Abstract: P973

Title: BRIDGING STRATEGIES FOR ANTI-BCMA CAR-T CELL THERAPIES IN MULTIPLE MYELOMA PATIENTS WITH PRIOR EXPOSURE TO BISPECIFIC ANTIBODIES

Abstract Type: Poster Presentation

Topic: Myeloma and other monoclonal gammopathies - Clinical

Background:

Idecabtagen-vicleucel (ide-cel) and ciltacabtagen-autoleucel (cilta-cel) have recently emerged as first-in-class anti-BCMA CAR-T cell therapies with unprecedented efficacy in heavily pretreated relapsed/ refractory multiple myeloma (RRMM). Preliminary data suggest that prior exposure to bispecific antibodies (bsAb) negatively affects successful T-cell manufacturing and outcomes after CAR-T. At the same time, bsAb remain an important bridging option for patients with triple-class refractory MM.

Aims:

To assess the impact of prior bsAb treatment on the efficacy of CAR-T cell therapies in RRMM

Methods:

Data from n=28 bsAb-exposed MM patients treated at nine different centers in Germany were retrospectively collected and analyzed. Manufacturing failure was noted in 2/28 (7%) patients. Another 3/28 (11%) individuals were excluded due to immature follow-up <4 weeks after CAR-T cell infusion. For the remaining cohort of n=23 patients, survival analyses were conducted using the Kaplan-Meier method. The log-rank test was used for survival comparison among groups.

Results:

Median age in this study was 62 (range 43-75) years. Patients were heavily pretreated with a median of 7 (range 4-13) prior lines of therapy. High-risk cytogenetics, defined as del17p, t(4;14), t(14;16) and/or ampl1q were identified in 13/23 (57%) patients, and extramedullary disease was present in 14/23 (61%) individuals. Treatment strategies before apheresis showed substantial heterogeneity with talquetamab depicting the most frequently used agent (n=8), followed by teclistamab (n=5) and CD38-antibody-based triplets (n=5). In 9/23 patients (39%), bridging was intensified after apheresis, e.g. by use of PACE-like regimens (n=4). The overall response rate was 65% and 83% in patients treated with ide-cel (n=17, 35% complete remission (CR)) and cilta-cel (n=6, 50% CR), respectively. At a median follow-up of 4.2 months after CAR-T infusion, progression-free survival (PFS) across the entire cohort was 2.7 months (0.7-NR). We observed no significant association of disease remission at time of apheresis (defined as stable disease or better) with longer duration of response (DoR) to CAR-T (DoR 14.2 vs. 2.4 months, Fig. 1A, *P=0.371*). Disease remission before lymphodepletion showed a trend towards longer durability of CAR-T response (DoR 9.6 vs. 2.1 months, Fig. 1B, *P=0.091*), thus underlining the need for effective tumor control at the time of CAR-T infusion. Best response to CAR-T was CR in n=9, (very good) partial remission (VGPR) in n=7, and progressive disease (PD) in n=7 patients. As expected, this translated into a significant PFS benefit of 10.7 vs. 9.1 vs. 1.8 months (Fig. 1C, *P=0.002*). To further dissect the impact of previous bsAb exposure, patients were grouped by prior duration of teclistamab and talquetamab exposure and respective wash-out times before apheresis. Interestingly, neither the duration of bsAb exposure prior to apheresis nor a wash-out period of <4 weeks, as previously reported, affected the DoR to CAR-T in our study. At last follow-up, 6/23 patients had died from disease progression and 1/23 patient had died from infectious complications.

Summary/Conclusion:

In summary, our study shows that bsAb-based bridging strategies did not negatively affect CAR-T efficacy. In

contrast, bsAb seemed beneficial if they led to better disease control before re-infusion of CAR-T. More mature follow-up data will be presented at the meeting.

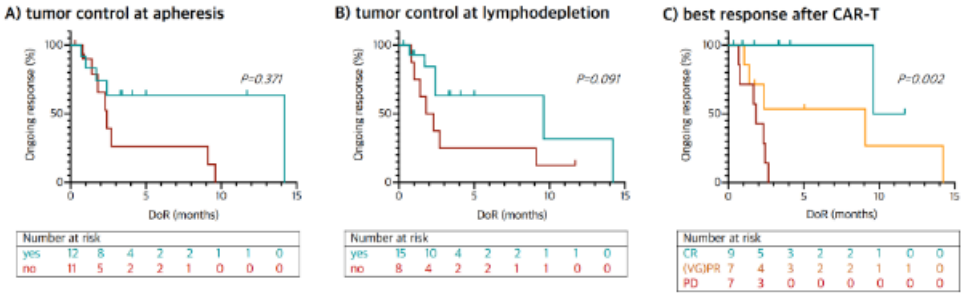

Figure 1. Efficacy of CAR-T in MM patients with prior bsAb exposure. Kaplan-Meier curves for duration of response (DoR) are shown as stratified by tumor control before apheresis **(A)** or lymphodepletion **(B)**, and by best response achieved after CAR-T infusion *(C). Abbreviations: CR= complete remission, (VG)PR= very good partial remission, PD= progressive disease.*

Keywords: Multiple myeloma, Bispecific, CAR-T, T cell reconstitution