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705.CELLULAR IMMUNOTHERAPIES: LATE PHASE AND COMMERCIALLY AVAILABLE THERAPIES

Comparison of Fludarabine/Cyclophosphamide Vs Bendamustine As Lymphodepleting Regimen for CAR-T: A Safety and Efficacy Analysis in Patients with Relapsed/ Refractory Multiple Myeloma

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Background
Two commercially available anti-BCMA chimeric antigen receptor T-cell therapies (CAR-T) are approved by FDA for use in patients with relapsed multiple myeloma (RRMM). Lymphodepletion (LD) with fludarabine in combination with cyclophosphamide (Flu/Cy) is used as a standard regimen sequentially prior to CAR-T. Due to a national shortage with regards to availability of fludarabine, bendamustine (B) has emerged as a possible alternative regimen for LD.
We evaluated the impact of bendamustine as an alternative lymphodepleting regimen to Flu/Cy on safety and efficacy profile of CAR-T therapy in patients with relapsed multiple myeloma.
Patients and methods
We conducted a single center, retrospective, IRB-approved study for patients with RRMM who received LD with B and FC at Hackensack University Medical Center (HUMC). Efficacy outcomes included overall response rates (ORR), Progression free survival (PFS) and Overall survival (OS). Response to CAR-T was assessed by the treating physician per International Myeloma Working Group (IMWG) criteria. Safety outcomes included the incidence and severity of adverse events (AEs). AEs were graded using National Cancer Institute Common Terminology Criteria for Adverse Events version 5.0 (NCI-CTCAE 5.0). Cytokine release syndrome (CRS) and immune effector associated neurotoxicity syndrome (ICANS) were graded as per the American Society for Transplantation and Cellular Therapy (ASTCT) criteria.
Results
We identified 53 patients with RRMM who received anti-BCMA CAR-T therapy between 6/2021 and 6/2023, who had a follow-up of at least 30 days following infusion. Due to shortage of fludarabine, the majority of pts (67.9%) received LD with B. Baseline characteristics are described in table 1. The median age of the entire cohort was 69.6 years, not significantly different between the B vs FC group. There were no statistically significant differences between the two groups with respect to the baseline characteristics except more pts were male in the B group (66.7% vs 32.1%, p=0.03) and the type of CAR-T product received. No significant differences were found with regards to the safety profile; however, the ORR were found to be

higher in the FC group compared to the B group (88.2% vs 69.4%) although not statistically significant (p=0.1). Median PFS (mPFS) was shorted in the B group compared with the FC group (7.7 months vs 13.1 months) respectively (p=0.0047). Median OS (mOS) was not reached in the FC group, whereas it was 12.4 months in the B group, p=0.5.

Conclusions

LD with B was not found to have any significant impact on the CRS or ICANS, however a lower ORR (although not statistically significant) was found. mPFS was shorter for the B group compared to the FC group which was a statistically significant finding. Although the follow-up is short, our experience suggests that the use of B as LD may have a negative impact on outcomes of pts receiving CAR-T therapy for RRMM.

Disclosures Biran: *Pfizer:* Membership on an entity's Board of Directors or advisory committees; *GSK:* Membership on an entity's Board of Directors or advisory committees; *Genomic Testing Cooperative:* Divested equity in a private or publicly-traded company in the past 24 months; *Abbvie:* Honoraria; *Takeda:* Honoraria, Membership on an entity's Board of Directors or advisory committees; *Sanofi:* Honoraria, Membership on an entity's Board of Directors or advisory committees; *Merck:* Research Funding; *BMS:* Honoraria, Membership on an entity's Board of Directors or advisory committees, Research Funding; *Karyopharm:* Membership on an entity's Board of Directors or advisory committees, Research Funding; *Amgen:* Membership on an entity's Board of Directors or advisory committees, Research Funding; *Janssen:* Honoraria, Membership on an entity's Board of Directors or advisory committees, Research Funding; *Boehringer Ingelheim:* Other: spouse of employee. **Suh:** *Kite Pharma:* Membership on an entity's Board of Directors or advisory committees. **Siegel:** *Janssen:* Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees, Research Funding, Speakers Bureau; *Karyopharm:* Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees, Research Funding, Speakers Bureau; *Novartis:* Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees, Research Funding, Speakers Bureau; *Celgene:* Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees, Research Funding, Speakers Bureau; *Celularity Scientific:* Consultancy, Membership on an entity's Board of Directors or advisory committees; *Takeda:* Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees, Research Funding, Speakers Bureau; *Amgen:* Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees, Research Funding, Speakers Bureau; *BMS:* Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees, Research Funding, Speakers Bureau. **Parmar:** *Sanofi:* Consultancy, Honoraria; *Cellectar Biosciences:* Consultancy, Honoraria.

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Variable	All	Benda	Flu/Cy	P-value
No of patients, N (%)	53	36 (67.9%)	17 (32.1%)	
Gender: Male	30 (56.6%)	24 (66.7%)	6 (35.3%)	0.03
Median age (years) (range)	69.6	69.5 (52.6-81.8)	70.5 (50.5-81.5)	0.42
Median prior lines of therapies (range)	5	5 (4-12)	6 (4-12)	0.8
Median time from diagnosis to therapy in years (range)	8.1	7.9 (2-21.6)	9.1 (2.4-17.7)	0.6
High risk FISH (%)	27 (60%)	21 (65.6%)	6 (46.2%)	0.23
ISS stage 2 or 3 (%)	24 (60%)	11 (40.7%)	5 (38.5%)	0.89
Triple class refractory (%)	50 (94.3%)	35 (97.2%)	15 (88.2%)	0.2
Ide-cel	35 (66.04%)	20 (57.1%)	15 (42.9%)	0.01
Cilta-cel	18 (33.96%)	16 (88.9%)	2 (11.1%)	
Prior ASCT (%)	52 (98.1%)	35 (97.2%)	17 (100%)	0.37
CRS (any grade)	42 (79.2%)	28 (77.8%)	14 (82.3%)	0.7
CRS (Grade III or higher)	1 (1.9%)	1 (2.8%)	0 (0%)	0.37
ICANS (any grade)	6 (11.3%)	5 (13.9%)	1 (5.9%)	0.4
ICANS (Grade III or higher)	2 (3.8%)	2 (5.6%)	0 (0%)	0.21
ORR (%)	40 (75.5%)	25 (69.4%)	15 (88.2%)	0.1
VGPR or better (%)	30 (56.6%)	19 (52.8%)	11 (64.7%)	0.4
Median PFS in months (Interquartile range)	11.9 (4.8-19)	7.7 (4.04-12.4)	13.1 (10.9-NR)	0.0047
Median OS months (Interquartile range)	NR(NR-NR)	12.4 (12.4-NR)	NR (NR-NR)	0.5

ISS= International Staging System; ASCT= Autologous Stem Cell Transplant; CRS= Cytokine Release Syndrome; ICANS= Immune effector cell-associated neurotoxicity syndrome; ORR= Overall Response Rate; VGPR= Very Good Partial Remission; PFS= Progression Free Survival; OS= Overall Survival.

Table 1. Baseline characteristics, safety and efficacy data for the entire cohort and those receiving lymphodepletion with bendamustine and Fludarabine/cyclophosphamide (Flu/Cy)

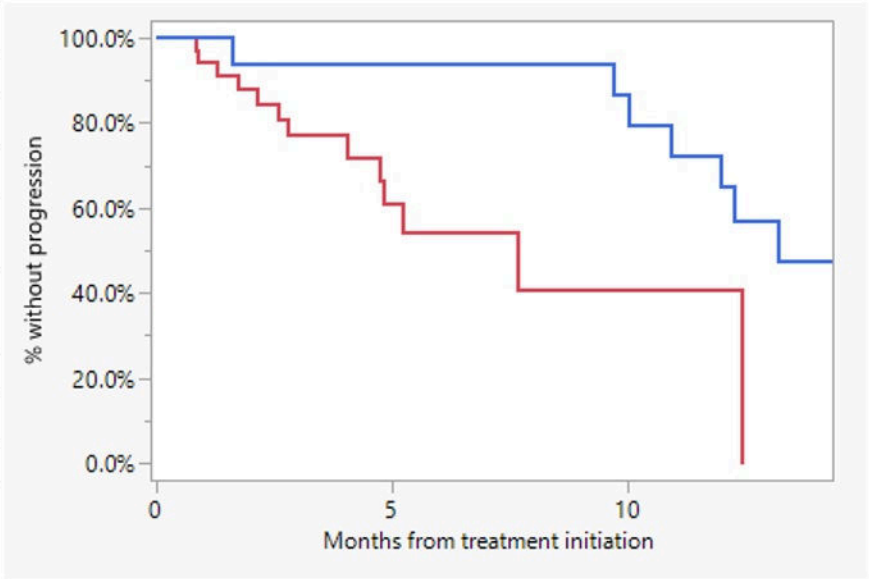

Figure 1. mPFS for patients receiving lymphodepletion with FC (blue)=11.9 mos vs B (red)=7.7mos

Figure 1