ELSEVIER

Blood 142 (2023) 3794–3796

The 65th ASH Annual Meeting Abstracts

POSTER ABSTRACTS

905.OUTCOMES RESEARCH-LYMPHOID MALIGNANCIES

Attrition after Referral for Chimeric Antigen Receptor T-Cell (CAR-T) Products in Multiple Myeloma (MM)

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Introduction:
Chimeric antigen receptor T-cell (CAR-T) products have shown an impressive response in relapsed/refractory MM patients (pts). The pivotal KarMMa-3 (Otero-Rodriguez P et al, NEJM, 2023) and CARTITUDE-4 (San Miguel J, et al, NEJM, 2023) studies showed that infusion of idecabtagene vicleucel (ide-cel) and ciltacabtagene autoleucel (cilta-cel) was superior to other standard of care therapies.
However, some pts in these studies were unable to receive CAR-T even after being deemed eligible for apheresis. In KarMMa-3, 12/140 pts who completed apheresis did not receive their cells, 3 due to disease progression/death and 1 due to a true manufacturing failure. In CARTITUDE-4, 16/113 pts who completed apheresis did not receive their cells, with 9 dying prior to infusion and 0 having true manufacturing failures. Other studies have shown that factors like peripheral CD3 count (PCD3) affected the probability of a successful apheresis (Rytlewski et al, ASCO 2022). Known reasons for CAR-T attrition include lack of available spots, true manufacturing failures, death post-apheresis but prior to infusion (PAD; due to infection and/or disease progression), and cell product issues necessitating an expanded access program (EAP). This study aimed to find patient- and disease-specific variables associated with increased rates of CAR-T attrition.
Methods:
We retrospectively reviewed the medical records of all pts who were approved for either ide-cel or cilta-cel as standard of care (SOC) treatment for MM at MD Anderson between August 2021 and June 2023. The study was approved by the Institutional Review Board at MD Anderson. Pts were classified by CAR-T product received, and the number of apheresis procedures required to produce viable product. They were then classified based on need for EAP.
Descriptive statistics including mean, standard deviation, median, and range for continuous variables such as age and lab measurements, and frequency counts and percentages for categorical variables such as stage, gender, comorbidity, treatment, and response were obtained. Fisher's exact test or Chi-square test was used to evaluate the association between two categorical variables. Wilcoxon rank sum test or Kruskal-Wallis test was used to evaluate the difference in a continuous variable between or among patient groups. Kaplan-Meier method was used to estimate overall survival and progression free

survival for the pts who received CAR-T infusion. Statistical software SAS 9.4 (SAS, Cary, NC) and S-Plus 8.2 (TIBCO Software Inc., Palo Alto, CA) were used for all the analyses.

Results:

Data from 153 pts were included. High-risk features, defined as the presence of high-risk cytogenetics, extramedullary disease, or R-ISS stage III, were present in 125 (81.7%), and 84 (54.9%) were penta-refractory. CAR-T cells were infused successfully in 86 (56.2%) pts, including 5 who were infused via EAP. Of the 67 pts who did not get infused, 26 (38.2%) died prior to apheresis, 8 (11.9%) were PAD, 10 (14.9%) were treated with a bispecific agent due to lack of available manufacturing slots, and 3 (4.5%) had true manufacturing failures. Of the 8 patients that were PAD, 2 died due to progression of disease, 4 died from complications of inpatient bridging chemo, and 2 died from complications from lymphodepleting chemo. For all pts with manufacturing failures, their apheresis had a low dose, with 2 out of 3 having PCD3 < 5%.

The mean absolute lymphocyte count (ALC) at apheresis was significantly higher in the EAP group (n=5) compared with the non-EAP group, but significantly lower in the manufacturing failures group (n=3) compared with the successful CAR-T manufacturing (n=86) group (Table 1).

For the overall cohort of pts receiving CAR-T (n=86), the median progression-free (PFS) and overall survival (OS) rates were 11.7 and 18.8 months, respectively (Figure 1).

Conclusion:

The PFS and OS for all pts, including those who received their CAR-T through EAP, were excellent. ALC at the time of apheresis was a predictor of true manufacturing failure. Surprisingly, pts successfully treated on EAP had an increased ALC compared with those receiving SOC. Further comparative studies of pts with barriers to CAR-T are needed to identify other variables that increase adverse outcomes so that these can be addressed. Hopefully, with a better understanding of the barriers patients have, we can ensure that more pts get access to this efficacious treatment.

Disclosures Lee: *Amgen:* Research Funding; *Takeda:* Consultancy, Research Funding; *Pfizer:* Consultancy; *Bristol Myers Squibb:* Consultancy, Research Funding; *Regeneron:* Consultancy, Research Funding; *GlaxoSmithKline:* Consultancy, Research Funding; *Sanofi:* Consultancy; *Allogene Therapeutics:* Consultancy; *Janssen:* Consultancy, Research Funding; *Genentech:* Consultancy. **Thomas:** *Ascentage Pharma:* Research Funding; *Cellectar Biosciences:* Research Funding; *Janssen Pharma:* Research Funding; *Genentech:* Research Funding; *X4 pharma:* Research Funding; *Cellectar Biosciences:* Consultancy; *Abbvie, Cellectar Biosciences:* Consultancy; *Bristol Myers Squibb, Janssen Pharma Genentech, X4 pharma, Cellectar Biosciences, Ascentage Pharma:* Research Funding. **Gaballa:** *Boxer Capital, LLC:* Consultancy. **Qazilbash:** *NexImmune:* Research Funding; *Bioline:* Other: Advisory board; *Janssen:* Research Funding; *Angiocrine:* Research Funding; *Amgen:* Research Funding. **Hawkins:** *Janssen:* Membership on an entity's Board of Directors or advisory committees; *BMS:* Membership on an entity's Board of Directors or advisory committees; *Legend Biotech:* Consultancy; *Kite:* Membership on an entity's Board of Directors or advisory committees. **Orlowski:** *BMS/Celgene Corporation, CARsgen Therapeutics, Exelixis Inc., Heidelberg Pharma, Janssen Biotech Inc., Sanofi/Genzyme, Takeda Pharmaceuticals USA Inc.:* Other: Clinical Research Funding, Research Funding; *Asylia Therapeutics, BioTheryX Inc., Heidelberg Pharma:* Other: Laboratory Research Funding, Research Funding; *AbbVie, Adaptive Biotech, Asylia Therapeutics, Inc., BioTheryX, Bristol-Myers Squibb Pharmaceuticals, Karyopharm Therapeutics, Meridian Therapeutics, Monte Rosa Therapeutics, Nanjing IASO Biotherapeutics, Neoleukin Corporation, Oncopeptides AB, Pfizer, In:* Consultancy, Honoraria; *Asylia Therapeutics:* Current equity holder in private company, Patents & Royalties. **Patel:** *Takeda:* Consultancy; *AbbVie; Allogene Therapeutics, Inc.; Arcellx; Bristol Myers Squibb/Celgene Corporation; Cellectis; Janssen Pharmaceuticals, Inc.; Nektar Therapeutic; Poseida Therapeutics; Precision BioSciences, Inc.; and Takeda Pharmaceuticals U.S.A., Inc.:* Research Funding; *AbbVie; Arcellx, AstraZeneca; Bristol Myers Squibb/Celgene Corporation; Caribou Science; Cellectis; Curio Bioscience; Genentech; Janssen Pharmaceuticals, Inc.; Karyopharm; Legend Biotech; Merck & Co., Inc.; Oncopeptides; Pfizer; Precision BioSciences:* Consultancy.

Variable	EAP vs non-EAP (n=86)			Manufacturing Failures vs SOC (n=89)		
	Non-EAP (n=81)	EAP (n=5)	p-value	Failure (n=3)	SOC CAR-T (n=86)	p-value
Male sex (%)	51 (63.0%)	3 (60.0%)	1.000	1 (33.3%)	54 (62.8%)	0.5554
Age at apheresis (years)	65.0 ± 11.6	64.2 ± 7.73	0.7257	68.7 ± 4.7	64.9 ± 11.3	0.6247
Prior Lines of Therapy (n)	7.47 ± 3.30	7.20 ± 4.87	0.5030	5.67 ± 1.53	7.45 ± 3.37	0.3901
Mean ALC at apheresis ($x10^3/\mu L$)	0.92 ± 0.56	1.77 ± 1.10	0.0346	0.27 ± 0.26	0.97 ± 0.63	0.0132
Mean ALC 2 weeks prior ($x10^3/\mu L$)	0.74 ± 0.47	0.62 ± 0.40	0.8908	0.33 ± 0.24	0.73 ± 0.46	0.0875
WBC at apheresis ($x10^3/\mu L$)	4.50 ± 1.73	4.68 ± 1.41	0.7188	3.30 ± 1.91	4.51 ± 1.71	0.3452

Table 1: Comparison of patient- and disease-specific variables between different subgroups. The first comparison is between the EAP (n=5) and non-EAP (n=81) subgroups, and the second comparison is between the successful CAR-T infusion (n=86) and the true manufacturing failure (n=3) subgroups.

Abbreviations: EAP, expanded access program; SOC, standard of care; CAR-T, chimeric antigen receptor T-cell; ALC, absolute lymphocyte count; WBC, white blood cell count

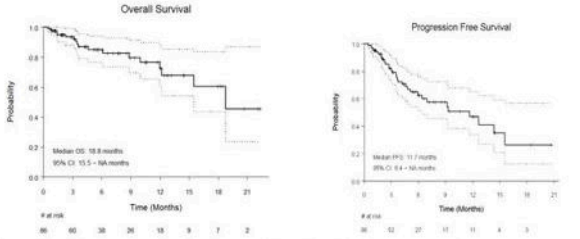

Figure 1: Kaplan-Meier curves for overall survival (OS) and progression-free survival (PFS) for overall CAR-T cohort. Most pts did not reach progression after CAR-T infusion.

Figure 1

https://doi.org/10.1182/blood-2023-187583