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ORAL ABSTRACTS

705.CELLULAR IMMUNOTHERAPIES: LATE PHASE AND COMMERCIALLY AVAILABLE THERAPIES

Real-World Outcomes of Brexucabtagene Autoleucel (brexu-cel) for Relapsed or Refractory (R/R) Adult B-Cell Acute Lymphoblastic Leukemia (B-cell ALL): Evidence from the CIBMTR Registry

Evandro Bezerra, MD[1], *Taha Itani, PhD MPH*[2], *Kistada Wudhikarn, MD*[3], *Miguel-Angel Perales, MD*[4], *Yang Yang, MD*[5], *Usama Gergis, MD MBA*[5], *Ahmed Aribi, MD*[6], *LaQuisa C. Hill, MD*[7], *Nitin Jain, MD*[8], *Jessica T. Leonard, MD*[9], *Forat Lutfi, MD*[10], *Soyoung Kim, PhD*[11], *Matthew Bye, MPH*[12], *Hai-Lin Wang, MPH*[2], *Tsveta Hadjivassileva, PhD*[2], *Liana Nikolaenko, MD*[2], *Ioana Kloos, MD*[2], *Amina Abdeldaim, MD MPH*[2], *David Dalton, PharmD*[2], *Hairong Xu, MD PhD*[2], *Marcelo Pasquini, MDMS*[11], *Partow Kebriaei, MD*[13]

[1] Division of Hematology, The Ohio State University Wexner Medical Center, Columbus, OH
[2] Kite, a Gilead Company, Santa Monica, CA
[3] Memorial Sloan Kettering Cancer Center, New York, NY
[4] Adult Bone Marrow Transplantation Service, Department of Medicine, Memorial Sloan Kettering Cancer Center, New York, NY
[5] Thomas Jefferson University, Philadelphia, PA
[6] Hematology/HCT, City of Hope National Medical Center, Duarte, CA
[7] Baylor College of Medicine, Center for Cell and Gene Therapy, Houston, TX
[8] Department of Leukemia, The University of Texas MD Anderson Cancer Center, Houston, TX
[9] Department of Hematology & Medical Oncology, Oregon Health and Science University, Portland, OR
[10] University of Kansas Medical Center, Westwood, KS
[11] Center for International Blood and Marrow Transplant Research, Medical College of Wisconsin, Milwaukee, WI
[12] Center for International Blood and Marrow Transplant Research (CIBMTR), Medical College of Wisconsin, Milwaukee, WI
[13] Department of Stem Cell Transplantation and Cellular Therapy, The University of Texas MD Anderson Cancer Center, Houston, TX

Background Brexu-cel is a CD19 CAR T therapy first approved by the FDA in 2021 for adult patients (pts) with R/R B-cell ALL. In the pivotal phase II ZUMA-3 single arm trial, brexu-cel achieved a high rate (71%) of complete remission or complete remission with incomplete hematological recovery (CR/CRi) with a manageable safety profile. Here, we report outcomes of brexu-cel in a broad real-world patient population.

Methods A total of 197 pts with B-cell ALL were infused with brexu-cel and prospectively enrolled between July 2021 and May 2023 in the CIBMTR registry across 67 centers in the US. In this analysis, we included 138 pts with at least one scheduled follow-up at Day 100 and evaluable safety and effectiveness outcomes. Descriptive statistics, Kaplan-Meier estimator and cumulative incidence functions were used to summarize outcomes.

Results Median age was 43 years (range, 19.4-79.4; 19% were age ≥60 years) and 52% were males. Pts had a diverse ethnic background: 50% non-Hispanic White, 28% Hispanic, 11% non-Hispanic Black and 7% non-Hispanic Asian. More than half (55%) of pts had poor cytogenic risk score at diagnosis. Prior to lymphodepletion (LD), the majority of pts had: ECOG performance status of 0 or 1 (80%); at least one clinically significant comorbidity (79%); and Ph-negative disease (64%). Furthermore, 44% had evidence of ≤5% bone marrow blasts; of these (n=49), 65% were MRD negative. Extramedullary disease and CNS involvement was observed in 22% and 10% of pts prior to LD, respectively. As such, based on adapted criteria available in the registry data, 91% of pts in this cohort would have been ineligible for ZUMA-3. Pts received a median of 4 prior lines of therapy (range 1-13); 46% had prior inotuzumab and 58% had prior blinatumomab. One third (35%) had prior allogeneic (allo) stem cell transplant (SCT). Moreover, 41% of pts received bridging therapy prior to LD. Median time from leukapheresis to brexu-cel infusion was 32 days (inter-quartile range [IQR] 27-42)) and median follow-up time was 5.9 months (95% CI: 5.1-6.1) (Table 1).

Overall CR/CRi rate by Day 100 post infusion was 76%; 70% were still in remission at 6 months post initial response (95% CI: 55-80). For those who were not in response before LD, 63% of them converted into a CR/CRi. Relapse free survival at 6 months was 53% (95% CI: 42-62). The overall survival rate at 6 months was 78% (95% CI: 69-84); primary causes of death were primary

disease (n=13/32, 41%) and infection (n=7/32, 22%). About one third (31%) of responders received a subsequent allo SCT. High response rates were observed in all pts regardless of age, prior exposure to blinatumomab, allo SCT, or presence of extramedullary disease prior to LD. Grade ≥3 cytokine release syndrome (CRS) and immune effector cell-associated neurotoxicity syndrome (ICANS, ASTCT consensus) occurred in 9% and 24% of pts, respectively (Table 2). Treatment for CRS and/or ICANS consisted mainly of tocilizumab (67%) and corticosteroids (51%). Most of these adverse events were resolved within 3 weeks of infusion (CRS, 94%; ICANS, 80%). Prolonged cytopenia and neutropenia 30 days post infusion was experienced by 42% and 33% of pts, respectively.

Conclusion In this largest-to-date real-world evidence study of brexu-cel in adult pts with B-cell ALL, response and safety outcomes were consistent with findings from ZUMA-3, even with 91% of patients not meeting ZUMA-3 eligibility criteria. Updated data with longer follow-up will be reported at the time of presentation.

*First and second authors are equal contributors

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*Kite/Gilead:* Consultancy. **Wang:** *Kite, a Gilead Company:* Current Employment. **Hadjivassileva:** *Kite, a Gilead Company:* Current Employment, Current equity holder in publicly-traded company. **Nikolaenko:** *Kite, a Gilead Company:* Current Employment, Current equity holder in publicly-traded company, Other; *City of Hope:* Current Employment; *Rafael Pharmaceuticals:* Research Funding. **Kloos:** *Kite, a Gilead Company:* Current Employment. **Abdeldaim:** *Gilead Sciences:* Current holder of *stock options* in a privately-held company; *Kite, a Gilead Company:* Current Employment, Other: Travel Support. **Dalton:** *Gilead Sciences:* Current holder of *stock options* in a privately-held company, Other; *Bristol Myers Squibb:* Current holder of *stock options* in a privately-held company, Other; *Kite, a Gilead Company:* Current Employment. **Xu:** *Kite, a Gilead Company:* Current Employment; *Gilead Sciences:* Current equity holder in publicly-traded company. **Pasquini:** *Kite, a Gilead Company:* Honoraria, Research Funding; 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Table 1: Baseline characteristics for adult pts with R/R B-cell ALL treated with brexu-cel

Variable	All pts (N=138)
Median age in years (range)	42.9 (19.4-79.4)
Age <60 / ≥60 years (n, %)	112 (81) / 26 (19)
Female (n, %)	66 (48)
Ethnicity (n, %)	
Non-Hispanic white / Black / Asian	69 (50) / 15 (11) / 9 (7)
Hispanic	39 (28)
Not reported	6 (4)
ECOG prior to LD (n, %)	
0 or 1 / ≥ 2	111 (80) / 15 (11)
Unknown	12 (9)
Presence of a clinically significant co-morbidity (n, %)	109 (79)
Cytogenic risk score at diagnosis (n, %)	
Normal / Poor	17 (12) / 76 (55)
Other / Not tested / Unknown / Not reported	38 (28) / 2 (1) / 4 (3) / 1 (< 1)
Ph+ chromosome any time prior to LD (n, %)	
Negative / Positive / Not reported	89 (64) / 46 (33) / 3 (2)
Blast in marrow prior to LD (n, %)	
≥ 0 to ≤ 5 / > 5 to ≤ 25	61 (44) / 12 (9)
> 25 to ≤ 50 / > 50 to ≤ 75	7 (5) / 6 (4)
> 75 / Not reported	8 (6) / 44 (32)
MRD status prior to LD (among responders) (n, %)	
CR/CRi, MRD- / CR/CRi, MRD+ / Not reported	32 (65) / 10 (20) / 7 (14)
Prior allo SCT (n, %)	48 (35)
Extramedullary disease / CNS involvement prior to LD, n (%)	30 (22) / 14 (10)
Number of prior lines (median, range)	4 (1-13)
Prior monoclonal antibody-based therapy (n=125)	
Prior blinatumomab / inotuzumab treatment (n, %)	73 (58) / 58 (46)
Prior blinatumomab or inotuzumab	97 (78)
Received Bridging therapy prior to LD (n, %)	57 (41)
Median time from leukapheresis to brexu-cel infusion (IQR), days	32 (27-42)
Median follow-up time (95% CI), months	5.9 (5.1-6.1)

Table 2: Safety and effectiveness outcomes for adult pts with R/R B-cell ALL treated with brexu-cel from July 2021 and May 2023

Outcome measure	All pts (N=138)	Age (years)		Prior blina exposure (N=125)		Prior allo SCT (N=138)		Extramedullary disease prior to infusion (N=123)	
		<60 (n=112)	≥ 60 (n=26)	Yes (n=73)	No (n=52)	Yes (n=48)	No (n=90)	Yes (n=30)	No (n=93)
CR/CRi rate (%, 95% CI)	76 (68-83)	73 (64-81)	88 (70-98)	82 (71-90)	71 (56-83)	75 (60-86)	76 (66-85)	70 (51-85)	80 (70-87)
DoR[1]									
At 6 months (%, 95% CI)	70 (55-80)	80 (67-89)	44 (17-68)	63 (41-78)	77 (55-89)	78 (55-90)	62 (41-78)	NE	69 (52-81)
Subsequent allo SCT rate (%, 95% CI)[2]	31 (22-41)	37 (27-48)	9 (1-28)	35 (23-48)	25 (12-42)	8 (2-22)	43 (31-55)	29 (11-52)	32 (22-44)
Relapse free survival (%, 95% CI)[3]									
At 6 months (%, 95% CI)	53 (42-62)	57 (46-66)	40 (17-63)	50 (34-64)	55 (40-68)	58 (42-71)	48 (33-61)	56 (35-73)	54 (41-65)
Overall survival									
At 6 months (%, 95% CI)	78 (69-84)	79 (70-86)	72 (48-87)	78 (65-87)	80 (66-89)	77 (61-87)	78 (68-86)	64 (40-80)	83 (73-89)
CRS- Any grade no. (%)	112 (81)	90 (80)	22 (85)	60 (82)	41 (79)	38 (79)	74 (82)	27 (90)	76 (82)
CRS-Grade ≥ 3 no. (%)	13 (9)	11 (10)	4 (15)	10 (14)	3 (6)	5 (10)	8 (9)	5 (17)	4 (4)
Time to CRS onset, days - median (range)	6.0 (1.0-14.0)	6.0 (1.0-14.0)	5.5 (1.0-12.0)	6.0 (1.0-14.0)	6.0 (1.0-11.0)	7.0 (2.0-12.0)	6.0 (1.0-14.0)	6.0 (1.0-13.0)	7.0 (1.0-14.0)
Time from CRS onset to resolution, days - median (range)	6.0 (2.0-27.0)	5.5 (2.0-27.0)	6.0 (2.0-14.0)	6.5 (2.0-21.0)	5.0 (2.0-14.0)	5.0 (2.0-21.0)	6.0 (2.0-27.0)	6.0 (2.0-21.0)	6.0 (2.0-27.0)
Neurotoxicity-Any grade no. (%)	66 (48)	49 (44)	17 (65)	33 (45)	26 (50)	27 (56)	39 (43)	19 (63)	41 (44)
Neurotoxicity-Grade ≥ 3 no. (%)	33 (24)	23 (21)	10 (38)	17 (23)	13 (25)	15 (31)	18 (20)	9 (30)	20 (22)
Time to ICANS onset, days - median (range)	8.0 (2.0-16.0)	8.0 (2.0-15.0)	7.0 (3.0-16.0)	8.0 (2.0-15.0)	8.0 (3.0-12.0)	8.0 (4.0-15.0)	8.0 (2.0-16.0)	8.0 (6.0-12.0)	8.0 (2.0-16.0)
Time from ICANS onset to resolution, days - median (range)	6.0 (1.0-68.0)	6.0 (1.0-27.0)	8.0 (2.0-68.0)	6.0 (1.0-68.0)	6.0 (1.0-27.0)	7.0 (1.0-66.0)	5.5 (1.0-68.0)	6.0 (1.0-24.0)	6.0 (1.0-68.0)

[1] Among patients achieved CR/CRi as best response. Subsequent allo-SCT was censored.
[2] Among patients achieved CR/CRi as best response.
[3] Subsequent allo-SCT was censored.

Figure 1

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