinical trial information: NCT06297226. Research Sponsor: Juno Therapeutics, Inc., a Bristol-Myers Squibb Company.