Abstract: P978

Title: CILTACABTAGENE AUTOLEUCEL VS STANDARD OF CARE IN LENALIDOMIDE-REFRACTORY MULTIPLE MYELOMA: PHASE 3 CARTITUDE-4 SUBGROUP ANALYSIS BY CYTOGENETIC RISK

Abstract Type: Poster Presentation

Topic: Myeloma and other monoclonal gammopathies - Clinical

Background:

The prognosis for patients with multiple myeloma (MM) who have high-risk cytogenetics is poor. In the phase 3 CARTITUDE-4 trial, ciltacabtagene autoleucel (cilta-cel) vs standard of care (SOC) significantly improved progression-free survival (PFS; $P<0.0001$) in patients with relapsed and lenalidomide-refractory MM after 1–3 prior lines of therapy. Additionally, the proportion of patients with an overall response (85% vs 67%), complete response or better (≥CR; 73% vs 22%), and minimal residual disease (MRD) negativity rate (10–5; 61% vs 16%) was higher with cilta-cel vs SOC.

Aims:

To report the efficacy of cilta-cel vs SOC in patients with high-risk and standard-risk cytogenetics, including by type of cytogenetic abnormality from a post hoc subgroup analysis of CARTITUDE-4.

Methods:

Eligibility criteria for CARTITUDE-4 have been previously described. Patients in the cilta-cel arm underwent apheresis, received bridging therapy (pomalidomide, bortezomib, and dexamethasone [PVd] or daratumumab, pomalidomide, and dexamethasone [DPd]), and then a single cilta-cel infusion (target dose, 0.75×106 CAR+ viable T cells/kg) 5–7 days after the start of lymphodepletion. The SOC arm received PVd or DPd until progressive disease. High-risk cytogenetics was defined as patients with ≥1 of the following cytogenetic abnormalities at baseline determined by fluorescence in situ hybridization: del(17p), t(4;14), t(14;16), or gain/amp(1q). Standard-risk cytogenetics was defined as patients without del(17p), t(4;14), t(14;16), or gain/amp(1q) at baseline. Efficacy analyses were assessed in the intent-to-treat population (all randomized patients) and are summarized descriptively.

Results:

In CARTITUDE-4, 394/419 patients were evaluable for cytogenetics and had non-missing data; of these patients, 255 patients had high-risk cytogenetics (cilta-cel, n=123; SOC, n=132) and 139 had standard-risk cytogenetics (cilta-cel, n=69; SOC, n=70). At the data cutoff (Nov 1, 2022), median follow-up was 15.9 months (range, 0.1–27.3). In patients with high-risk cytogenetics, median PFS was not reached (NR; 95% CI, 18.4–not estimable [NE]) with cilta-cel vs 10.3 months (95% CI, 7.6–12.5) with SOC; 12-month PFS rates were 76% vs 43%, respectively. Among patients with standard-risk cytogenetics, median PFS was NR (95% CI, NE–NE) with cilta-cel vs 20.6 months (95% CI, 11.2–NE) with SOC; 12-month PFS rates were 77% vs 59%, respectively. In patients with high-risk cytogenetics, a greater proportion had an overall response (85% vs 66%), ≥CR (73% vs 20%), and MRD negativity (10–5; 70% vs 14%) with cilta-cel vs SOC. Similarly, in patients with standard-risk cytogenetics a greater proportion had an overall response (86% vs 71%), ≥CR (74% vs 26%), and MRD negativity (10–5; 49% vs 19%) with cilta-cel vs SOC. Improved efficacy with cilta-cel vs SOC was observed by type of cytogenetic abnormality (**Table**). Efficacy in patients with t(14;16) was excluded because the small number of patients in the cilta-cel (n=3) and SOC (n=7) arms precludes meaningful analyses.

Summary/Conclusion:

A single infusion of cilta-cel demonstrated favorable efficacy outcomes vs SOC in lenalidomide-refractory MM patients who had high-risk and standard-risk disease, with generally consistent results across different

cytogenetic abnormalities although sample sizes for some individual types were small. Of note, cilta-cel induced comparable overall response, ≥CR, and MRD-negativity rates in patients with high-risk and standard-risk disease, supporting the role of cilta-cel as a potential new SOC in patients with lenalidomide-refractory MM after 1–3 prior lines of therapy.

Table: Efficacy outcomes by type of cytogenetic abnormality

	High-risk cytogenetics	
gain/amp(1q)	**Cilta-cel (n=89)**	**SOC (n=107)**
Median PFS, months (95% CI)	NR (18.4–NE)	10.3 (7.5–14.0)
ORR, n (%)	77 (87)	70 (65)
≥CR, n (%)	64 (72)	24 (22)
MRD negativity (10^{-5}), n (%)[a]	63 (71)	16 (15)
del(17p)	**Cilta-cel (n=49)**	**SOC (n=43)**
Median PFS, months (95% CI)	19.3 (12.9–NE)	8.7 (5.1–11.8)
ORR, n (%)	39 (80)	27 (63)
≥CR, n (%)	31 (63)	4 (9)
MRD negativity (10^{-5}), n (%)[a]	32 (65)	4 (9)
t(4;14)	**Cilta-cel (n=30)**	**SOC (n=30)**
Median PFS, months (95% CI)	NR (12.9–NE)	6.7 (3.8–13.8)
ORR, n (%)	24 (80)	20 (67)
≥CR, n (%)	23 (77)	5 (17)
MRD negativity (10^{-5}), n (%)[a]	20 (67)	4 (13)

[a]MRD was assessed centrally by next-generation sequencing on bone marrow samples.
Cilta-cel, ciltacabtagene autoleucel; CR, complete response; MRD, minimal residual disease; NE, not evaluable; NR, not reached; ORR, overall response rate; PFS, progression-free survival; SOC, standard of care (pomalidomide, bortezomib, and dexamethasone [PVd] or daratumumab, pomalidomide, and dexamethasone [DPd]).

Keywords: Multiple myeloma, CAR-T, Cytogenetic abnormalities, Clinical trial