IBCL-1346

# Comparative Effectiveness of Epcoritamab, Lenalidomide, and Rituximab in EPCORE FL-1 vs Real-World Chemoimmunotherapy in Relapsed/Refractory Follicular Lymphoma

**Habte Yimer,[1] Lorenzo Falchi,[2] Rong Tao,[3] Loic Ysebaert,[4] Michal Kwiatek, [5] Abel Costa,[6] Theodoros P Vassilakopoulos,[7] Marcel Nijland,[8] Shane Gangatharan,[9] Dai Maruyama,[10] Abualbishr Alshreef,[11] Anthony Wang,[11] Junhua Yu,[11] David Tybor,[11] Yves Mbous,[11] Kavita Sail,[11] Zhijie Ding,[12] Gauri Sunkersett,[11] JP Mei,[11] Kim Linton[13]**

[1]Texas Oncology-Tyler, US Oncology Research, Tyler, TX, USA; [2]Lymphoma Service, Memorial Sloan Kettering Cancer Center, New York, NY, USA; [3]Fudan University Cancer Hospital, Shanghai, China; [4]Hematology Department, Univ Toulouse, CHU Toulouse, IUCT-Oncopole, Toulouse, France; [5]Aidport Clinical Trials Hospital, Skórzewo (Poznan), Poland; [6]Department of Hematology, D'Or Institute for Research and Education, São Paulo, Brazil; [7]Laikon General Hospital, National and Kapodistrian University of Athens, Athens, Greece; [8]University Medical Center Groningen, University of Groningen, Groningen, Netherlands; [9]Fiona Stanley Hospital, Murdoch, WA, Australia; [10]Department of Hematology Oncology, Cancer Institute Hospital, Japanese Foundation for Cancer Research, Tokyo, Japan; [11]AbbVie Inc., North Chicago, IL, USA; [12]Genmab US, Inc, Plainsboro, NJ, USA; [13]The Christie NHS Foundation Trust, Manchester Cancer Research Centre, and Division of Cancer Sciences, University of Manchester, Manchester, England, UK

## Objective

- To compare the efficacy of epcoritamab + R² from EPCORE FL-1 with real-world CIT in R/R FL using an IPTW-adjusted indirect treatment comparison

## Conclusion

- This comparative IPTW-adjusted analysis against CIT showed that epcoritamab + R² resulted in deep and durable responses in patients with 2L+ FL, similar to the findings of the EPCORE FL-1 trial
- Comparative efficacy analysis showed that epcoritamab + R² significantly improved response rates, PFS, and OS compared with real-world CIT regimens
  - There was a 67% reduction in risk of progression or death and 82% reduction in risk of mortality in patients treated with epcoritamab + R² vs CIT
  - Increased rates and deeper responses were observed with epcoritamab + R² vs CIT (complete response rate: 84.2% vs 55.8%)
- Limitations of the analysis include potential confounding of DOR/DOCR by frequency and timing of scans in the real-world vs clinical trial setting and the lower PFS observed with real-world CIT compared with clinical trials
- Overall, the findings presented here combined with the manageable safety profile and superior efficacy vs R² demonstrated in the EPCORE FL-1 trial position epcoritamab + R² as a new chemotherapy-free standard of care for 2L+ FL



## References

1. Matasar MJ, et al. *Oncologist*. 2019;24:e1236-1250.
2. Casulo C, et al. *Blood*. 2025;146:1782-1791.
3. EPKINLY [prescribing information]. Plainsboro, NJ; Genmab US, Inc; November 2025.
4. Tepkinly [summary of product characteristics]. Ludwigshafen, Germany: AbbVie Deutschland GmbH & Co. KG; February 2026.
5. Falchi L, et al. *Lancet*. 2026;407:161-173.
6. Ghione P, et al. *Haematologica*. 2023;108:822-832.
7. Austin PC and Stuart EA. *Stat Med*. 2015;34:3661-79.

## Acknowledgments

On behalf of all the authors, AbbVie and Genmab would like to thank the patients participating in this clinical trial and their families, and all the study investigators, coordinators, and support staff.

Epcoritamab is being developed in collaboration between AbbVie and Genmab. AbbVie funded this study and participated in the study design, research, analysis, data collection, interpretation of data, reviewing, and approval of the publication. All authors had access to relevant data and participated in the drafting, review, and approval of this publication. No honoraria or payments were made for authorship. Medical writing support was provided by Hilary Durbano, PhD, of Bio Connections LLC, and funded by AbbVie.

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

## Author Disclosures

**L Falchi** has received research funding from Roche, Genentech, Genmab, AbbVie, Innate Pharma, BeOne, and AstraZeneca; has received consultancy fees from Roche, Genentech, Genmab, AbbVie, Sanofi, AstraZeneca, Merck, and NOBO Medicine; has served in an advisory role for AbbVie, Genentech, ADC Therapeutics, Seagen, Ipsen, Johnson & Johnson, Regeneron, Chugai, and Bristol Myers Squibb; has received honoraria from Roche, Genmab, AbbVie, and Kite; and has received travel support from Genmab, AbbVie, Roche, Kite, and Chugai.

**R Tong** has served in a consultancy role for AbbVie.

**L Ysebaert** has received honoraria from AbbVie, AstraZeneca, BeOne, Bristol Myers Squibb, Gilead, Johnson & Johnson, Eli Lilly, and Roche.

**M Kwiatek** declares no competing interests.

**A Costa** has received honoraria from Johnson & Johnson, AbbVie, AstraZeneca, Eli Lilly, Knight, BeiGene, Regeneron, IPSEN, and Pfizer; and has received research funding from AbbVie.

**TP Vassilakopoulos** has received research support/PI for Merck, Roche, AbbVie, Bristol Myers Squibb, and Karyopharm; has received honoraria from Takeda, Roche, Genesis Pharma, AbbVie, Gilead, AstraZeneca, Eli Lilly, Janssen, and Swixx; and has served in an advisory role for Roche, Genesis Pharma, Takeda, AbbVie, Merck, Gilead, AstraZeneca, Winmedica, Swixx, and Eli Lilly.

**M Nijland** has received research funding from Takeda and consulting fees from AbbVie. All payments to institution.

**S Gangatharan** declares no competing interests.

**H Yimer** has served on speaker bureaus for AbbVie, Amgen, BeOne, Genmab, Karyopharm, Janssen, Pharmacosmos, and Regeneron; and has served in an advisory role for AstraZeneca, Bristol Myers Squibb, and Pfizer.

**D Maruyama** has received research funding from Ono, Janssen, Eisai, Chugai, Kyowa Kirin, MSD, Sanofi, SymBio, Takeda, AbbVie, AstraZeneca, Bristol Myers Squibb, Genmab, Novartis, Otsuka, Pfizer, Astellas, BeOne, Eli Lilly, Daiichi-Sankyo, and Meiji Seika Pharma; has served on an advisory board for Janssen, AstraZeneca, Chugai, AbbVie, Genmab, Sanofi, Bristol Myers Squibb, and Pfizer; and has received honoraria from Ono, Nippon Shinyaku, Janssen, Mundipharma, Eisai, Chugai, Roche, Kyowa Kirin, MSD, Zenyaku, Sanofi, SymBio, Takeda, AbbVie, AstraZeneca, Bristol Myers Squibb, Genmab, Novartis, and BeOne.

**A Alshreef, A Wang, J Yu, D Tybor, Y Mbous, K Sail, G Sunkersett, and JP Mei** are currently employed by and are shareholders of AbbVie.

**Z Ding** reports employment by Genmab and owns Genmab stock or options.

**K Linton** has served in a consultancy role for Kite, Gilead, Genmab, Roche, AbbVie, BeOne, Bristol Myers Squibb, and Celgene; has received research funding from Kite/Gilead, Genmab, Roche, AbbVie, BeOne, Bristol Myers Squibb, ADC Therapeutics, AstraZeneca, CellCentric, Janssen, MorphoSys, MSD, Nurix, Regeneron, Step Pharma, Viracta, and Celgene; has participated on speaker bureaus for AbbVie, Bristol Myers Squibb, and Celgene; has received travel support from Bristol Myers Squibb and Celgene; has served as a member of the Epcoritamab Global Council; and has received research funding from the National Institute for NIHR Manchester Biomedical Research Center (NIHR203308).

Previously presented at the Annual Congress of the European Hematology Association; June 11–14, 2026; Stockholm, Sweden; DV-019917

*Presented at the Society of Hematologic Oncology (SOHO) 2026 Annual Meeting; September 9–12, 2026; Houston, TX; DV-021147*

## Introduction

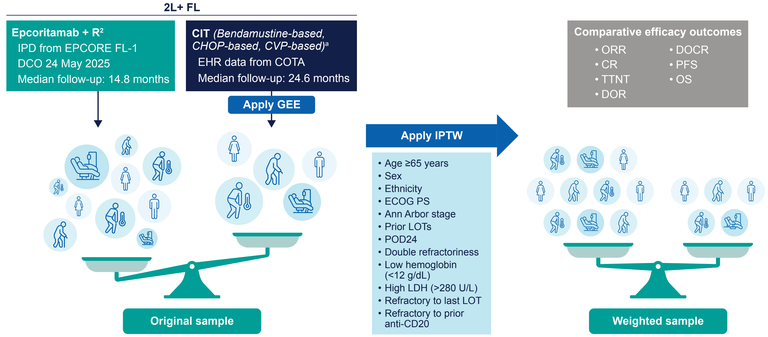
- Patients with relapsed/refractory follicular lymphoma (R/R FL) often experience repeated relapse, with shorter remissions after each subsequent therapy[1,2]
- Chemoimmunotherapy (CIT) remains used in routine practice, but cumulative toxicity and limited durability highlight the need for more effective chemotherapy-free options[2]
- Epcoritamab is a subcutaneous CD3×CD20 bispecific antibody approved in the United States (US) and Europe as monotherapy in third line and beyond (3L+) FL and approved in the US as combination therapy with lenalidomide and rituximab ($R^2$) in 2L+ FL[3,4]
- In EPCORE FL-1 (NCT05409066), fixed-duration epcoritamab + R² demonstrated superior response rates and progression-free survival (PFS) versus R² (hazard ratio [HR], 0.21 [95% CI, 0.14–0.31]; *P*<.0001), with a 79% reduction in the risk of progression or death, and a manageable safety profile[5]
- Because CIT is commonly used in real-world practice,[6] this analysis compares epcoritamab + R² with real-world CIT regimens

## Methods

### Data Sources

- Individual patient data from 2 sources were compared:
  - EPCORE FL-1 trial[5] (data cutoff: 24 May 2025)
    - Adults aged ≥18 years who had histologically confirmed CD20+ FL
    - FL Grade 1–3A, stage II–IV
    - ≥1 prior treatment containing ≥1 anti-CD20 monoclonal antibody therapy plus an alkylating agent
    - Met ≥1 Groupe d'Etude des Lymphomes Folliculaires criterion
  - COTA US electronic health records database (COTA Healthcare, New York, NY)
    - Contains real-world patient data (de-identified demographic, diagnostic, treatment, and outcomes data) submitted by geographically dispersed US academic medical centers and community practice sites
    - Patients were selected for inclusion based on criteria similar to the FL-1 trial
      - Adults aged ≥18 years who had a diagnosis of R/R FL based on record of pathological confirmation of an initial FL diagnosis from January 2010 through December 2024
      - Eastern Cooperative Oncology Group performance status ≤2
      - FL Grade 1–3A
      - ≥1 prior treatment, including ≥1 anti-CD20 monoclonal antibody-containing therapy and an alkylating agent or lenalidomide
      - Second-line (2L) initiation not earlier than 1 January 2010
- Generalized estimating equations identified the best-matched CIT line of therapy (LOT) and inverse probability of treatment weighting (IPTW) balanced baseline characteristics[7]

### *IPTW Was Used to Balance Demographics and Clinical Baseline Characteristics*




Despite IPTW adjustment, residual confounding may remain due to unmeasured or incompletely captured prognostic variables.
[a]CIT regimens contained rituximab or obinutuzumab.
2L+, second line and beyond; CHOP, cyclophosphamide, doxorubicin, vincristine, and prednisolone; CIT, chemoimmunotherapy; CR, complete response; CVP, cyclophosphamide, vincristine, and prednisone; DCO, data cutoff; DOCR, duration of complete response; DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; EHR, electronic health record; FL, follicular lymphoma; GEE, generalized estimating equations; IPD, individual patient data; IPTW, inverse probability of treatment weighting; LDH, lactate dehydrogenase; LOT, line of therapy; ORR, overall response rate; OS, overall survival; PFS, progression-free survival; POD24, disease progression occurring within 24 months of initiating first-line therapy; R², lenalidomide and rituximab; TTNT, time to next treatment.

## Results

### *IPTW-Adjusted Demographics and Clinical Baseline Characteristics Were Well Balanced*

| Characteristic | Unadjusted | | Adjusted | |
|---|---|---|---|---|
| | Epcoritamab + R² (n=243) | CIT (n=274) | Epcoritamab + R² (ESS=199) | CIT (ESS=220) |
| Age ≥65 years, % | 36.2 | 59.1 | 47.8 | 51.5 |
| Female, n (%) | 42.8 | 42.7 | 40.9 | 42.3 |
| Hispanic or Latino ethnicity, n (%)[a] | 11.9 | 21.2 | 14.9 | 16.7 |
| Prior LOT, n (%) | | | | |
| 1 | 59.7 | 71.9 | 66.5 | 68.8 |
| 2 | 23.9 | 17.5 | 20.6 | 18.6 |
| ≥3 | 16.5 | 10.6 | 12.9 | 12.6 |
| ECOG performance status, n (%) | | | | |
| 0 | 68.3 | 51.5 | 64.1 | 60.7 |
| 1 | 29.6 | 41.6 | 33.3 | 34.8 |
| 2 | 2.1 | 6.9 | 2.6 | 4.5 |
| POD24, n (%) | 43.6 | 40.5 | 42.4 | 42.0 |
| High LDH, n (%) | 35.0 | 18.2 | 28.0 | 26.1 |
| Abnormal hemoglobin, n (%) | 34.6 | 29.2 | 31.7 | 31.6 |
| Stage III–IV, n (%) | 84.8 | 90.1 | 87.3 | 89.1 |
| Double refractory, n (%) | 37.4 | 38.7 | 35.6 | 36.5 |

[a]Race, including African American, was not adjusted for as groups were equally balanced.
CIT, chemoimmunotherapy; ECOG, Eastern Cooperative Oncology Group; ESS, effective sample size; IPTW, inverse probability of treatment weighting; LDH, lactate dehydrogenase; LOT, lines of therapy; POD24, disease progression occurring within 24 months of initiating first-line therapy; R², lenalidomide and rituximab.

### *Demographics and Clinical Baseline Characteristics*

- The analysis included 243 patients from EPCORE FL-1 who received epcoritamab + R² and 274 patients from COTA who received CIT for the treatment of 2L+ FL
- Patients in the CIT arm received bendamustine-based (69.3%), CHOP-based (16.4%), CVP-based (6.2%), other (6.9%), and other alkylator-based (1.1%) therapy
- Prior to IPTW adjustment, the epcoritamab + R² arm included lower proportions of older patients, lower proportions of Hispanic/Latino patients, higher proportions of patients with elevated lactate dehydrogenase (LDH), and higher proportions of patients with 2+ prior lines of therapy than the CIT arm, but the arms were balanced after weighting
  - Before weighting, the epcoritamab + R² cohort was more heavily pretreated and had higher LDH

### *Comparative Efficacy*

- Epcoritamab + R² showed improved response, durability, and survival compared with CIT

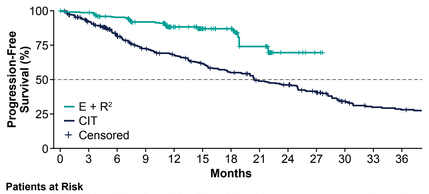
#### IPTW-Adjusted ORR and CRR Were Higher With Epcoritamab + R² vs CIT




CIT, chemoimmunotherapy; CRR, complete response rate; IPTW, inverse probability of treatment weighting; ORR, overall response rate; R², lenalidomide and rituximab; RR, relative risk.

### *Comparative Efficacy, continued*

#### IPTW-Adjusted PFS Was Improved With Epcoritamab + R² vs CIT



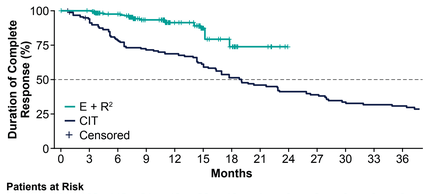

| Adjusted PFS | Epcoritamab + R² (n=243, ESS=199) | CIT (n=274, ESS=220) |
|---|---|---|
| Median (95% CI), months | NE | 20.4 (17.4–25.9) |
| HR (95% CI), *P* value | 0.33 (0.21–0.50), *P*<.0001 | |
| 16-month rate (95% CI), % | 86.9 (82.1–92.1) | 58.4 (51.5–66.3) |

| Patients at Risk | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| E + R² | 227 | 223 | 206 | 171 | 107 | 73 | 59 | 24 | 4 | 1 | 0 | 0 | 0 |
| CIT | 269 | 226 | 170 | 144 | 130 | 115 | 102 | 85 | 80 | 67 | 48 | 40 | 37 |

CIT, chemoimmunotherapy; E, epcoritamab; ESS, effective sample size; IPTW, inverse probability of treatment weighting; NE, not estimable; PFS, progression-free survival; HR, hazard ratio; R², lenalidomide and rituximab.

- After IPTW-adjustment, patients receiving epcoritamab + R² had improved PFS compared with CIT and had 67% reduction in the risk of progression or death

#### IPTW-Adjusted DOCR Was Improved With Epcoritamab + R² vs CIT



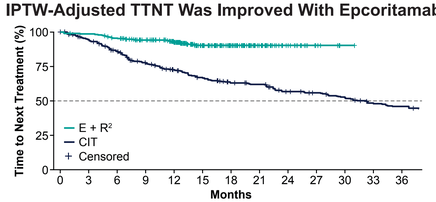

| Adjusted DOCR | Epcoritamab + R² (n=243, ESS=199) | CIT (n=274, ESS=220) |
|---|---|---|
| Median (95% CI), months | NE | 19.0 (15.0–28.0) |
| HR (95% CI), *P* value | 0.28 (0.14–0.55), *P*<.001 | |
| 16-month rate (95% CI), % | 79.3 (64.9–96.9) | 58.3 (47.4–71.6) |

| Patients at Risk | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| E + R² | 191 | 182 | 142 | 81 | 48 | 26 | 13 | 4 | 0 | 0 | 0 | 0 | 0 |
| CIT | 150 | 78 | 65 | 59 | 57 | 50 | 42 | 38 | 34 | 32 | 28 | 26 | 25 |

CIT, chemoimmunotherapy; DOCR, duration of complete response; E, epcoritamab; ESS, effective sample size; HR, hazard ratio; IPTW, inverse probability of treatment weighting; NE, not estimable; R², lenalidomide and rituximab.

- After IPTW-adjustment, patients receiving epcoritamab + R² had improved duration of response (DOR) (accessible in the Supplemental Materials via the QR code) and duration of complete response (DOCR) compared with CIT and had:
  - 74% reduction in risk of loss of response or mortality
  - 72% reduction in risk of loss of complete response (CR) or mortality

#### IPTW-Adjusted TTNT Was Improved With Epcoritamab + R² vs CIT

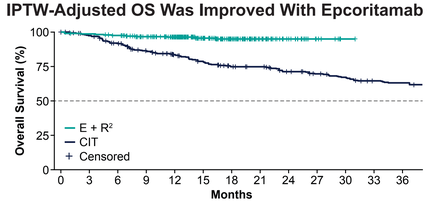



| Adjusted TTNT | Epcoritamab + R² (n=243, ESS=199) | CIT (n=274, ESS=220) |
|---|---|---|
| Median (95% CI), months | NE | 32.3 (25.7–41.5) |
| HR (95% CI), *P* value | 0.22 (0.13–0.37), *P*<.0001 | |
| 16-month rate (95% CI), % | 90.4 (86.2–94.7) | 64.7 (58.4–71.7) |

| Patients at Risk | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| E + R² | 227 | 223 | 213 | 188 | 163 | 97 | 68 | 31 | 15 | 5 | 1 | 0 | 0 |
| CIT | 269 | 249 | 223 | 195 | 176 | 160 | 145 | 138 | 121 | 115 | 108 | 96 | 91 |

CIT, chemoimmunotherapy; E, epcoritamab; ESS, effective sample size; HR, hazard ratio; IPTW, inverse probability of treatment weighting; NE, not estimable; R², lenalidomide and rituximab; TTNT, time to next treatment.

#### IPTW-Adjusted OS Was Improved With Epcoritamab + R² vs CIT




| Adjusted OS | Epcoritamab + R² (n=243, ESS=199) | CIT (n=274, ESS=220) |
|---|---|---|
| Median (95% CI), months | NE | 60.7 (44.5–90.2) |
| HR (95% CI), *P* value | 0.18 (0.09–0.38), *P*<.0001 | |
| 16-month rate (95% CI), % | 95.6 (92.6–98.7) | 76.4 (70.7–82.5) |

| Patients at Risk | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| E + R² | 227 | 223 | 217 | 194 | 170 | 103 | 70 | 33 | 16 | 6 | 1 | 0 | 0 |
| CIT | 269 | 257 | 239 | 216 | 198 | 184 | 169 | 164 | 150 | 141 | 135 | 126 | 123 |

CIT, chemoimmunotherapy; E, epcoritamab; ESS, effective sample size; HR, hazard ratio; IPTW, inverse probability of treatment weighting; NE, not estimable; OS, overall survival; R², lenalidomide and rituximab.

- After IPTW-adjustment, patients receiving epcoritamab + R² had improved overall survival compared with CIT and had 82% reduction in mortality risk