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POSTER ABSTRACTS

705.CELLULAR IMMUNOTHERAPIES: LATE PHASE AND COMMERCIALLY AVAILABLE THERAPIES

The Impact of Inotuzumab Ozogamicin (InO) Treatment on Brexucabtagene Autoleucel (Brexu-cel) Outcomes in Adults with Relapsed/Refractory B-Cell Acute Lymphoblastic Leukemia (B-ALL)

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Cellular Immunotherapies: Late Phase and Commercially Available Therapies

The Impact of Inotuzumab Ozogamicin (InO) Treatment on Brexucabtagene Autoleucel (Brexu-cel) Outcomes in Adults with Relapsed/Refractory B-cell Acute Lymphoblastic Leukemia (B-ALL)

Introduction: Brexu-cel is the first approved CD19-directed chimeric antigen receptor (CAR) T-cell therapy for adult patients (pts) with relapsed/refractory (r/r) B-ALL. InO, an anti-CD22 antibody drug conjugate, is also approved for the same indication. With the accessibility to several targeted therapies in r/r B-ALL, the optimal sequence remains uncertain. The effect of prior treatment with InO on brexu-cel outcomes remains underreported, especially as a bridging therapy, as well as the effect of previous response to InO on post brexu-cel outcomes.

Methods: This is a retrospective multicenter analysis from 25 U.S. institutions of adults (≥18 years) with r/r B-ALL treated with commercial brexu-cel from 2021 to 2023 post FDA approval. Methodologies for assessing minimal residual disease (MRD) (minimal threshold of 10^{-4}) included flow cytometry, NGS, or qPCR depending on institutional practice. Progression-free survival (PFS) and overall survival (OS) were calculated from day of brexu-cel infusion and were not censored for hematopoietic cell transplant (HCT) or maintenance. All living patients were censored at the time of last follow-up prior to data lock, which occurred on June 30, 2023.

Results: Among 152 infused, 83 (54.6%) had pre-CAR InO therapy (InO-exposed), with a median of 3 administered doses (range: 1-22). Within the InO-exposed cohort, 23 (28%) pts received InO as a CAR T-cell bridging therapy (ie, between apheresis and lymphodepletion) with or without pre-apheresis and 60 (72%) pts received InO only during pre-apheresis. Baseline characteristics for InO exposed and InO-naïve pts are shown in Table 1. InO-exposed pts had higher median prior lines of therapies (4 vs. 3; p= 0.05), more frequently had active disease (≥5% marrow blasts) at the time of apheresis (67% vs. 44%, p= 0.02), and had lower incidence of Ph+ disease (19% vs. 45%, p=0.003), compared to InO-naïve pts, respectively.

The incidences of cytokine release syndrome (CRS) (85% vs. 85%, p= 0.26) and ICANS (58% vs. 57%, p= 0.36) post infusion were similar, and post-infusion death in remission occurred in 17% and 12% among InO-exposed and InO-naïve pts, respectively. Morphological complete remission (CR) and MRD- rates following brexu-cel infusion were 89% and 77% for InO-exposed pts, and 92% and 70% for InO-naive pts, respectively. Post CAR therapy, more InO-naïve pts underwent consolidation/maintenance therapy (transplant, chemotherapy, or TKIs) compared to InO-exposed pts (41% vs. 19%, p= 0.004).

The median follow-up after brexu-cel was 8.4 (range) months. Median OS (not reached (NR) vs. 12 months; p= 0.033) and median PFS (NR vs. 7 months; p= 0.029) were superior in InO-naïve pts compared to InO-exposed pts, respectively. However, after adjusting for pre-apheresis disease burden and post-CAR maintenance therapy, there were no longer significant differences in OS (HR= 1.25;95%CI: 0.62-2.53; p= 0.53) or PFS (HR= 1.24;95%CI:0.71-2.16, p=0.45) based on pre-CAR InO exposure. When InO-exposed pts were stratified based on prior InO-response (CR vs. no response), InO-responsive pts had superior estimated 12-month OS (64%) and PFS (38%) relative to InO-refractory pts (OS: 33%; PFS: 34%), but inferior to InO-naïve pts (OS: 75%; PFS 56%), with p-values of 0.0001 and 0.021 for OS and PFS, respectively (Figure 1). The timing of pre-CAR InO therapy did not impact brexu-cel survival outcomes, with comparable estimated 12-month OS (43% vs. 58%, p= 0.35) and PFS (46% vs. 38%, p= 0.57) for InO-exposed pts during bridging therapy and patients who received InO as a therapy prior to apheresis.

Conclusion: After adjusting for pre-CAR disease burden and post-CAR consolidation/maintenance, we found that prior InO exposure does not significantly associate with PFS or OS following brexu-cel. However, relative to InO-responsive patients, patients who were InO-refractory appear to have worse post-CAR survival outcomes. Finally, timing of InO administration (ie as a prior line of therapy or as CAR bridging) did not influence outcomes brexu-cel outcomes.

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Table 1. Baseline Characteristics	N	%	N	%
	InO-exposed (n= 83; 55%)		InO-naïve (n= 69; 45%)	
Age at infusion, years				
Median (IQR)	46 (32-62)		46 (31-59)	
Sex				
Male	48	58	39	57
Race/Ethnicity				
Non-Hispanic White	42	51	35	51
Hispanic	28	34	24	35
Asian/PI	6	7	4	6
Black	5	6	4	6
Other	2	2	2	3
ALL Sub-Type				
Ph+	16	19	31	45
Ph-	45	54	28	41
Ph-Like	19	23	10	14
MPAL	3	4	0	0
Prior Therapies				
Lines of Prior Therapy: median (IQR)	4 (2-5)		3 (2-4)	
Blinatumomab pre-apheresis	47	57	41	59
Allogeneic HCT	31	37	31	45
Pre-Apheresis Disease Burden				
Active disease (>=5% marrow blasts)	51	67	28	44
CR with MRD-Positive	12	16	23	37
CR with MRD-Negative	11	14	11	17
CR with MRD- Unknown	2	3	1	2
Toxicity	**N**	**%**	**N**	**%**
CRS (ASTCT Criteria) (n= 147)				
Any CRS	68	85	57	85
Grade 1	30	38	28	42
Grade 2	28	35	25	37
Grade >=3	10	13	3	4
ICANS (ASTCT Criteria) (n= 148)				
Any ICANS	46	58	39	57
Grade 1	8	10	6	9
Grade 2	9	11	12	18
Grade >=3	29	36	19	28
Outcomes	**N**	**%**	**N**	**%**
Response (among N=134 with response data)				
No response				
CR/CRi	8	11	5	8
MRD+ among CR/CRi	63	89	58	92
MRD- among CR/CRi	6	8	12	19
MRD unknown among CR/CRi	55	77	44	70
	2	3	2	3
Progression-Free Survival (PFS)				
Median PFS	7 months		Not reached	
6-month PFS	55%		67%	
12-month PFS	40%		56%	
Overall Survival (OS)				
Median OS	12 months		Not reached	
6-month OS	77%		85%	
12-month OS	55%		75%	

Figure 1. OS post brexu-cel by InO exposure and response

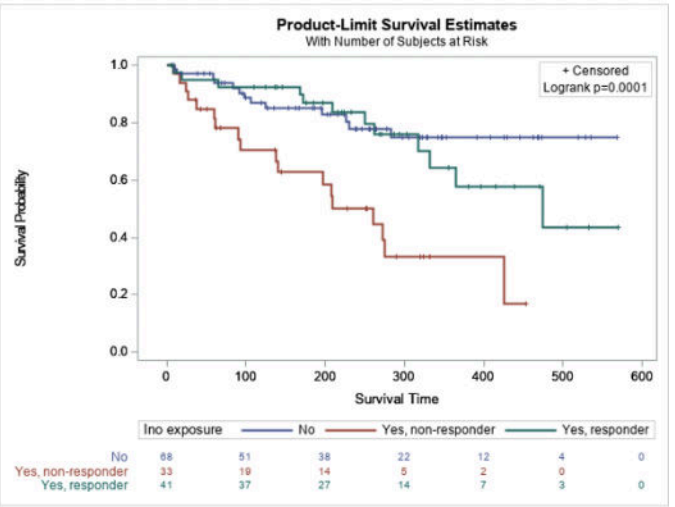

Figure 1