Poster
4865

A Retrospective Intrapatient Analysis From ZUMA-5: Axicabtagene Ciloleucel (Axi-Cel) Compared With Prior Standard-of-Care Therapy in Patients With Relapsed/Refractory Follicular Lymphoma

Emmanuel Bachy, MD, PhD[1]; Sattva Neelapu, MD[2]; Julio Chavez, MD[3]; Ibrahim Yakoub-Agha, MD, PhD[4]; Christine Lui, MS[5]; Jacob Wulff, DrPH[5]; Harry Miao, MD, PhD[5]; Olga Nikolajeva, MD[5]; Timothy Best, PhD[5]; Camille Linot, PharmD, PhD[5]; and Caron Jacobson, MD[6]

[1]Centre Hospitalier Lyon Sud, Pierre-Bénite, France; [2]The University of Texas MD Anderson Cancer Center, Houston, TX, USA; [3]Moffitt Cancer Center, Tampa, FL, USA; [4]CHU de Lille, Univ Lille, INSERM U1286, Infinite, F-59000, Lille, France; [5]Kite, a Gilead Company, Santa Monica, CA, USA; and [6]Dana-Farber Cancer Institute, Boston, MA, USA

BACKGROUND

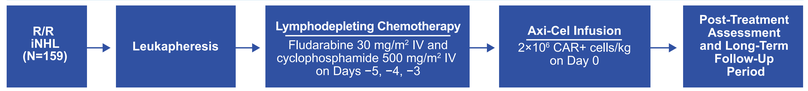
- Axi-cel, an autologous anti-CD19 chimeric antigen receptor T-cell therapy, is approved for adults with relapsed/refractory (R/R) follicular lymphoma (FL)[1,2]
- Approval was supported by ZUMA-5, a Phase 2, multicenter, single-arm study of axi-cel in patients with R/R indolent non-Hodgkin lymphoma[3]
  - After a median of ≥3 years of follow-up in patients with FL, median duration of response was 38.6 months and 53% of patients were in ongoing response[4]
- While responses were higher with axi-cel in ZUMA-5 compared with a matched standard-of-care (SOC) cohort (SCHOLAR-5), differences in patient characteristics between the groups limited comparison[5]
- Here we report a retrospective, intrapatient assessment of axi-cel versus prior SOC from the 4-year analysis of ZUMA-5

OBJECTIVE

- To evaluate the efficacy of axi-cel versus patients' most recent prior line of SOC therapy among those with R/R FL in ZUMA-5

METHODS

Figure 1. ZUMA-5 Study Design[4]



Key ZUMA-5 Eligibility Criteria
- R/R FL (Grades 1-3a) or MZL (nodal or extranodal)[a]
- ≥2 prior lines of therapy that must have included an anti-CD20 mAb combined with an alkylating agent[b]

Primary Endpoint
- ORR (centrally assessed per Lugano[6])

Key Secondary Endpoints
- CR rate
- DOR, PFS, OS
- AEs
- CAR T-cell and cytokine levels

[a] Patients with stable disease (without relapse) >1 year from completion of last therapy were not eligible. [b] Single-agent anti-CD20 antibody did not count as line of therapy for eligibility.
AE, adverse event; axi-cel, axicabtagene ciloleucel; CAR, chimeric antigen receptor; CR, complete response; DOR, duration of response; FL, follicular lymphoma; INHL, indolent non-Hodgkin lymphoma; IV, intravenous; mAb, monoclonal antibody; MZL, marginal zone lymphoma; ORR, overall response rate; OS, overall survival; PFS, progression-free survival; R/R, relapsed/refractory.

Intrapatient Efficacy Analysis

- This analysis used efficacy data from the 4-year data cutoff date (March 31, 2023)
- Efficacy outcomes were compared between axi-cel and a patient's most recent prior therapy (MRPT)
  - Progression-free survival (PFS) after the MRPT was calculated from the date of therapy initiation to progression; those who did not have progression reported prior to leukapheresis were censored at leukapheresis
    - If multiple regimens were used in the same line, the earliest date of initiation and latest date of progression were used
  - Time to next treatment (TTNT) after the MRPT was calculated as the time from initiation of the MRPT to leukapheresis
  - For axi-cel, PFS was defined as time from leukapheresis to progression or death and TTNT was defined as time from leukapheresis to the start of subsequent anticancer therapy or death
- All efficacy endpoints were per investigator assessment

RESULTS

Table 1. Common Regimens in the MRPT

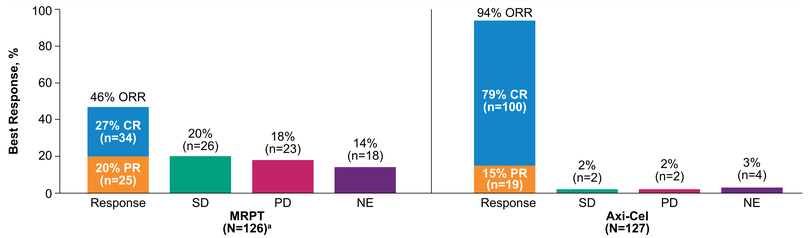
	Patients with FL (N=127)
Patients with any prior therapy, n (%)	126 (99)[a]
Anti-CD20 mAb-containing chemoimmunotherapy	91 (72)
Bendamustine-containing	25 (20)
ICE-containing	18 (14)
Lenalidomide-containing	14 (11)
CHOP-containing	13 (10)
Chemotherapy multiple agent	12 (9)
Other	9 (7)
PI3K inhibitors	17 (13)
Other therapy	18 (14)

Multiple prior therapies within the same line are counted as one incidence.
[a] One patient received previous therapy for DLBCL instead of for the primary disease of FL.
CHOP, cyclophosphamide, doxorubicin, vincristine, and prednisone; DLBCL, diffuse large B-cell lymphoma; FL, follicular lymphoma; ICE, ifosfamide, carboplatin, and etoposide; mAb, monoclonal antibody; MRPT, most recent prior therapy; PI3K, phosphoinositide 3-kinase.

- Common MRPT regimens included anti-CD20 mAb-containing chemoimmunotherapy and PI3K inhibitors (**Table 1**)

RESULTS (CONTINUED)

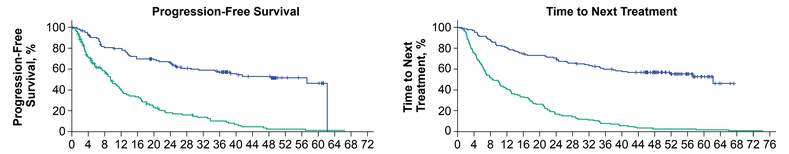
Figure 2. Best Response to MRPT and Axi-Cel



[a] One patient received previous therapy for DLBCL instead of for the primary disease of FL.
Axi-cel, axicabtagene ciloleucel; CR, complete response; DLBCL, diffuse large B-cell lymphoma; FL, follicular lymphoma; MRPT, most recent prior therapy; NE, undefined/not done/not evaluable; ORR, overall response rate; PD, progressive disease; PR, partial response; SD, stable disease.

- A total of 46% of patients responded to their MRPT (27% complete response [CR] rate; **Figure 2**)
- In contrast, 94% of patients had a subsequent overall response to axi-cel (79% CR rate; **Figure 2**)
- Among patients who responded to MRPT (n=59), 97% had a response to axi-cel (83% CR rate)
- Among those who did not respond to MRPT (n=67), 91% responded to axi-cel (76% CR rate)

Figure 3. Progression-Free Survival and Time to Next Treatment With MRPT and Axi-Cel



No. at Risk

Axi-Cel	127	115	98	96	84	80	75	64	61	57	42	38	38	12	10	9	1	0							
MRPT[a]	126	84	61	41	34	23	17	15	12	9	6	4	2	2	2	1	1	0							

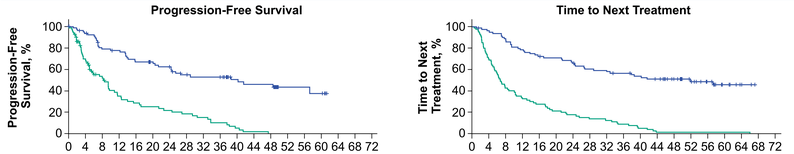
No. at Risk

Axi-Cel	127	122	111	102	94	91	88	81	78	72	69	66	52	40	27	14	5	0							
MRPT[a]	126	95	65	52	42	33	21	18	14	10	7	4	3	3	3	2	2	1	1	0					

[a] One patient received previous therapy for DLBCL instead of for the primary disease of FL.
Axi-cel, axicabtagene ciloleucel; DLBCL, diffuse large B-cell lymphoma; FL, follicular lymphoma; MRPT, most recent prior therapy.

- Prior to leukapheresis, 83% of patients (106/127) had disease progression
  - Median time between prior progression and leukapheresis was 1.4 months
- Median PFS with MRPT was 9.4 months (95% CI, 7.5-11.9; **Figure 3**)
- Median PFS with subsequent axi-cel was substantially longer than MRPT at 57.3 months (95% CI, 30.9-not estimable; **Figure 3**)
- Median TTNT with MRPT was 8.6 months (95% CI, 6.5-11.7) and median TTNT with axi-cel was 62.2 months (95% CI, 37.8-not estimable; **Figure 3**)

Figure 4. Progression-Free Survival and Time to Next Treatment With MRPT and Axi-Cel Among Patients With ≥3 Lines of Therapy



No. at Risk

Axi-Cel	80	72	59	57	49	45	41	34	32	31	22	20	20	7	7	6	0								
MRPT	80	50	32	21	17	15	13	11	9	6	3	1	0												

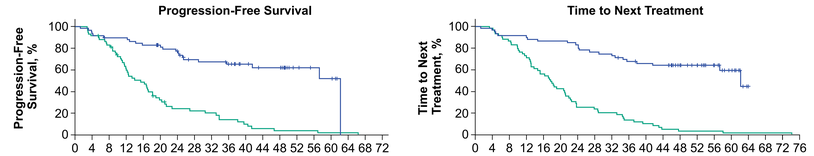
No. at Risk

Axi-Cel	80	76	70	62	57	55	52	46	45	42	39	36	28	22	16	8	4	0							
MRPT	80	56	34	27	22	17	14	11	10	7	4	1	1	1	1	1	1	0							

Axi-cel, axicabtagene ciloleucel; MRPT, most recent prior therapy.

- In a subgroup analysis of patients with ≥3 prior lines of therapy prior to axi-cel infusion (n=80), medians of PFS with MRPT and axi-cel were 8.5 and 40.2 months, respectively (**Figure 4**)
- Median TTNT in those with ≥3 prior lines of therapy was 6.7 months with MRPT and 51.8 months with axi-cel (**Figure 4**)

Figure 5. Progression-Free Survival and Time to Next Treatment With Axi-Cel and MRPT Among Patients With a Response to MRPT



No. at Risk

Axi-Cel	59	55	52	52	48	45	41	33	32	29	23	20	20	8	6	5	0								
MRPT	59	54	48	34	27	17	12	11	10	7	5	3	2	2	2	1	1	0							

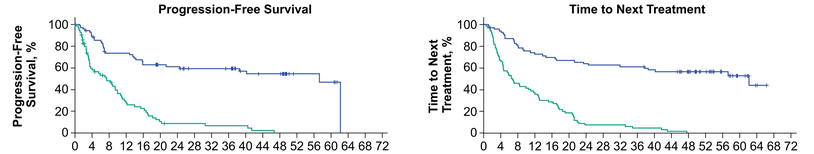
No. at Risk

Axi-Cel	59	58	54	54	51	51	49	45	44	39	37	36	28	24	17	9	1	0							
MRPT	59	57	51	43	33	25	15	14	12	8	6	3	2	2	2	1	1	1	1	0					

Axi-cel, axicabtagene ciloleucel; MRPT, most recent prior therapy.

- Among patients who responded to MRPT (n=59), medians of PFS and TTNT after axi-cel were 62.2 months and 62.2 months, respectively (**Figure 5**)
  - Those who did not respond to MRPT (n=67) had medians of PFS and TTNT post axi-cel of 34.9 and 40.2 months, respectively

Figure 6. Progression-Free Survival With Axi-Cel and MRPT Among Patients With POD24



No. at Risk

Axi-Cel	70	60	48	48	41	38	37	32	32	31	23	21	21	7	7	6	0								
MRPT	70	38	29	16	13	6	4	4	3	3	3	1	0												

No. at Risk

Axi-Cel	70	65	56	51	48	46	44	43	43	42	39	38	30	23	15	9	4	0							
MRPT	70	47	32	26	20	13	5	5	5	3	3	1	0												

Axi-cel, axicabtagene ciloleucel; MRPT, most recent prior therapy; POD24, progression <2 years after initial chemoimmunotherapy.

- Among patients who had progression <2 years after initial chemoimmunotherapy (POD24; n=70), the medians of PFS after later-line MRPT and axi-cel were 7.4 and 57.3 months, respectively (**Figure 6**)
  - Among those without POD24 (n=41), the medians of PFS after MRPT and axi-cel were 12.0 and 48.6 months, respectively
- Median TTNT among those with POD24 was 6.6 months with MRPT and 62.2 months with axi-cel (**Figure 6**)

CONCLUSIONS

- Through this retrospective analysis, axi-cel demonstrated robust improvement in median PFS and TTNT compared with the MRPT among patients with R/R FL in ZUMA-5, a population with substantial high-risk characteristics
  - Improvement was sustained in high-risk subgroups, including in patients with POD24 and ≥3 prior lines of therapy
- Results support use of axi-cel earlier in the treatment paradigm for R/R FL

REFERENCES

1. YESCARTA® (axicabtagene ciloleucel) Prescribing information. Kite Pharma, Inc; 2022.
2. YESCARTA® (axicabtagene ciloleucel) [summary of product characteristics]. Amsterdam, The Netherlands: Kite Pharma EU B.V.; 2022.
3. Jacobson CA, et al. *Lancet Oncol*. 2022;23:91-103.
4. Neelapu SS, et al. *Blood*. 2023; blood.2023021243. Epub ahead of print.
5. Ghione P, et al. *Blood*. 2022;140:851-860.
6. Cheson BD, et al. *J Clin Oncol*. 2014;32:3059-3068.

ACKNOWLEDGMENTS

- The patients, families, friends, and caregivers
- The study investigators, coordinators, and healthcare staff at each study site
- Medical writing support was provided by Danielle Fanslow, PhD, of Nexus Global Group Science, funded by Kite, a Gilead Company
- This study was funded by Kite, a Gilead Company

DISCLOSURES

Full author disclosures are available through the virtual meeting platform

Presented at the 2023 American Society of Hematology Annual Meeting