Abstract: P922

Title: ADJUSTED COMPARISONS OF CILTACABTAGENE AUTOLEUCEL WITH THERAPIES FROM REAL-WORLD CLINICAL PRACTICE: TWO-YEAR FOLLOW-UP ANALYSES FROM CARTITUDE-1 AND THE PROSPECTIVE LOCOMMOTION STUDY

Abstract Type: Poster Presentation

Session Title: Myeloma and other monoclonal gammopathies - Clinical

Background:

Patients with triple-class exposed, relapsed and refractory multiple myeloma (TCE-RRMM) have a poor prognosis and limited options for treatment. The single arm phase 1b/2 CARTITUDE-1 study demonstrated the efficacy and safety of Ciltacabtagene autoleucel (cilta-cel) in heavily pre-treated patients with TCE RRMM (Martin et al. 2022). Previously presented adjusted indirect comparisons between CARTITUDE-1 and LocoMMotion, a prospectively collected cohort of patients with TCE-RRMM receiving Real World Clinical Practice (RWCP), provided valuable information on the relative effectiveness and safety benefits of cilta-cel over current RWCP. In this analysis we present updated results of the comparative analyses, using data 2 years after last patient in from CARTITUDE-1 and LocoMMotion.

Aims:

To compare cilta-cel and RWCP outcomes in patients with TCE-RRMM after a median follow-up of 28 months and 26 months in the CARTITUDE-1 and LocoMMotion studies, respectively.

Methods:

Individual patient data (IPD) available from both CARTITUDE-1 (clinical cut-off January 2022) and LocoMMotion (clinical cut-off October 2022) were combined to perform comparative analyses. Inverse probability weighting methods were used to account for differences between cohorts for important baseline characteristics. Propensity scores estimated using multivariable logistic regression were used to derive average treatment effect on the treated (ATT) population weights. These weights were applied to the population of patients from the LocoMMotion cohort such that the weighted RWCP cohort reflected the CARTITUDE-1 population. Relative estimates of effect for binary endpoints (ORR and ≥VGPR; expressed as response rate ratios [RR] with 95% CI) were estimated using weighted logistic regression, while weighted Cox proportional hazards modeling was used for time-to-event outcomes (OS, PFS; expressed as hazard ratios [HR] with 95% CI). Main analyses included all infused patients from CARTITUDE-1 and an aligned RWCP cohort of patients from LocoMMotion who were alive and progression-free 52 days after starting treatment. Additional analyses included all patients who were enrolled in either study.

Results:

CARTITUDE-1 enrolled 113 patients, of whom 97 received cilta-cel. LocoMMotion enrolled 248 patients who received RWCP therapies. The most common regimens initiated at baseline in the RWCP cohort were carfilzomib-dexamethasone (Kd, 12.9%), pomalidomide-cyclophosphamide-dexamethasone (PCd, 10.9%) and pomalidomide-dexamethasone (Pd, 9.7%). 152 patients in LocoMMotion received subsequent anti-myeloma therapy, of which 76 (50%) patients received at least one novel agent including, belantamab (n=49), selinexor (n=21), bispecific antibodies (n=14) and CAR-T (n=3). Following application of ATT weights, the cohorts were well balanced on key characteristics. Comparisons of outcomes between cilta-cel and RWCP are summarized in **Table 1**. In the main analyses, cilta-cel was associated with statistically significant improvements compared to RWCP for ORR (RR 2.86 [95% CI 1.94-4.21], \geq VGPR (RR 4.82 [95% CI 2.98-7.81]), PFS (HR 0.19 [95% CI 0.10-0.38]) and OS (HR 0.25 [95% CI 0.14-0.47]).

Summary/Conclusion:

After two years of follow-up, outcomes of patients with TCE-RRMM treated with cilta-cel were significantly

improved compared to those treated with RWCP. Results were consistent with those observed in analyses of shorter follow-up. These data further support the conclusion that cilta-cel can play a valuable role in addressing the unmet treatment needs of patients with TCE-RRMM.

Table 1

Main analysis: Clita-cel infused population versus RWCP from LocoMMotion	
(aligned):	
RR / HR (95% CI)	
Outcome Measure	IPTW Adjusted Comparison
ORR	RR 2.86 (1.94, 4.21)
\geq VGPR	RR 4.82 (2.98, 7.81)
PFS	HR 0.19 (0.10, 0.38)
OS	HR 0.25 (0.14, 0.47)
Additional analysis: Cilta-cel enrolled population versus RWCP from	
LocoMMotion:	
RR / HR (95% CI)	
Outcome Measure	IPTW Adjusted Comparison
ORR	RR 3.59 (2.33, 5.53)
\geq VGPR	RR 6.34 (3.64, 11.04)
PFS	HR 0.23 (0.14, 0.40)
OS	HR 0.30 (0.19, 0.49)

Abbreviations: CI = confidence interval; HR = hazard ratio; IPTW = inverse probability of treatment weighting; ORR = overall response rate; OS = overall survival; PFS = progression-free survival; RR = response rate ratio; RWCP = real-world clinical practice; \geq VGPR = very good partial response or better rate.

Keywords: CAR-T, Multiple myeloma, Cellular therapy