Poster #2038

# A 3-Year Follow-up 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)

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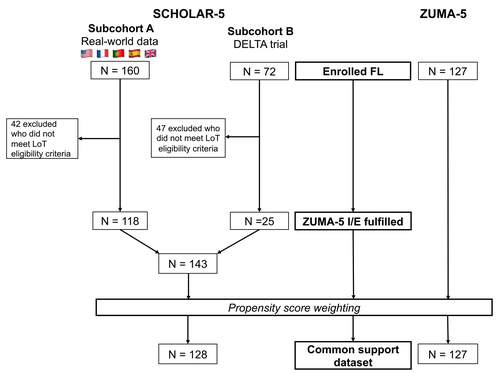
## BACKGROUND

- In the pivotal ZUMA-5 trial, axicabtagene ciloleucel (axi-cel; an autologous anti-CD19 chimeric antigen receptor T-cell therapy) demonstrated high rates of durable response in relapsed/refractory follicular lymphoma (r/r FL) patients.[1]
- The international SCHOLAR-5 external cohort was constructed to allow the comparison of ZUMA-5 to alternative available therapies for r/r FL.
- Previously we have compared the inferential analysis set of ZUMA-5 data at 18-month minimum follow-up to SCHOLAR-5 using propensity score methods. This analysis showed a substantial clinical benefit of axi-cel in overall response rate (ORR), complete response (CR), progression-free survival (PFS), and overall survival (OS).[2]
- Here, we present an updated comparative analysis at 36 months using the intention-to-treat population.

## METHODS

- The international SCHOLAR-5 external control cohort consists of r/r FL patients from 5 countries who initiated a third or higher (3L+) line of therapy (LOT) and patients from the pivotal DELTA trial. To avoid overrepresentation of idelalisib, the first eligible LoT after idelalisib was selected as the index LoT for DELTA (**Figure 1**).

### Figure 1. Patient enrollment, selection, and analysis




- ZUMA-5 trial eligibility criteria were applied to the SCHOLAR-5 cohort with patients excluded/censored upon transformation.
- The SCHOLAR-5 and ZUMA-5 cohorts were balanced for patient characteristics through propensity score standardized mortality ratio weighting on prespecified prognostic factors.[3]
- OS, PFS and time-to-next treatment (TTNT) were evaluated using Kaplan-Meier analysis and Cox proportional hazards regression. ORR and CR were compared using odds ratios.

## RESULTS

- 143 patients were identified in SCHOLAR-5, reducing to 128 patients after applying propensity score weights, versus 127 patients in ZUMA-5.
- Variables that were successfully balanced (standardized mean difference <0.1) after weighting included POD24, number of prior LOT, relapsed vs refractory, prior stem cell transplant, size of largest nodal mass, response to prior LOT, time since last therapy, and age (**Table 1**).
- Median follow-up time for ZUMA-5 and SCHOLAR-5 were 36.8 and 26.2 months, respectively.

### Table 1. Baseline characteristics before and after weighting

| | SCHOLAR-5 before weighting (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 lines of therapy, median (range)*** | 2 (2-8) | 3 (1-10) | 3 (2-8) | 0.079 (.62) |
| **Refractory to prior line, 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) |
| **Size of 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 |
| **1** | 79 (66.9%) | 48 (37.8%) | 72 (67.4%) | (<.001) |

*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.
- In the subgroup analysis of ≥4th LoT patients with confirmed biopsies by central review prior to axi-cel, these differences were more pronounced (**Table 2**). This sub-group analysis compared 75 ZUMA-5 to 74 SCHOLAR-5 patients (after weighting).

### 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 |
| **≥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-based 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

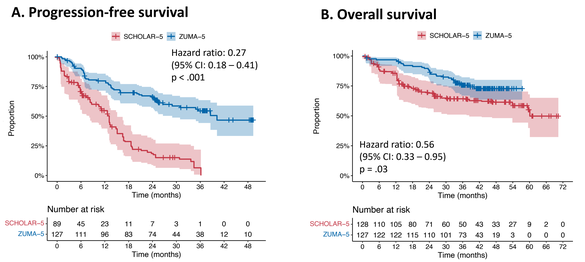
- In patients initiating ≥3rd LoT, the median PFS was 40.21 months in ZUMA-5 compared to 12.97 months in SCHOLAR-5 (**Table 3**). At 36-months, 54.4% of ZUMA-5 patients had not progressed, compared to only 6.5% of SCHOLAR-5 patients.
- Median OS was not reached in either ZUMA-5 or SCHOLAR-5, and the hazard ratios for both PFS and OS were statistically significant, favoring axi-cel (**Figure 2**).
- TTNT, which is not subject to measurement bias between groups, was also significantly different between the groups, with a hazard ratio of 0.60.

### Table 3. Comparison of time to event outcomes

| | | 36 months % (95% CI) | | Median months (95% CI) | | Hazard ratio (95% CI) | p value |
|---|---|---|---|---|---|---|---|
| | | SCHOLAR-5 | ZUMA-5 | SCHOLAR-5 | ZUMA-5 | | |
| **≥3rd LoT** | **OS** | 64.2 (52.1-76.3) | 75.5 (66.9-82.2) | NR* (38.4-NE) | NR (NE-NE) | 0.56 (0.33-0.95) | .03 |
| | **PFS** | 6.5 (0.0-17.0) | 54.4 (44.2-63.5) | 12.97 (7.75-15.47) | 40.21 (28.94-NE) | 0.27 (0.18-0.41) | <.001 |
| | **TTNT** | 45.7 (33.1, 58.4) | 59.5 (50.2-67.6) | 26.61 (12.65-NE) | NE (37.85-NE) | 0.60 (0.39 – 0.93) | .02 |
| **≥4th LoT** | **OS** | 49.7 (34.8-64.5) | 73.8 (62.0-82.4) | 32.23* (12.53-NE) | NR (NE-NE) | 0.36 (0.20-0.64) | <.001 |
| | **PFS** | NE† | 52.0 (38.7-63.8) | 4.75 (2.22-12.97) | 40.21 (24.18-NE) | 0.18 (0.11-0.30) | <.001 |
| | **TTNT** | 42.3 (27.4-57.2) | 56.2 (44.1-66.7) | 16.44 (5.97-NE) | NR (26.61-NE) | 0.55 (0.33-0.93) | .02 |

DOR: duration of response; 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; †by 36 months all patients had either progressed or been censored so PFS was not evaluable.

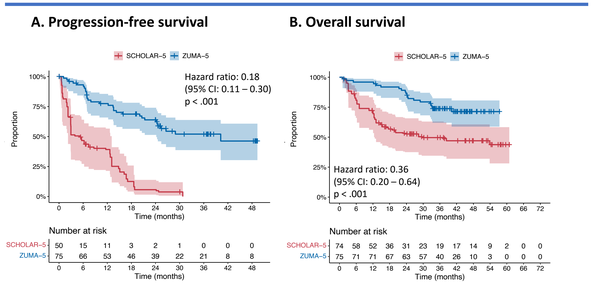
### Figure 2. Time to event curves, ≥3rd LoT




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 the pattern of results was the same as at ≥3rd LoT, but the effects were more pronounced.
  - The median PFS was again 40.21 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 were again statistically significant (**Figure 3**), as was the hazard ratio for TTNT.

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




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

## CONCLUSIONS

- After a median follow-up of 36.8 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 three years post-treatment.

## REFERENCES

1. Jacobson, CA et al. Axicabtagene ciloleucel in relapsed or refractory indolent non-Hodgkin lymphoma (ZUMA-5): a single-arm, multicentre, phase 2 trial (2022) The Lancet Oncology, Volume 23, Issue 1, 91 - 103

2. Ghione, P. et al. Comparative effectiveness of ZUMA-5 (axi-cel) vs SCHOLAR-5 external control in relapsed/refractory follicular lymphoma. Blood (2022) 140 (8): 851–860.

3. Brookhart, M.A. et al. Variable selection for propensity score models. Brookhart et al. Am J Epidemiol 2006; 163(12): 1149-56.

## ACKNOWLEDGMENTS

We thank the patients who participated in the study and their family, friends, caregivers.

We thank Anna Purdum, Julia Thornton Snider, Hairong Xu, Christine Lui, Yin Yang, and Long Ma of Kite, a Gilead Company; Victoria Tse, Herve Besson, Nikita Jeswani, and Domitilla Masi, of IQVIA; Janet Matthews and Sarah Mueller of Cancer Research UK Barts Centre; Clare Day, and Emma Armstrong of the Christie NHS Foundation; Marion Choquet and Maryam Idlhaj of Hopital Lyon Sud; Michelle Okwali of Memorial Sloan Kettering Cancer Centre; Yasmina Bernabe of Vall d'Hebron Institute of Oncology; Marina Borges and Maria José Bento of Instituto Português de Oncologia do Porto Francisco Gentil for study conduct.

Presented at the ASH meeting in 2022