IBCL-278

Epcoritamab With Rituximab + Lenalidomide (R^2) in Previously Untreated (1L) Follicular Lymphoma (FL) and Epcoritamab Maintenance Therapy in FL: EPCORE NHL-2 Arms 6 and 7

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OBJECTIVE

- To assess the long-term safety and efficacy of first-duration epcoritamab + R^2 in 1L FL (updated data from arm 6) and single-agent epcoritamab as maintenance treatment after SOC in FL (first disclosure of arm 7)

CONCLUSIONS

- Longer follow-up showed that fixed-duration epcoritamab + R^2 in previously untreated FL leads to deep and durable responses that translate to favorable long-term outcomes
  - ORR 95%, CR rate 85%
  - At 18 months, an estimated 90% of patients remained progression free and alive
- First disclosure of a CD3xCD20 bispecific antibody as maintenance therapy in patients with FL (epcoritamab given Q8W for up to 2 years after 1–2 lines of SOC treatment) shows the regimen was well tolerated with no new safety signals and led to deepening responses
  - 100% of partial responses converted to complete responses, most by first assessment (around week 12)
- Results support the continued evaluation of epcoritamab-based, chemotherapy-free regimens in FL; two phase 3 trials are actively enrolling
  - EPCORE FL-1, epcoritamab + R^2 vs R^2 alone in relapsed or refractory FL (NCT05409066)
  - EPCORE FL-2, epcoritamab + R^2 vs chemoimmunotherapy or R^2 alone in previously untreated FL (NCT06191744)

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Abbreviations

1L, previously untreated; AE, adverse event; ASCT, autologous stem cell transplant; C, cycle; CMV, cytomegalovirus; CR, complete response; CRS, cytokine release syndrome; CT, computed tomography; d, day(s); DOCR, duration of complete response; DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; FL, follicular lymphoma; FLIPI, Follicular Lymphoma International Prognostic Index; ICANS, immune effector cell–associated neurotoxicity syndrome; IR, indeterminate response; IV, intravenous; mAb, monoclonal antibody; mo, month(s); MRI, magnetic resonance imaging; ORR, overall response rate; OS, overall survival; PD, progressive disease; PFS, progression-free survival; PR, partial response; QD, every day; QW, every week; Q4W, every 4 weeks; R^2, rituximab + lenalidomide; SC, subcutaneous; SD, stable disease; SOC, standard of care; SUD, step-up dose; SUD 1, first step-up dose; SUD 2, second step-up dose; TEAE, treatment-emergent adverse event; wk, week(s); y, year(s).

Disclosures

Falchi: AbbVie, Genentech: Consultancy, Honoraria. Membership on an Entity's Board of Directors or Advisory Committees, Research Funding; Evolveimmune, Genmab, Roche: Consultancy, Honoraria, Research Funding; Kaplan: CME Presentation: Projects in Knowledge: Memorial Sloan Kettering Cancer Center: Current Employment; Sanofi: Honoraria; Taylor & Francis: Journal Editor; ADC Therapeutics, Ipsen, Seagen: Membership on an Entity's Board of Directors or Advisory Committees; BeiGene, Innate: Research Funding. **Vermaat:** Servier, Bristol Myers Squibb, Janssen, Takeda, AbbVie, Incyte, Genmab: Consultancy, Honoraria, Advisory Board. **Nijland:** AbbVie: Advisory Board; Nordic Nanovector, Takeda: Research Funding. **Christensen:** Takeda: Research Funding. **Offner:** There are no relationships to disclose. **Leslie:** AbbVie, ADC Therapeutics, AstraZeneca, BeiGene, BMS, Lilly, Epizyme, Genmab, Janssen, Kiyoypharm, Kite, Merck, Pharmacyclics, Seagen: Consultancy. **Brody:** ADC Therapeutics, Epizyme, Seagen: Advisory Board; BMS, Genentech, GlaxoSmithKline, Merck: Research Funding. **Hoehn:** Genmab: Current Employment. **Marek:** Genmab: Current Employment. **Wang:** Genmab: Current Employment. **Mei:** AbbVie: Current Employment. **Belada:** AbbVie, BMS, Genmab, Gilead, MorphoSys, Roche, Sobi, Takeda: Consultancy, AbbVie, Gilead, Janssen, MorphoSys, Roche, Takeda: Honoraria; AbbVie, Recordati, Roche: Travel Expenses/Accommodations. **Abrisqueta:** AbbVie, AstraZeneca, BMS, Janssen: Consultancy, Speakers Bureau.

BACKGROUND

- Most patients with advanced 1L FL are not cured[1]:
  - R^2 is a recommended treatment that has shown improved outcomes compared with rituximab alone,[2] and outcomes are comparable with rituximab + chemotherapy (CR rates, ~50%)[3,4]
  - Outcomes are still suboptimal, and novel, chemotherapy-free combinations that induce deep and durable responses translating to favorable long-term outcomes in a larger proportion of patients with 1L FL are needed[5]
- Anti-CD20 maintenance therapy (up to 2 y) is a consideration for advanced FL after response to induction therapy; however, no OS benefit was reported[6,7]:
  - A safe, novel maintenance approach that deepens responses or improves durability of initial responses may provide long-term survival benefit

STUDY DESIGN: EPCORE® NHL-2 Arms 6 (1L FL) and 7 (FL Maintenance After SOC)

A phase 1b/2, open-label trial evaluating the safety and antitumor activity of fixed-duration epcoritamab + R^2 in adults with previously untreated FL (arm 6) and fixed-duration epcoritamab maintenance after SOC in patients with FL (arm 7)

Key inclusion criteria
- 1L CD20$^+$ FL
  - Grade 1, 2, or 3A
- ECOG PS 0–2
- Measurable disease by CT or MRI
- Adequate organ function

Key inclusion criteria
- CD20$^+$ FL
  - Grade 1, 2, or 3A
- In CR or PR after 1–2 lines of SOC treatment
- ECOG PS 0–2
- Adequate organ function

Step-up dosing[a]

Arm 6 (1L FL) expansion, N=41

Epcoritamab (SC) 48 mg	Rituximab (IV) 375 mg/m^2	Lenalidomide (oral) 20 mg
QW C1–2, Q4W C3+ (28 d/C) Treatment up to 2 y	QW C1, Q4W C2–6	QD for 21 d in C1–12

Data cutoff: January 31, 2024
Median follow-up: 22.8 mo
- **Primary objective:** Antitumor activity (ORR)[b]
- **Key secondary endpoints:** Safety/tolerability, DOR, DOCR, PFS, OS

Arm 7 (FL maintenance after SOC treatment) expansion, N=20

Epcoritamab (SC) 48 mg
QW C1 (28 d), Q8W C2–13 (56 d/C) Treatment up to 2 y

Data cutoff: January 31, 2024
Median follow-up: 22.1 mo
- **Primary objective:** Safety/tolerability
- **Key secondary endpoints:** CR rate,[c] DOCR

[a]SUD 1: priming, 0.16 mg; SUD 2: intermediate, 0.8 mg. [b]Radiographic disease evaluation was performed every 12 wk until CR, then every 24 wk until disease progression. [c]Radiographic disease evaluation was performed every 12 wk for the first 24 wk (12 and 24 wk), then every 24 wk until disease progression. ClinicalTrials.gov: NCT04663347. EudraCT: 2020-000845-15.

RESULTS

Arm 6 (1L FL): Baseline Characteristics, Treatment Exposure, and Follow-Up

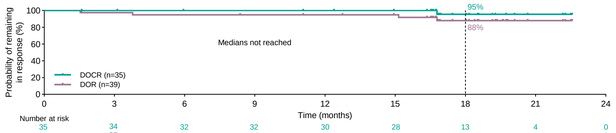
Characteristic	N=41
Median age, y (range)	57 (39–78)
Male, n (%)	21 (51)
Ann Arbor stage, n (%)[a]	
III	16 (39)
IV	22 (54)
FLIPI, n (%)[b]	
2	15 (37)
3–5	14 (34)
ECOG PS, n (%)	
0	34 (83)
1	6 (15)
2	1 (2)

Treatment Exposure and Follow-Up	N=41
Median follow-up, mo (range)	22.8 (1.4+ to 25.6)
Epcoritamab treatment exposure[c]	
Median number of treatment cycles initiated (range)[d]	23 (1–27)
Median duration of treatment, mo (range)	22.0 (0.5–24.2)
Ongoing treatment, n (%)	12 (29)
Completed treatment per protocol, n (%)	14 (34)
Discontinued treatment, n (%)	15 (37)
AE	9 (22)
Patient withdrawal	2 (5)
PD	1 (2)
Other[e]	3 (7)

[a]Ann Arbor stage was I–II in 3 patients. [b]FLIPI was 0–1 in 12 patients. [c]Median time from diagnosis to first dose was 11.6 wk (range, 2.3–352). [d]Patients initiated a median of 6 cycles of rituximab (range, 1–6) and 12 cycles of lenalidomide (range, 1–12). [e]Other reasons for treatment discontinuation were maximum clinical benefit, complications from infection, and COVID-19 (n=1 each).

Arm 6 (1L FL): Epcoritamab + R^2 Continued to Show Deep, Durable Responses

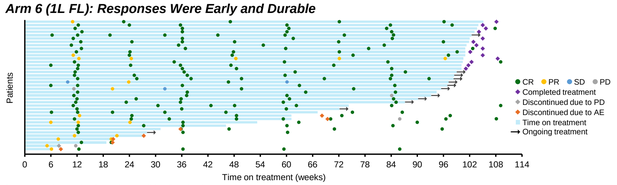
	N=41[a]
Overall response, n (%)	39 (95)
Complete response, n (%)	35 (85)
Partial response, n (%)	4 (10)
Progressive disease, n	0
Median time to response, mo (range)	2.7 (1.2–5.5)
Median time to complete response, mo (range)	2.8 (1.4–11.4)



Kaplan–Meier estimates of DOR and DOCR assessed by investigator. [a]A total of 2 patients were not evaluable.

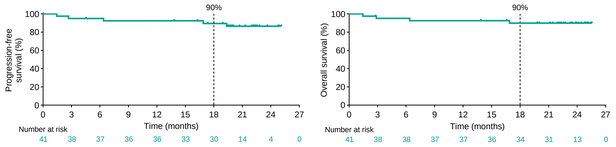
- High rates of patients remaining in response and complete response were observed at 18 months

Arm 6 (1L FL): Responses Were Early and Durable



Per protocol, patients continued to receive scans if they discontinued treatment for reasons other than PD.

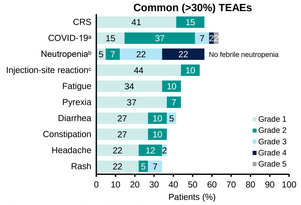
Arm 6 (1L FL): Progression-Free and Overall Survival



Kaplan–Meier estimate of progression-free survival assessed by investigator.

- High rates of progression-free and overall survival were observed at 18 months

Arm 6 (1L FL): Safety Was Consistent With Prior Reports

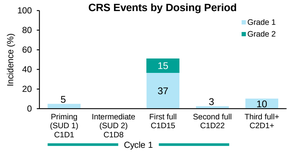


[a]Combined term includes COVID-19, COVID-19 pneumonia, and post-acute COVID-19 syndrome. [b]Combined term includes neutropenia and decreased neutrophil count. [c]Combined term includes injection-site reaction, erythema, rash, pain, hypersensitivity, and swelling.

- Common TEAEs were mostly low grade
- TEAEs leading to epcoritamab discontinuation were COVID-19 (n=5), CMV reactivation (n=1), ovarian epithelial cancer and pleural effusion (n=1), pneumonitis (n=1), and toxic skin eruption (n=1)
  - Pleural effusion and ovarian epithelial cancer were not deemed to be related to epcoritamab by the investigator
- Fatal TEAEs were COVID-19 pneumonia and septic shock (n=1 each)
- There is an increased risk of morbidity and mortality due to infections for patients with hematologic malignancies being treated with B-cell–depleting therapies

Arm 6 (1L FL): CRS Was Low Grade and Consistent With Prior Reports, With Predictable Timing

	N=41
CRS, n (%)[a]	23 (56)
Grade 1	17 (41)
Grade 2	6 (15)
Median time to onset after first full dose, d (range)	2 (1–6)
CRS resolution, n/n (%)	23/23 (100)
Median time to resolution,[b] d (range)	3 (1–6)
Treated with tocilizumab, n (%)	4 (10)
Leading to epcoritamab discontinuation, n (%)	**0**



[a]Graded by Lee et al 2019 criteria. [b]Median is based on longest CRS duration in patients with >1 CRS event.

- CRS timing was predictable; CRS events were primarily confined to cycle 1
- CRS events were low grade and resolved
- No ICANS or clinical tumor lysis syndrome

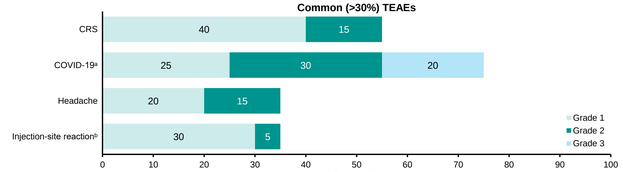
Arm 7 (FL Maintenance After SOC): Baseline Characteristics, Treatment History, Exposure, and Follow-Up

Characteristic	N=20
Median age, y (range)	54.5 (31–78)
Male, n (%)	11 (55)
FLIPI, n (%)[a]	
2	3 (15)
3–5	5 (25)
ECOG PS, n (%)	
0	17 (85)
1	3 (15)
Treatment History	**N=20**
Median time from end of SOC therapy to first dose, mo (range)	2.5 (0.7–6.0)
Median time from end of last anti-CD20 therapy to first dose, mo (range)	2.9 (1.2–9.7)
SOC line of therapy, n (%)[b]	
First line	16 (80)
Second line	3 (15)
Prior ASCT, n (%)	1 (5)
Best response to SOC therapy, n (%)	
Complete response	12 (60)
Partial response	8 (40)
Treatment Exposure and Follow-Up	**N=20**
Median follow-up, mo (range)	22.1 (5.8+ to 23.5)
Epcoritamab treatment exposure[c]	
Median number of treatment cycles initiated (range)	9.5 (2–13)
Median duration of treatment, mo (range)	19.7 (1.0–23.1)
Ongoing treatment, n (%)	8 (40)
Completed treatment per protocol, n (%)	4 (20)
Discontinued treatment, n (%)	8 (40)
AE	3 (15)
Patient withdrawal	3 (15)
PD	2 (10)

[a]FLIPI was 0–1 in 10 patients and unknown in 2 patients. [b]One patient came on to trial with SOC in the fourth line, noted as a protocol deviation. [c]Median time from diagnosis to first dose was 10.1 mo (range, 5.3–260).

- Prior SOC treatments included anti-CD20 mAb–containing regimens (100%), alkylating agent–containing regimens (80%), anthracyclines (50%), and others (75%)

Arm 7 (FL Maintenance After SOC): No New Safety Signals With Extended Q8W Dosing

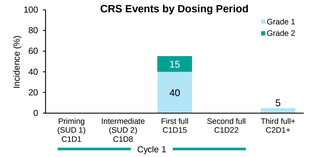


[a]Combined term includes COVID-19, COVID-19 pneumonia, and post-acute COVID-19 syndrome. [b]Combined term includes injection-site reaction, erythema, extravasation, and swelling.

- Common TEAEs were mostly low grade
- TEAEs leading to epcoritamab discontinuation were myelodysplastic syndrome and respiratory failure (n=1 each)
  - Myelodysplastic syndrome was not deemed to be related to epcoritamab by the investigator
- One fatal TEAE occurred (respiratory failure, post-acute COVID syndrome after 2 cycles of epcoritamab)

Arm 7 (FL Maintenance After SOC): CRS Was Low Grade, Mostly Confined to the C1D15 Dose, and Not Observed With Extended Q8W Dosing

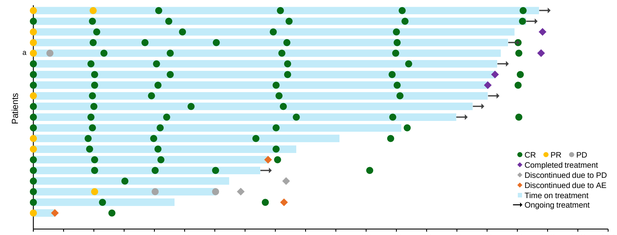
	N=20
CRS, n (%)[a]	11 (55)
Grade 1	8 (40)
Grade 2	3 (15)
Median time to onset after first full dose, d (range)	2 (1–3)
CRS resolution, n/n (%)	11/11 (100)
Median time to resolution,[b] d (range)	2 (1–8)
Treated with tocilizumab, n (%)	1 (5)
Leading to epcoritamab discontinuation, n (%)	**0**



[a]Graded by Lee et al 2019 criteria. [b]Median is based on longest CRS duration in patients with >1 CRS event.

- CRS timing was predictable; events were primarily confined to cycle 1, and all were low grade and resolved
- No ICANS or clinical tumor lysis syndrome

Arm 7 (FL Maintenance After SOC): Onset and Durability of Responses



Per protocol, patients continued to receive scans if they discontinued treatment for reasons other than PD. [a]PD shown was confirmed as a pseudoprogression (IR1) by investigator.

- All 8 patients enrolling with partial response (100%) converted to complete response; 6/8 conversions occurred by the first assessment (around week 12)
- An estimated 83% of patients remained in response and an estimated 90% of patients remained alive at 21 months

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