Abstract: P413

Title: BREXUCABTAGENE AUTOLEUCEL (BREXU-CEL) AS CONSOLIDATION TREATMENT IN ADULTS WITH B-CELL ACUTE LYMPHOBLASTIC LEUKEMIA WITH MARROW BLASTS <5%, INCLUDING PATIENTS (PTS) WITH NGS MRD NEGATIVE DISEASE

Abstract Type: Poster Presentation

Topic: Acute lymphoblastic leukemia - Clinical

Background:

Brexu-cel is an CD19 CAR T cell approved for adults with R/R B-cell ALL. In the ZUMA-3, pts were required to have >5% marrow blasts at study entry.

Aims:

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

Methods:

We retrospectively analyzed pts (≥18y) with B-ALL who received brexu-cel (not on clinical trial) at MDACC, Houston. Pts were included in this analysis if they had marrow blasts <5% at the time of most recent evaluation prior to lymphodepletion (LD) and without any clinical (and imaging, if performed) evidence of extra-medullary disease (EMD) at the time of LD. Event-free survival was calculated from the time of infusion to an event (defined as morphologic/MRD relapse requiring initiation of next line of therapy, or death from any cause). Allo-SCT after CAR T was at the discretion of the treating physician; outcomes were not censored for allo-SCT.

Results:

34 pts received brexu-cel from Feb 2022 to Dec 2023. Median age at cell infusion was 37 yrs. 9 pts (26%) had Ph+ ALL, 8 pts (24%) had Ph-like ALL, including 6 pts with CRLF2 fusion. The median number of prior therapies was 2 (range 1-7). Prior therapy included blinatumomab (94%), inotuzumab (88%), allo-SCT (24%). 7 pts received CAR T in CR1 [due to recurrent/persistent MRD +/- high-risk genomics]; the remaining pts had >1 prior line of therapy.

At the time of most recent disease assessment prior to LD, all pts had marrow blasts <5% with no clinical/imaging evidence of EMD. 29/34 pts had NGS MRD (clonoSEQ) results available from the last marrow prior to LD (4 pts NGS not done; 1 no trackable clone). 21/29 pts had NGS MRD undetectable at 10-6 sensitivity; the remaining 8 pts were positive at values ranging from 2-3283 cells/million.

For the 8 pts with NGS MRD+ disease prior to LD, the best response post CAR T was NGS MRD undetectable at 10-6 sensitivity in 6 pts (0 cells/million, n=3; <1 cells/million, n=3); 1 pt remained NGS MRD+ post CAR T; 1 pt had no NGS done post CAR T.

29 pts had serial CAR T levels assessed by peripheral blood flow-cytometry. The median peak expansion level was 12 cells/µl (range <1-1270) at a median of D+8. Among the 21 pts who were marrow NGS undetectable prior to LD, the median peak expansion level was 12 cells/µl (range <1-1270 n=18 with available data); among the 8 pts who were marrow NGS+ prior to LD, peak expansion was median 53 cells/µl (range 3-381, n=7 with available data).

19 pts (56%) had CRS [G3, 2 pts] and 7 pts (21%) had ICANS [G3-4, 2 pts]. 3 pts had either G3-4 CRS/ICANS. Tocilizumab was needed in 15 pts (44%), dexamethasone 7 pts (21%), and 2 pts needed ICU care. Among the 3 pts with G3-4 CRS/ICANS, 2 had CAR T expansion data available with peak expansion of 102 and 1270 cells/µl, respectively.

6 (18%) pts had subsequent allo-SCT in remission at a median of 3.6 mos (range 2.8-8.8) from cell infusion. With a median follow-up of 9.3 mos (range 1-21), the 6-mo and 12-mo EFS is 69.9% and 59.5%, respectively. The 6-mo and 12-mo OS was 95.8% and 88.4%, respectively. Among the pts with CAR T expansion data (n=29), those with CAR T peak expansion ≥20 cells/µl (n=12), no pt had MRD/clinical relapse compared to 7/17 pts with <20 cells/µl peak expansion.

Summary/Conclusion:

Use of brexu-cel in pts with low tumor burden is associated with low rates of G3-4 CRS/ICANS. We noted CAR T expansion in pts with no morphologic disease prior to LD. Prospective trials are planned to assess role of CAR T in low tumor burden setting, including MRD+ and as consolidation strategy.

Table 1: Baseline characteristics, CAR T expansion, and toxicity		
Parameters		**N (%), median [range] (N=34)**
Age		37 [20-84]
	Age ≥60 years	5 (15)
Gender	Male	23 (68)
Disease / Prior therapy details	Median lines of therapy	2 [1-7]
	Prior blinatumomab	32 (94)
	Prior inotuzumab	30 (88)
	Prior allo-SCT	8 (24)
	Prior CNS disease	11 (32)
	Prior EMD (incl prior CNS disease)	14 (41)
	Ph+ ALL	9 (26)
	Ph-like ALL	8 (24)
Time from apheresis to infusion (days)		40 [26-188]
Post CAR T complications	CRS	19 (56)
	• Grade 3	2 (6)
	• Grade 4	0
	ICANS	7 (21)
	• Grade 3-4	2 (6)
Therapy for CRS/ICANS	Tocilizumab	15 (44)
	Dexamethasone	7 (21)
	Anakinra	0
	Intensive care support	2 (6)
CAR T expansion (n=29)	Day to peak expansion (days)	8 [6-28]
	Peak CAR T expansion (cell/µl)	12 [<1-1270]

Keywords: Acute lymphoblastic leukemia, Cellular therapy