ABCL-500

Longer Follow-up Reaffirms Subcutaneous Epcoritamab Induces Deep and Durable Complete Remissions in Patients With Relapsed/Refractory Large B-Cell Lymphoma: Updated Results From the Pivotal EPCORE NHL-1 Trial

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OBJECTIVE

To evaluate the longer-term clinical efficacy and safety of epcoritamab monotherapy in patients with R/R LBCL

CONCLUSIONS

Epcoritamab SC is a bispecific antibody that has demonstrated unprecedented single-agent activity in R/R LBCL

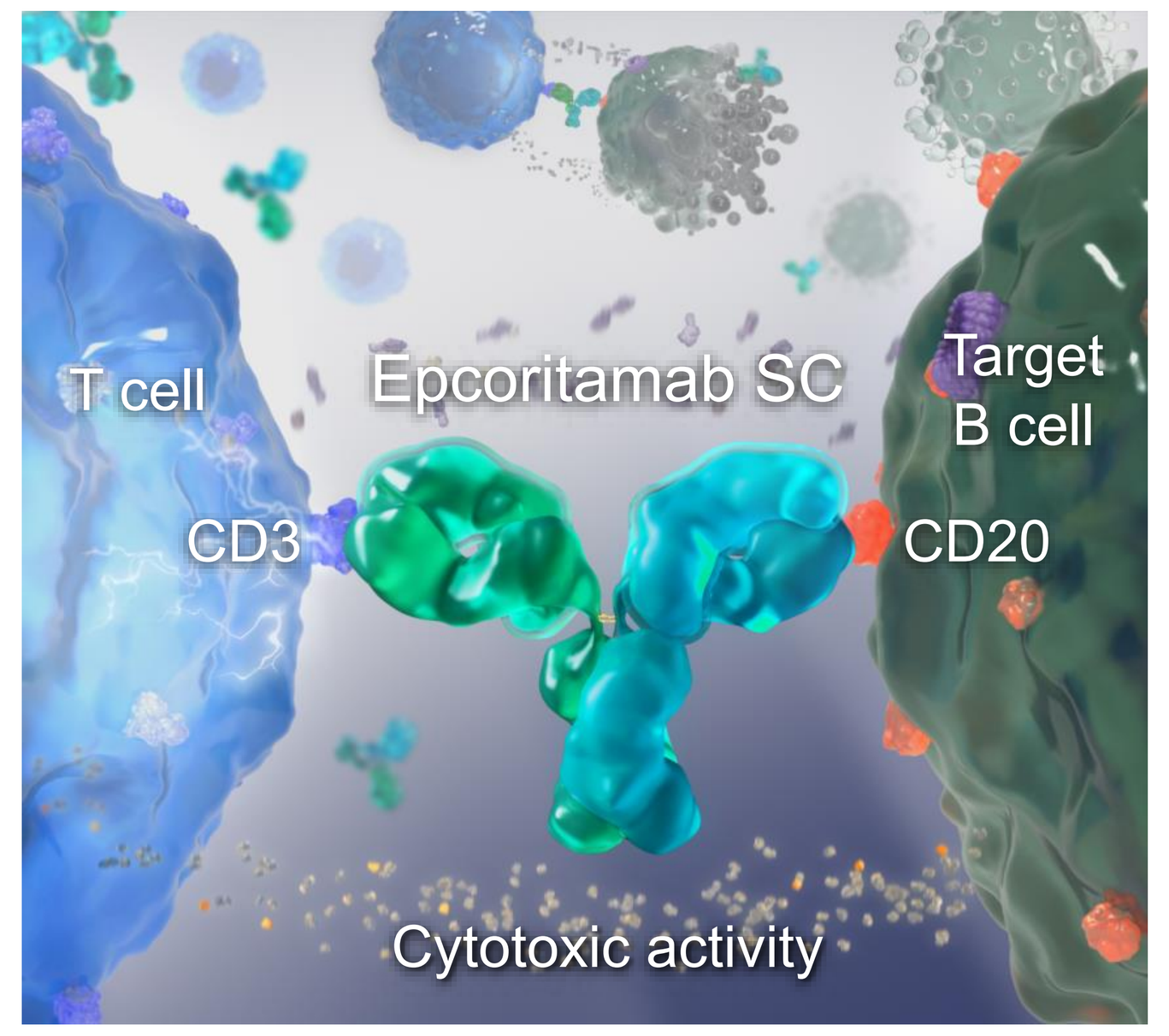
With longer follow-up, we continue to observe durable complete responses

Patients who achieved a complete response had favorable long-term outcomes, with median overall survival not reached

Safety was manageable and consistent with previous reports; there were no new safety signals

BACKGROUND

- Outcomes are poor for patients with relapsed or refractory (R/R) large B-cell lymphoma (LBCL)[1-7]
- Epcoritamab SC is a CD3xCD20 bispecific antibody
  - Developed using the DuoBody® platform
  - Demonstrated deep and durable responses (ORR: 63%; CR: 39%) and a manageable safety profile as a single agent in patients with R/R LBCL in the EPCORE NHL-1 phase 1/2 trial[8]
  - Approved by the US FDA for the treatment of adult patients with R/R DLBCL, NOS, including DLBCL arising from indolent lymphoma, and HGBCL after ≥2L systemic therapy[9]
- Here, we present longer follow-up of the ongoing EPCORE NHL-1 trial



STUDY DESIGN: EPCORE™ NHL-1 LBCL Expansion

Dose escalation

B-NHL:
- ✓ No DLTs
- ✓ MTD not reached
- ✓ RP2D identified
- ✓ Manageable safety profile
- ✓ Encouraging antitumor activity

Dose expansion data cutoff: November 18, 2022
Median follow-up: 20.0 mo

Key inclusion criteria:
- R/R CD20+ mature B-cell neoplasm
- ECOG PS 0–2
- ≥2 prior lines of antineoplastic therapy, including ≥1 anti-CD20 mAb
- Measurable disease by PET/CT
- Prior CAR T allowed

Step-up dosing[a]

Epcoritamab SC RP2D 48 mg
Treatment until PD[b,c] or unacceptable toxicity
LBCL cohort, N=157
DLBCL & HGBCL, n=148; PMBCL, n=4; FL G3B, n=5

SC injections in minutes

	QW			Q2W						Q4W
C	1	2	3	4	5	6	7	8	9	10
Wk	0	4	8	12	16	20	24	28	32	36

- **Primary endpoint:** ORR by independent review committee (IRC)
- **Key secondary endpoints:** DOR, TTR, PFS, OS, CR rate, and safety/tolerability

[a]Step-up dosing (SUD; priming [SUD 1] 0.16 mg and intermediate [SUD 2] 0.8 mg dosing before first full dose) and corticosteroid prophylaxis were used to mitigate CRS. [b]Radiographic disease evaluation was performed every 6 wk for the first 24 wk (6, 12, 18, and 24 wk), then every 12 wk (36 and 48 wk), and every 6 mo thereafter. [c]≥2 measurable (by CT/MRI) and FDG PET–positive lesions. ClinicalTrials.gov: NCT03625037. EudraCT: 2017-001748-36.

RESULTS

Highly Refractory Patient Population

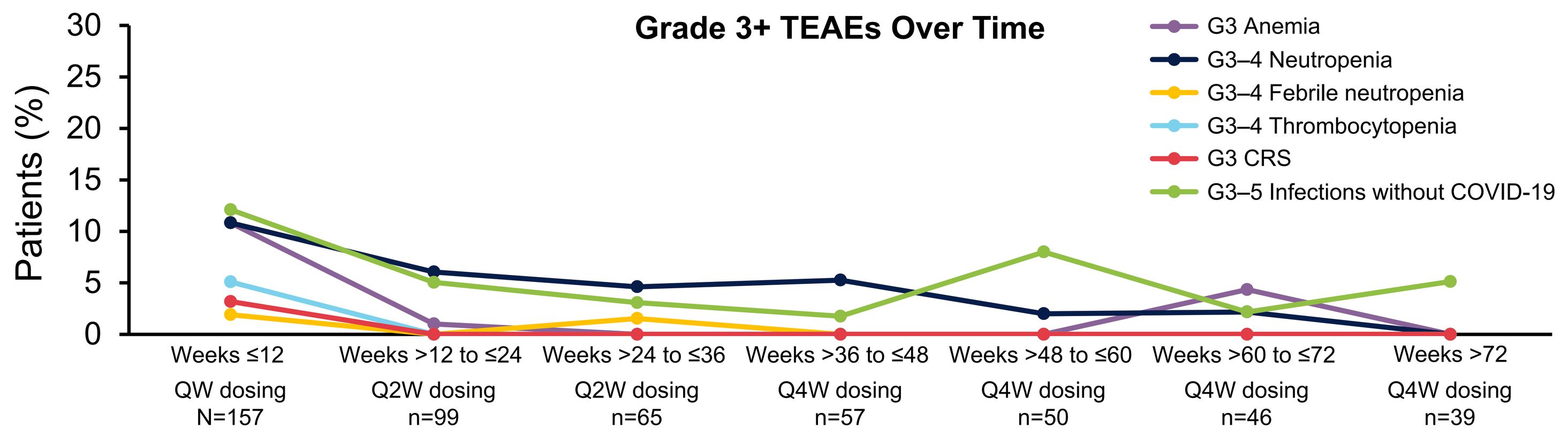
Demographics	DLBCL & HGBCL, n=148	LBCL, N=157
Median age (range), y	65 (22–83)	64 (20–83)
≥75 y, n (%)	29 (20)	29 (18)
ECOG PS, n (%)		
0	71 (48)	74 (47)
1	72 (49)	78 (50)
2	5 (3)	5 (3)
Disease Type, n (%)	**DLBCL & HGBCL, n=148**	**LBCL, N=157**
DLBCL[a]	127 (86)	127 (81)
De novo	92/127 (72)	92/127 (72)
Transformed	33/127 (26)	33/127 (26)
HGBCL	21 (14)	21 (13)
PMBCL	0	4 (3)
FL G3B	0	5 (3)
Prior Treatments	**DLBCL & HGBCL, n=148**	**LBCL, N=157**
Median time from initial diagnosis to first dose, mo	19	19
Median time from end of last therapy to first dose, mo	2.4	2.4
Median prior lines of therapy (range)	3 (2–11)	3 (2–11)
≥3 Lines of therapy, n (%)	104 (70)	110 (70)
Primary refractory[b] disease, n (%)	88 (59)	95 (61)
Refractory[b] to last systemic therapy, n (%)	122 (82)	130 (83)
Refractory[b] to ≥2 consecutive lines of therapy, n (%)	112 (76)	118 (75)
Prior ASCT, n (%)	27 (18)	31 (20)
Prior CAR T therapy, n (%)	58 (39)	61 (39)
Refractory[b] to CAR T therapy	43/58 (74)	46/61 (75)

[a]De novo versus transformed status of 2 patients with DLBCL was unknown. [b]Refractory disease is defined as disease that either progressed during therapy or progressed within <6 mo of completion of therapy.

Patient Disposition and Exposure

Follow-up	DLBCL & HGBCL, n=148	LBCL, N=157
Median follow-up (range), mo	20.0 (0.3+ to 28.2)	20.0 (0.3+ to 28.2)
Mean number of treatment cycles	9	9
Ongoing treatment, n (%)	34 (23)	36 (23)
Discontinued treatment, n (%)	114 (77)	121 (77)
PD	84 (57)	88 (56)
AE	18 (12)	18 (11)
Allogeneic transplant	5 (3)	7 (4)
Withdrawal by patient	4 (3)	5 (3)
Other	3 (2)	3 (2)

Treatment-Emergent Adverse Events in LBCL Patients



- Safety was consistent with previous findings; the most common TEAEs of any grade were CRS (51%), neutropenia (24%), pyrexia (24%), fatigue (23%), nausea (22%), and diarrhea (21%)
- Ten patients (6%) experienced ICANS; 9 (6%) had G1–2 events, and 1 patient (1%) with several confounding factors experienced a fatal ICANS event
- Fatal TEAEs occurred in 15 patients (COVID-19 [n=8])
  - 2 were considered related events (COVID-19 pneumonia and ICANS)

CRS Was Predictable and Primarily Low Grade

	LBCL, N=157
CRS, n (%)[a]	80 (51)
Grade 1	50 (32)
Grade 2	25 (16)
Grade 3	5 (3)
Median time to onset after first full dose, h	20
Treated with anticytokine therapy, n (%)	23 (15)
Leading to treatment discontinuation, n (%)	1 (1)
CRS resolution, n/n (%)	79/80 (99)
Median time to resolution, d (range)[b]	2 (1–27)

[a]Graded by Lee et al 2019 criteria.[10] [b]Median is Kaplan–Meier estimate based on longest CRS duration in patients with CRS.

- CRS occurred primarily following the first full dose (C1D15)
- Tocilizumab was used predominantly to treat CRS events following the first full dose (C1D15) in patients who experienced grade 2 or grade 3 CRS events

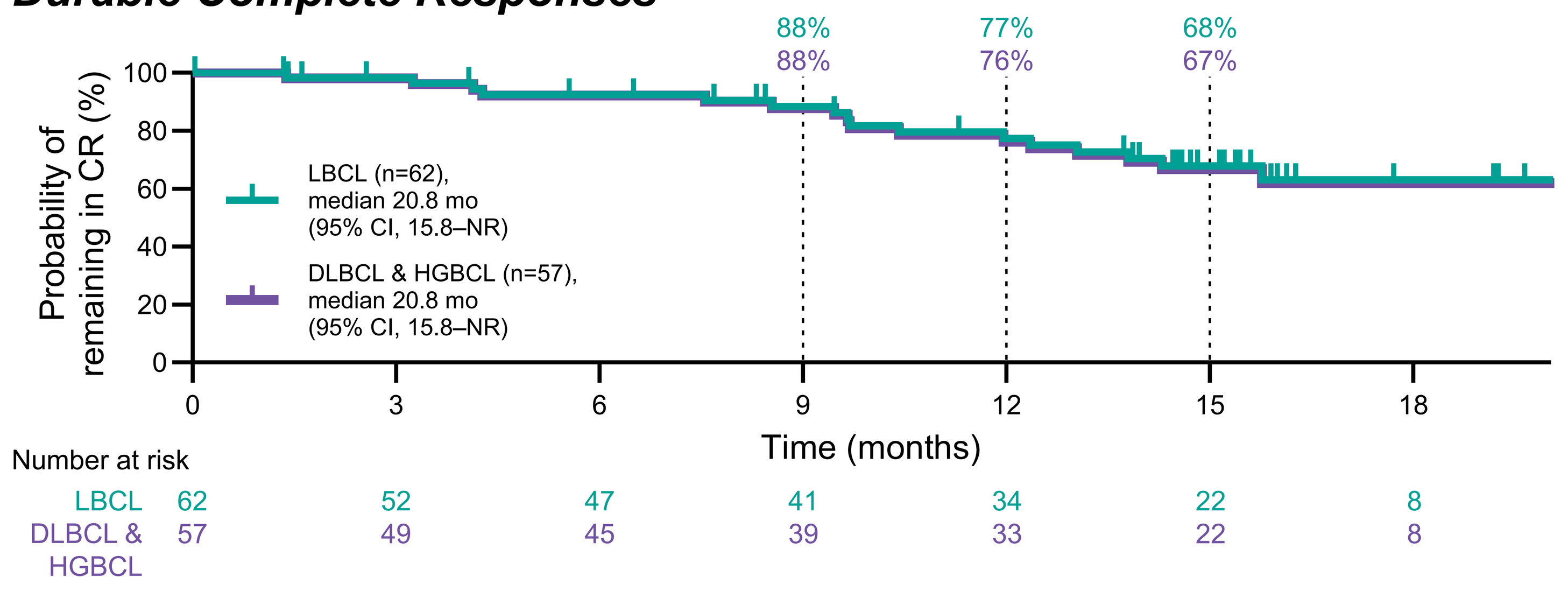
High Rates of Complete Response

Best Overall Response, n (%)	LBCL N=157[a]	DLBCL & HGBCL n=148[a]	PMBCL n=4	FL G3B n=5
Overall response	99 (63)	90 (61)	4 (100)	5 (100)
Complete response	62 (39)	57 (39)	2 (50)	3 (60)
Partial response	37 (24)	33 (22)	2 (50)	2 (40)
Stable disease	5 (3)	5 (3)	—	—
Progressive disease	37 (24)	37 (25)	—	—

Based on IRC per Lugano criteria. [a]16 patients were not evaluable.

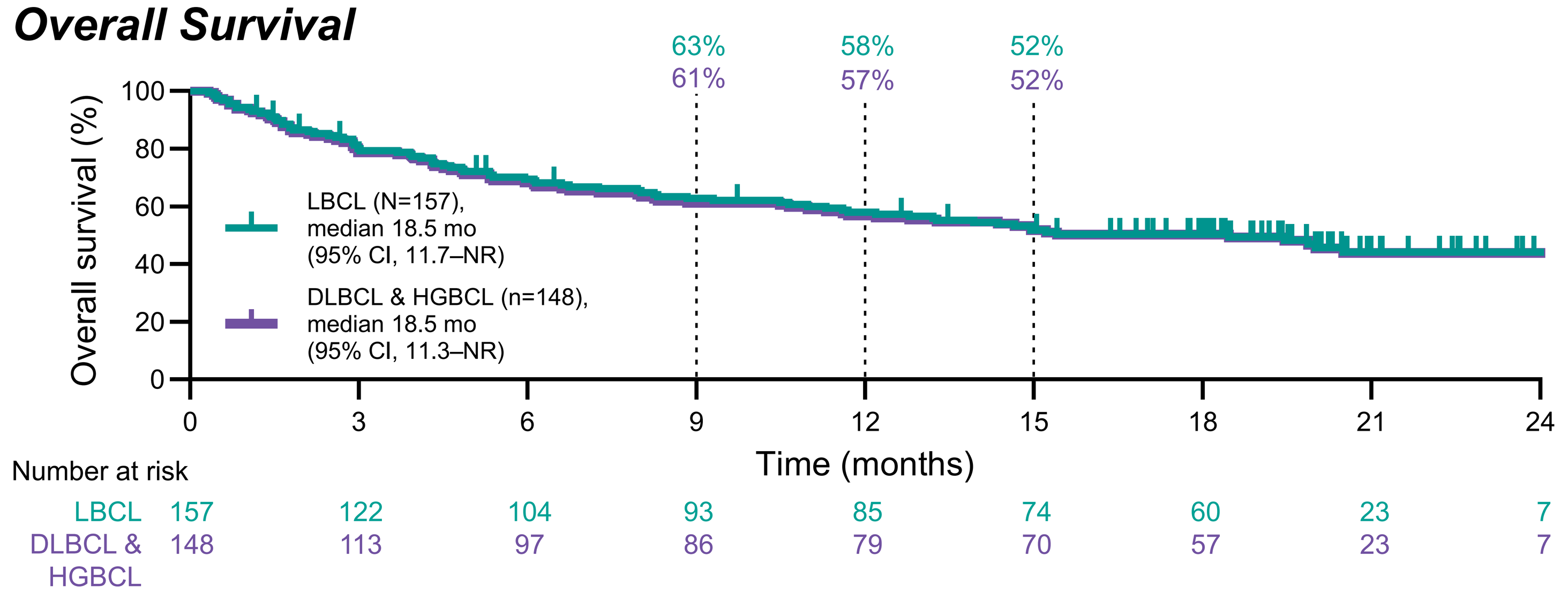
- In patients with DLBCL & HGBCL, median DOR was 15.5 mo (95% CI, 9.7–20.8)
- For patients with LBCL previously treated with CAR T, median DOR was not reached
- Median overall survival was 18.5 mo (95% CI, 11.7–NR) in patients with LBCL (N=157) and 18.5 mo (95% CI, 11.3–NR) for DLBCL & HGBCL patients (n=148)

Durable Complete Responses



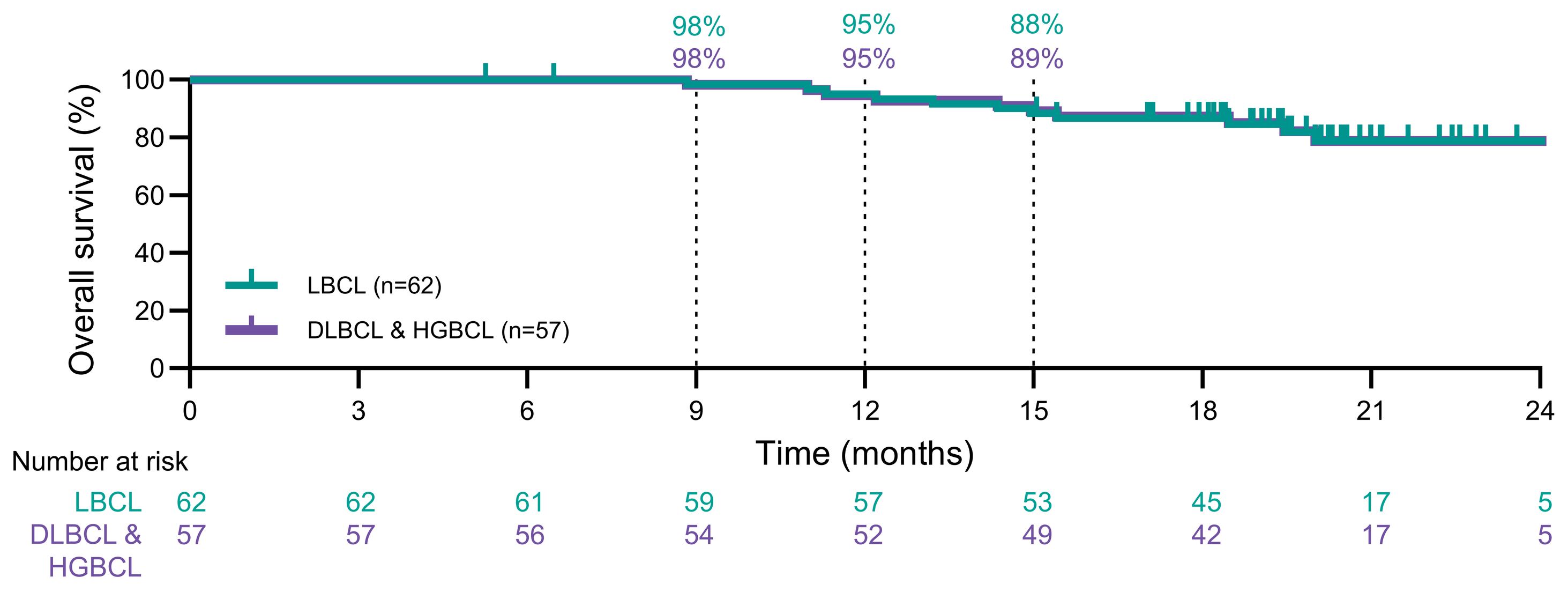
Percentages shown are Kaplan–Meier estimates for complete responders remaining in complete response at the specified time point.

Overall Survival



Percentages shown in the graph are Kaplan–Meier estimates for patients remaining alive at the specified time point.

Overall Survival Among Complete Responders



Percentages shown in the graph are Kaplan–Meier estimates for complete responders remaining alive at the specified time point.

- Additionally, median progression-free survival was not reached among DLBCL & HGBCL complete responders (n=57)
  - At 9, 12, and 15 mo, an estimated 91%, 87%, and 80% of patients remained progression free, respectively

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