Poster #4869

An Updated Comparison of Clinical Outcomes From 4-Year Follow-Up of ZUMA-5 (Axicabtagene Ciloleucel) and the International SCHOLAR-5 External Control Cohort in Relapsed/Refractory Follicular Lymphoma

John G Gribben[1], Paola Ghione[2,3], M Lia Palomba[2], Markqayne D Ray[4], Eve Limbrick-Oldfield[5], Steve Kanters[5], Sabela Bobillo[6], Maria Teresa Ribiero[7], Caron A Jacobson[8], Sattva S Neelapu[9], Herve Ghesquieres[10], Olga Nikolajeva[4], Jiali Yan[4], Hailin Wang[4] and Anik R Patel[4]

[1]Barts Cancer Institute, London, UK , [2]Memorial Sloan Kettering Cancer Center, New York, NY, USA , [3]Roswell Park Comprehensive Cancer Center, Buffalo, NY, USA , [4]Kite, A Gilead Company, Santa Monica, CA , [5]RainCity Analytics, Vancouver, BC, Canada, [6]Vall D'Hebron Insitute of Oncology, Barcelona, Spain , [7]Portuguese Oncology Institute of Porto, Porto, Portugal, [8]Dana-Farber Cancer Institute, Boston, MA, USA, [9]The University of Texas MD Anderson Cancer Center, Houston, TX, USA ,[10]Centre Hospitalier Lyon Sud, Lyon, France

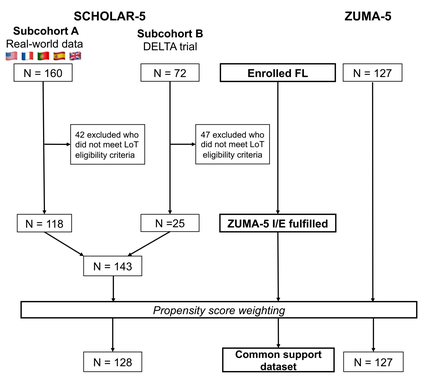
INTRODUCTION

- Axicabtagene ciloleucel (axi-cel) is an autologous anti-CD19 chimeric antigen receptor (CAR) T-cell therapy. ZUMA-5, the pivotal trial of axi-cel as a treatment for relapsed/refractory follicular lymphoma (R/R FL), demonstrated high rates of durable response in these patients.[1]
- SCHOLAR-5 is an external cohort created to allow for the comparison of ZUMA-5 to other commercially available therapies.
- Previously, we compared ZUMA-5 to SCHOLAR-5 using propensity score methods, and axi-cel showed a substantial clinical benefit in outcomes including overall response rate (ORR), complete response (CR), progression-free survival (PFS), and overall survival (OS).[2] This benefit was maintained at later timepoints using the intent-to-treat (ITT) population with no minimum follow-up.[3]

METHODS

- The SCHOLAR-5 external control cohort consists of R/R FL patients from 7 institutions across 5 countries.
- Eligible patients had R/R FL and initiated a third or higher line of therapy (LoT) after July 2014. Patients initiating an eligible LoT after receipt of idelalisib in the DELTA trial were also included (**Figure 1**).

Figure 1. Patient enrollment, selection, and analysis



- Eligibility criteria from ZUMA-5 were applied to SCHOLAR-5 and patients were excluded/censored upon transformation.
- Patient characteristics in SCHOLAR-5 were matched to ZUMA-5 patient characteristics via propensity score standardized mortality ratio weighting on prespecified prognostic factors.[4]
- OS, PFS, and time-to-next treatment (TTNT) were evaluated using Kaplan-Meier (KM) analysis and Cox proportional hazards regression, while ORR and CR were evaluated using odds ratios.

RESULTS

- 143 patients identified in SCHOLAR-5 were reduced to 128 patients after propensity score weighting, compared to 127 patients from the ITT population of ZUMA-5. Variables balanced after weighting (standardized mean difference <0.1) included POD24, number of prior lines of therapy (LOT), relapsed vs refractory, prior stem cell transplant, size of largest nodal mass, response to prior LOT, and time since last therapy (**Table 1**).
- Median follow-up times for ZUMA-5 and SCHOLAR-5 were 47.6 months and 26.2 months, respectively.

Table 1. Patient characteristics before and after weighting

	≥3rd LOT analysis			
	SCHOLAR-5 (n = 143)	ZUMA-5 (n = 127)	SCHOLAR-5 after weighting (n = 128)	SMD (p-value)
Median age (range), years*	64 (36 – 89)	60 (34 – 79)	60 (36 – 89)	0.119 (.47)
Male, n (%)	81 (56.6)	75 (59.1)	79 (61.3)	0.046 (.76)
POD24, n (%)	51 (35.7)	70 (55.1)	73 (57.1)	0.039 (.79)
Prior LOT, median (range)*	2 (2-8)	3 (1-10)	3 (2-8)	0.079 (.62)
Refractory to prior LOT, n (%)*	86 (60.5)	87 (68.5)	93 (72.3)	0.083 (.56)
Prior SCT, n (%)*	31 (21.7)	30 (23.6)	33 (25.5)	0.043 (.78)
Largest nodal mass (cm), median (IQR)*	4.14 (2.81 – 6.75)	4.30 (3.23 – 6.10)	3.96 (2.74 – 6.03)	0.079 (.60)
Time since last therapy (months), median (IQR)*	6.79 (1.18 – 22.67)	3.76 (1.91 – 10.04)	2.30 (0.76 - 11.59)	0.066 (.59)
Time since diagnosis (months), median (IQR)	84.79 (52.99 – 130.47)	55.41 (31.47– 99.29)	60.89 (39.53 – 105.00)	0.023 (.87)
ECOG, n (%): 0	39 (33.1)	79 (62.2)	35 (32.6)	0.621 (<.001)
1	79 (66.9)	48 (37.8)	72 (67.4)	

*Included in propensity score. IQR: interquartile range; ECOG: Eastern Cooperative Oncology Group performance status; POD24: progression of disease within 24 months of first line chemoimmunotherapy; SCT: Stem cell transplant; SMD: standardized mean difference after weighting.

- In patients initiating ≥3rd LoT, ORR and CR were higher in ZUMA-5 compared to SCHOLAR-5 (**Table 2**).
- These differences were more pronounced in the subgroup analysis of ≥4th LoT patients with confirmed biopsies by central review prior to axi-cel.

Table 2. Comparison of response outcomes

		SCHOLAR-5 (n=128)	ZUMA-5 (n=127)	Odds ratio (95% CI)	P value
≥3rd LoT	**ORR, n (%)**	69 (54)	119 (93.7)	12.66 (5.24, 30.57)	<.001
	CR, n (%)	45 (34.9)	100 (78.7)	6.9 (3.62, 13.18)	<.001
		SCHOLAR-5 (n=74)	**ZUMA-5 (n=75)**	**Odds ratio (95% CI)**	**P value**
≥4th LoT	**ORR, n (%)**	31 (41.6)	70 (93.3)	19.63 (6.57, 58.64)	<.001
	CR, n (%)	16 (21.8)	58 (77.3)†	12.21 (5.22, 28.55)	<.001

†Response assessments includes CT-based and PET scans with limited confirmatory bone marrow biopsies. Thirteen patients with imaging CRs did not receive a confirmatory bone marrow biopsy. CI: Confidence interval; CR: complete response; LoT: line of therapy; ORR: overall response rate.

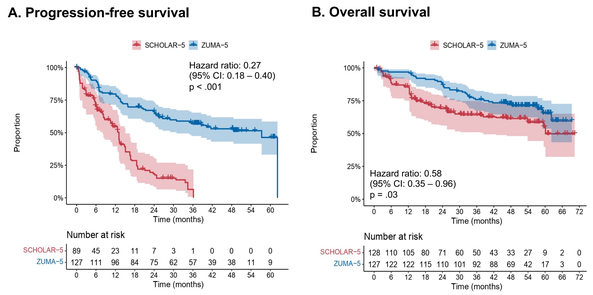
- The median PFS among patients initiating ≥3rd LoT was 57.30 months in ZUMA-5 compared to 12.97 months in SCHOLAR-5 (**Table 3**). PFS at 48-months was 53.0% in ZUMA-5 while SCHOLAR-5 was not evaluable as all patients had either progressed or been censored.
- Median OS was not reached in either ZUMA-5 or SCHOLAR-5. OS at 48 months was 72.4% in ZUMA-5 versus 61.4% in SCHOLAR-5. Hazard ratios for PFS and OS were both statistically significant in favor of axi-cel (**Figure 2**).
- TTNT was also significantly different between the groups, with a hazard ratio of 0.62 (95% CI: 0.40 – 0.95).

Table 3. Comparison of time to event outcomes

		48 months % (95% CI)		Median months (95% CI)		Hazard ratio (95% CI)	p value
		SCHOLAR-5	ZUMA-5	SCHOLAR-5	ZUMA-5		
≥3rd LoT	**OS**	61.4 (41.9-73.7)	72.4 (63.6-79.4)	NR* (38.4-NE)	NR (62.19-NE)	0.58 (0.35-0.96)	.03
	PFS	NE†	53.0 (43.1-61.9)	12.97 (7.75-15.47)	57.30 (30.92-NE)	0.27 (0.18-0.40)	<.001
	TTNT	41.9 (28.7, 55.0)	56.6 (47.4-64.8)	26.61 (12.65-NE)	62.19 (37.85-NE)	0.62 (0.40 – 0.95)	.03
≥4th LoT	**OS**	47.0 (32.1-61.9)	69.3 (57.1-78.6)	32.23* (12.53-NE)	NR (57.3-NE)	0.41 (0.24-0.71)	<.01
	PFS	NE†	49.2 (36.0-61.1)	4.75 (2.22-12.97)	41.59 (24.18-NE)	0.18 (0.11-0.29)	<.001
	TTNT	40.0 (25.0-55.1)	51.8 (39.7-62.6)	16.44 (5.97-NE)	51.84 (26.61-NE)	0.58 (0.35-0.96)	.04

NE: not evaluable; NR: not reached; OS: overall survival; PFS: progression-free survival; TTNT: time to next treatment; * For SCHOLAR-5 the median estimates were less reliable, due to the small number of events and the small number of patients that remained at risk when the median was reached; †PFS not evaluable as by 48 months all patients had either progressed or been censored.

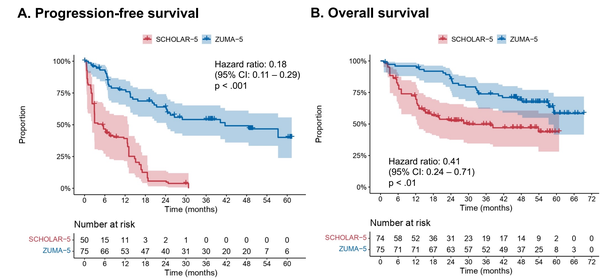
Figure 2. Time to event curves, ≥3rd LoT



Kaplan-Meier curves showing survival time from enrollment for outcomes in ZUMA-5 (blue), compared to SCHOLAR-5 (red) in patients at ≥3rd LoT.

- In patients at ≥4th LoT, results were in the same direction as ≥3rd LoT, but the effects more pronounced (**Figure 3**).
  - The median PFS was 41.59 months in ZUMA-5, compared to 4.75 months in SCHOLAR-5 (**Table 3**).
  - Median OS was not reached in ZUMA-5 and was 32.23 months in SCHOLAR-5.
- In patients at ≥4th LoT, the hazard ratios for PFS, OS and TTNT were again statistically significant in favor of axi-cel.

Figure 3. Time to event curves, ≥4th LoT



Kaplan-Meier curves showing survival time from enrollment for outcomes in ZUMA-5 (blue), compared to SCHOLAR-5 (red) in patients at ≥4th LoT.

- Response outcomes remained the same as those previously observed using the 36-month data and the observed HRs were very similar to those previously observed using the 36-month data.[3]

CONCLUSION

- After a median follow-up of 47.6 months, axi-cel continues to demonstrate a substantial and statistically significant improvement in meaningful clinical endpoints compared to currently available therapies for r/r FL patients. These results are consistent with the previously published data that included fewer ZUMA-5 patients.
- This demonstrates the benefit of axi-cel is durable, which will help inform clinical decision-makers and patients.
- These findings suggest that axi-cel addresses an important unmet medical need for r/r FL patients, and that the observed treatment effects are significant for at least four years post-treatment.

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