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Matching-Adjusted Indirect Comparison of Epcoritamab With Rituximab + Lenalidomide Versus Tafasitamab With Rituximab + Lenalidomide in Second-Line or Later Follicular Lymphoma

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OBJECTIVE

- In the absence of head-to-head trials, this study aimed to compare epcoritamab + R^2 to tafasitamab + R^2 as 2L+ therapy for patients with R/R FL using a matching-adjusted indirect comparison (MAIC)

CONCLUSIONS

- Findings from this MAIC highlight the potential of epcoritamab + R^2 to deliver meaningful improvement in ORR, CR, and PFS versus tafasitamab + R^2
- Results showed a significant improvement in ORR and CR and a 45% reduction in risk of progression or death with epcoritamab + R^2 in 2L+ patients with FL

BACKGROUND

- Follicular lymphoma (FL), the most common indolent B-cell lymphoma, is characterized by chronic periods of relapse and remission with reduced survival odds after relapse[1-5]
- There is no standard of care for patients with relapsed or refractory (R/R) FL, so there remains a need for safe and highly efficacious treatment to improve outcomes in this population[2,6]
- Epcoritamab, a subcutaneous CD3xCD20 bispecific antibody approved in the United States and other countries,[7,8] provides deep, durable responses and manageable safety in R/R FL after ≥2 systemic therapies, based on results from the EPCORE NHL-1 trial (NCT03625037)[9,10]
- The therapeutic benefit of epcoritamab + rituximab and lenalidomide (R^2) in R/R FL is being investigated in ongoing multinational trials[6] (EPCORE NHL-2 [NCT04663347, phase 1b/2] and EPCORE FL-1 [NCT05409066, phase 3]) with varied treatment durations, and this combination has earned the US Food and Drug Administration's breakthrough therapy designation for the treatment of adult patients with R/R FL[11]
- The combination of tafasitamab, a humanized CD19-directed monoclonal antibody, and R^2 has demonstrated efficacy and manageable safety in patients with R/R FL in the inMIND trial (NCT04680052, phase 3)[3]
- To our knowledge, to date, no head-to-head clinical study has compared the outcomes of epcoritamab + R^2 versus tafasitamab + R^2 in second-line or later (2L+) R/R FL

METHODS

Data sources

- Arm 2 of the EPCORE NHL-2 trial (data cutoff: May 2024)
  - Individual patient data for epcoritamab (48 mg) + R^2
- inMIND study (data cutoff: February 2024)
  - Aggregate data for tafasitamab + R^2

Patient population

- To mirror inMIND's inclusion criteria, 3 patients in the epcoritamab + R^2 cohort with prior R^2 use were excluded
- Patients receiving epcoritamab + R^2 were matched to those receiving tafasitamab + R^2 on the following key baseline characteristics:
  - Aged ≥75 years
  - Gender
  - Eastern Cooperative Oncology Group performance status
  - Follicular Lymphoma International Prognostic Index score
  - Number of prior lines of therapy
  - Groupe d'Etude des Lymphomes Folliculaires (GELF) criteria
  - Progression of disease within 24 months
    - Epcoritamab + R^2: FL progression in ≤24 months of first-line therapy
    - Tafasitamab + R^2: disease progression within 24 months of initial diagnosis
  - Refractory to last therapy
  - Refractory to prior anti-CD20

Outcomes of interest

- Overall response rates (ORRs), complete response (CR) rate, and progression-free survival (PFS)

Statistical analysis

- Weighted log-binomial regression analysis was used to estimate relative risks and 95% confidence intervals (CIs) for ORRs and CR rates
- Weighted Cox proportional-hazard models were used to estimate hazard ratios (HRs) and 95% CIs for PFS
- Outcomes (ORR, CR, and PFS) as assessed by investigators were used in this analysis

RESULTS

Key baseline characteristics

- Before matching
  - A higher proportion of patients in the tafasitamab + R^2 cohort (N=273) were aged ≥75 years and were refractory to last therapy as compared to patients in the epcoritamab + R^2 cohort (N=108) (**Table 1**)
  - In comparison, a higher proportion of patients in the epcoritamab + R^2 cohort than the tafasitamab + R^2 cohort met GELF criteria, suggesting a higher tumor burden
- After matching
  - The key baseline characteristics were well balanced, creating comparable cohorts (**Table 1**)

Table 1. Baseline comparisons before and after MAIC in 2L+ FL

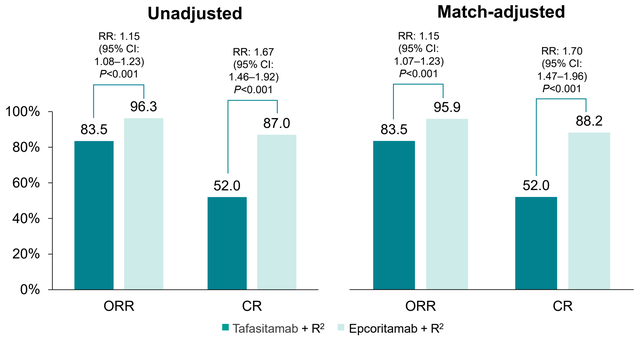
Key baseline characteristics	Before MAIC epcoritamab + R^2 (48 mg; N=108)	After MAIC epcoritamab + R^2 (48 mg; ESS = 50)	Tafasitamab + R^2 (N=273)
Aged ≥75 years	11.1%	19.8%	19.8%
Male	50.9%	54.9%	54.9%
ECOG PS			
0	63.9%	66.3%	66.3%
1–2	36.1%	33.7%	33.7%
FLIPI score			
0 or 1	12.9%	20.9%	20.9%
2–5	87.1%	79.1%	79.1%
High tumor burden per GELF criteria	96.3%	81.3%	81.3%
LOTs, n			
1	53.9%	53.8%	53.8%
2	24.2%	24.2%	24.2%
≥3	21.9%	22.0%	22.0%
POD24[a]	50.0%	31.1%	31.1%
Refractory to last therapy	35.2%	41.0%	41.0%
Refractory to prior anti-CD20	43.5%	43.2%	43.2%

[a]POD24 (epcoritamab + R^2): FL progression within ≤24 months of first-line therapy; POD24 (tafasitamab + R^2): disease progression within ≤24 months of initial diagnosis.
2L+, second-line or later; ECOG, Eastern Cooperative Oncology Group; ESS, effective sample size; FL, follicular lymphoma; FLIPI, Follicular Lymphoma International Prognostic Index; GELF, Groupe d'Etude des Lymphomes Folliculaires; LOT, line of therapy; MAIC, matching-adjusted indirect comparison; POD24, progression of disease within 24 months; PS, performance status; R^2, rituximab + lenalidomide.

Response rate estimates

- After matching, epcoritamab + R^2 provided significantly higher ORR (95.9% vs 83.5%; *P*<0.001) versus tafasitamab + R^2 (**Figure 1**)
  - CR rates were also significantly higher with epcoritamab + R^2 versus tafasitamab + R^2 (88.2% vs 52.0%; *P*<0.001)

Figure 1. Response rate comparisons of epcoritamab + R^2 and tafasitamab + R^2 in 2L+ FL

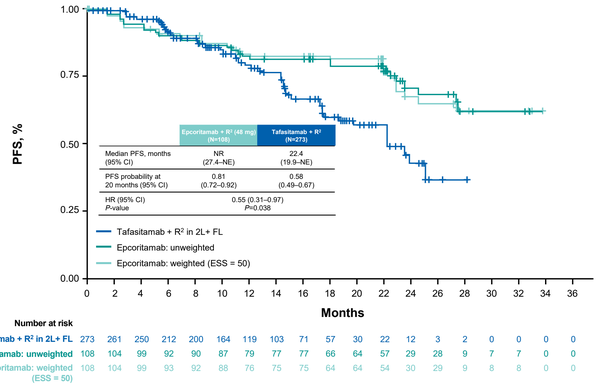


2L+, second-line or later; CI, confidence interval; CR, complete response; FL, follicular lymphoma; ORR, overall response rate; R^2, rituximab + lenalidomide; RR, relative risk.

Time-to-event outcomes

- The median follow-up time was 25.3 months for the epcoritamab + R^2 cohort and 14.1 months for the tafasitamab + R^2 cohort
- Median PFS was not reached in the epcoritamab + R^2 cohort, while median PFS in the tafasitamab + R^2 cohort was 22.4 months (**Figure 2**)
  - PFS probability at 20 months was 81.3% in the epcoritamab + R^2 cohort versus 57.5% in the epcoritamab + R^2 cohort
- The HR for epcoritamab + R^2 versus tafasitamab + R^2 (HR [95% CI]: 0.55 [0.31–0.97]; *P*=0.038) indicated a 45% reduction in the risk of progression or death with epcoritamab + R^2

Figure 2. PFS in epcoritamab + R^2 versus tafasitamab + R^2 in 2L+ FL



Number at risk

Tafasitamab + R^2 in 2L+ FL	273	261	250	212	200	164	119	103	71	57	30	22	12	3	2	0	0	0	0
Epcoritamab: unweighted	108	104	99	92	90	87	79	77	77	66	64	57	29	28	9	7	7	0	0
Epcoritamab: weighted (ESS = 50)	108	104	99	93	92	88	76	75	75	64	64	54	30	29	9	8	8	0	0

2L+, second-line or later; CI, confidence interval; ESS, effective sample size; FL, follicular lymphoma; HR, hazard ratio; NE, not estimable; NR, not reached; PFS, progression-free survival; R^2, rituximab + lenalidomide.

Limitations

- Although this analysis adjusted for confounding variables between studies, indirect treatment comparisons are subject to bias due to variations in patient populations, study designs, and outcome measures across the included trials. As such, outcomes may still be subject to uncertainty relative to head-to-head randomized trials[12]

Strengths

- Given the available evidence, the described comparative analysis is a transparent and methodologically sound approach to compare epcoritamab + R^2 with tafasitamab + R^2 in patients with R/R FL[12]

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