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Epcoritamab + R² Regimen and Responses in Patients With High-Risk Follicular Lymphoma, Regardless of POD24 Status

Reid W. Merryman, MD,[1] David Belada, MD, PhD,[2] Anna Sureda, MD, PhD,[3] Sirpa Leppä, MD, PhD,[4] Joost S.P. Vermaat, MD, PhD,[5] Harald Holte, MD, PhD,[6] Martin Hutchings, MD, PhD,[7] Pieternella Lugtenburg, MD, PhD,[8] Sven de Vos, MD, PhD,[9] Pau Abrisqueta, MD, PhD,[10] Marcel Nijland, MD, PhD,[11] Jacob Haaber Christensen, MD, PhD,[12] Björn E. Wahlin, MD, PhD,[13] Kim M. Linton, MBChB, PhD,[14] Liwei Wang, PhD,[15] Aqeel Abbas, MS,[15] Ali Rana, MD, PhD,[15] Syed Quadri, PharmD,[16] Lorenzo Falchi, MD[17]

[1]Dana-Farber Cancer Institute, Boston, MA; USA; [2]4th Department of Internal Medicine – Hematology, University Hospital and Faculty of Medicine, Hradec Králové, Czech Republic; [3]Institut Català d'Oncologia, Hospital Duran i Reynals, IDIBELL, Universitat de Barcelona, L'Hospitalet de Llobregat, Barcelona, Spain; [4]University of Helsinki and Helsinki University Hospital Comprehensive Cancer Center, Helsinki, Finland; [5]Leiden University Medical Center, Leiden, Netherlands; [6]Oslo University Hospital and KG Jebsen Center for B-cell Malignancies, Oslo, Norway; [7]Rigshospitalet, Copenhagen University Hospital, Copenhagen, Denmark; [8]On behalf of the Lunenburg Lymphoma Phase I/II Consortium-HOVON/LLPC, Erasmus MC Cancer Institute, University Medical Center, Department of Hematology, Rotterdam, Netherlands; [9]Ronald Reagan University of California Los Angeles Medical Center, Los Angeles, CA, USA; [10]Hospital Universitario Vall d'Hebron, Barcelona, Spain; [11]University Medical Center Groningen and University of Groningen, Groningen, Netherlands; [12]Odense University Hospital, Odense, Denmark; [13]Karolinska Institutet, Stockholm, Sweden; [14]The Christie NHS Foundation Trust and Manchester Cancer Research Centre, Manchester, UK; [15]Genmab, Plainsboro, NJ, USA; [16]AbbVie, North Chicago, IL, USA; [17]Lymphoma Service, Memorial Sloan Kettering Cancer Center, New York, NY, USA

OBJECTIVE

To evaluate epcoritamab SC + R² in R/R FL, including high-risk subgroups

CONCLUSIONS

Addition of epcoritamab SC to R² drives deep and durable remissions in R/R FL patients, including POD24 and other high-risk populations

High overall response and CMR rates were observed regardless of POD24 or other high-risk features

Manageable safety profile with no new safety signals; consistent with previous reports

CRS occurrence was predictable, and events were primarily low grade

Epcoritamab SC combination regimens are being studied in the ongoing randomized, phase 3 EPCORE FL-1 trial (NCT05409066) and in a POD24 cohort in the EPCORE NHL-2 trial (NCT04663347)

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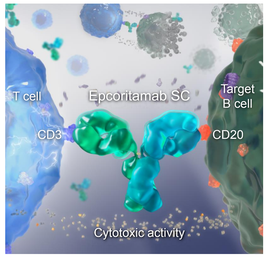
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BACKGROUND

- Follicular lymphoma (FL) is the second most common lymphoma, with a subset of patients exhibiting high-risk features associated with worse outcomes[1-4]
- Poor outcomes are seen in:
  - POD24: Patients who progress within 24 mo after first-line chemoimmunotherapy[3,4]
  - Double refractory: Patients refractory to both an anti-CD20 mAb and an alkylating agent[5,6]
- No established standard of care for POD24, as current therapeutic options provide suboptimal outcomes:
  - 5-year overall survival with POD24 versus non-POD24 is ~35%–70% versus ~90%[3,4]
  - R² in POD24: ORR ~50%–80% with a CR rate ~10%–30%[a,6,7]
  - T-cell engagers have shown improved outcomes that can be further optimized[b,8-10]
- Despite therapeutic advances, outcomes in relapsed or refractory (R/R) FL with high-risk features are suboptimal

[a]CT/MRI. [b]PET-CT.

Epcoritamab SC



- Epcoritamab is a subcutaneously (SC) administered CD3xCD20 bispecific antibody developed using the DuoBody® platform[11-14]
- Single-agent epcoritamab SC has demonstrated deep and durable responses with manageable safety in the EPCORE NHL-1 trial[14]
- Based on these data, epcoritamab SC is approved by the US FDA for the treatment of adults with R/R DLBCL, NOS, including DLBCL arising from indolent lymphoma, and HGBCL after ≥2L systemic therapy[15]
- Epcoritamab SC + R² is being assessed in the ongoing EPCORE NHL-2 trial (NCT04663347)
- Epcoritamab SC + R² have nonoverlapping modes of action[11,16]
- The immunomodulatory properties of lenalidomide may increase the therapeutic potential of epcoritamab SC[11,16]

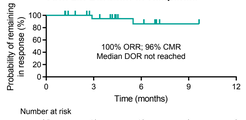
Previously Reported for Epcoritamab SC + R² in R/R FL

EPCORE™ NHL-2: A phase 1b/2, open-label trial evaluating the safety and antitumor activity of epcoritamab SC + R² in adults with R/R FL[a]

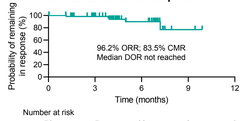
Step-up dosing → **Arm 2a** R² C1–12 + **Epcoritamab SC 48 mg** QW C1–3, Q2W C4–9, Q4W C10+ **Treatment up to 2 years**

Step-up dosing → **Arm 2b** R² C1–12 + **Epcoritamab SC 48 mg** QW C1–2, Q4W C3+ **Treatment up to 2 years**

Arm 2a: Duration of Response[17,b]



Arm 2b: Duration of Response[18,c]



[a]Patients received epcoritamab SC with step-up dosing (ie, priming and intermediate doses before first full dose), corticosteroid prophylaxis to mitigate CRS, and protocol-mandated hospitalization for 24 h after the first full dose. Epcoritamab SC was administered in 28-d cycles. Rituximab regimen: 375 mg/m² IV QW in C1 and Q4W C2–5; lenalidomide regimen: 20 mg QD (oral administration) for 21 d in C1–12. [b]Data cutoff: March 25, 2022. Median follow-up: 8.6 mo. [c]Data cutoff: October 31, 2022. Median follow-up: 5.6 mo.

STUDY DESIGN AND PATIENT DISPOSITION

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[19]
- ECOG PS 0–2
- Measurable disease by CT or MRI
- Adequate organ function

Data cutoff: January 31, 2023
Median follow-up: 11.4 mo
Primary objectives: Safety and antitumor activity[9]

Epcoritamab SC 48 mg (N=111)

High risk
[Patients could be counted in ≥1 high-risk subgroup]

POD24[a] (n=42)	Primary refractory[b] (n=38)	Refractory[b] to prior anti-CD20 (n=48)	Double refractory[b,c] (n=37)	High FLIPI (3–5; n=64)

POD24[a] 2L[d] (n=23)	POD24[a] 3L+[e] (n=19)

Non–high risk[f] (n=21)

- First pooled analysis for epcoritamab SC + R² in R/R FL patients

[a]POD24: Progression within 2 y of initiating first-line treatment that included chemoimmunotherapy. [b]Refractory: No response or relapse within 6 mo after therapy. [c]Double refractory: Refractory to both anti-CD20 and an alkylating agent. [d]Patients received epcoritamab SC in second line. [e]Patients received epcoritamab SC in third line or beyond. [f]Non–high risk: Patients who do not meet criteria for any of the predefined high-risk factors (eg, POD24, primary refractory, refractory to prior anti-CD20, double refractory, and high FLIPI). [g]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.

RESULTS

Baseline Characteristics

	Total N=111
Median age, y (range)	65 (30–80)
Female, n (%)	55 (50)
Ann Arbor stage, n (%)	
I–II	20 (18)
III	24 (22)
IV	67 (60)
Histologic grade, n (%)[a]	
1	9 (8)
2	64 (58)
3A	28 (25)
FLIPI, n (%)[b]	
0–1	13 (12)
2	34 (31)
3–5	64 (58)
ECOG PS, n (%)	
0	71 (64)
1	37 (33)
2	3 (3)
Bulky disease, n (%)	
>7 cm	32 (29)
Bone marrow involvement, n (%)[c]	
Yes	39 (35)
No	69 (62)
Beta-2 microglobulin, n (%)[d]	
High	48 (43)
Normal	53 (48)

[a]Histologic grade was unknown or missing for 10 patients. [b]FLIPI was prior to first dose on study. [c]Bone marrow involvement was missing for 3 patients. [d]Beta-2 microglobulin was missing for 10 patients.

Treatment History and Prior Systemic Therapies

Treatment History	Total N=111
Median time from diagnosis to first dose, mo (range)	63 (4–331)
Median time from end of last line of therapy to first dose, mo (range)	17 (0.6–213)
Median number of prior lines of therapy (range)	1 (1–7)
1 prior line, n (%)	63 (57)
2 prior lines, n (%)	28 (25)
≥3 prior lines, n (%)	20 (18)
Prior Systemic Therapies, n (%)	**Total N=111**
Anti-CD20	111 (100)
Alkylating agents	103 (93)
Anthracyclines	71 (64)
PI3K inhibitor	9 (8)
IMiD	5 (5)
CAR T	2 (2)

Treatment Exposure and Disposition

	Total N=111
Median follow-up, mo (range)	11.4 (2.1–22.1)
Epcoritamab SC treatment exposure	
Median number of treatment cycles initiated (range)	10 (1–25)
Median duration of treatment, mo (range)	9 (0.3–22)
Ongoing treatment, n (%)	81 (73)
Discontinued treatment, n (%)	30 (27)
AE	13 (12)
COVID-19	8 (7)
Other[a]	5 (5)
PD	12 (11)
Patient withdrawal	4 (4)
Other[b]	1 (1)

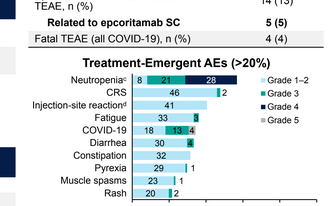
[a]Other AEs included cellulitis, colitis, dementia, mania, and neutrophil count decreased (n=1 each). Colitis and neutrophil count decreased were epcoritamab SC related. [b]Treatment-related immunosuppression and related infections outweighed the benefits of resuming treatment.

- As of data cutoff, 73% of patients continued to receive treatment

Safety Profile

	Total N=111
Grade ≥3 TEAE, n (%)	84 (76)
Related to epcoritamab SC	45 (41)
ICANS, n (%)[a]	2 (2)
Median time to resolution, d (range)[b]	5.5 (4–7)
CTLS, n (%)	0
Epcoritamab SC dose delay due to TEAE, n (%)	68 (61)
Related to epcoritamab SC	32 (29)
Epcoritamab SC discontinuation due to TEAE, n (%)	14 (13)
Related to epcoritamab SC	**5 (5)**
Fatal TEAE (all COVID-19), n (%)	4 (4)

Treatment-Emergent AEs (>20%)



[a]ICANS events were grade 1 and grade 2 (n=1 each). [b]Based on longest ICANS duration in patients with ICANS. [c]Combined term includes neutropenia and neutrophil count decreased; 4 patients (4%) had febrile neutropenia. [d]Combined term includes injection-site reaction, erythema, pain, pruritus, rash, and swelling.

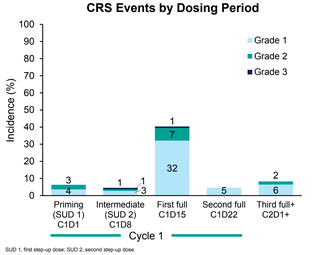
- Findings are consistent with previous reports

CRS Summary

	Total N=111
CRS, n (%)[a]	53 (48)
Grade 1	38 (34)
Grade 2	13 (12)
Grade 3	2 (2)
Median time to onset after first full dose, d (range)	2 (1–9)
CRS resolution, n (%)	53 (100)
Median time to resolution, d (range)[b]	3 (1–23)
Treated with tocilizumab, n (%)	14 (13)
Leading to epcoritamab SC discontinuation, n (%)	**0**

[a]Graded by Lee *et al* 2019 criteria. [b]Median is Kaplan–Meier estimate based on longest CRS duration in patients with CRS.

CRS Events by Dosing Period



SUD 1, first step-up dose; SUD 2, second step-up dose.

- CRS occurrence was predictable
- Majority of events were low grade
- All events resolved

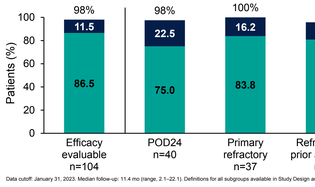
Antitumor Activity With Epcoritamab SC + R²

Response[a]	Efficacy Evaluable for Epcoritamab SC + R² n=104
Overall response	**98%**
CMR	87%
PMR	12%
Stable disease	1%
Progressive disease	1%

Data cutoff: January 31, 2023. Median follow-up: 11.4 mo (range, 2.1–22.1). [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.

- High overall response and CMR rates observed with epcoritamab SC + R²

Antitumor Activity in Subgroups



Data cutoff: January 31, 2023. Median follow-up: 11.4 mo (range, 2.1–22.1). Definitions for all subgroups available in Study Design and Patient Disposition.

- High overall response and CMR rates regardless of subgroup

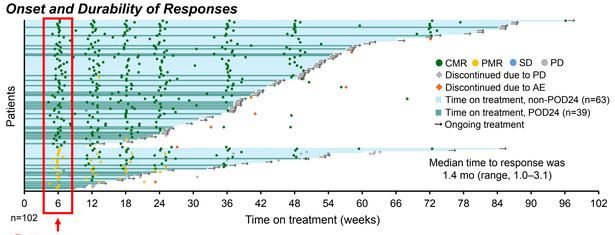
Antitumor Activity in POD24

Response, %	Non-POD24 n=64	POD24 n=40	POD24 2L n=21	POD24 3L+ n=19
ORR	98	98	100	95
CMR	94	75	86	63

Definitions for all subgroups available in Study Design and Patient Disposition.

- High overall response and CMR rates regardless of POD24 status and line of therapy

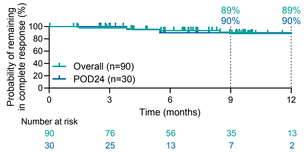
Onset and Durability of Responses



Data cutoff: January 31, 2023. Per protocol, patients continued to receive scans if they discontinued treatment for reasons other than PD. Of 21 PMRs, 12 converted to CMRs, the majority by the second assessment; 3 of 4 SDs converted to PMRs by the second assessment.

- Responses occurred early and were deep and durable

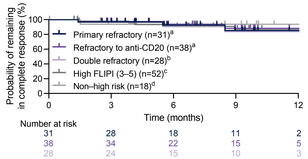
Duration of Complete Response – Overall and POD24



Data cutoff: January 31, 2023. Definitions for all subgroups available in Study Design and Patient Disposition. DoCR is among complete responders in response-evaluable set. The 9-mo/12-mo PFS estimates for POD24 2L (n=23) and POD24 3L+ (n=19) are 81%/81% and 72%/72%, respectively. Median follow-up for overall population: 11.4 mo (range, 2.1–22.1). Median follow-up for POD24: 9.5 mo (range, 2.4+ to 19.4). Median follow-up for POD24 2L: 9.2 mo (range, 3.5–19.4). Median follow-up for POD24 3L+: 9.5 mo (range, 2.4+ to 16.7). Percentages are Kaplan–Meier estimates.

- Epcoritamab SC + R² led to durable complete responses, including in POD24 patients

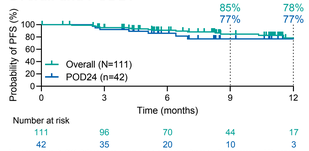
Duration of Complete Response – Other High-Risk Subgroups and Non–High Risk



Data cutoff: January 31, 2023. Definitions for all subgroups available in Study Design and Patient Disposition. [a]Median follow-up: 10.4 mo (range, 3.0–19.4). [b]Median follow-up: 10.1 mo (range, 3.0–19.4). [c]Median follow-up: 12.5 mo (range, 2.1–22.1). [d]Median follow-up: 11.2 mo (range, 3.7–19.0).

- Epcoritamab SC + R² led to durable complete responses in other high-risk and non–high risk populations

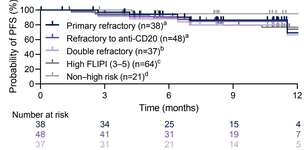
Progression-Free Survival – Overall and POD24



Data cutoff: January 31, 2023. Definitions for all subgroups available in Study Design and Patient Disposition. PFS is among full analysis set. The 9-mo/12-mo PFS estimates for POD24 2L (n=23) and POD24 3L+ (n=19) are 81%/81% and 72%/72%, respectively. Median follow-up for overall population: 11.4 mo (range, 2.1–22.1). Median follow-up for POD24: 9.5 mo (range, 2.4+ to 19.4). Median follow-up for POD24 2L: 9.2 mo (range, 3.5–19.4). Median follow-up for POD24 3L+: 9.5 mo (range, 2.4+ to 16.7). Percentages are Kaplan–Meier estimates.

- Epcoritamab SC + R² led to durable remissions, including in POD24 patients

Progression-Free Survival – Other High-Risk Subgroups and Non–High Risk



Data cutoff: January 31, 2023. Definitions for all subgroups available in Study Design and Patient Disposition. [a]Median follow-up: 10.4 mo (range, 3.0–19.4). [b]Median follow-up: 10.1 mo (range, 3.0–19.4). [c]Median follow-up: 12.5 mo (range, 2.1–22.1). [d]Median follow-up: 11.2 mo (range, 3.7–19.0).

- Epcoritamab SC + R² led to durable remissions in other high-risk and non–high risk populations

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