Poster 272

The prognostic value of POD24 in relapsed/refractory follicular lymphoma – A SCHOLAR-5 analysis

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INTRODUCTION

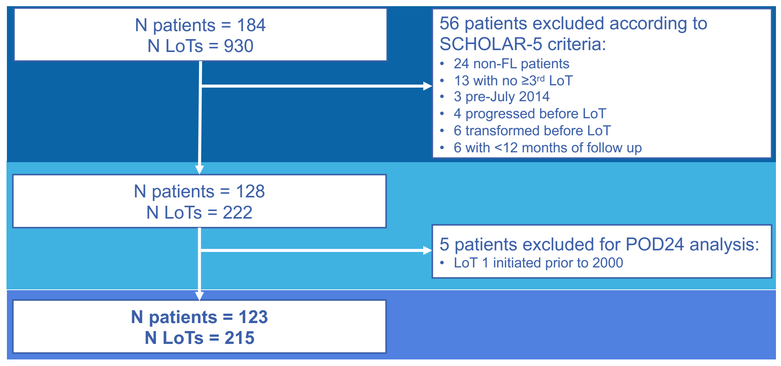
- Follicular lymphoma (FL) has a heterogeneous prognosis with multiple risk factors associated with shorter overall survival (OS), including early progression of disease after front-line therapy.
- Patients whose FL progresses within 24 months (POD24) after frontline chemo-immunotherapy (CIT) have poor OS (50% survival at 5 years vs 90% for non-POD24, hazard ratio [HR] of 7.17, 95% confidence interval [CI]: 4.83-10.65).[1,2] As such POD24 has become an important prognostic factor that is used to guide clinical decision-making.
- However, whether POD24 status remains prognostic in later lines is unclear.
- We sought to investigate whether POD24 remains a key prognostic factor in relapsed/refractory (R/R) FL patients initiating ≥3rd line of therapy (LoT).

METHODS

- SCHOLAR-5 is an international retrospective cohort study of R/R FL patients with ≥2 prior LoT. Patient selection was as reported previously,[3] but with the additional removal of patients who received front-line therapy prior to 2000, when rituximab became widely available (**Figure 1**).
- POD24 was defined as relapsing within 24-months of initiating frontline CIT. Patients who relapsed within 24 months of initiating rituximab monotherapy or another class of frontline therapy were non-POD24, as per the ZUMA-5 trial definition.[4]
- OS was analysed using Cox regression with time-dependent covariates and a single outcome for each patient. Progression-free survival (PFS) was analyzed using repeated measures Cox regression. Overall response rate (ORR) and complete response (CR) were analyzed using repeated measures logistic regression producing an odds ratio (OR).
- All analyses included LoT, sex and prior stem-cell transplant (SCT) in current LoT as covariates.
- Additional analyses explored alternative prognostic factors, including progression by 12 months (POD12), and relapsed or refractory to prior line.

RESULTS

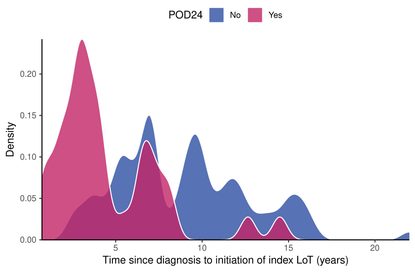
Figure 1. SCHOLAR-5 patient selection



FL:, follicular lymphoma, LoT: Line of therapy, POD24: Progression of disease with 24-months after front-line chemoimmunotherapy.

- A total of 123 patients met the inclusion criteria (**Figure 1**), with 34 (27.6%) defined as POD24. Age, FLIPI and stage at diagnosis were all comparable between POD24 and non-POD24 groups (**Table 1**).

Figure 2. Time from diagnosis to index LoT



- At the first eligible ≥3rd LoT, age and number of prior LoTs did not differ between the groups, but POD24 patients had a significantly shorter time since diagnosis (**Figure 2**), and there was a trend for a higher proportion of POD24 patients to be refractory to their prior LoT.

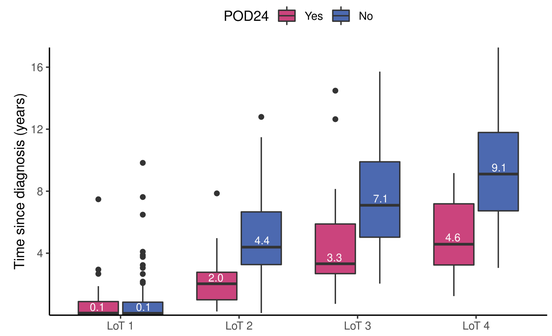
RESULTS

Table 1. Baseline patient characteristics

		POD24 (n = 34)	Non-POD24 (n = 89)	P value
Characteristics at diagnosis				
Median age, years (range)		58.0 (35.0, 79.0)	58.0 (32.0, 82.0)	.18
FLIPI, n (%)	Low	5 (21.7%)	12 (20.0%)	.45
	Medium	7 (30.4%)	27 (45.0%)	
	High	11 (47.8%)	21 (35.0%)	
	Missing	*11*	*29*	
Disease stage, n (%)	I	1 (4.0%)	3 (4.3%)	.89
	II	3 (12.0%)	5 (7.1%)	
	III	8 (32.0%)	22 (31.4%)	
	IV	13 (52.0%)	40 (57.1%)	
	Missing	9	19	
Characteristics at first eligible ≥3rd LoT				
Median age, years (range)		62.0 (37.0, 85.0)	65.0 (36.0, 86.0)	.52
Median time since diagnosis, months (range)		42.0 (8.8, 173.8)	106.9 (29.6, 263.7)	**< .0001**
Prior lines of treatment (range)		2.0 (2.0, 8.0)	2.0 (2.0, 9.0)	.68
Response to previous LoT, n (%)	*Relapsed*	16 (47.1%)	59 (67.8%)	.06
	Refractory	18 (52.9%)	28 (32.2%)	
	Missing	0	2	

FLIPI: Follicular lymphoma international prognostic index. LoT: line of therapy. POD24: Progression of disease with 24-months after front-line chemoimmunotherapy.

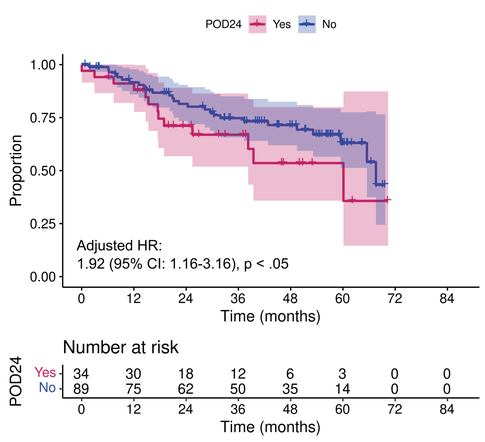
Figure 3. Time from diagnosis to initiation of each LoT



Box-plot showing median, interquartile-range and minimum/maximum. Outlying points are beyond 1.5 * the interquartile range.

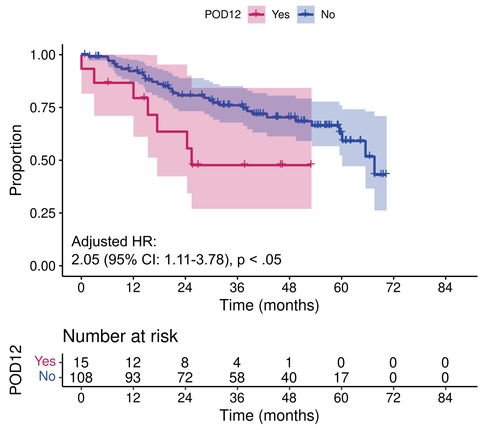
- There was no difference in between POD24 and non-POD24 patients in time to initiation of first LoT, but by LoT 2, the time to initiation of the LoT was shorter for POD24 patients (**Figure 3**), and this pattern continued to LoT 4.

Figure 4. Unadjusted Kaplan-Meier curves of OS by POD24



- POD24 status was associated with shorter OS from qualifying LoT, with an HR of 1.92 (95% CI: 1.16 - 3.16, p < .05; **Figure 4**).

Figure 5. Unadjusted Kaplan-Meier curves of OS by POD12



- Secondary analyses revealed POD12 was also associated with shorter OS (**Figure 5**).
- POD24 was not significantly associated with PFS or response, although the effect was directionally consistent as was observed for OS (**Table 2**).

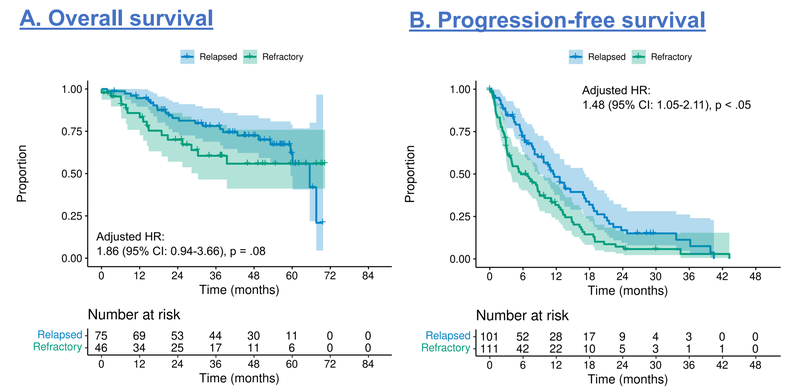
Table 2. Results across all prognostic factors

	Treatment effect (95% CI)
POD24 vs non-POD24	
Overall survival (HR)	**1.92 (1.16 – 3.16)**
Progression-free survival (HR)	1.28 (0.96 – 1.70)
Overall response rate (OR)	1.44 (0.80 – 2.97)
Complete response (OR)	1.45 (0.65 – 3.30)
POD12 vs non-POD12	
Overall survival (HR)	**2.05 (1.11 – 3.78)**
Progression-free survival (HR)	1.40 (0.94 – 2.08)
Refractory* vs Relapsed to prior LoT**	
Overall survival (HR)	1.86 (0.94 – 3.66)
Progression-free survival (HR)	**1.48 (1.05 – 2.11)**

*Defined as progressing during or within 6 months after completion of the most recent prior treatment.
**Defined as progressing after complete response, partial response, or stable disease > 6 months after completion of the most recent prior treatment. Bold text indicates significant p <.05. HR: Hazard ratio. OR: Odds ratio.

- In addition, refractory status to prior LoT was significantly associated with shorter time to progression, but not OS, compared to relapsed patients (**Figure 6**).

Figure 6. Unadjusted Kaplan-Meier curves for R/R status



- The evidence suggests that POD24 remains a prognostic factor amongst R/R FL patients initiating later LoT, although with a smaller effect size than observed at earlier LoT.[1,2]
- Differences in time since diagnosis and R/R status between POD24 and non-POD24 patients suggest that POD24 may capture the degree of disease aggression regardless of LoT.
- The limitations of this study were the limited sample size and unavailability ability of some prognostic factors, such as FLIPI and disease stage at diagnosis.

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DISCLOSURES

ARP: Employment or leadership position – Kite, a Gilead company; Stock ownership – Kite, a Gilead company. EHLO: Employment or leadership position: RainCity Analytics. SK: Employment or leadership position: RainCity Analytics; Research funding: RainCity Analytics has received funds from for-profit healthcare companies for research. MDR: Employment or leadership position – Kite, a Gilead company; Stock ownership – Kite, a Gilead company. TB: Employment or leadership position – Kite, a Gilead company; Stock ownership – Kite, a Gilead company. PG: Consultant or advisory position: AstraZeneca, Kyowa Hakko Kirin, Secura Bio; Research funding: Kite, a Gilead company. SSN: Consultant or advisory position: Kite, a Gilead company, Merck, BMS, Novartis, Celgene, Pfizer, Allogene Therapeutics, Cell Medica/Kuur, Incyte, Precision Biosciences, Adicet Biolegend Biotech, Calibr, Unum Therapeutics, Bluebird Bio, Medscape, Aptitude Health, Bio Ascend; Honoraria: Kite, a Gilead company, Merck, BMS, Novartis, Celgene, Pfizer, Allogene Therapeutics, Cell Medica/Kuur, Incyte, Precision Biosciences, Adicet Bio, Legend Biotech, Calibr, Unum Therapeutics, Bluebird Bio, Medscape, Bio Ascend; Research funding: Kite, a Gilead company, Merck, BMS, Celgene, Allogene Therapeutics, Precision Biosciences, Adicet Bio, Unum Therapeutics, Aptitude Health, Poseida, Cellectis, Karus Therapeutics, Acerta; Other remuneration: Kite, a Gilead company, Merck, BMS, Novartis, Celgene, Pfizer, Allogene Therapeutics, Cell Medica/Kuur, Incyte, Precision Biosciences, Legend Biotech, Adicet Bio, Calibr, Unum Therapeutics, Takeda Pharmaceuticals. JGG: Honoraria – Janssen, AbbVie, AstraZeneca, Amgen, BMS, Kite, a Gilead company, Novartis; Research funding: Celgene, AstraZeneca, BMS; Other remuneration: Janssen, AbbVie, Roche/Greentech. SB: Employment or leadership position –Kite, a Gilead company; Research funding - Kite, a Gilead company. SB: No conflicts of interest pertinent to the abstract to be declared.

Presented at the International Conference on Malignant Lymphoma, 2023