



The 65th ASH Annual Meeting Abstracts

ORAL ABSTRACTS

705.CELLULAR IMMUNOTHERAPIES: LATE PHASE AND COMMERCIALY AVAILABLE THERAPIES

Brexucabtagene Autoleucel in Adults with Relapsed/Refractory B-Cell ALL: Outcomes and Novel Insights from the Real-World Outcomes Collaborative of CAR T in Adult ALL (ROCCA)

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Introduction

In October 2021, brexucabtagene autoleucel (brexu-cel) received U.S. FDA approval as the first CAR T-cell therapy for adults with relapsed/refractory (r/r) B-cell acute lymphoblastic leukemia (B-ALL) based on the 55-patient ZUMA-3 Phase II study. We subsequently established ROCCA and now report on the largest cohort of patients treated with commercial brexu-cel for r/r B-ALL to date.

Methods

Adults (18+) with r/r B-ALL infused with commercial brexu-cel across 25 U.S. institutions were included. ASTCT consensus criteria were used to score CRS and ICANS. Methodologies for assessing MRD (minimal threshold of 10^{-4}) included flow cytometry, NGS, or qPCR depending on institution practice. Duration of remission (DOR) was calculated from time of complete response (CR); 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, the median age was 46 (range, 18-81), 57% were male, and 34% were Hispanic. Most (67%) had Ph-ALL, were heavily pre-treated (median 4 prior lines), and entered apheresis with high disease burden (57%). At time of apheresis, 23% of patients only had MRD+ disease and 15% were in complete molecular remission. While 82% developed CRS, the majority was grade 1-2, with 9% of the overall cohort experiencing grade 3-4 CRS. In contrast, 55% developed ICANS, with 32% of the entire cohort experiencing grade 3-4 ICANS. Eight patients (5%) died of toxicity/infection prior to D+28 response assessment.

Among 133 patients with response assessment, 120 (90%) achieved morphologic CR, of whom 82% were MRD-, 15% were MRD+, and 3% MRD unknown. The median follow-up for survivors was 8.4 months; 45 patients have relapsed and 42 patients died. Median DOR was not reached. Median PFS and OS were 8.6 months and 15.6 months, respectively. Estimated PFS and OS of the entire cohort at 6-months were 61% (95% CI, 52-68) and 81% (95% CI, 73-87) and at 12-months were 47% (95% CI, 37-56) and 63% (95% CI, 53-72), respectively. We found no association between pre-CAR disease burden and post-CAR PFS/OS. However, patients with MRD- response to CAR had superior PFS relative to patients with MRD+ CR (median 14 months vs. 5 months, $P=0.002$). Forty-four patients received post-CAR consolidation/maintenance therapy while in CR: 25 allogeneic HCT, 15 TKI, 2 POMP, and 3 other/unknown. To examine the effect of consolidation/maintenance following brexu-cel, we performed a landmark analysis of PFS limited to patients alive and in CR at 2-months post-CAR infusion ($N=113$) and suggests superior PFS in patients receiving either HCT or other forms maintenance, relative to those receiving no further therapy following brexu-cel ($P=0.055$). We then investigated post-CAR MRD-response in combination with receipt of post-CAR consolidation/maintenance and found that even among patients achieving MRD-negative response, post-CAR consolidation/maintenance led to superior PFS (Figure 1).

Conclusions

Among 152 adults treated with commercial brexu-cel for r/r B-ALL across 25 U.S. institutions, we found very high response rates (CR/CRi: 90%; 82% MRD-) consistent with the Zuma-3 data. While rates of severe CRS are low, grade 3-4 ICANS was observed in 32% of patients and warrants further investigation. We demonstrate the prognostic impact of achieving an MRD-negative CR and an emerging role for consolidation/maintenance therapies to enhance the durability of response following brexu-cel in adults r/r B-ALL.

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Figure 1. PFS by Post-CAR MRD Response and Use of Post-CAR Consolidation/Maintenance

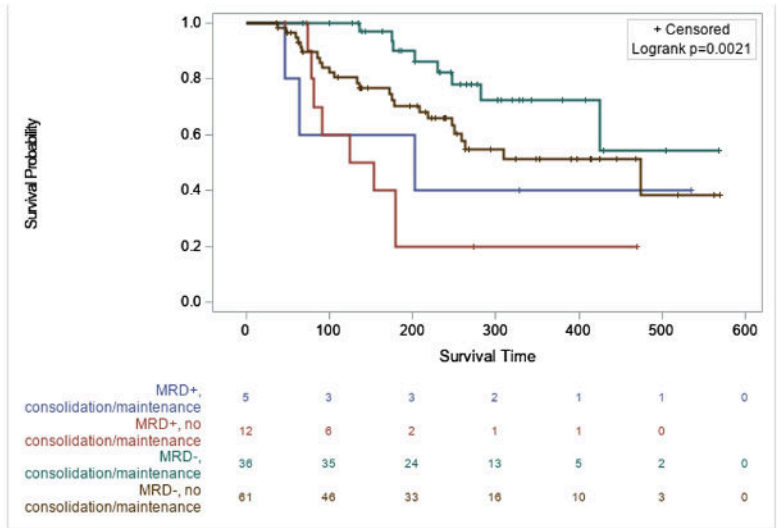


Figure 1

| Baseline Characteristics | N | % |
|-----------------------------------------------------------------|-------------|----------|
| Age at infusion, years | | |
| Median (Range) | 46 | (18-81) |
| Sex | | |
| Male | 87 | 57 |
| Race/Ethnicity | | |
| Non-Hispanic White | 77 | 51 |
| Hispanic | 52 | 34 |
| Asian/PI | 10 | 7 |
| Black | 9 | 6 |
| Other | 4 | 3 |
| ALL Sub-Type | | |
| Ph+ | 47 | 31 |
| Ph- | 102 | 67 |
| MPAL | 3 | 2 |
| Prior Therapies | | |
| Lines of Prior Therapy: median (range) | 4 | (1-12) |
| Blinatumomab | 88 | 58 |
| Inotuzumab | 72 | 47 |
| Allogeneic HCT | 62 | 41 |
| Other CAR T-Cell | 3 | 2 |
| Pre-Apheresis Disease Burden | | |
| High Burden (>=5% marrow blasts and/or extra-medullary disease) | 78 | 51 |
| Low Burden (<5% marrow blasts), MRD-Positive | 35 | 23 |
| Low Burden, MRD-Negative | 23 | 15 |
| Low Burden, MRD Unknown | 3 | 2 |
| Unknown | 13 | 9 |
| Toxicity | N | % |
| CRS (ASTCT Criteria) | | |
| Any CRS | 124 | 82 |
| Grade 1 | 58 | 38 |
| Grade 2 | 53 | 35 |
| Grade 3 | 9 | 6 |
| Grade 4 | 4 | 3 |
| Unknown | 5 | 3 |
| ICANS (ASTCT Criteria) | | |
| Any ICANS | 83 | 55 |
| Grade 1 | 14 | 9 |
| Grade 2 | 21 | 14 |
| Grade 3 | 34 | 23 |
| Grade 4 | 14 | 9 |
| Unknown | 4 | 3 |
| Outcomes | N | % |
| Response (among N=133 with response data) | | |
| CR/CRi | 120 | 90 |
| MRD+ among CR/CRi | 18 | 15 |
| MRD- among CR/CRi | 98 | 82 |
| MRD unknown among CR/CRi | 4 | 3 |
| Less than CR/CRi | 13 | 10 |
| Unknown/Unavailable (of total N=152 in cohort) | 19 | 13 |
| Duration of Response (DOR, among N=120 responders) | | |
| Median DOR | Not Reached | |
| 6-month DOR | 70% | (59, 78) |
| 12-month DOR | 62% | (50, 71) |
| Progression-Free Survival (PFS) | | |
| Median PFS | 8.6 months | |
| 6-month PFS | 61% | (52, 68) |
| 12-month PFS | 47% | (37, 56) |
| Overall Survival (OS) | | |
| Median OS | 15.6 months | |
| 6-month OS | 81% | (73, 87) |
| 12-month OS | 63% | (53, 72) |
| Death in Remission by Day +28 | 8 | 5 |
| Loss of CD19 at Relapse (among N= 45 relapsed) | 15 | 33 |
| Post-CAR T-Cell Consolidation/Maintenance | | |
| Total Receiving Consolidation/Maintenance | 44 | 29 |
| Allogeneic HCT | 25 | 16 |
| TKI | 15 | 10 |
| POMP | 2 | 1 |
| Other | 3 | 2 |