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A COMPARISON OF CLINICAL OUTCOMES FROM ZUMA-5 (AXICABTAGENE CILOLEUCEL) AND THE INTERNATIONAL SCHOLAR-5 EXTERNAL CONTROL COHORT IN RELAPSED/REFRACTORY FOLLICULAR LYMPHOMA (R/R FL)

Topic: 25. Gene therapy, cellular immunotherapy and vaccination - Clinical

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Background: In the pivotal ZUMA-5 (Z-5) trial, axicabtagene ciloleucel (axi-cel; an autologous anti-CD19 chimeric antigen receptor T-cell therapy) demonstrated high rates of durable response in r/r FL patients, including those with high-risk disease such as patients who progressed within 24 months of initiating first-line chemoimmunotherapy (POD24).

Aims: To compare clinical outcomes from updated 18-month Z-5 to a matched sample from the international SCHOLAR-5 (S-5) external control cohort.

Methods: The international S-5 cohort source data were extracted for r/r FL patients from 7 institutions in 5 countries who initiated a third or higher (3L+) line of therapy (LOT) after July 2014. Data from the pivotal idelalisib DELTA trial was also included in the S-5 cohort. Z-5 trial eligibility criteria were applied to the S-5 cohort, with patients excluded or censored upon transformation. The S-5 and Z-5 cohorts were balanced for patient characteristics through propensity scoring on prespecified prognostic factors and standardized mortality ratio weighting. Differences between treatment groups with a standardized mean difference (SMD) <0.1 were deemed balanced. Overall response rate (ORR) was compared using odds ratio (OR). Overall survival (OS), progression-free survival (PFS) and time to next treatment (TTNT) were evaluated using Kaplan-Meier analysis and hazard ratios (HR).

Results: 143 patients were identified in S-5, reducing to 85 patients after applying propensity score weights along with 86 patients in Z-5. Median follow-up time for Z-5 was 23.3 months and for S-5 was 26.2 months. Variables that were successfully matched (SMD<0.1) included POD24, number of prior LOT, relapsed vs refractory, prior stem cell transplant, size of largest node, response to prior LOT, time since last therapy and age. Despite matching, the S-5 cohort had a higher proportion of ECOG 1 vs 0 (71.0% vs 40.7%) at baseline.

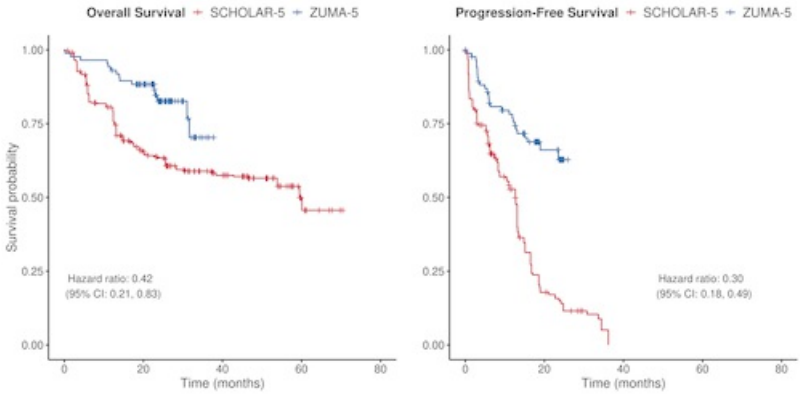
In 3L+ patients, the ORR was 42/85 (49.9%) in S-5 compared to 81/86 (94.2%) for an OR of 16.2 (95% confidence interval [CI]: 5.6-46.9). The median PFS and OS were not reached in Z-5 and in S-5 were 12.7 months and 59.8 months, respectively (Table 1). The HRs for OS and PFS were 0.42 (95%CI: 0.21-0.83) and 0.30 (95%CI: 0.18-0.49; Figure 1). In sub-group analysis of 4L+ patients, improvements in all time-to-event outcomes were more

pronounced (Table 1).

Table 1. Matched time-to-event outcomes

		18 months %(95% CI)		Median month (95% CI)		Hazard ratio (95% CI)	p-value
		SCHOLAR-5	ZUMA-5	SCHOLAR-5	ZUMA-5		
Primary analysis: 3L+	OS	67.1 (54.1, 80.2)	88.3 (79.4, 93.5)	59.8 (21.9, -)	NR (31.6, -)	0.42 (0.21, 0.83)	0.013
	PFS	23.8 (11.0, 36.5)	68.8% (57.4, 77.8)	12.7 (6.2, 14.7)	NR (23.5, -)	0.30 (0.18, 0.49)	<0.001
	TTNT	47.2 (34.2, 60.2)	69.7 (58.8, 78.3)	14.4 (6.2, 25.8)	NR (-, -)	0.42 (0.26, 0.68)	<0.001
Sub-group analysis: 4L+	OS	55.0 (39.6, 70.3)	88.3 (77, 94.2)	28.4 (12.3, -)	NR (31.6, -)	0.31 (0.15, 0.66)	0.003
	PFS	12.7 (0.7, 24.6)	67.0 (52.7, 77.8)	3.5 (1.8, 12.9)	NR (19.0, -)	0.20 (0.11 to 0.34)	<0.001
	TTNT	37.7 (22.0, 53.4)	68.3 (54.9, 78.5)	6.9 (5.1, 23.5)	NR (22.8, -)	0.38 (0.21, 0.68)	0.001

Image:



Summary/Conclusion: Compared to currently available therapies in r/r FL patients, axi-cel demonstrated a substantial and statistically significant improvement in meaningful clinical endpoints including ORR, PFS, TTNT and OS, highlighting the durable treatment effect of axi-cel. These findings suggest that axi-cel addresses an important unmet medical need for r/r FL patients.

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