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POSTER ABSTRACTS

705.CELLULAR IMMUNOTHERAPIES: LATE PHASE AND COMMERCIALLY AVAILABLE THERAPIES

Impact of Prior Response to Blinatumomab on Outcomes of Brexucabtagene Autoleucel (Brexu-cel) in Adult Patients with Relapsed or Refractory (r/r) B-Cell Acute Lymphoblastic Leukemia (B-ALL): Results from the Real-World Outcomes Collaborative of CAR-T in Adult ALL (ROCCA)

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Introduction: Brexucabtagene autoleucel (brexu-cel) is an autologous anti-CD19 chimeric antigen receptor (CAR) T-cell therapy approved for adults with relapsed or refractory (r/r) B-cell acute lymphoblastic leukemia (B-ALL). Blinatumomab is a CD19-directed bispecific T-cell engager that is also approved for r/r B-ALL, and often used as early salvage therapy. Data in the pediatric/AYA population suggest that patients who did not respond to blinatumomab may have inferior outcomes to CD19-directed CAR-T products compared to those who have achieved a response to blinatumomab or were blinatumomab-naïve (Myers *et al*. J Clin Oncol 2022). In this study, we evaluate the response to blinatumomab and subsequent response to brexu-cel in adults with r/r B-ALL.

Methods: Retrospective data were collected from 25 centers across the U.S. as part of the real-world outcomes collaborative study of CAR-T in B-ALL (ROCCA). Consecutive patients treated with brexu-cel from 2021 to 2023 were categorized by blinatumomab exposure status. Those exposed were separated into "blinatumomab responders" (B-R), defined as patients achieving a CR/CRi in response to any number of cycles of blinatumomab, and "non-responders" (B-NR). Each cohort was compared for outcomes of interest. The primary outcome was CR/CRi rate at day 28 following brexu-cel administration. Secondary outcomes were duration of response (DOR), progression-free survival (PFS), and overall survival (OS). Survival outcomes were calculated from day of brexu-cel infusion and were not censored for allogeneic hematopoietic cell transplantation or maintenance therapy. All living patients were censored at data cutoff on June 30, 2023. Survival comparisons were made by log rank test.

Results: Among 152 patients who received brexu-cel, the median follow-up time was 8.4 months. Eighty-eight (57%) of 152 r/r B-ALL brexu-cel recipients had received blinatumomab prior to apheresis. The median number of pre-apheresis blinatumomab cycles was 2 (range 1-12). The baseline characteristics of B-R, B-NR, and blinatumomab-naïve (B-NV) patients were similar, including pre-apheresis disease burden and receipt of maintenance therapy following brexu-cel infusion (Table 1). Seventy percent (N= 62) of the blinatumomab-exposed patients were B-R, while 30% (N=26) were B-NR. Rates of CR/CRi at day 28 following brexu-cel infusion were similar between B-R, B-NR, and B-NV patients (79% vs 84% vs 78%, respectively). Most of these remissions were negative for measurable residual disease (MRD), with similar MRD negativity rates in the three groups (table 2). 1-year DOR and PFS were significantly higher in the B-NV group compared to B-R or B-NR (77% vs 49% vs 50%, $p<.0001$; 60% vs 37% vs 30%, $p<.0001$). B-NV and B-R had better 1-year survival compared to B-NR (71% vs 65% vs 32%, $p<.0001$). There were more CD19-negative relapses following brexu-cel in B-NR (29%) and B-R (18%) compared to B-NV patients (8%), although this was not statistically significant.

Conclusions: Brexu-cel induced deep responses in a majority of adults with r/r B-ALL, irrespective of prior exposure or response to blinatumomab. Similar to data published by the pediatric CAR-T cell groups, our data draw speculation that adult patients who did not respond to blinatumomab experience shorter overall survival following brexu-cel compared to those who responded to or did not receive blinatumomab. This should be confirmed in a larger, prospective clinical trial. Because this analysis could not account for patients who achieved durable remission after blinatumomab, these differences may not reflect superiority of sequencing brexu-cel before blinatumomab. The higher number of CD19-negative relapses in the blinatumomab-exposed cohort add to the interest in pursuing strategies to address antigen escape following CAR-T cell therapy directed against a previously targeted antigen.

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Table 1. Baseline cohort description stratified by blinatumomab exposure and response prior to CAR

	Blinatumomab-exposed; responder N = 62		Blinatumomab-exposed; non-responder N = 26		Blinatumomab-naïve N = 64	
	n	%	n	%	n	%
Age at CAR T-cell infusion, median (IQR) (n = 151)	51 (37, 62)		40 (29, 62)		40 (28, 60)	
Sex						
Female	31	50	8	31	26	41
Male	31	50	18	69	38	59
Race/ethnicity						
American Indian/Alaskan Native	2	3	0	0	0	0
Asian/Pacific Islander	2	3	4	15	4	6
Black	3	5	3	12	3	5
Hispanic	23	37	7	27	22	34
Mixed	0	0	0	0	1	2
Non-Hispanic White	32	52	12	46	33	52
Unknown	0	0	0	0	1	2
Leukemia type						
Ph+ ALL	21	34	5	19	21	33
Ph- ALL	30	48	12	46	31	48
Ph-like ALL	10	16	8	31	11	17
Mixed phenotype acute leukemia	1	2	1	4	1	2
Number of lines of therapy, median (IQR)	4 (3, 5)		4 (3, 5)		3 (2, 4)	
Pre-apheresis disease burden						
Active disease at time of apheresis	25	40	16	62	38	59
CR with MRD+	21	34	3	12	11	17
CR with MRD-	9	15	3	12	10	16
CR with unknown MRD	2	3	0	0	1	2
Unknown	5	8	4	15	4	6
Blin pre-apheresis	62	100	26	100	0	0
# cycles of blin, median (min, max)*	2 (1, 12)		1 (1, 4)		--	
Best response to blin pre-apheresis						
No response/active disease	0	0	26	100	--	
Complete remission with MRD+	19	31	0	0	--	
Complete remission with MRD-	39	63	0	0	--	
Complete remission achieved by morphology without MRD testing	3	5	0	0	--	
Received maintenance	19	31	8	31	17	27

*Cumulative across all subsequent lines of therapy.

Table 2. Post-CAR outcomes by blinatumomab exposure and response

	Blinatumomab-exposed; responder N = 62		Blinatumomab-exposed; non-responder N = 26		Blinatumomab-naïve N = 64		p-value
	n	%	n	%	n	%	
Day 28 post CAR T-cell therapy response							0.88
No response	6	10	1	4	6	9	
CR with MRD+	8	13	5	19	5	8	
CR with MRD-	40	65	16	62	43	67	
CR with unknown MRD	1	2	1	4	2	3	
Unknown	7	11	3	12	8	13	
CD19 negative relapse (n = 94)							0.05
Yes	8	18	4	29	3	8	
No	32	73	6	43	30	83	
Unknown	4	9	4	29	3	8	
Death in remission	10	16	4	15	8	13	0.82
1-year duration of response (% survived)	49		50		77		<.0001
1-year progression-free survival (% survived)	37		30		60		<.0001
1-year overall survival (% survived)	65		32		71		<.0001

Figure 1

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