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ORAL ABSTRACTS

705.CELLULAR IMMUNOTHERAPIES: LATE PHASE AND COMMERCIALLY 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)

Gregory W Roloff, MD[1], Ibrahim Aldoss, MD[2], Noam E. Kopmar, MD[3], Chenyu Lin, MD[4], Simone E. Dekker, MD PhD[5], Vishal K Gupta, MD[6], Nikeshan Jeyakumar, MD[7], Timothy E O'Connor, MD[8], Amy Zhang, PhD[9], Katharine Miller, PhD MPH[9], Kaitlyn C Dykes, MD[10], Mohamed Ahmed[11], Hector Zambrano[12], Danielle Bradshaw, MD[13], Santiago Mercadal, MD[14], Marc Schwartz, MD[15], Sean Tracy, MDPhD[16], Bhagirathbhai Dholaria, MBBS[17], Michal Kubiak, MD[18], Akash Mukherjee, MD[19], Navneet Majhail, MD[20], Minoo Battiwalla, MD[20], Luke Mountjoy, DO[21], Shahbaz A. Malik, MD[22], John Mathews, MD[23], Paul Shaughnessy, MD[24], Aaron C. Logan, MD PhD[25], Abdullah Ladha, MD[26], George Yaghmour, MD[26], Anjali S. Advani, MD[27], Maryann Stefan[27], Caitlin Guzowski, MBA[28], Rasmus T. Hoeg, MD[29], Talal Hilal, MD[30], Jozal Moore, MD[31], Kristen M. O'Dwyer, MD[31], Stephanie B. Tsai, MD MS[8], Joshua Sasine, MD[11], Melhem M. Solh, MD[28], Catherine J. Lee, MD[32], Vamsi K. Kota, MD[18], Divya Koura, MD[10], Muthu Veeraputhiran, MD[19], Betsy Blunk[12], Jessica T. Leonard, MD[33], Veronika Bachanova, MD PhD[34], Wendy Stock, MD[1], Ahmed Galal, MD[4], Vinod Pullarkat, MD[2], Ryan D Cassaday, MD[3], Bijal D. Shah, MD[35], Rawan Faramand, MD[35], Lori S. Muffly, MD[9]

[1] University of Chicago, Chicago, IL
[2] City of Hope, Duarte, CA
[3] University of Washington, Seattle, WA
[4] Duke University School of Medicine, Durham, NC
[5] Department of Hematology & Medical Oncology, Oregon Health & Science University, Portland, OR
[6] University of California Los Angeles, Los Angeles, CA
[7] Division of Blood and Marrow Transplantation & Cellular Therapy, Stanford University School of Medicine, Palo Alto, CA
[8] Loyola University, Maywood, IL
[9] Stanford University School of Medicine, Stanford, CA
[10] University of California San Diego, La Jolla, CA
[11] Cedars-Sinai Medical Center, Los Angeles, CA
[12] Sarah Cannon Research Institute, Nashville, TN
[13] Georgia Cancer Center, Augusta University Medical Center, Augusta, GA
[14] University of Utah, Salt Lake City, UT
[15] Division of Hematology, University of Colorado, Aurora, CO
[16] Division of Hematology, Oncology and Transplantation, University of Minnesota, Minneapolis
[17] Division of Hematology/Oncology, Vanderbilt University Medical Center, Nashville, TN
[18] Georgia Cancer Center, Augusta University, Augusta, GA
[19] University of Arkansas for Medical Sciences, Little Rock, AR
[20] Sarah Cannon Transplant and Cellular Therapy Program at TriStar Centennial Medical Center, Nashville, TN
[21] Colorado Blood Cancer Institute and Sarah Cannon Cancer Institute at Presbyterian/St Luke's Medical Center, Denver, CO
[22] St. David's South Austin Medical Center, Austin, TX
[23] Sarah Cannon and Texas Oncology Transplant and Cellular Therapy Program at Medical City Dallas, Dallas, TX
[24] Sarah Cannon Transplant and Cellular Therapy Program at Methodist Hospital, San Antonio, TX
[25] Helen Diller Family Comprehensive Cancer Center, University of California San Francisco, San Francisco, CA
[26] Norris Comprehensive Cancer Center, University of Southern California, Los Angeles, CA
[27] Cleveland Clinic Foundation, Cleveland, OH
[28] Northside Hospital Cancer Institute, Atlanta, GA
[29] Department of Internal Medicine, Division of Cellular Therapy, Bone Marrow Transplantation and Malignant Hematology, University of California Davis, Sacramento, CA

[30] Mayo Clinic, Phoenix, AZ
[31] University of Rochester, Rochester, NY
[32] Clinical Research Division, Fred Hutchinson Cancer Center, Seattle, WA
[33] Oregon Health & Science University, Portland, OR
[34] Division of Hematology, Oncology and Transplantation, University of Minnesota, Minneapolis, MN
[35] Department of Blood and Marrow Transplantation and Cellular Immunotherapy, Moffitt Cancer Center, Tampa, FL

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.

Disclosures Aldoss: *Jazz:* Consultancy; *Amgen:* Consultancy, Honoraria; *Takeda:* Consultancy; *KiTE:* Consultancy; *Sobi:* Consultancy; *Pfizer:* Consultancy. **Lin:** *Biomarin:* Current equity holder in publicly-traded company; *Rigel Pharmaceuticals:* Consultancy. **Schwartz:** *Jazz Pharmaceuticals:* Consultancy; *Novartis:* Consultancy. **Dholaria:** *Poseida:* Research Funding; *Boxer Capital:* Consultancy; *AstraZeneca:* Research Funding; *Molecular Templates:* Research Funding; *Atara:* Research Funding; *NCI:* Research Funding; *Allovir:* Research Funding; *Pluri Biotech:* Consultancy; *ADC therapeutics:* Consultancy, Honoraria; *Wugen:* Research Funding; *Gilead:* Research Funding; *Arivan:* Consultancy; *Takeda:* Research Funding; *Pfizer:* Research Funding; *Ellipsis pharma:* Consultancy; *Lumanity:* Consultancy; *Orca Bio:* Research Funding; *MEI:* Research Funding; *Adicet:* Research Funding; *Angiocrine:* Research Funding; *BEAM therapeutics:* Consultancy; *gamida cel:* Consultancy; *Janssen:* Consultancy, Honoraria, Research Funding; *BMS:* Research Funding; *Poseida:* Research Funding. **Battiwalla:** *Novartis:* Research Funding; *Fate Therapeutics:* Research Funding. **Shaughnessy:** *Sanofi:* Speakers Bureau; *BMS:* Speakers Bureau. **Logan:** *Amgen, Autolus Therapeutics, Kadmon, Kite, Pharmacyclics, Talaris:* Research Funding; *AbbVie, Amgen, Actinium, BMS, Pfizer, Sanofi, Takeda:* Consultancy. **Advani:** *Jazz:* Honoraria, Membership on an entity's Board of Directors or advisory committees; *Kura:* Honoraria; *Servier:* Research Funding; *Beam:* Honoraria; *Immunogen:* Research Funding; *OBI:* Research Funding; *Kite:* Honoraria, Other: consulting, Research Funding; *Pfizer:* Honoraria, Research Funding; *Glycomimetics:* Membership on an entity's Board of Directors or advisory committees, Research Funding; *Seattle Genetics:* Research Funding; *Macrogenics:* Research

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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

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

Figure 1