3. RELAPSED/REFRACTORY MULTIPLE MYELOMA

ARLOCABTAGENE AUTOLEUCEL, A GPRC5D-TARGETED CAR T-CELL THERAPY FOR PATIENTS WITH RELAPSED/REFRACTORY MULTIPLE MYELOMA: UPDATED PHASE 1 SAFETY AND EFFICACY RESULTS IN PATIENTS WITH 1–3 PRIOR REGIMENS

S. Bal[1], M. Htut[2], J. Berdeja[3], L. Anderson[4], A. Rossi[5], T. Gregory[6], L. Costa[1], H. Hu[7], Z. Guo[7], J. Chen[7], K. Jordahl[7], N. Sarkis[7], S. Ziyad[7], W. -M. Kao[7], A. Kaeding[7], M. Burgess[7], O. Nadeem[8]

[1]University of Alabama at Birmingham, USA; [2]City of Hope Comprehensive Cancer Center, Duarte, USA; [3]Greco-Hainsworth Tennessee Oncology Center for Research, Nashville, USA; [4]Hematologic Malignancies and Cellular Therapy Program, Simmons Comprehensive Cancer Center, UT Southwestern Medical Center, Dallas, USA; [5]Icahn School of Medicine at Mount Sinai, New York, USA; [6]Colorado Blood Cancer Institute, Sarah Cannon Cancer Network, Denver, USA; [7]Bristol Myers Squibb, Princeton, USA; [8]Dana-Farber Cancer Institute, Boston, USA

https://doi.org/10.3324/haematol.2026.s2.14112

Introduction. There is an urgent need for new therapeutic options with alternative targets or mechanisms of action for patients (pts) with relapsed and refractory multiple myeloma (RRMM). Arlocabtagene autoleucel (arlo-cel; CC-95266; BMS-986393) is a chimeric antigen receptor (CAR) T cell therapy targeting GPRC5D that is being evaluated in the multicohort phase 1 trial (NCT04674813). We report updated safety and efficacy data for the cohort of pts with 1–3 prior lines of therapy.

Methods. Pts had 1–3 prior anti-MM regimens, including a proteasome inhibitor and an immunomodulatory agent. Anti-CD38 therapy was not required; BCMA-directed therapies, including CAR T cells, were allowed. After screening and leukapheresis (bridging therapy optional), pts received lymphodepleting chemotherapy followed by a single infusion of arlo-cel at the recommended phase 2 dose (150×10^6 CAR T cells). The primary objective was safety; secondary objectives included clinical activity per IMWG Uniform Response Criteria and pharmacokinetics.

Results. As of June 6, 2025, 31 pts had been enrolled and 100% received arlo-cel following successful manufacturing; 61% (19/31) received optional systemic bridging therapy. Median age was 62 y (range 31–78); 68% were male. Overall, 26% had high-risk cytogenetics (del[17p], t[4;14], and/or t[14;16]), 68% had 1q21 gain/amp, and 32% had extramedullary disease. Pts had a median of 2 prior regimens; 29% received 3 prior regimens. All 31 pts had a treatment-emergent (TE) adverse event (AE); 87% had grade (G) 3/4 TEAEs. No deaths were attributed to AEs. Treatment-related AEs occurred in 97% (48% G3/4). Cytokine release syndrome occurred in 84% (all G1/2 resolved); no pts had macrophage activation syndrome/hemophagocytic lymphohistiocytosis. Immune effector cell-associated neurotoxicity syndrome occurred in 10% (all G1/2 resolved). On-target/off-tumor nail, skin, and oral TEAEs were reported in 36%, 26% and 42%, respectively. Other select neurotoxicity occurred in 6.5% of patients, including 1 event of ataxia, 1 event of dysarthria, 2 events of gait disturbance; all events were grade ≤2 and ongoing. TE infections occurred in 55% (all G1/2). In the efficacy-evaluable population (n=24), after a median 18.3 mo follow-up (range 3.8–24.3 mo) the ORR was 96% (23/24) and CR rate was 67% (16/24); 11/23 responses were still ongoing. The 12-mo PFS rate was 74%. Of 16 pts with minimal residual disease (MRD) data, the MRD negative (10^{-5} depth) CR rate was 56.3%.

Conclusion. A one-time administration of arlo-cel in pts with RRMM and 1–3 prior lines of therapy was well tolerated and led to a high response rate that deepened over time, with few early relapses after 18.3 mo median follow-up. The favorable benefit-risk profile for this dose and population was consistent with prior disclosures. Notably, frequency and grade of infections were lower than those reported for BCMA-targeted therapies. These data support arlo-cel as a safe and effective potential early-line treatment in RRMM, with a phase 3 trial (QUINTESSENTIAL 2; NCT06615479) underway.