3. RELAPSED/REFRACTORY MULTIPLE MYELOMA

LONG-TERM PROGRESSION-FREE SURVIVAL BENEFIT WITH CILTACABTAGENE AUTOLEUCEL IN STANDARD-RISK RELAPSED/REFRACTORY MULTIPLE MYELOMA

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Introduction. CARTITUDE-4 (NCT04181827) enrolled patients with lenalidomide-refractory multiple myeloma (MM) after 1–3 prior lines of therapy (pLOT) and showed a significant benefit of ciltacabtagene autoleucel (cilta-cel) over established triplet regimens. However, the benefit of cilta-cel for patients with standard-risk cytogenetics is less characterized. Here, outcomes in patients with standard-risk cytogenetics from CARTITUDE-4 are reported.

Methods. In CARTITUDE-4, patients randomized to cilta-cel underwent apheresis and bridging therapy (pomalidomide, bortezomib, and dexamethasone [PVd] or daratumumab, pomalidomide, and dexamethasone [DPd]), followed by lymphodepletion (cyclophosphamide and fludarabine), and a subsequent single cilta-cel infusion. A validated computerized algorithm was used to assess progression-free survival (PFS). The intent-to-treat (ITT) population included 208 patients; 32 progressed or died on bridging therapy and 176 were included in the as-treated population. Patients with high-risk cytogenetics (del(17p), t(14;16), t(4;14), gain/amp(1q); n=105), or with unknown cytogenetics (n=12), were not included in the as-treated analysis. Twelve-month minimal residual disease (MRD)-negative complete response (CR) was defined per the International Myeloma Working Group criteria. PFS rates were determined from the time of cilta-cel infusion for the as-treated population.

Results. In the ITT population of CARTITUDE-4, patients with standard-risk cytogenetics had a 30-month PFS rate (95% CI) of 71.0% (58.8–80.2) with cilta-cel (N=69) vs 43.2% (31.3–54.5) with standard of care (N=70) at a median follow-up of 33.6 months. Participants with standard-risk cytogenetics in the as-treated population (n=59) had a 30--month PFS rate of 80.5% (95% CI, 67.2–88.8). In CARTITUDE-1 (NCT03548207), evaluating cilta-cel in patients with heavily pretreated relapsed/refractory MM (RRMM; ≥3 pLOT), the 30-month PFS rate among patients with standard-risk cytogenetics (negative for del(17p), t(14;16), or t(4;14); n=68) was 59.9% (95% CI, 47.2–70.5). The CARTITUDE-4 as-treated population with standard-risk cytogenetics experienced 8 PFS events within 1 year and 4 PFS events beyond 1 year of cilta-cel infusion. MRD-negative CR was achieved by 26 patients at 12 months after cilta-cel, 100.0% of whom were progression free at 30 months. Fourteen patients were not assessed for MRD because of calibration failure (n=12), no sample availability for testing (n=1), or indeterminate results post baseline (n=1).

Conclusions. The PFS rate at 2.5 years for participants with standard-risk RRMM was higher in CARTITUDE-4 compared with CARTITUDE-1, supporting the use of cilta-cel as early as second line. Among as-treated patients in CARTITUDE-4, 80.0% of those with standard-risk cytogenetics were progression free and off treatment at 2.5 years; this rate increased to 100.0% in patients with standard-risk disease who attained MRD-negative CR at 1 year. The low rate of progression events in cilta-cel-treated patients with standard-risk cytogenetics demonstrated the profound benefit of a single cilta-cel infusion in this population.