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Subcutaneous epcoritamab with rituximab + lenalidomide (R^2) in patients (pts) with relapsed or refractory (R/R) follicular lymphoma (FL): update from phase 1/2 trial

Lorenzo Falchi, MD,[1]* Sirpa Leppä, MD,[2] Björn E. Wahlin, MD, PhD,[3] Marcel Nijland, MD, PhD,[4] Jacob Haaber Christensen, MD, PhD,[5] Sven de Vos, MD, PhD,[6] Harald Holte, MD, PhD,[7] Kim M. Linton, MBChB, PhD,[8] Aqeel Abbas, MS,[9] Liwei Wang, PhD,[9] Minh Dinh, MD,[10] Brian Elliott, MD,[9] David Belada, MD, PhD[11]

[1]Lymphoma Service, Memorial Sloan Kettering Cancer Center, New York, NY, USA; [2]Helsinki University Hospital Comprehensive Cancer Center and University of Helsinki, Helsinki, Finland; [3]Karolinska Institutet, Stockholm, Sweden; [4]University Medical Center Groningen and University of Groningen, Groningen, Netherlands; [5]Odense University Hospital, Odense, Denmark; [6]Ronald Reagan University of California Los Angeles Medical Center, Los Angeles, CA, USA; [7]Oslo University Hospital and KG Jebsen Center for B-cell Malignancies, Oslo, Norway; [8]The Christie NHS Foundation Trust and Manchester Cancer Research Centre, Manchester, UK; [9]Genmab, Princeton, NJ, USA; [10]AbbVie, North Chicago, IL, USA; [11]4th Department of Internal Medicine – Hematology, University Hospital and Faculty of Medicine, Hradec Králové, Czech Republic

*Email address for questions: falchil@mskcc.org

Objectives

- The EPCORE NHL-2 trial (phase 1/2; NCT04663347) is evaluating epcoritamab combined with different standard of care therapies in patients with B-cell NHL
- To present data from epcoritamab + R^2 in patients with R/R FL

Conclusions

- Epcoritamab + R^2 showed encouraging responses, with all patients in arm 2a achieving a response:
  - ORR 100%; CMR 96%
- Based on response rates at week 6, patients in arm 2b showed similarly encouraging efficacy
- Epcoritamab + R^2 demonstrated a manageable safety profile
  - Mainly low-grade CRS; all CRS resolved
  - One ICANS event (grade 2, resolved)
- These updated data support further exploration of epcoritamab + R^2 in patients with R/R FL

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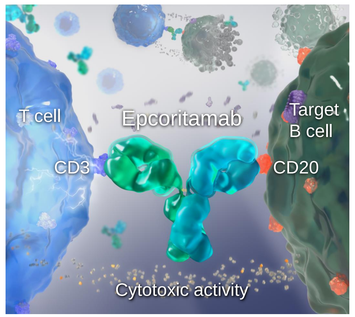
Background



- Despite treatment advances, FL remains incurable, and most patients will eventually experience disease progression[1-3]
- R/R FL becomes more aggressive with each line of therapy, and the choice of treatment varies widely; better treatment options are needed[1-3]
- Epcoritamab (DuoBody®-CD3xCD20) is a subcutaneously administered bispecific antibody that binds to CD3 on T cells and CD20 on B cells to induce T-cell–mediated killing of CD20+ malignant B cells[4,5]
- Single-agent epcoritamab had substantial antitumor activity in patients with heavily pretreated B-cell NHL in the dose-escalation portion of the first-in-human phase 1/2 trial (EPCORE NHL-1)[6]
- Epcoritamab is well suited for combination therapy due to its mechanism of action, distinct from that of the components of the R^2 regimen[4,7,8]

Study Design: EPCORE NHL-2 Arm 2

Arm 2 of EPCORE NHL-2, a phase 1b/2, open-label, multicenter trial, is evaluating the safety and antitumor activity of SC epcoritamab + standard R^2 for 12 cycles of 28 days, followed by epcoritamab monotherapy for a total of 2 years, in adults with R/R FL[a]

Key inclusion criteria
- R/R CD20+ FL
  - Grade 1, 2, or 3A
  - Stage II–IV
- Need for treatment based on symptoms or disease burden, as determined by GELF criteria[9]
- ECOG PS 0–2
- Measurable disease by CT or MRI
- Adequate organ function

Dose escalation, n=6

Step-up dosing

Cohort 2a
Epcoritamab (SC) 24 mg (n=3) or 48 mg (n=3)
QW C1–3, Q2W C4–9, Q4W C10+
+ R^2
C1–12

Expansion, n=68

Step-up dosing

Cohort 2a
Epcoritamab (SC) 48 mg
QW C1–3, Q2W C4–9, Q4W C10+
+ R^2
C1–12

Cohort 2b
Epcoritamab (SC) 48 mg
QW C1–2, Q4W C3+
+ R^2
C1–12

Data cutoff: March 25, 2022
Median follow-up for arm 2a: 8.6 mo

Primary objectives: DLT/Safety and tolerability
Key secondary objective: Antitumor activity[b]

Primary objective: Antitumor activity[b]
Treatment up to 2 years

[a]Patients received SC epcoritamab with step-up dosing (ie, priming and intermediate doses before first full dose) and corticosteroid prophylaxis as previously described[1] to mitigate CRS. Epcoritamab was administered in 28-d cycles as shown. Rituximab regimen: 375 mg/m^2 IV QW in C1 and Q4W in C2–5; lenalidomide regimen: 20 mg QD (oral administration) for 21 d in C1–12. [b]Tumor response was evaluated by PET-CT obtained at 6, 12, 18, 24, 36, and 48 wk, and every 24 wk thereafter, until disease progression. Lugano criteria and LYRIC were used to assess response. AEs were graded by CTCAE v5.0; CRS was evaluated by Lee et al[10] criteria. ClinicalTrials.gov Identifier: NCT04663347.

Results

Baseline Demographics, Characteristics, and Prior Therapies

Characteristic	Arm 2a N=30	Arm 2b N=44
Median age, y (range)	68 (42–80)	66 (30–79)
Female, n (%)	17 (57)	22 (50)
Ann Arbor stage, n (%)[a]		
II	3 (10)	2 (5)
III	6 (20)	14 (32)
IV	21 (70)	27 (61)
Histologic grade, n (%)[b]		
1	4 (13)	3 (7)
2	20 (67)	21 (48)
3A	5 (17)	14 (32)
FLIPI, n (%)[c]		
0–1	2 (7)	1 (2)
2	8 (27)	11 (25)
3–5	20 (67)	20 (45)
Median time from diagnosis to first dose, mo (range)	89 (6–281)	73 (4–331)
Median number of prior lines of therapy (range)	1 (1–5)	2 (1–9)
1 prior line, n (%)	18 (60)	20 (45)
2 prior lines, n (%)	5 (17)	13 (30)
≥3 prior lines, n (%)	7 (23)	9 (20)
Primary refractory disease, n (%)[d]	9 (30)	12 (27)
Progressed within 24 mo of initial therapy, n (%)	12 (40)	19 (43)
Refractory to last line of therapy, n (%)[d]	8 (27)	12 (27)
Median time from end of last line of therapy to first dose, mo (range)	31 (1–213)	17 (2–198)

Data cutoff: March 25, 2022. [a]Ann Arbor stage was missing for 1 patient in arm 2b. [b]Histologic grade was unknown or missing for 1 patient in arm 2a and 6 patients in arm 2b. [c]FLIPI was unknown for 12 patients in arm 2b. [d]Refractory indicates no response or relapse within 6 mo after therapy.

- Overall, arm 2b patients were later line (median of 2 prior lines vs 1 in arm 2a) with higher ECOG PS (0/1/2, 61%/32%/7% vs 73%/27%/0% in arm 2a) and shorter median time since last therapy (17 mo vs 31 mo in arm 2a)

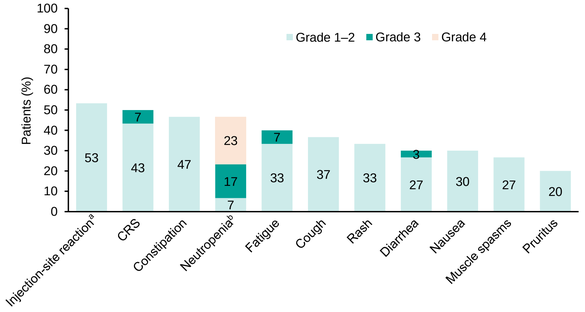
Follow-Up and Treatment Exposure in Arm 2a

	Arm 2a N=30
Median follow-up, mo (range)[a]	8.6 (3.3–14.6)
Ongoing treatment, n (%)	23 (77)
Discontinued treatment, n (%)	7 (23)
Treatment exposure	
Median number of epcoritamab 28-d cycles initiated (range)	10 (1–14)
Median duration of treatment, mo (range)	8.5 (0.3–13.3)
Patients with epcoritamab dose delay due to TEAE, n (%)	13 (43)

Data cutoff: March 25, 2022. [a]Median is Kaplan–Meier estimate.

- Additional patients enrolled with the arm 2b schedule (median [range] follow-up, 2.2 [0–4.7] mo; median [range] duration of treatment, 2.1 [0.03–4.5] mo)

Treatment-Emergent Adverse Events (≥20%) by Grade in Arm 2a



Data cutoff: March 25, 2022. [a]Combined term includes injection-site erythema, pain, rash, and reaction. [b]Combined term includes neutropenia and neutrophil count decreased; 1 patient (3%) had febrile neutropenia (grade 3).

- **Arm 2a:** Based on follow-up (median 8.6 mo) for patients in arm 2a:
  - Two patients had TEAEs that led to discontinuation of epcoritamab: one patient had cellulitis not related to epcoritamab; the other had CRS, flatulence, and generalized edema (related to epcoritamab), as well as agitation and mania (not related to epcoritamab)
  - One patient (3%) had ICANS (grade 2), which resolved in 4 days and did not lead to epcoritamab discontinuation
  - No fatal TEAEs were reported
- **Arm 2b:** Based on initial data and limited follow-up (median 2.2 mo) for patients in arm 2b, AE incidences are not reported, but no new safety signals were observed

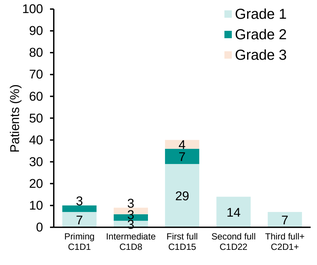
CRS Graded by Lee et al[10] 2019 Criteria in Arm 2a

	Arm 2a N=30
CRS, n (%)	15 (50)
Grade 1	9 (30)
Grade 2	4 (13)
Grade 3	2 (7)
CRS resolution, n (%)	15 (100)
Median time to resolution, d (range)[a]	4 (1–15)
CRS leading to treatment discontinuation, n (%)	1 (3)
Tocilizumab use, n (%)	3 (10)

Data cutoff: March 25, 2022. [a]Median is Kaplan–Meier estimate based on longest CRS duration in patients with CRS; range is defined by shortest and longest CRS duration.

- CRS was mostly low grade; all cases resolved

CRS Events by Dosing Period in Arm 2a



Data cutoff: March 25, 2022. Priming dose: n=30; intermediate dose: n=29; first full dose and later: n=28.

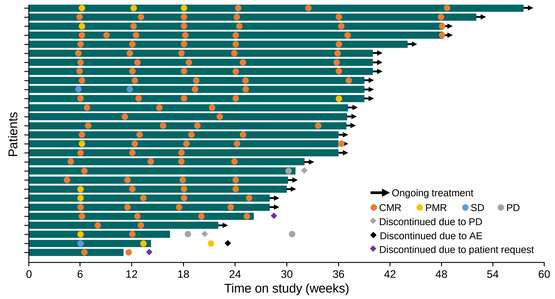
- CRS occurrence was predictable; most cases occurred following the first full dose with a median time to onset of 2 days (range, 1–5)

Best Overall Responses at Any Time and at 6 Weeks (First Assessment)

Response, n (%)[a]	At any time Arm 2a n=28[b]	At 6 weeks Arm 2a n=27	At 6 weeks Arm 2b n=28
Overall response	28 (100)	25 (93)	26 (93)
CMR	27 (96)	19 (70)	17 (61)
PMR	1 (4)	6 (22)	9 (32)
Stable disease	0	2 (7)	1 (4)
Progressive disease	0	0	1 (4)

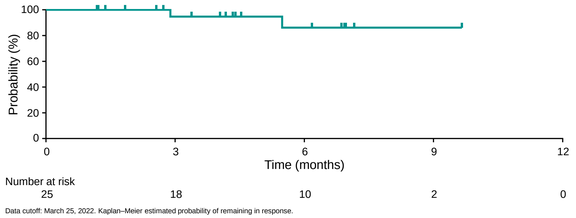
Data cutoff: March 25, 2022. [a]Based on modified response-evaluable population, defined as patients with ≥1 target lesion at baseline and ≥1 postbaseline response evaluation and patients who died within 60 d of first dose. [b]Excludes 2 patients who discontinued before first assessment.

Response Profile for Arm 2a



Data cutoff: March 25, 2022. Per protocol, patients continued to receive scans if they discontinued treatment for reasons other than PD.

Duration of Response for Arm 2a (48 mg)



Data cutoff: March 25, 2022. Kaplan–Meier estimated probability of remaining in response.

References

1. Matasar MJ, et al. *Oncologist*. 2019;24:e1236-50. **2.** Casulo C, et al. *Ann Oncol*. 2017;28:2094-106. **3.** Rivas-Delgado A, et al. *Br J Haematol*. 2019;184:753-9. **4.** Engelberts PJ, et al. *EBioMedicine*. 2020;52:102625. **5.** van der Horst HJ, et al. *Blood Cancer J*. 2021;11:38. **6.** Hutchings M, et al. *Lancet*. 2021;398:1157-69. **7.** Chiu CW, et al. AACR 2021. Abstract 1574. **8.** Linton KM, et al. ASH 2021. Abstract 3535. **9.** Brice P, et al. *J Clin Oncol*. 1997;15:1110-7. **10.** Lee DW, et al. *Biol Blood Marrow Transplant*. 2019;25:625-38.

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