Abstract: S202

Title: CARTITUDE-1 FINAL RESULTS: PHASE 1B/2 STUDY OF CILTACABTAGENE AUTOLEUCEL IN HEAVILY PRETREATED PATIENTS WITH RELAPSED/REFRACTORY MULTIPLE MYELOMA

Abstract Type: Oral Presentation

Session Title: MM and CLL final analyses/long term follow up of clinical trials

Background:

Heavily pretreated patients with relapsed/refractory multiple myeloma (RRMM) treated with standard of care therapy have median overall survival (OS) of ~12 months. In the single-arm, phase 1b/2 CARTITUDE-1 study (NCT03548207), patients received a single infusion of ciltacabtagene autoleucel (cilta-cel), a chimeric antigen receptor-T cell therapy targeting B-cell maturation antigen. At the final protocol-specified analysis (27.7-month median follow-up), overall response rate (ORR) was 98%, with 83% stringent complete response; 27-month rates of progression-free survival (PFS) and OS were 55% and 70%, respectively.

Aims:

To report CARTITUDE-1 study close out efficacy and safety results.

Methods:

Informed consent was obtained prior to study entry. Enrolled patients had received ≥3 prior lines of therapy (LOT) or were double refractory to a proteasome inhibitor (PI) and immunomodulatory drug (IMiD); and had received prior PI, IMiD, and anti-CD38 antibody therapy. Primary endpoint was ORR and safety; secondary endpoints included PFS, OS, and minimal residual disease (MRD)-negativity at 10^{-5}.

Results:

97 patients received cilta-cel (59% male; median age 61 years; median of 6 prior LOT; 42% penta-drug refractory; 88% triple-class refractory; 99% refractory to last LOT). As of October 14, 2022, median follow-up was 33.4 months (range, 1.5–45.2). Median duration of response was 33.9 month (95% CI, 25.5–not estimable [NE]). Median PFS was 34.9 months (95% CI, 25.2–NE), with an estimated 47.5% of patients progression free and alive at 36 months. Median OS was not reached, with an estimated 62.9% survival at 36 months. Of 49 MRD-evaluable patients, 26 had MRD-negativity sustained for ≥12 months, of which 20 had sustained MRD-negative complete response (CR) or better. Median PFS was not reached in these subgroups (Table). Eighteen patients were MRD-negative with ≥CR at 24-months post infusion. No new safety signals and no new neurotoxicity events were reported since the 27.7-month median follow-up. Six new cases of second primary malignancy were reported, including 2 cases of basal cell carcinoma and 1 case each of myelodysplastic syndrome, B-cell lymphoma, melanoma, and prostate cancer. Five additional deaths occurred (progressive disease [PD], n=3; pneumonia and sepsis, n=1 each [both unrelated to cilta-cel]), for a total of 35 deaths (PD, n=17; unrelated to cilta-cel, n=12; related, n=6).

Summary/Conclusion:

Longer median PFS was observed after a single infusion of cilta-cel than any previously reported therapy in heavily pretreated patients with RRMM. Achieving CR and/or sustained MRD-negativity was associated with prolonged PFS. Patients continue to be followed for safety and survival in the 15-year CARTINUE long-term study (NCT05201781; MMY4002).

TABLE: PFS at ~3-year median follow-up

Subgroup	n	PFS, median (95% CI), mo	30-month PFS rate	36-month PFS rate
All patients	97	34.9 (25.2–NE)	54.2%	47.5%
≥CR	76	38.2 (34.9–NE)	66.8%	59.8%
12-month sustained MRD negativity[a]	26	NR (NE–NE)	74.9%	NE
12-month sustained MRD-negative CR[a]	20	NR (NE–NE)	78.5%	NE

[a]≥2 MRD-negative assessments 6 or 12 months apart, with no MRD-positive samples in that interval.
CR, complete response; MRD, minimal residual disease (10^{-5}); NE, not estimable; NR, not reached; PFS, progression-free survival.

Keywords: Phase I/II, Clinical trial, CAR-T, Multiple myeloma