Brexucabtagene Autoleucel (Brexu-cel) as Consolidation Treatment in Adults with B-Cell Acute Lymphoblastic Leukemia: Efficacy and Toxicity in a real world setting

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INTRODUCTION

- Brexu-cel is a CD19 CAR T cell approved for adult patients (pts) with R/R B-cell ALL
- In the ZUMA-3 trial, pts were required to have >5% marrow blasts at study entry[1]

AIMs and OBJECTIVES

- To evaluate toxicity/efficacy with Brexu-cel in real world setting in adult pts with marrow blasts <5%

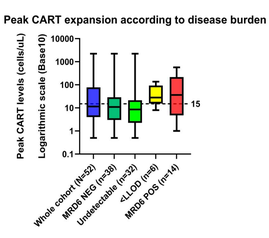
METHODS

- Retrospective analysis of adult patients who received commercial Brexu-cel between 02/2022 to 02/2025 at MDACC, Houston
- Inclusion criteria
  - Marrow blasts <5% at the time of most recent evaluation prior to lymphodepletion (LD)
  - Absence of any active EMD/CNS disease
  - Availability of NGS MRD (assessed by clonoSEQ assay) as well as CAR T expansion data
- Serial CAR T levels monitored in peripheral blood (PB) by flow cytometry based on anti-FMC63 Ab

RESULTS

Characteristic	n(%) or median [range]
Age (years)	36.5 [20 – 84]
• ≥60	11 (21)
Sex (Male)	32 (62)
Disease Subtype	
• Ph Positive	18 (35)
• Ph Like	10 (19)
○ CRLF2 rearranged	8 (15)
• KMT2A	1 (2)
• CK	13 (25)
• TP53	10 (19)
• Therapy Related ALL	5 (10)
Prior Extramedullary Disease (including CNS)	19 (37)
• Prior CNS disease	11 (21)
Prior Lines of therapy	2 [1 - 8]
• 1	10 (19)
• 2	25 (48)
• 3	10 (19)
• ≥ 4	7 (14)
Prior therapies	
• Blinatumomab	51 (98)
• Inotuzumab	40 (77)
• Allo-SCT	8 (15)
• CD19 CART	2 (4)
Pre CART BM MRD by NGS (Clonoseq)	
• MRD6 POS	14 (27)
• MRD6 NEG	38 (73)

Table 1 : Patient Characteristics (N=52)



Pre CAR T BM NGS Status / Disease status	Peak CAR T cells/µL Median [range]	Peak Expansion ≥ 15 cells/µL n(%)
Whole Cohort (N=52)	11.5 [1-2222]	25 (48)
MRD6 NEG (n=38)	11 [1-2222]	17 (44)
• Undetectable (n=32)	8.5 [1-2222]	12 (38)
• <LLOD (n=6)	28 [8-129]	5 (83)
MRD6Pos (n=14)	36.5 [1-573]	8 (57)

Figure 1: Pre CAR T BM NGS MRD and CAR T expansion, n=52

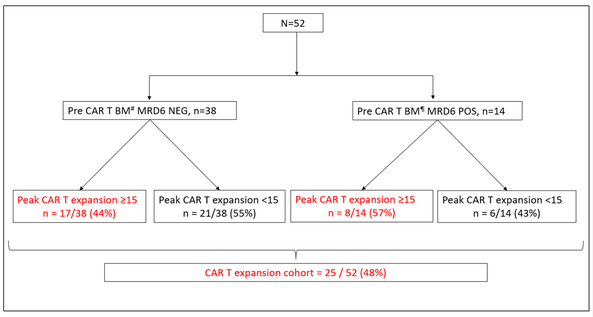
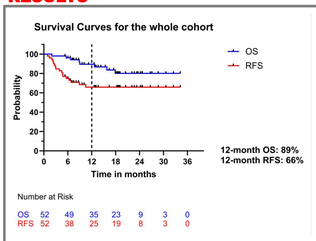


Figure 2: Pre CAR T BM NGS MRD and CAR T expansion, n=52

RESULTS



Median follow up 16.1 mos

Post CAR T consolidation
Allo-SCT (n=5)
Median time from CAR T to allo-SCT 3.5 mos [range, 1.6-4.2]

TKI (n=15)
Started at a median of 1 mos [range, 0.6-2.6]

Figure 3: OS and RFS of whole cohort

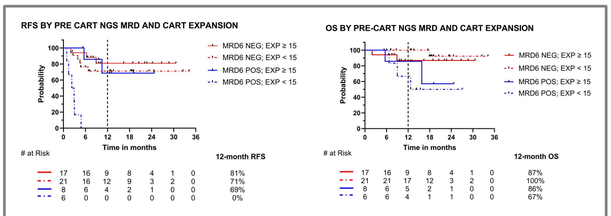


Figure 4: OS and RFS of whole cohort by pre CAR T NGS MRD and peak CAR T expansion

Characteristic n(%) or median[range]	Peak CART ≥ 15 cells/µL	Peak CART <15 cells/µL	P
N	25	27	
Age (years)	39 [22-84]	32 [20-77]	0.126
• ≥60	6/11 (55)	5/11 (45)	0.4
Sex (Male)	17/32 (53)	15/32 (47)	0.4
Disease Subtype			
• Ph Positive	13/18 (72)	5/18 (28)	0.019
• Ph Like	4/10 (40)	6/10 (60)	0.73
○ CRLF2r	3/8 (17)	5/8 (63)	0.70
• KMT2Ar	0	1 (100)	1.0
• CK	6/13 (46)	7/13 (54)	1.0
• TP53m	5/10 (50)	5/10 (50)	1.0
• Therapy Related ALL	2/5 (40)	3/5 (60)	1.0
Prior CNS Disease	7/11 (64)	4 (36)	0.32
Prior extramedullary disease	10/19 (53)	9/19 (47)	0.77
Prior Lines of therapy	2 [1-5]	2 [1-8]	0.40
• 1	6/25 (24)	4/27 (15)	0.84
• 2	12/25 (48)	13/27 (48)	
• 3	4 (16)	6/27 (22)	
• ≥ 4	3 (12)	4/27 (15)	
Prior used therapies			
• Blinatumomab	24/51 (47)	27/51 (53)	0.48
• Inotuzumab	15/40 (38)	25/40 (63)	0.008
• Allo-SCT	6/8 (75)	2/8 (25)	0.14
• CART	1/2 (50)	1/2 (50)	1.0
• Radiation therapy	6/10 (60)	4/10 (40)	0.49
Interval from prior therapy			
• Blinatumomab (days)	88 [7-690]	38 [12-757]	0.075
• Inotuzumab (days)	120 [22-1272]	111.5 [18-845]	0.21
• Radiation	20.5 [15-1042]	67 [11-159]	1.0

Table 2: Characteristics to predict peak CAR T expansion ≥15 cells/µL

Parameter	n(%) or median [range]
CRS	
• All Grade	28 (54)
• Grade 3	1 (2)
• Grade 4	0
ICANS	
• All Grade	11 (21)
• Grade 3	3 (6)
• Grade 4	2 (4)
Post CART Cytopenia	
• Grade 3-4 neutropenia @ D28	5 (10)
• Grade 3-4 neutropenia @ D42	3 (6)
• Grade 3-4 thrombocytopenia @ D28	17 (33)
• Grade 3-4 thrombocytopenia @ D42	14 (27)
Other Grade 3 / 4 Toxicity	
• Severe acute GVHD	1 (2)
Therapy for CRS/ICANS	
• Tocilizumab	22 (42)
• Dexamethasone	13 (25)
• Intensive Care Support	4 (13)

Table 3: CAR T Toxicity

Patients with G3-4 CRS or ICANS had high CAR T expansion (102, 124, 573, 1270 and 2222 cell/µL) and 2/5 had recent CNS disease

CONCLUSIONS

- Brexu-cel in pts with <5% marrow blasts is associated with low rates of grade 3-4 CRS/ICANS
- We noted CAR T expansion in pts with no morphologic detectable disease prior to LD
  - 12 mo RFS and OS for the entire cohort was 66% and 89%, respectively
  - Pts with higher CAR T expansion had lower likelihood of relapse

REFERENCES

1. Shah BD, Ghobadi A, et al. KTE-X19 for relapsed or refractory adult B-cell acute lymphoblastic leukaemia: phase 2 results of the single-arm, open-label, multicentre ZUMA-3 study. Lancet. 2021Aug 7;398(10299):491-502.

CONTACT INFORMATION

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