3. RELAPSED/REFRACTORY MULTIPLE MYELOMA

EFFECTIVENESS OF BRIDGING THERAPY CORRESPONDS TO IMPROVED OUTCOMES AFTER CILTACABTAGENE AUTOLEUCEL: PHASE 3 CARTITUDE-4 STUDY OF PATIENTS WITH RELAPSED, LENALIDOMIDE-REFRACTORY MULTIPLE MYELOMA

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Introduction. In patients treated with ciltacabtagene autoleucel (cilta-cel), effective tumor burden reduction using bridging therapy correlates with better progression-free survival (PFS) and safety In CARTITUDE-4 (median follow-up, 33.6 months), a single cilta-cel infusion significantly improved PFS (hazard ratio [HR] weighted, 0.29 [95% CI, 0.22–0.39]) and overall survival (OS; HR, 0.55 [0.39–0.79]; *P*=0.0009) vs standard of care in relapsed and lenalidomide-refractory multiple myeloma after 1–3 prior lines of therapy. Here, we examine the association between bridging therapy responses before cilta-cel with the post-infusion efficacy and safety.

Methods. The CARTITUDE-4 study design was described previously. Patients receiving cilta-cel underwent apheresis, ≥1 cycle of bridging therapy (pomalidomide, bortezomib, and dexamethasone [PVd] or daratumumab, pomalidomide, and dexamethasone [DPd]), lymphodepletion (cyclophosphamide and fludarabine), and subsequently a single cilta-cel infusion 5–7 days after the lymphodepletion initiation.

Results. Of 196 patients receiving cilta-cel in CARTITUDE-4, 172 (87.8%) were treated with DPd and 24 (12.2%) received PVd while bridging (median bridging cycles, 2 [range, 1–6]). Following bridging therapy, 42 patients had very good partial response or better (≥VGPR), 70 had partial response (PR), 61 had minimal response (MR)/stable disease (SD), 20 had progressive disease (PD), and 3 were not evaluable. Thirty-month PFS rates (95% CI) with cilta-cel were 75.9% (59.8–86.2), 72.9% (60.4–82.1), 56.5% (42.8–68.1), and 30.0% (12.3–50.1), respectively. Thirty-month OS rates (95% CI) were 85.1% (69.9–93.0), 91.4% (81.9–96.1), 74.8% (61.6–84.0), and 40.0% (19.3–60.0), respectively. In patients with ≥VGPR or PR, no movement or neurocognitive treatment-emergent adverse events (MNTs) were reported. One case of MNT in patients with PD and 1 in a patient with a best response of SD were observed. In participants with ≥VGPR, PR, MR/SD, and PD, cranial nerve palsy occurred in 11.9%, 7.1%, 8.2%, and 5.0%, and fatal infections in 2.4%, 4.3%, 13.1%, and 15.0%, respectively. Prolonged (grade 3/4 that did not recover to grade 2 by day 60 post cilta-cel) thrombocytopenia was lowest among patients achieving ≥VGPR (9.5%), PR (11.4%) or MR/SD (11.5%) after bridging therapy, and higher in those with PD (50%). Prolonged neutropenia was lowest in participants achieving ≥VGPR before cilta-cel (2.4%) vs 9.8–15.7% in those with PR or lower. In participants with ≥VGPR, PR, MR/SD, and PD, non-relapse mortality was 7.1%, 8.6%, 18.0%, and 30.0%, respectively.

Conclusions. Better responses to bridging therapy were associated with with longer PFS and OS in CARTITUDE-4. No MNTs were reported in patients who achieved PR or greater following bridging therapy. Poorer responses to bridging therapy were linked to fatal infections, prolonged thrombocytopenia and neutropenia, and higher rates of non-relapse mortality following cilta-cel infusion. These data highlight optimizing bridging therapy for disease control before receiving cilta-cel.