Abstract: P863

Title: CLINICAL BIOMARKERS ASSOCIATED WITH PROGRESSION FREE SURVIVAL TO CILTACABTAGENE AUTOLEUCEL IN CHINESE PATIENTS WITH RELAPSED/REFRACTORY MULTIPLE MYELOMA FROM CARTIFAN-1 STUDY

Abstract Type: Poster Presentation

Topic: Myeloma and other monoclonal gammopathies - Biology & translational research

Background:

In the CARTIFAN-1 phase 2 study (NCT03758417), a single infusion of ciltacabtagene autoleucel (cilta-cel), a BCMA-targeting CAR-T cell therapy, induced deep and durable responses in Chinese patients (pts) with relapsed/refractory multiple myeloma (RRMM). With median follow-up of 32.8 months, the overall response rate (ORR) was 87.5% and the median progression free survival (mPFS) was 25.5 months (Mi J et al, CSCO, 2023).

Aims:

Here we present correlative data from biospecimens collected during the CARTIFAN-1 study and evaluate clinical biomarkers associated with PFS.

Methods:

CARTIFAN-1 enrolled 48 pts with RRMM in China who had previously received 3 or more prior lines of therapy, including a proteasome inhibitor and an immunomodulatory drug. Pts received a single infusion of cilta-cel at a target dose of 0.75×106 CAR+ viable T cells/kg. The primary endpoint was ORR, secondary endpoints included PFS, overall survival, and safety. Blood and bone marrow biospecimens were collected before and after cilta-cel infusion. Cellular kinetics were analyzed by flow cytometry. PFS was assessed by Kaplan-Meier curves with optimized cut point selection via a maximally selected rank statistics method. Log-rank test and logistic regression analysis were used to explore biomarker association with long-term efficacy.

Results:

Similar ORR was observed in high-risk (HR) cytogenetics pts (n=21) vs standard risk (SR) pts (n=27), 85.7% (95% CI, 63.7-97.0) vs 88.9% (95% CI, 70.8-97.6); p=1.0. However, mPFS for pts with HR cytogenetics was 24.4 months (95% CI, 15.2-not estimable [NE]), which is numerically shorter than 30.1 months (95% CI, 20.8-NE) for SR pts.

Baseline soluble BCMA (sBCMA), a surrogate of tumor burden, was significantly higher in pts with ISS stage III vs II or I (p<0.05), as well as in pts with bone marrow plasma cells ≥60% vs <60% (p<0.001). Higher baseline sBCMA was associated with shorter PFS (p=0.032). Notably, CAR-T peak expansion (Cmax) was associated with longer PFS when normalized to baseline sBCMA (effector to target ratio; p=0.014). Furthermore, higher baseline CD8+ but not CD4+ naïve T cells in both blood and bone marrow biospecimens were significantly associated with longer PFS (p<0.05).

In pts with autologous stem-cell transplantation (ASCT) as prior treatment (n=17, 35.4%), PFS was significantly longer compared to pts without ASCT as prior treatment (NE vs 20.0 months, p=0.024). Moreover, in pts with ASCT as prior treatment, higher baseline lymphocyte counts significantly associated with longer PFS (p=0.0026, Figure 1), which was not seen in pts without ASCT as prior treatment. Similarly, higher baseline CD3+, CD8+ and CD4+ T cell counts trended with longer PFS in pts with ASCT as prior treatment (p=0.058, 0.058, and 0.066, respectively).

Summary/Conclusion:

In the CARTIFAN-1 study, despite of similar ORR, a trend towards shorter mPFS was observed in pts with HR

cytogenetics. Biomarker analyses showed that longer PFS was associated with lower baseline sBCMA, higher post-treatment effector to target ratio (CAR-T peak expansion/sBCMA), and higher baseline CD8+ naïve T cells. Lastly, longer PFS was also associated with higher baseline lymphocyte counts in pts with ASCT as prior treatment. These results suggest that improved T cell fitness is one of the contributing factors, which could potentially override subpar tumor characteristics to enable durable responses to cilta-cel.

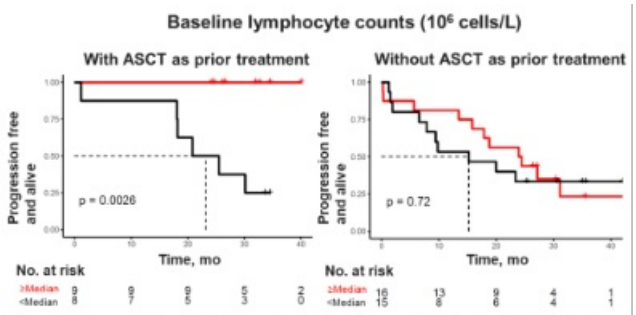

Figure 1. Among patients with ASCT as prior treatment, those with higher baseline lymphocyte counts (≥Median) significantly associated with longer PFS (left); Among patients without ASCT as prior treatment, there is no significant association of baseline lymphocyte counts with PFS (right).

Keywords: B-cell maturation antigen, CAR-T, Multiple myeloma, Cellular therapy