Epcoritamab with rituximab + lenalidomide (R^2) provides durable responses in high-risk follicular lymphoma, regardless of POD24 status

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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]

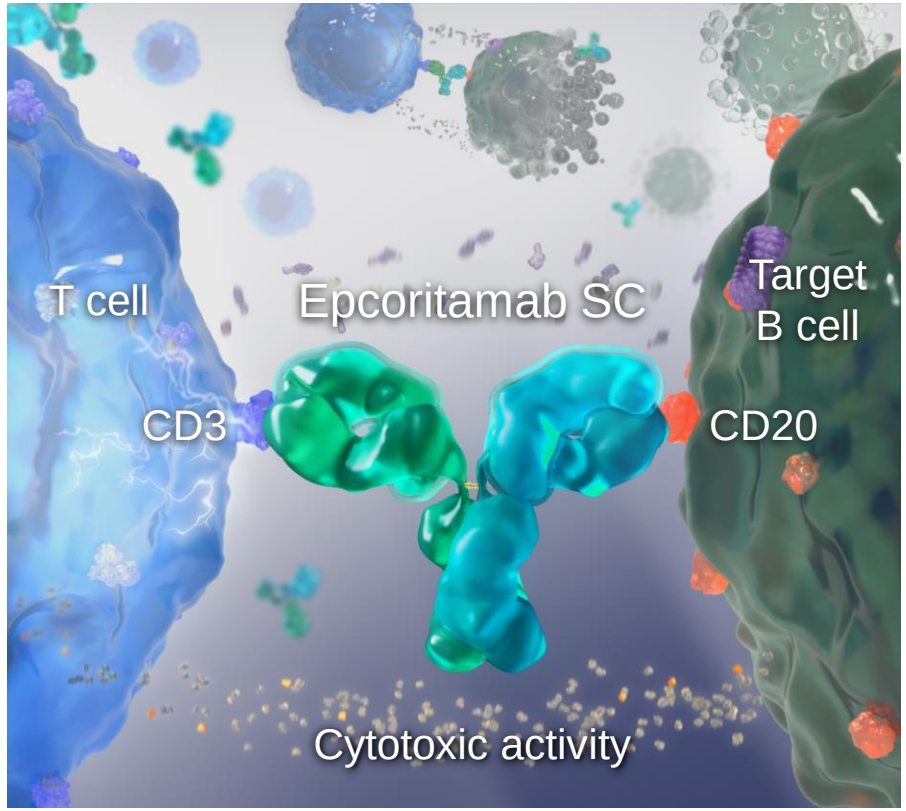
- **No established standard of care for POD24, as current therapeutic options provide suboptimal outcomes:**
  - 5-year overall survival with POD24 versus non-POD24 is ~35%–70% versus ~90%[3,4]
  - R^2 in POD24: ORR ~50%–80% with a CR rate ~10%–30%[a,6,7]
  - T-cell engagers have shown improved outcomes that can be further optimized[b,8-10]

Despite therapeutic advances, outcomes in R/R FL with high-risk features are suboptimal

[a]CT/MRI. [b]PET-CT. **1.** Link BK, et al. *Br J Haematol*. 2019;184:660-3. **2.** Alonso-Álvarez S, et al. *Eur J Cancer*. 2021;157:132-9. **3.** Casulo C, et al. *J Clin Oncol*. 2015;33:2516-22. **4.** Casulo C, et al. *Blood*. 2022;139:1684-93. **5.** Salles G, et al. *Hemasphere.* 2022;6:e745. **6.** Andorsky DJ, et al. *J Clin Oncol*. 2017;35(suppl). Abstract 7502. **7.** Leonard J, et al. *Hematol Oncol*. 2019;37(S2). Abstract 069. **8.** Budde LE, et al. *Blood*. 2021;138(suppl 1). Abstract 127. **9.** Jacobson CA, et al. *J Clin Oncol*. 2021;39(suppl). Abstract 7515. **10.** Dreyling M, et al. *Blood*. 2022;140(suppl 1). Abstract 608.

Epcoritamab SC

- Epcoritamab is a subcutaneously (SC) administered CD3xCD20 bispecific antibody developed using the DuoBody® platform[1-4]
- Single-agent epcoritamab SC has demonstrated deep and durable responses with manageable safety in the EPCORE NHL-1 trial[4]
- Based on these data, epcoritamab SC is approved by the US FDA for the treatment of adults with relapsed or refractory (R/R) DLBCL, NOS, including DLBCL arising from indolent lymphoma, and HGBCL after ≥2L systemic therapy[5]
- Epcoritamab SC + R² is being assessed in the ongoing EPCORE NHL-2 trial (NCT04663347)
- Epcoritamab SC + R² have nonoverlapping modes of action[1,6]
- The immunomodulatory properties of lenalidomide may increase the therapeutic potential of epcoritamab SC[1,6]



1. Engelberts PJ, et al. *EBioMedicine*. 2020;52:102625. **2.** van der Horst HJ, et al. *Blood Cancer J*. 2021;11:38. **3.** Hutchings M, et al. *Lancet*. 2021;398:1157-69. **4.** Thieblemont C, et al. *J Clin Oncol*. 2023;41:2238-47. **5.** EPKINLY [prescribing information]. Plainsboro, NJ: Genmab US, Inc.; 2023. **6.** Chiu CW, et al. AACR 2021. Abstract 1574.

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

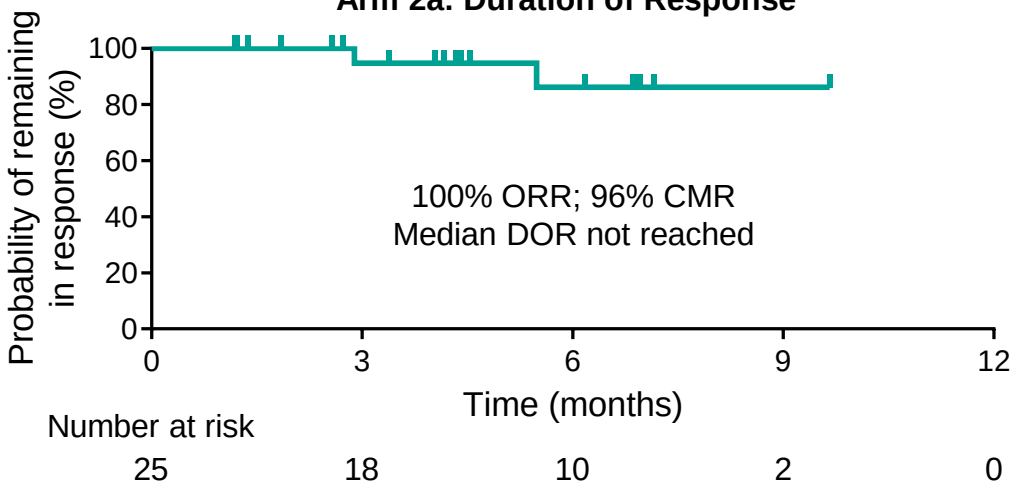
R² C1–12
+
Epcoritamab SC 48 mg
QW C1–3, Q2W C4–9, Q4W C10+
Treatment up to 2 years

Step-up dosing

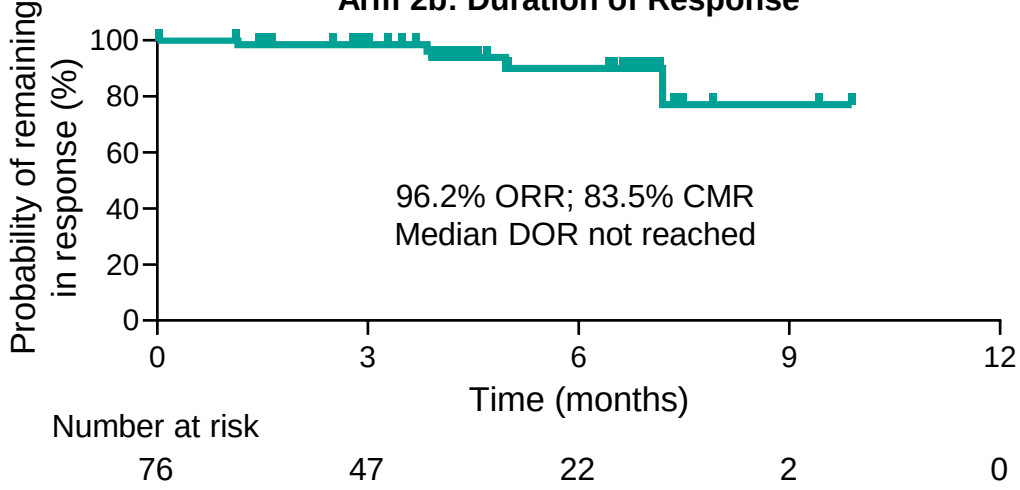
Arm 2b

R² C1–12
+
Epcoritamab SC 48 mg
QW C1–2, Q4W C3+
Treatment up to 2 years

Arm 2a: Duration of Response[1]



Arm 2b: Duration of Response[2]

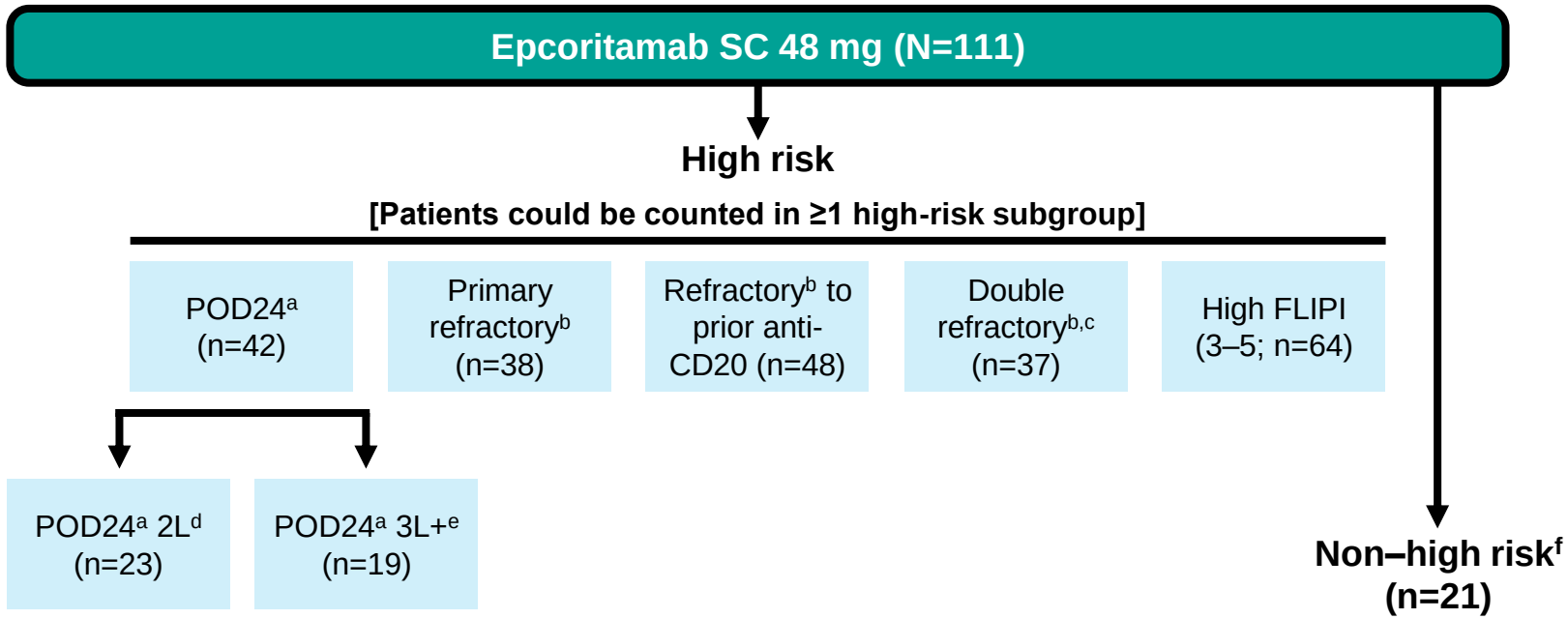


[a]Patients received epcoritamab SC with step-up dosing (ie, priming and intermediate doses before first full dose), corticosteroid prophylaxis to mitigate CRS, and protocol-mandated hospitalization for 24 h after the first full dose. Epcoritamab SC was administered in 28-d cycles. Rituximab regimen: 375 mg/m² IV QW in C1 and Q4W C2–5; lenalidomide regimen: 20 mg QD (oral administration) for 21 d in C1–12. **1.** Falchi L, et al. ASCO 2022. Abstract 7524. Data cutoff: March 25, 2022. Median follow-up: 8.6 mo. **2.** Falchi L, et al. ASH 2022. Abstract 609. 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[1]
- 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[g]

First pooled analysis for epcoritamab SC + R^2 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. **1.** Brice P, et al. *J Clin Oncol*. 1997;15:1110-7.

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)

	Total N=111
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

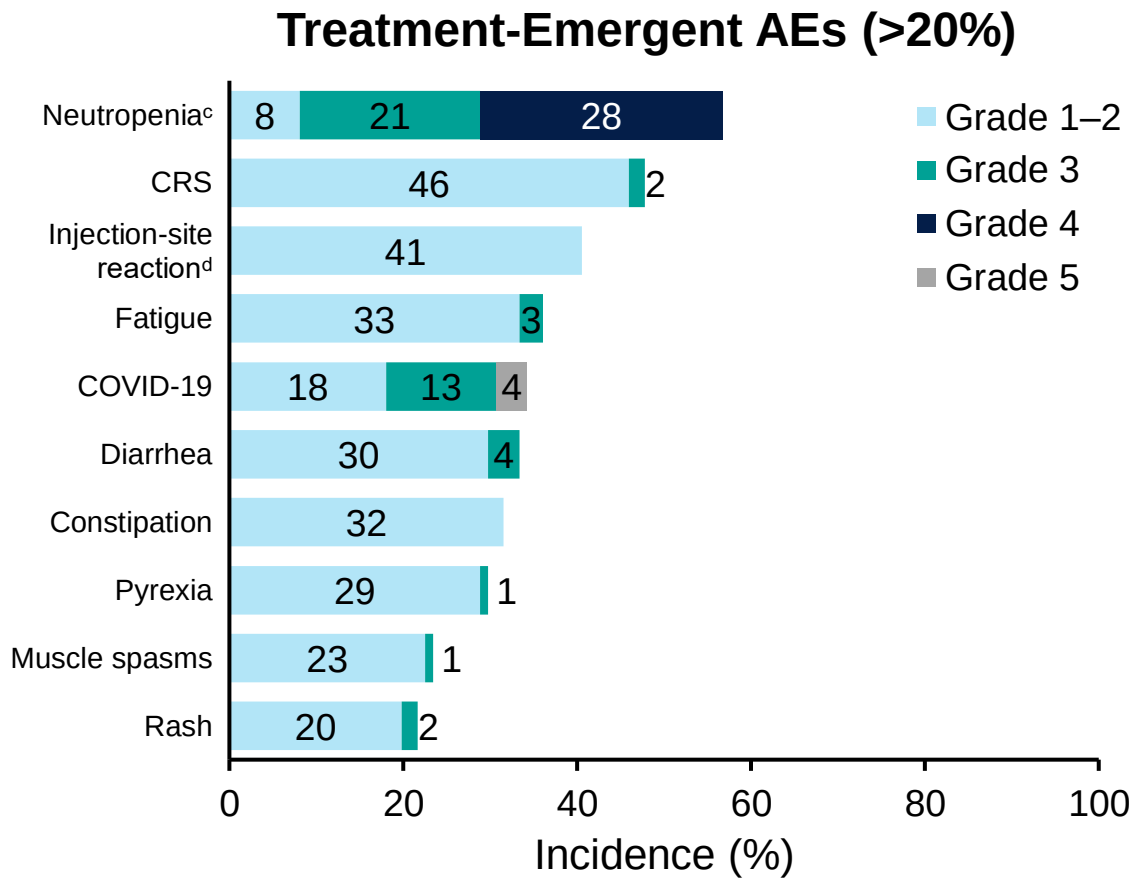
	Total N=111
Median follow-up, mo (range)	11.4 (2.1–22.1)
Epcoritamab SC treatment exposure	
Median number of treatment cycles initiated (range)	10 (1–25)
Median duration of treatment, mo (range)	9 (0.3–22)
Ongoing treatment, n (%)	81 (73)
Discontinued treatment, n (%)	30 (27)
AE	13 (12)
COVID-19	8 (7)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



Findings are consistent with previous reports

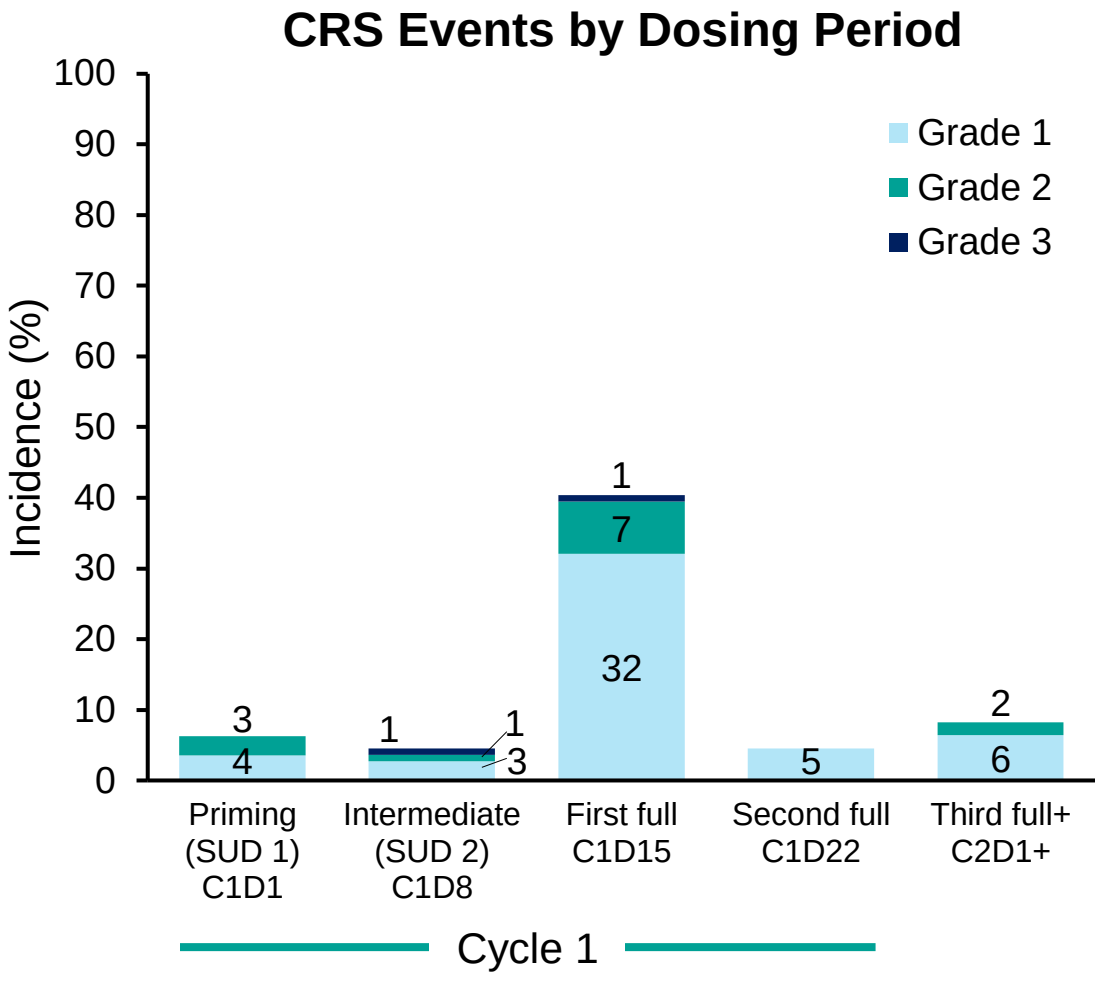
[a]ICANS events were grade 1 and grade 2 (n=1 each). [b]Based on longest ICANS duration in patients with ICANS. [c]Combined term includes neutropenia and neutrophil count decreased; 4 patients (4%) had febrile neutropenia. [d]Combined term includes injection-site reaction, erythema, pain, pruritus, rash,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

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



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

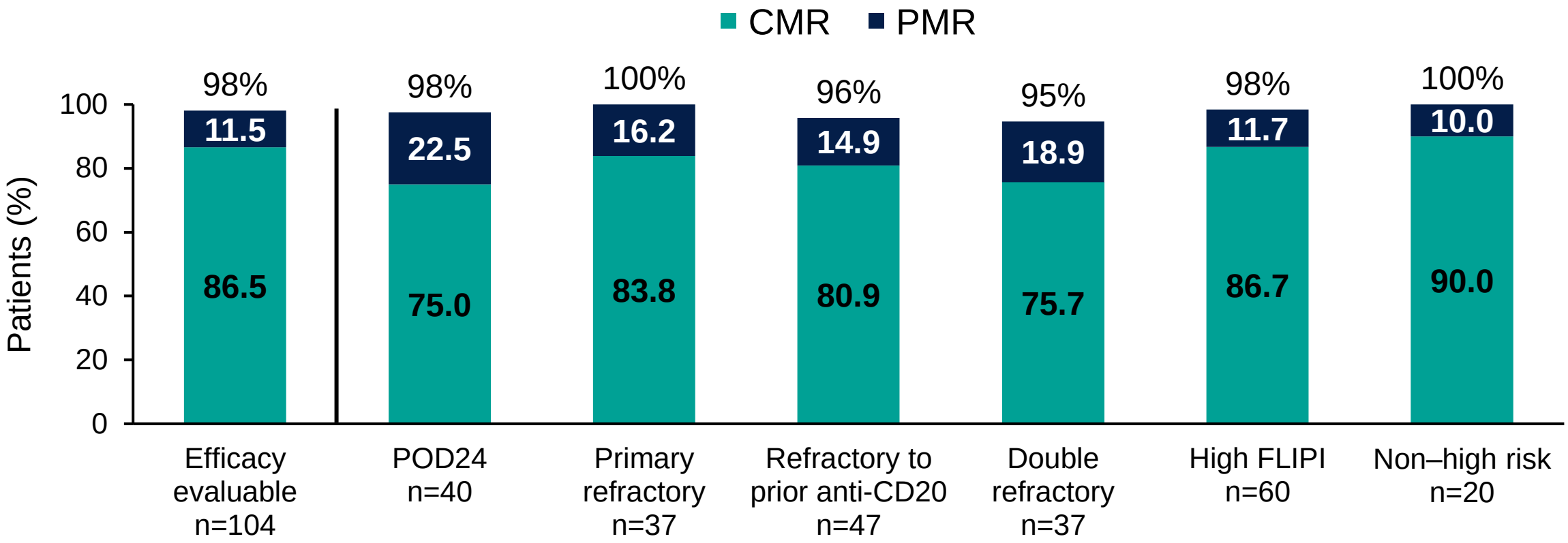
Antitumor Activity With Epcoritamab SC + R²

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



High overall response and CMR rates regardless of subgroup

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.

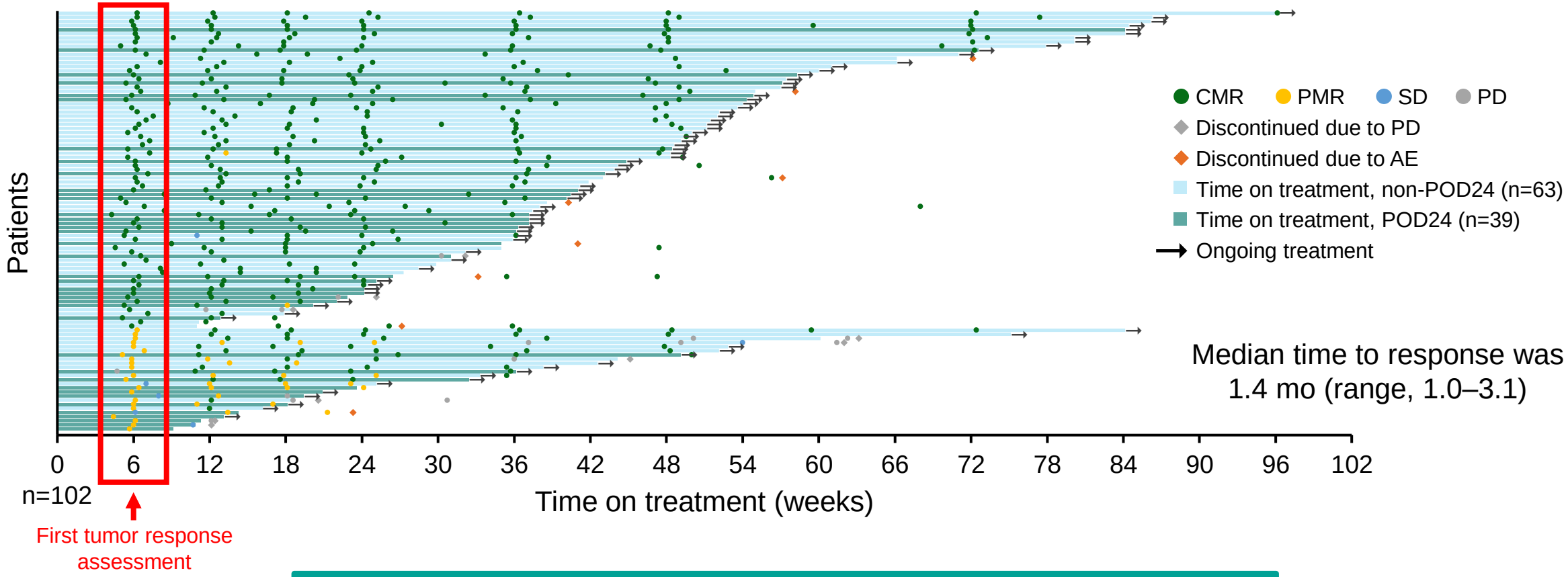
Antitumor Activity in POD24

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

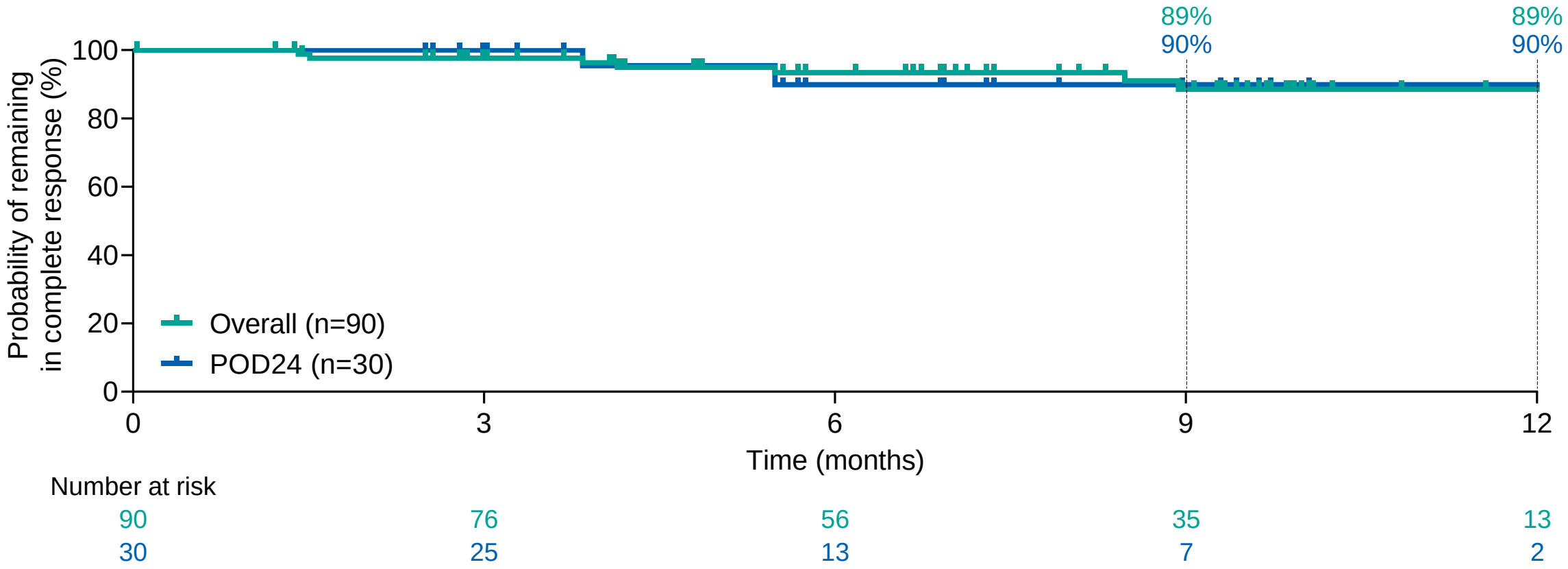
Onset and Durability of Responses



Responses occurred early and were deep and durable

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.

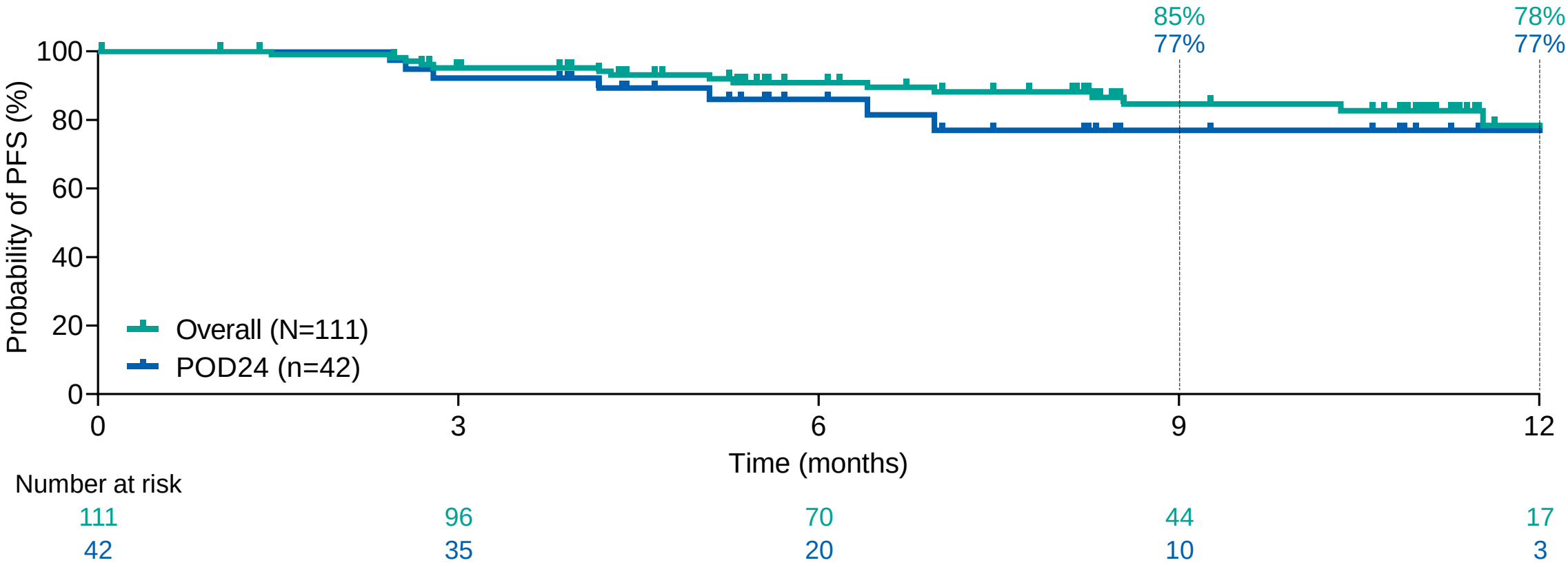
Duration of Complete Response – Overall and POD24



Epcoritamab SC + R^2 led to durable complete responses, including in POD24 patients

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 DoCR estimates for POD24 2L (n=18) and POD24 3L+ (n=12) are 85%/85% and 100%/100%, 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, 3.0–19.4). Median follow-up for POD24 3L+: 9.5 mo (range, 2.4+ to 16.7). Percentages are Kaplan–Meier estimates.

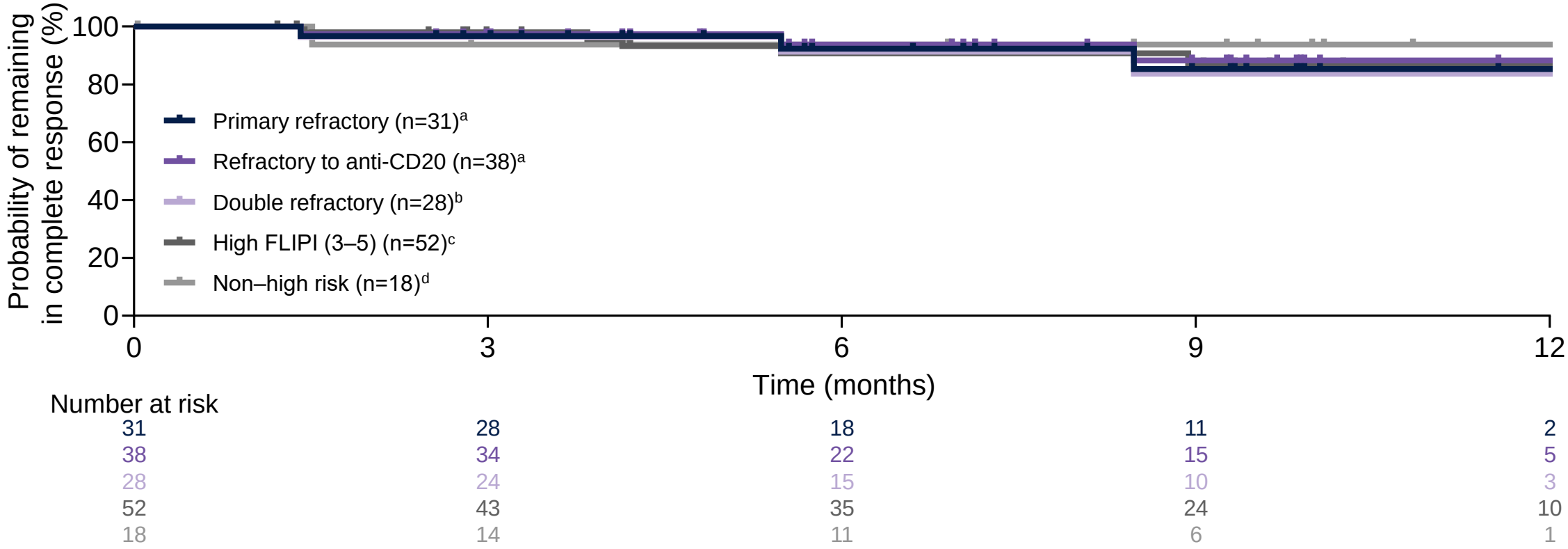
Progression-Free Survival – Overall and POD24



Epcoritamab SC + R^2 led to durable remissions, including in POD24 patients

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, 3.0–19.4). Median follow-up for POD24 3L+: 9.5 mo (range, 2.4+ to 16.7). Percentages are Kaplan–Meier estimates.

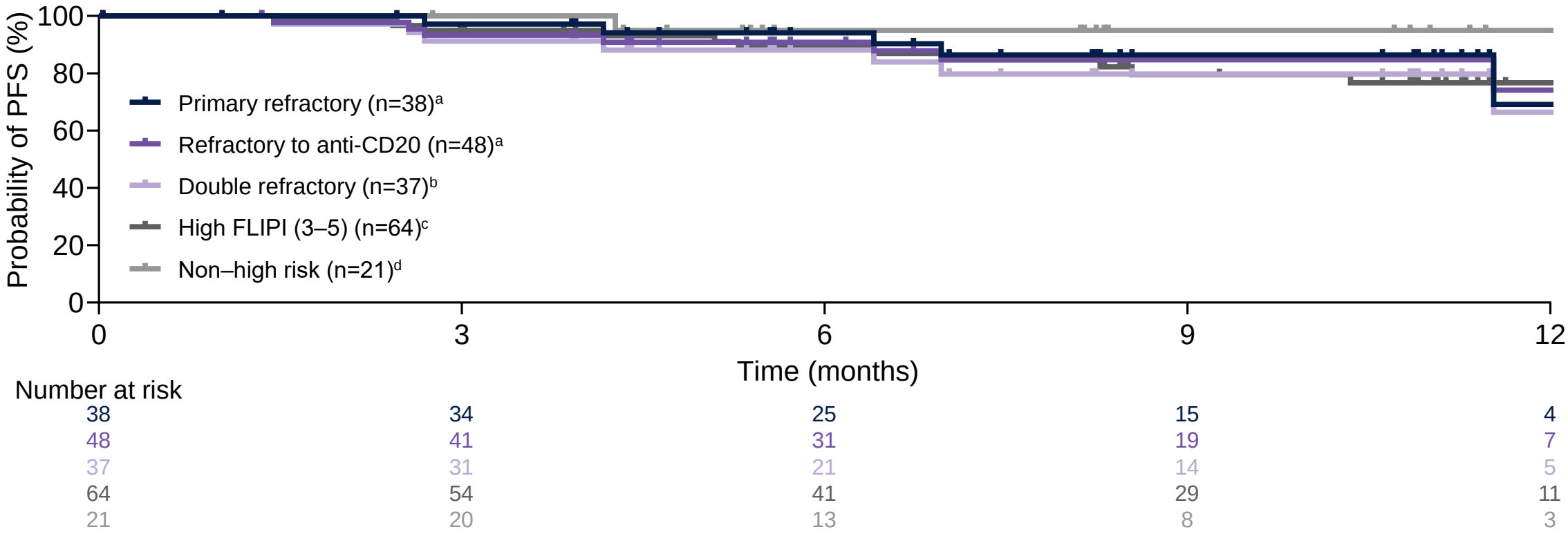
Duration of Complete Response – Other High-Risk Subgroups and Non–High Risk



Epcoritamab SC + R^2 led to durable complete responses in other high-risk and non–high risk populations

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).

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



Epcoritamab SC + R^2 led to durable remissions in other high-risk and non–high risk populations

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).

Conclusions

- **Addition of epcoritamab SC to R^2 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) as well as in a POD24 cohort in the EPCORE NHL-2 trial (NCT04663347)**

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