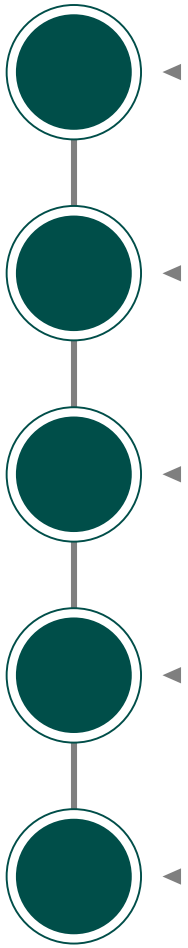
Administration of Epcoritamab

ICD-10 Coordination and Maintenance Committee Meeting
March 7, 2023

Epcoritamab* is a novel CD3xCD20 bispecific antibody intended for the treatment of third line plus Large B-cell Lymphoma (LBCL)



- Currently under consideration by the FDA for **treatment of relapsed/refractory Large B-cell Lymphoma** patients who have **failed at least two prior therapies** (3L+ R/R LBCL)[a]
- Under consideration for a **New Technology Add-On Payment (NTAP) for FY2024**[b]
- Epcoritamab is a **full-length IgG1 bispecific antibody** derived from a **humanized mouse anti-human CD3 mAb and a human anti-CD20 mAb**[c]
- **Induces T-cell mediated killing of malignant B-cells**[d]
- Epcoritamab would be **administered subcutaneously by a healthcare provider**[a]

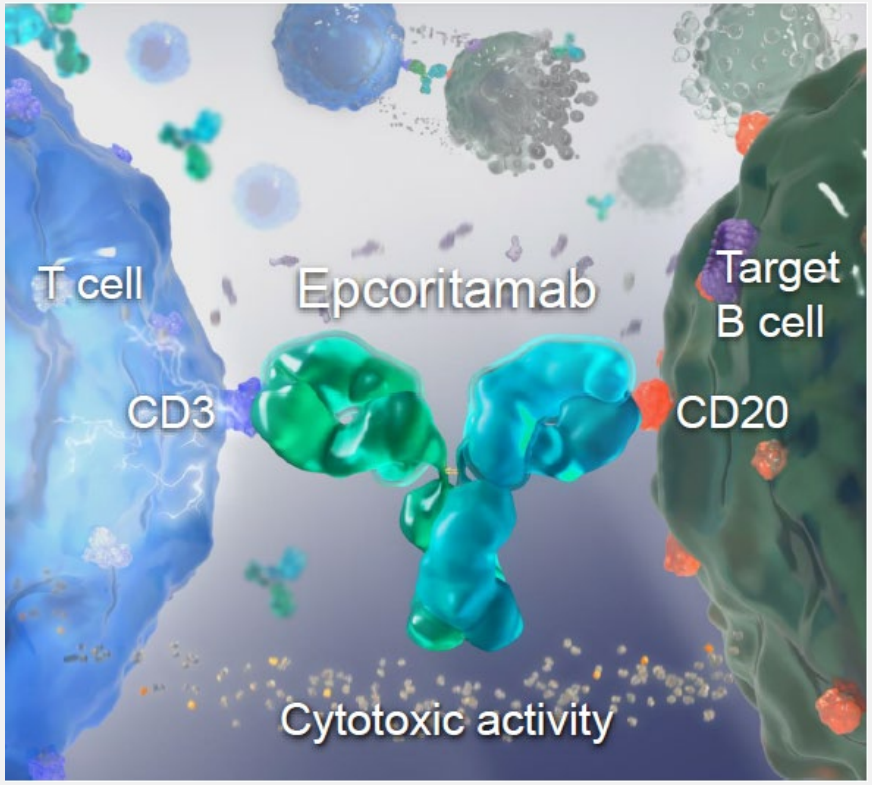
*Epcoritamab is a non-proprietary name; subject to FDA approval, a trade name will be finalized

[a.] https://ir.genmab.com/news-releases/news-release-details/genmab-announces-submissions-regulatory-applications-epcoritamab; [b.] New Technology Add-on Payments Submission (NTP221012JQM0G); [c.] Labrijn, A. F. et al. (2013). PNAS; [d.] Engelberts, P. J. et al. (2020). EBioMedicine

FDA – U.S. Food & Drug Administration; mAb – Monoclonal Antibody

Epcoritamab* induces T-cell–mediated killing of CD20-expressing tumors

Epcoritamab binds a CD3 T-cell and a CD20 B-Cell



- **Induces T-cell activation** by binding to CD3 on T-cells and CD20 on malignant B-cells[a]
- **Promotes** immunological synapse between bound cells, resulting in **apoptosis of B-cells**[a]
- **Binds to a distinct epitope on CD20**, different from the epitopes of rituximab and obinutuzumab[a]
- **Subcutaneous epcoritamab was well tolerated and drove strong responses across multiple patient subgroups**[b]

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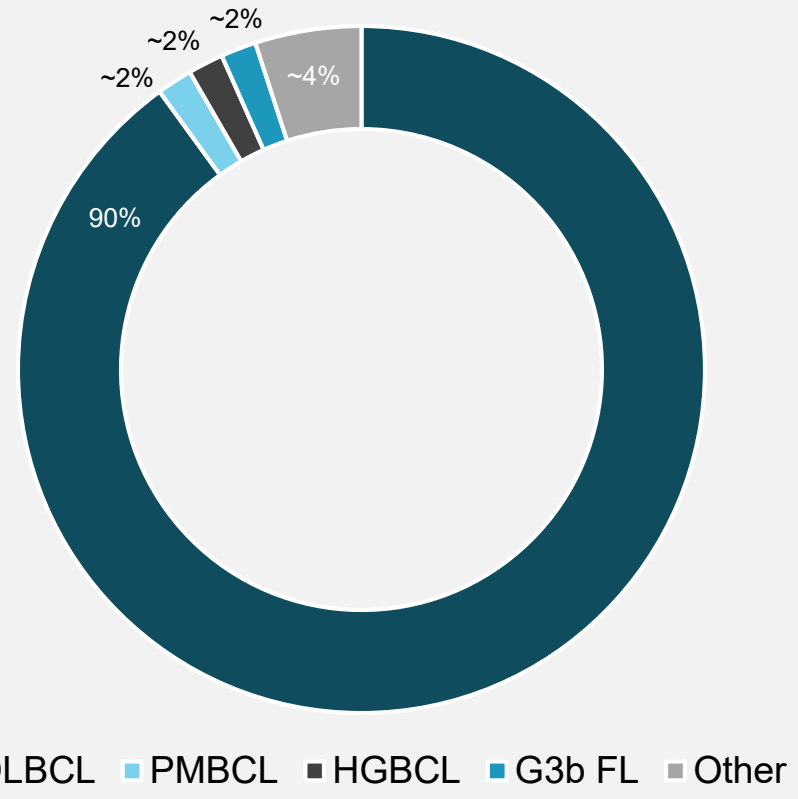
[a] Engelberts, P. J. et al. (2020). EBioMedicine; [b] Hutchings, M. et al (2021) Lancet

Large B-cell Lymphoma is an aggressive constellation of B-cell lymphomas for which there is no cure

LBCL Subtypes

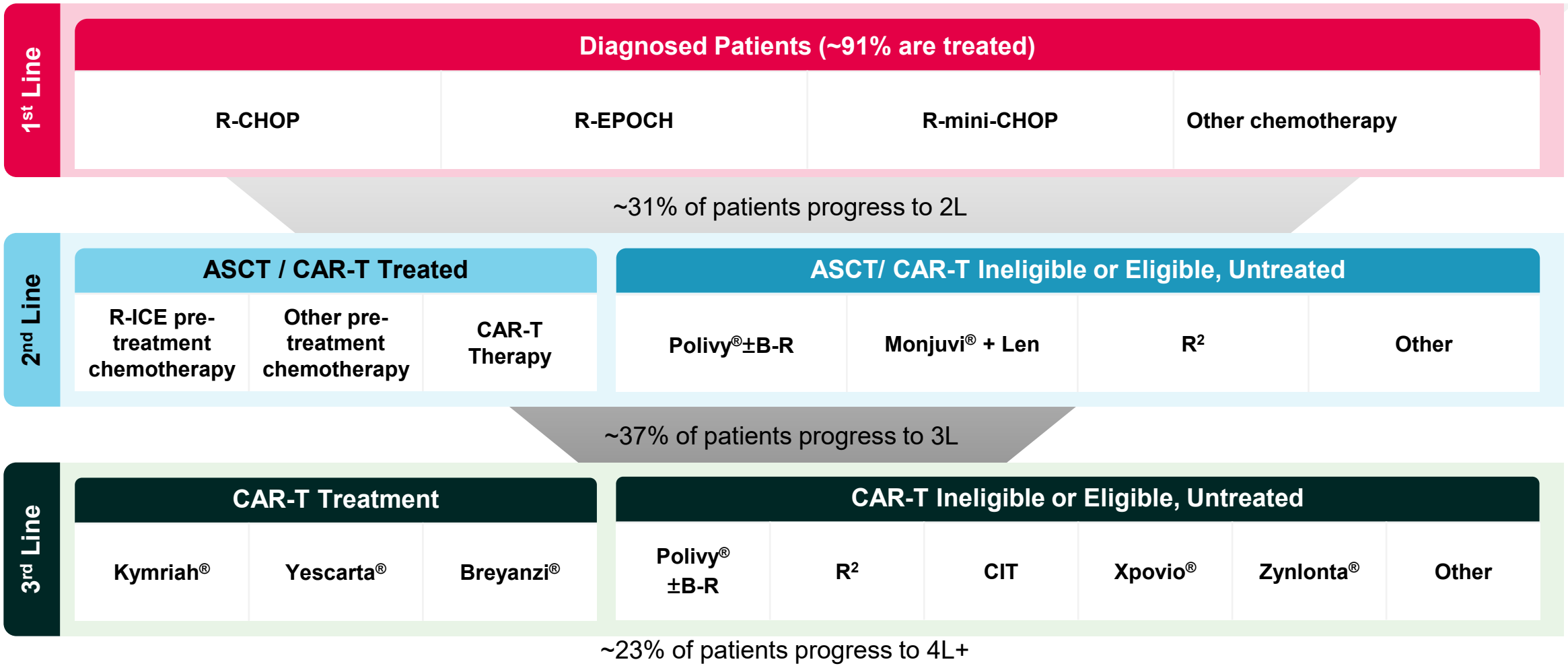


LBCL is an aggressive lymphoma that requires quick intervention[a]

- **Non-Hodgkin's lymphoma (NHL) represent ~90% of all lymphomas**, of which
  - ***B-cell lymphomas comprise 85% of all NHLs***
  - *~4% of all cancers in the US are NHLs with 80,500 people currently diagnosed with NHL*
- **Large B cell lymphoma is an aggressive subtype of NHL**
  - ***Diffuse Large B-cell Lymphoma*** *(DLBCL) is the most common LBCL subtype* ***(~90% of all cases)***
  - *Primary Mediastinal B-cell Lymphoma (PMBCL), High Grade B-cell Lymphoma (HGBCL), and Grade 3B Follicular Lymphoma (G3b FL) make up ~5% of LBCL*
- **Average age of onset is 65[b] and lifespan is limited:**
  - *<1 year without treatment*
  - ***5-year relative survival of DLBCL is only ~65%[b]***

a. https://www.cancer.org/cancer/non-hodgkin-lymphoma b .https://seer.cancer.gov/statfacts/html/dlbcl.html

There is no clear standard of care for third line plus LBCL



[a] Kanas G et al. (2021) Leuk Lymphoma - (Monjuvi is approved for 2L+ patients) Treatment paradigm shown is not exhaustive and focuses on recommended / approved treatments

2L – Second Line; 3L – Third Line; 4L+ - Fourth Line Plus; ASCT – Autologous Stem Cell Transplant; B – Bendamustine; CAR-T – Chimeric Antigen Receptor T-cell; CIT – Chemoimmunotherapy; R-CHOP - Rituximab, Cyclophosphamide, Doxorubicin, Vincristine, and Prednisone; R-EPOCH – Rituximab, Etoposide Phosphate, Prednisone, Vincristine Sulfate, Cyclophosphamide, Doxorubicin Hydrochloride; R-ICE - Rituximab, Ifosfamide, Carboplatin, Etoposide

A need remains for novel 3L+ LBCL agents that will provide deep and durable responses with manageable toxicity[a-i]

	Chemotherapy-based Regimens (R^2, CIT, R-chemo)	Novel Regimens (Polivy®, Xpovio®, Zynlonta®)	CAR-T Therapy (Kymriah®, Yescarta®, Breyanzi®)
Unmet Needs	**Low Efficacy** *(ORR <50%)*	**Low Efficacy** *(ORR: ~40-50%)*	**Eligibility and Safety** *(most 3L+ patients are ineligible; Grade 3+ CRS: 13%-22%)*
	Substantial AE profile *(Adverse event related discontinuation: up to 30%)*	**Substantial AE profile** *(Adverse event related discontinuation: up to 20%)*	**Subsequent Treatment** *(effective in <50%) of patients)*

Epcoritamab was demonstrated to be both safe and effective in a pivotal phase II trial for 3L+ LBCL patients

[a.] SCHOLAR-1 trial (2017) Blood; [b.] Susanibar-Adaniya, S., & Barta, S. K. (2021) AJH; [c.] Jalbert, J. J. et al. (2022) Advances in Therapy; [d.] Sehn, L. H., et al. (2022) Blood Advances. NCT02257567; [e.] Kalakonda, N. et al., (2020) Lancet Haem. NCT02227251; [f.] Caimi, P. F., et al. (2021) Lancet Onco. NCT03589469; [g.] Schuster, S. J., et al. (2019) NEJM. NCT02445248; [h.] Neelapu, S. S., et al. (2017) NEJM. NCT02348216; [i.] Abramson, J. S., et al. (2020) Lancet. NCT02631044

AE – Adverse Event; CRS – Cytokine Release Syndrome; ORR – Overall Response Rate;

EPCORE NHL-1 dose expansion cohort included challenging to treat, heavily pretreated, and highly refractory patients[a]

Demographics	LBCL, N=157
Median age (range), y	64 (20-83)
<65 y, n (%)	80 (51)
65 to <75 y, n (%)	48 (31)
≥75 y, n (%)	29 (18)
ECOG PS, n (%)	
0	74 (47)
1	78 (50)
2	5 (3)

Disease Characteristics[1]	LBCL, N=157
Disease type, n (%)	
DLBCL	139 (89)
De novo	97/139 (70)
Transformed	40/139 (29)
Unknown	2/139 (1)
HGBCL	9 (6)
PMBCL	4 (3)
FL Gr3B	5 (3)

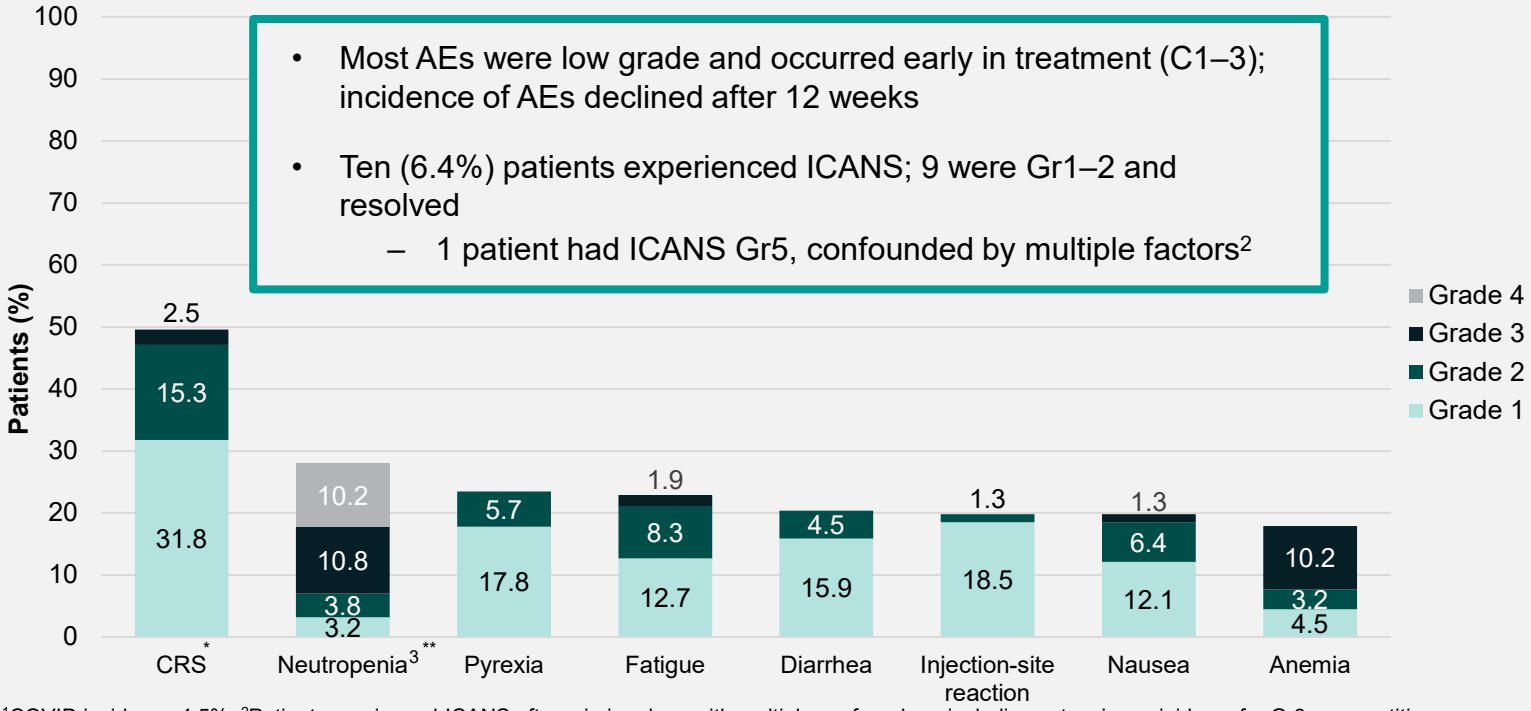
Prior Treatments	LBCL, N=157
Median time from initial diagnosis to first dose, y	1.6
Median time from end of last therapy to first dose, mo	2.4
Median number of prior lines of therapy (range)	3 (2-11)
3L+, n (%)	111 (71)
Primary refractory disease, n (%)	96 (61)
Refractory[2] to last systematic therapy, n (%)	130 (83)
Refractory[2] to ≥2 consecutive lines of therapy, n (%)	119 (76)
Prior ASCT, n (%)	31 (20)
Prior CAR T-cell therapy, n (%)	61 (39)
Progressed within 6 mo of CAR T-cell therapy	46/61 (75)

Median time from initial diagnosis was 1.6 y; median number of prior lines was 3

[1]Double/Triple-hit patients included, many with responses; central lab analysis pending. [2]Refractory disease is defined as disease that either progressed during therapy or progressed within 6 mo (<6 mo) of completion of therapy.
[a.] EPCORE NHL-1 clinical trial (GCT-3013-01), Jan 31st 2022 data cut off
ECOG PS – Eastern Cooperative Oncology Group Performance Score

Epcoritamab demonstrated low rates of treatment-related adverse events[a]

Treatment-emergent Adverse Events (AE)[1] (≥15% by Grade)



[1]COVID incidence 4.5%. [2]Patient experienced ICANS after priming dose with multiple confounders, including extensive opioid use for Gr3 pancreatitis, hyperammonemia, multifocal cerebral infarcts in setting of possible microangiopathy, and tocilizumab administration. [3]Combined term includes neutropenia and decreased neutrophil count.

Follow-up	LBCL, N=157
Median follow-up (range), mo	10.7 (0.3-17.9)
Median number of treatment cycles (range)	5 (1-20)
Ongoing treatment, n (%)	51 (32)
Discontinued treatment, n (%)	106 (68)
PD	83 (53)
AE	11 (7)
Related[4]	3 (2)
Allogenic transplant	7 (4)
Withdrawal by patient	4 (3)
Other	1 (1)

[4]Worsening CLIPPERS, CRS/fatigue, and ICANS.

Very few patients discontinued treatment due to adverse events

*CRS time of onset was predictable, events were transient and primarily low grade and occurred early in treatment
**Neurologic events were low and largely concurrent with CRS events
[a.] EPCORE NHL-1 clinical trial (GCT-3013-01), Jan 31st 2022 data cut off
C – Cycle; Gr – Grade; ICANS – Immune Effector Cell-associated Neurotoxicity Syndrome; PD – Progressive Disease

Epcoritamab drives deep and durable complete responses[a]

Best Overall response by IRC, n(%)[1]	LBCL, N=157
Overall response (ORR)	**99 (63)** [95% CI: 55-71]
Complete response (CR)	**61 (39)** [95% CI: 31-47]
Partial response (PR)	38 (24)
Stable disease	5 (3)
Progressive disease	37 (24)

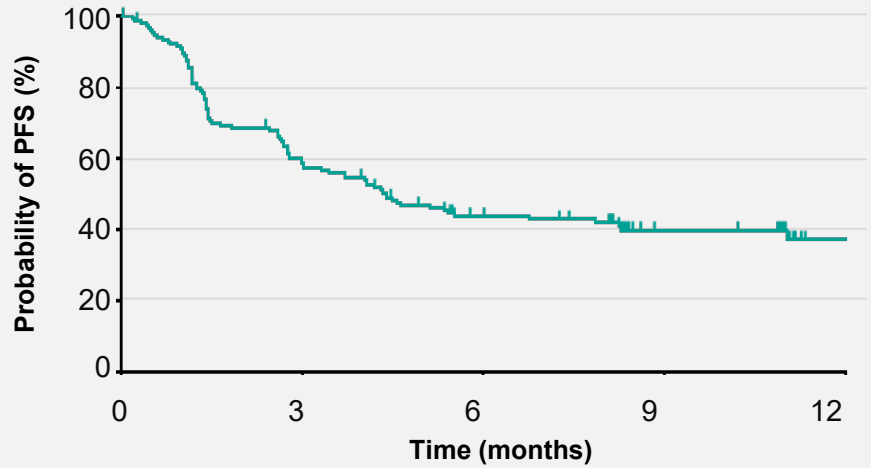
Response Characteristics, mo (range)	
Median time to response	**1.4 (1.0–8.4)**
Median time to CR	2.7 (1.2–11.1)
Median duration of response[2]	12 (0+ to 15.5+)
Median duration of response for patients in CR	Not reached

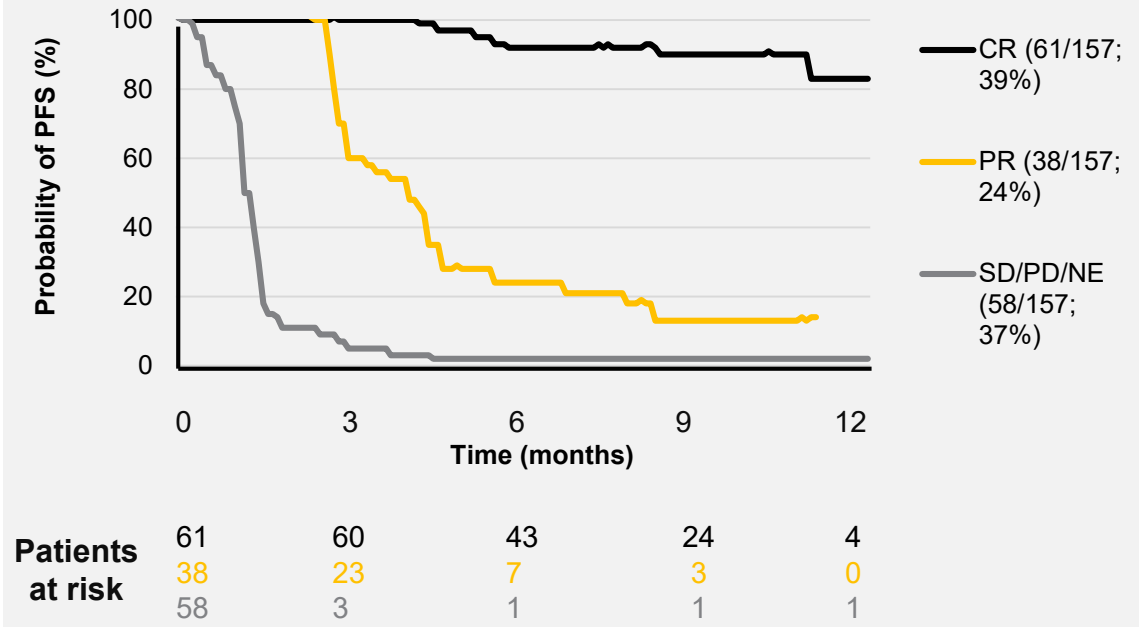
- **Majority of CRs** were **achieved by the first or second assessment**
- Some **conversions from PR to CR were still observed at ≥36 weeks**

[1]Based on IRC assessment and Lugano criteria.
[2]Median duration of response data not yet mature.
[3]Patients without arrows discontinued treatment to receive transplant
[a]EPCORE NHL-1 clinical trial (GCT-3013-01), Jan 31st 2022 data cut off

Epcoritamab demonstrated deep and durable responses[a]

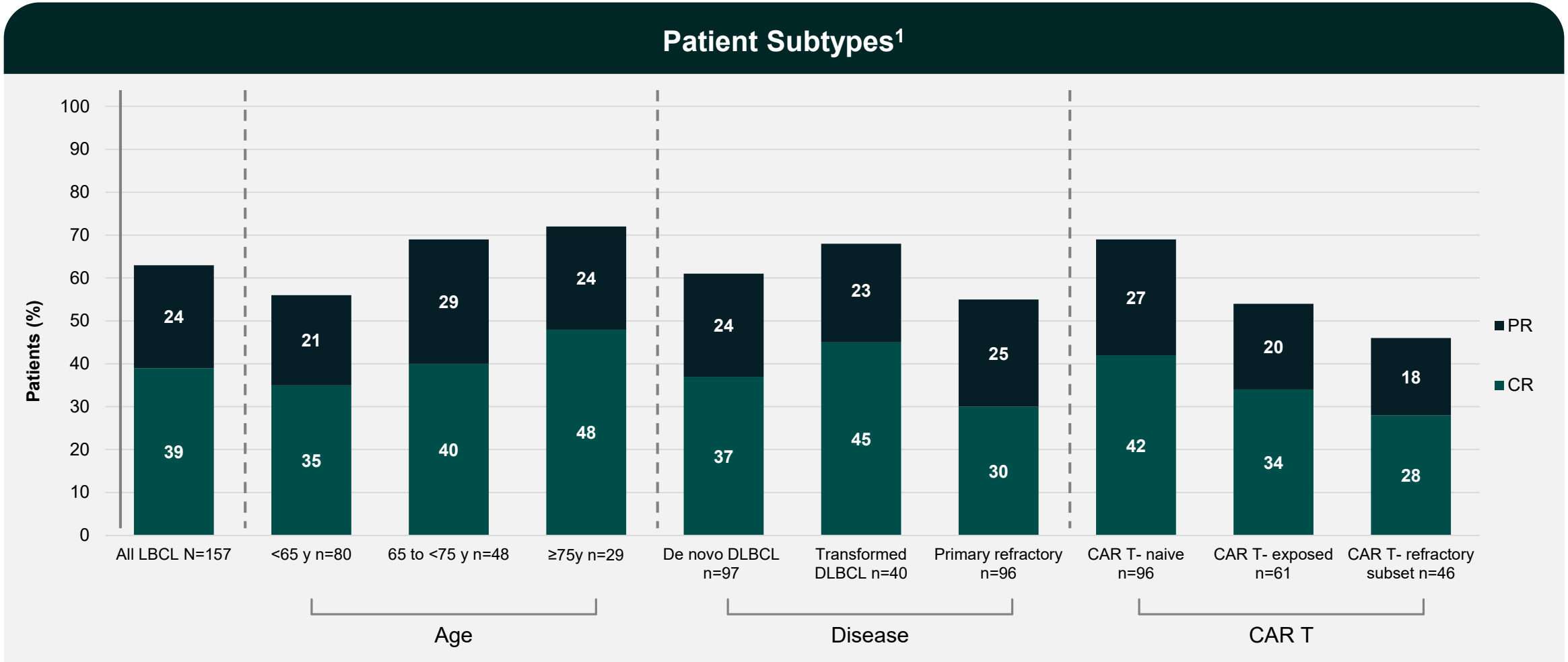
Kaplan-Meier Estimate[1]	
Median PFS for complete responders (n=61)	Not reached
Complete responders remaining in response at 9 mo	89%
Median PFS, mo (95% CI)	4.4 (3.0-7.9)
PFS at 6 mo, % (95% CI)	43.9 (35.7-51.7)





[1]Based on IRC assessment and Lugano criteria.
[a.] EPCORE NHL-1 clinical trial (GCT-3013-01), Jan 31st 2022 data cut off
PFS – Progression Free Survival

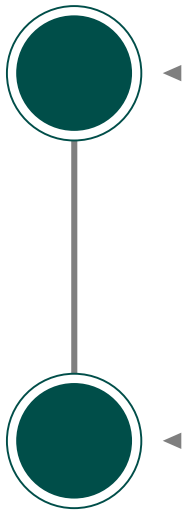
Epcoritamab demonstrated efficacy across patient subtypes[a]



[1]Based on IRC assessment and Lugano criteria.

[a.] EPCORE NHL-1 clinical trial (GCT-3013-01), Jan 31st 2022 data cut off

Administration and Documentation



Epcoritamab will be **administered via subcutaneous injection by a healthcare provider over the course of 28-day cycles**

In the inpatient setting, **epcoritamab will be documented in the "Medications and Orders" section** of medical record

Overview of CRS Events[a]	LBCL N=157
CRS events, n (%)[1]	78 (49.7)
Grade 1	50 (31.8)
Grade 2	24 (15.3)
Grade 3	**4 (2.5)**
Median time to onset from first full dose, d	**0.8 (20 h)**
CRS resolution, n (%)	77 (98.7)
Median time to resolution from first full dose, d	**2 (48 h)**
Treated with tocilizumab, n (%)	22 (14.0)
Treated with corticosteroids, n (%)	16 (10.2)
Leading to treatment discontinuation, n (%)	**1 (0.6)**

[1]Graded by Lee et al. 2019 criteria

[a] EPCORE NHL-1 clinical trial (GCT-3013-01), Jan 31st 2022 data cut off