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Clinically Relevant Subgroup Analysis From the Randomized Phase 3 EPCORE FL-1 Trial: Treatment Effect of Epcoritamab With Lenalidomide and Rituximab in Relapsed/Refractory Follicular Lymphoma

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Objective

- Here we present subgroup analyses from EPCORE FL-1 demonstrating that epcoritamab + R² provides consistent efficacy and tolerability across broad patient populations

Conclusion

- Fixed-duration epcoritamab + R² was superior to R² in the Phase 3 EPCORE FL-1 study in patients with 2L+ FL
  - There was a 79% reduction in the risk of disease progression or death
  - Higher rates and durable, deep responses were observed, with improved complete response rate (83% for epcoritamab + R² vs 50% for R²)
- Epcoritamab + R² led to sustained, improved efficacy with manageable safety across clinically relevant subgroups, consistent with the findings in the overall EPCORE FL-1 study population
  - Epcoritamab + R² treatment resulted in consistently greater efficacy when compared with R² and was comparable across both low- and high-risk clinically relevant subgroups
- In patients with reduced Len RDI, PFS was improved with epcoritamab + R² compared with R² alone, reinforcing that treatment benefit is maintained despite dose modifications
- Collectively, these findings further support fixed-duration epcoritamab + R² as a new standard of care in 2L+ FL, with the potential to improve treatment expectations across a broad patient population

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To submit a medical question, please visit abbviemedinfo.com.

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Introduction

- Chemoimmunotherapy or lenalidomide and rituximab (R²) are standard of care options for relapsed/refractory follicular lymphoma (R/R FL); however, an unmet need for novel treatments with improved outcomes remains[1]
- Epcoritamab, a subcutaneous CD3×CD20 bispecific antibody, is approved in the United States, Brazil, and China and received a positive Committee for Medicinal Products for Human Use opinion in the European Union in May 2026 as fixed-duration therapy with R² in 2L+ FL based on the Phase 3 EPCORE FL-1 study (NCT05409066)[2,3]
  - Dual primary endpoints were met with epcoritamab + R² showing superiority over R²
  - At 14.8 months of follow-up, epcoritamab + R² had higher overall response rate (95% vs 79%), higher complete response rate (83% vs 50%), longer progression-free survival (PFS; hazard ratio, 0.21 [95% CI, 0.14–0.31]), and increased durability[3]
- Subgroup analyses can inform optimal treatment decisions based on patient characteristics, including in both low- and high-risk clinically relevant subgroups
- In addition, lenalidomide (Len) relative dose intensity (RDI) was evaluated to assess efficacy

Methods

EPCORE FL-1: Phase 3, Global, Randomized, Open-Label Study[3]

Key eligibility criteria
- Histologically confirmed CD20+ R/R FL
- Grade 1–3a, Stage II–IV
- ≥1 prior treatment, including anti-CD20 mAb plus an alkylating agent
- Met ≥1 GELF criterion

- **Dual primary endpoints: ORR per IRC and PFS per IRC**
- Select secondary endpoints: CR rate per IRC, OS, and safety

Data cutoff: May 24, 2025
Median follow-up: 14.8 months[d]
Enrollment period: Oct 2022 to Jan 2025

Randomization 1:1

Fixed-Duration: 12 Cycles (28-Day Cycles)

Epcoritamab (48 mg) plus R²
- **Epcoritamab** 3-SUD cycle 1,[a] QW; cycles 2–3, QW; cycles 4–12, Q4W
- **Rituximab (375 mg/m²)** 5 cycles: cycle 1, QW; cycles 2–5, Q4W
- **Lenalidomide (20 mg)** 12 cycles QD, D1–21

R²
- **Rituximab (375 mg/m²)** 5 cycles: cycle 1, QW; cycles 2–5, Q4W
- **Lenalidomide (20 mg)** 12 cycles, QD, D1–21

Post Hoc Subgroup Analyses

Clinically relevant subgroups:
- Age (<70 vs ≥70 years)
- NHL-5 comorbidity index (low vs high/intermediate)[4]
- Prior LOTs (1 vs ≥2)
- FLIPI (0–2 vs 3–5)
- POD24 status[b]
- Bulky disease status[b,c]
- Double refractory status[b]

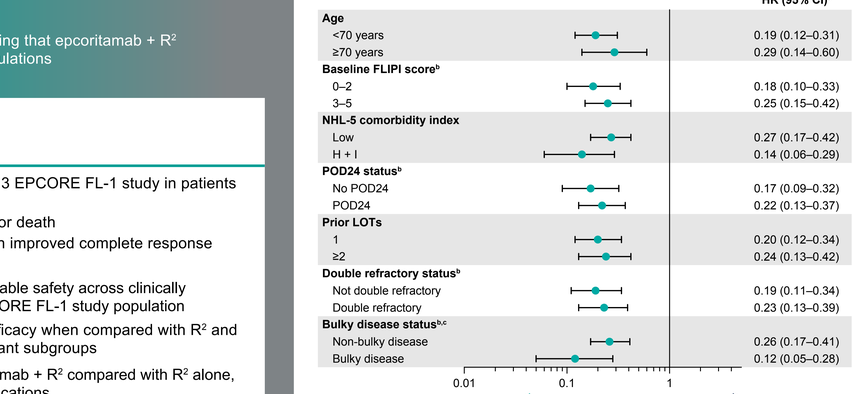
Len RDI subgroups: <50% vs ≤70% vs >70%

[a]Two SUD regimens were evaluated during cycle 1 to mitigate the risk of CRS: either a 2-SUD (0.16 mg on cycle 1 day 1, 0.8 mg on cycle 1 day 8), or 3-SUD (0.16 mg on cycle 1 day 1, 0.8 mg on cycle 1 day 8, 3 mg on cycle 1 day 15) regimen, followed by full dose 48 mg. The 3-SUD regimen was implemented after reduced CRS severity and incidence had been observed in the EPCORE NHL-1 FL trial (NCT03625037).[b]Pre-specified subgroup per the study statistical analysis plan. [c]Bulky disease was defined by the presence of a lymph node ≥7 cm at baseline/screening. [d]The data presented here are from the second planned interim analysis (May 24, 2025) after 76% information fraction for PFS had occurred.
CR, complete response; CRS, cytokine release syndrome; D, day; FL, follicular lymphoma; FLIPI, Follicular Lymphoma International Prognostic Index; GELF, Groupe d'Etude des Lymphomes Folliculaires; IRC, independent review committee; Len, lenalidomide; LOT, line of therapy; mAb, monoclonal antibody; NHL-5, non-Hodgkin lymphoma comorbidity score; ORR, overall response rate; OS, overall survival; PFS, progression-free survival; POD24, progression of disease ≤2 years from the date of initiation of frontline therapy; Q4W, once every 4 weeks; QD, once daily; QW, once every week; R², lenalidomide and rituximab; RDI, relative dose intensity; R/R, relapsed/refractory; SUD, step-up dosing.

Results

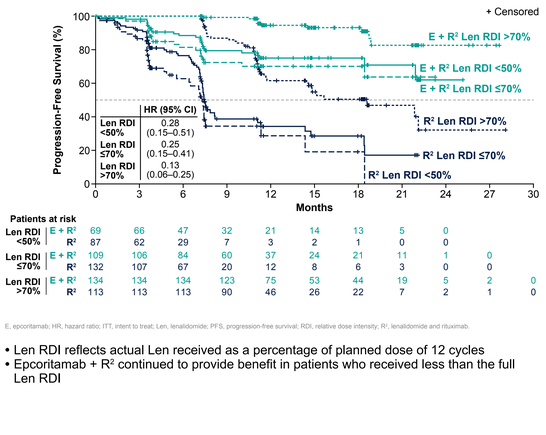
Efficacy Was Improved With Epcoritamab + R² vs R² Alone

Both Low- and High-Risk Clinically Relevant Subgroups Showed Improved PFS With Epcoritamab + R² Over R²



[a]HRs were determined by unstratified Cox proportional hazards model. [b]Response rates and PFS curves for FLIPI, POD24, double refractory status, and bulky disease status subgroups are accessible in the Supplemental Materials via the QR code. [c]Bulky disease was defined by the presence of a lymph node ≥7 cm at baseline/screening.
FLIPI, Follicular Lymphoma International Prognostic Index; HR, hazard ratio; LOT, line of therapy; NHL-5, non-Hodgkin lymphoma comorbidity score; PFS, progression-free survival; POD24, progression of disease ≤2 years from the date of initiation of frontline therapy; R², lenalidomide and rituximab.

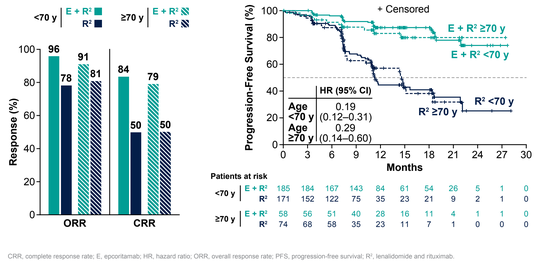
PFS Favored Epcoritamab + R² Compared With R² Alone Regardless of Len RDI Levels



E, epcoritamab; HR, hazard ratio; ITT, intent to treat; Len, lenalidomide; PFS, progression-free survival; RDI, relative dose intensity; R², lenalidomide and rituximab.

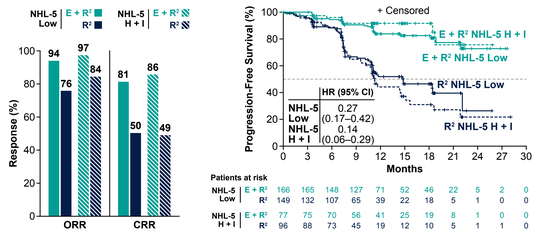
- Len RDI reflects actual Len received as a percentage of planned dose of 12 cycles
- Epcoritamab + R² continued to provide benefit in patients who received less than the full Len RDI

Efficacy Benefit With Epcoritamab + R² Was Maintained Across Patient Age Subgroups



CRR, complete response rate; E, epcoritamab; HR, hazard ratio; ORR, overall response rate; PFS, progression-free survival; R², lenalidomide and rituximab.

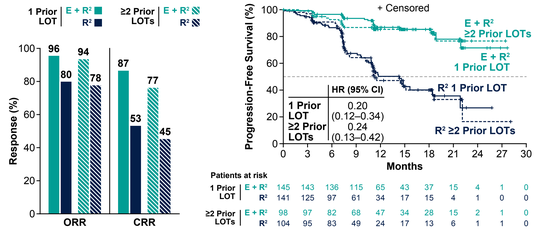
Regardless of Comorbidity Burden[a] Epcoritamab + R² Resulted in Higher Response Rates and Improved PFS



[a]Comorbidity burden was based on the NHL-5 Comorbidity Score Sum, Range (0–5) and defined as 0=low, 1+intermediate, ≥2=high.*
CRR, complete response rate; E, epcoritamab; H + I, high and intermediate; HR, hazard ratio; NHL-5, non-Hodgkin lymphoma comorbidity score; ORR, overall response rate; PFS, progression-free survival; R², lenalidomide and rituximab.

- The NHL-5 comorbidity score is a five-category score that classifies patients as low, intermediate, or high risk based on vascular disease, congestive heart failure, chronic obstructive pulmonary disease, diabetes mellitus, and renal disease[4]

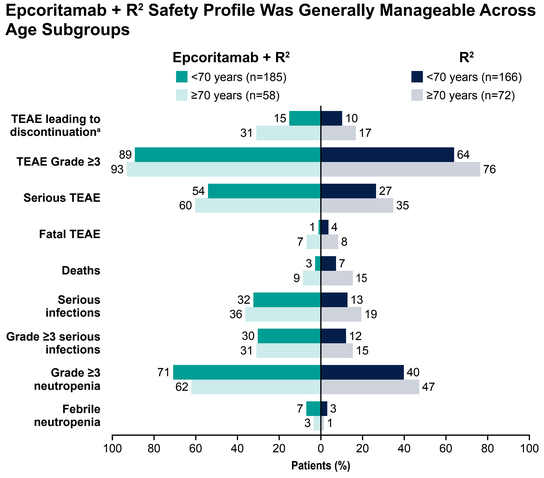
Epcoritamab + R² Showed Favorable Efficacy Over R² Across Prior LOT Subgroups



CRR, complete response rate; E, epcoritamab; HR, hazard ratio; LOT, line of therapy; ORR, overall response rate; PFS, progression-free survival; R², lenalidomide and rituximab.

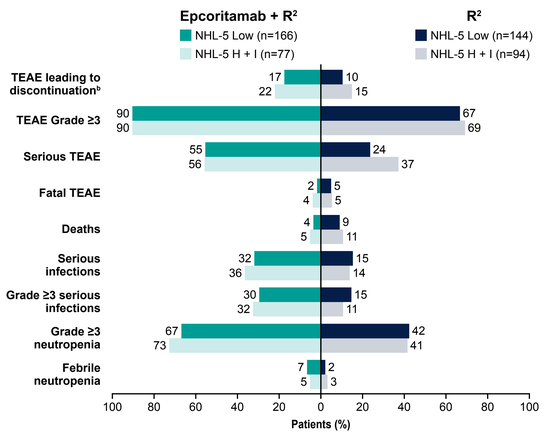
The Safety Profile of Epcoritamab + R² Was Manageable

Epcoritamab + R² Safety Profile Was Generally Manageable Across Age Subgroups



[a]TEAE leading to discontinuation of any study drug.
R², lenalidomide and rituximab; TEAE, treatment-emergent adverse event.

The Epcoritamab + R² Safety Profile Remained Generally Manageable Even in Patients With Increased Comorbidity Burden[a]



*Comorbidity burden was based on the NHL-5 Comorbidity Score Sum, Range (0–5) and defined as 0=low, 1+intermediate, ≥2=high.†TEAE leading to discontinuation of any study drug.
H + I, high and intermediate; NHL-5, non-Hodgkin lymphoma comorbidity score; R², lenalidomide and rituximab; TEAE, treatment-emergent adverse event.