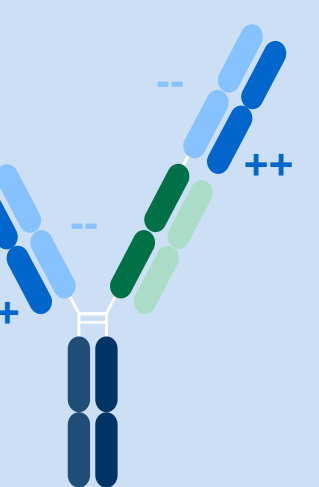


Glofitamab step-up dosing (SUD): Updated efficacy data show high complete response rates in heavily pretreated relapsed/refractory (R/R) non-Hodgkin lymphoma (NHL) patients (pts)

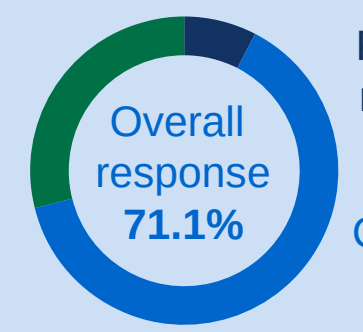
Carmelo Carlo-Stella,¹ Cyrus Khan,² Martin Hutchings,³ Fritz C. Offner,⁴ Franck Morschhauser,⁵ Emmanuel Bachy,⁶ Michael Crump,⁷ Anna Sureda,⁸ Gloria Iacoboni,⁹ Corinne Haioun,¹⁰ David Perez-Callejo,¹¹ Linda Lundberg,¹¹ James Relf,¹² Emma Clark,¹² David Carlile,¹² Emily Piccione,¹³ Anton Belousov,¹¹ Kathryn Humphrey,¹² Michael J. Dickinson¹⁴

Summary

Glofitamab is a novel T-cell-engaging bispecific antibody.



Glofitamab SUD showed high, durable responses in pts with R/R NHL.



SUD of glofitamab can be used for cytokine release syndrome mitigation in addition to obinutuzumab pretreatment, allowing administration of a high effective target dose (30mg).

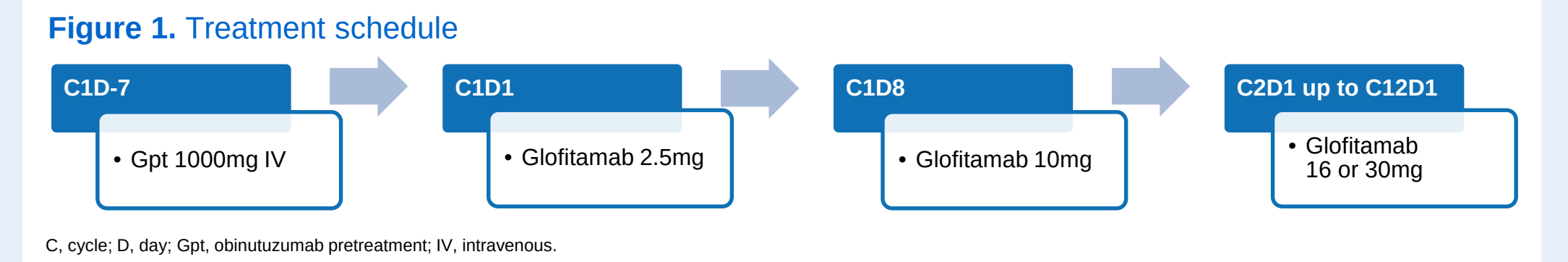
Cytokine release syndrome, the most commonly reported adverse event, was mostly of low grade and confined to cycles 1 and 2.

Background

- The prognosis of patients with relapsed or refractory B-cell NHL is often dismal, and there remains a clear unmet medical need for novel 'off-the-shelf' therapeutic agents.
- Glofitamab is a T-cell-engaging bispecific antibody with a novel '2:1' format shown pre-clinically to offer greater avidity, potency, and combinability with other anti-CD20 IgG antibodies than alternative bispecific formats.¹
- Glofitamab 0.6–25mg fixed-dosing with obinutuzumab pretreatment (Gpt), showed high, durable complete responses and manageable safety in heavily pretreated R/R NHL.² SUD, in addition to Gpt, allowed dose-escalation up to 30mg to maximize efficacy, while mitigating cytokine release syndrome (CRS).²
- Here, we present updated efficacy data for the glofitamab SUD cohorts (day [D]1/D8/target dose from cycle [C]2D1): 2.5/10/16mg and 2.5/10/30mg.

NP30179 (NCT03075696): an ongoing Phase I/II dose-escalation and expansion study in R/R NHL

- Pts aged ≥18 years with histologically confirmed B-cell NHL expected to express CD20, who had ≥1 prior lymphoma treatment, ≥1 measurable target lesion, adequate hematologic, renal and liver functions and an Eastern Cooperative Oncology Group performance status ≤1 were included.



- 1000mg Gpt 7 days prior to glofitamab administration.
- Glofitamab intravenous [IV] step-up doses on C1D1 and D8 and at target dose from C2D1 (2.5/10/16mg or 2.5/10/30mg).
- C1 was 14-days long. After SUD in C1, glofitamab was given every 3 weeks for a fixed duration of treatment up to 12 cycles.
- The primary objectives of the study were to evaluate safety, tolerability, pharmacokinetics, and the anti-tumor efficacy (per Lugano criteria³) of glofitamab as well as its maximum tolerated dose, optimal biological dose and the recommended Phase II dose (RP2D).
- Data from the December 01, 2020 cut-off date are presented here.

Most patients had heavily pretreated NHL

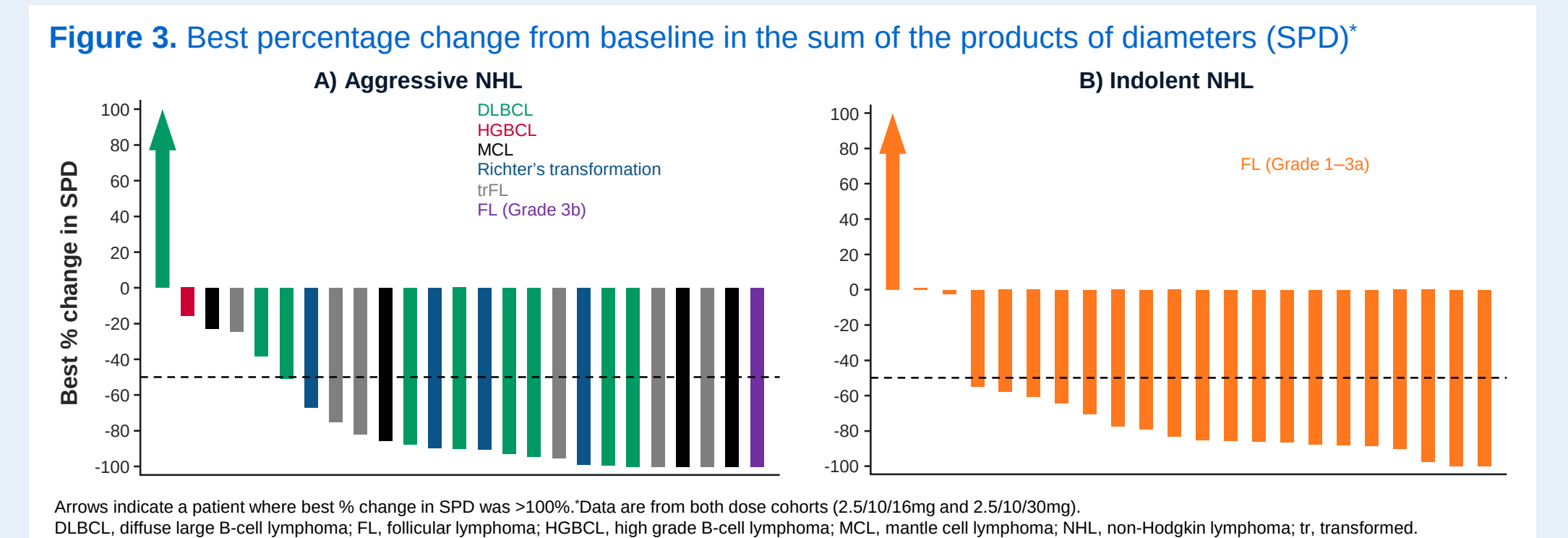
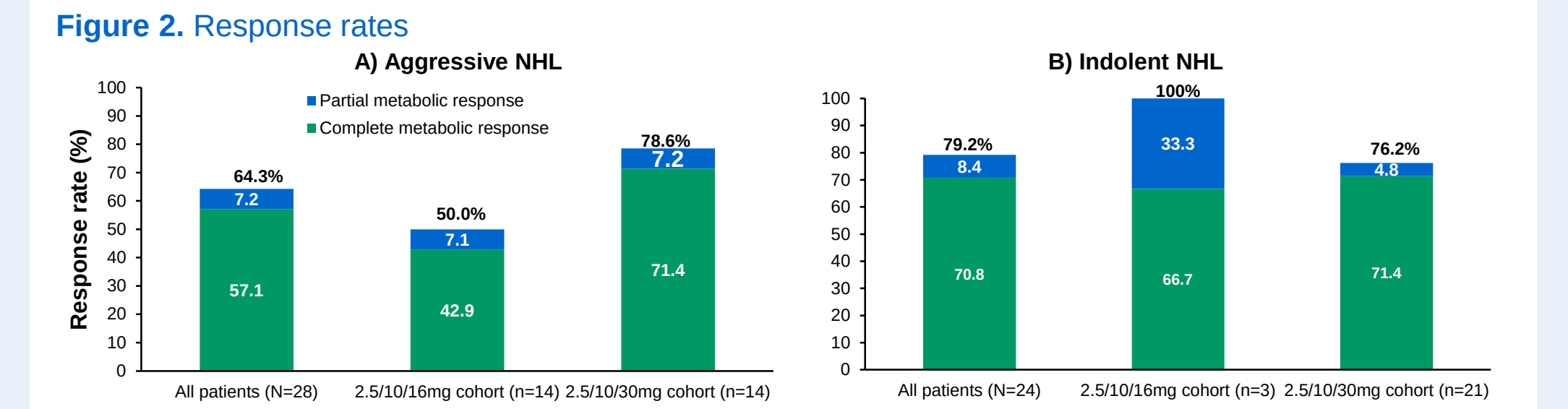
- Fifty-two pts received glofitamab SUD: 17 and 35 pts received 2.5/10/16mg and 2.5/10/30mg, respectively.

Baseline characteristics		2.5/10/16 and 2.5/10/30mg cohorts (N=52)
Median age (range), years		68 (44–85)
Male gender, n (%)		28 (53.8)
Prior lines of therapy, median (range)		3 (1–12)
Prior therapy, n (%)		
Chemotherapy and anti-CD20 monoclonal antibody		52 (100)
Autologous stem-cell transplant		11 (21.2)
PI3Ki		5 (9.6)
CAR-T		3 (5.8)
Cancer immunotherapy		1 (1.9)
Refractory status, n (%)		
Refractory to any prior therapy		44 (84.6)
Refractory to most recent therapy line		40 (76.9)
Refractory to any prior anti-CD20		38 (73.1)
Aggressive NHL, n (%)		28 (53.8)
DLBCL		10 (19.2)
Transformed FL		6 (11.5)
Richter's transformation		5 (9.6)
MCL		5 (9.6)
High-grade B-cell lymphoma		1 (1.9)
FL Grade 3b		1 (1.9)
Indolent NHL, n (%)		24 (46.2)
FL Grade 1–3a		24 (46.2)

CAR-T, chimeric antigen receptor T-cell; DLBCL, diffuse large B-cell lymphoma; FL, follicular lymphoma; MCL, mantle cell lymphoma; NHL, non-Hodgkin lymphoma; PI3Ki, phosphoinositide 3-kinase inhibitor.

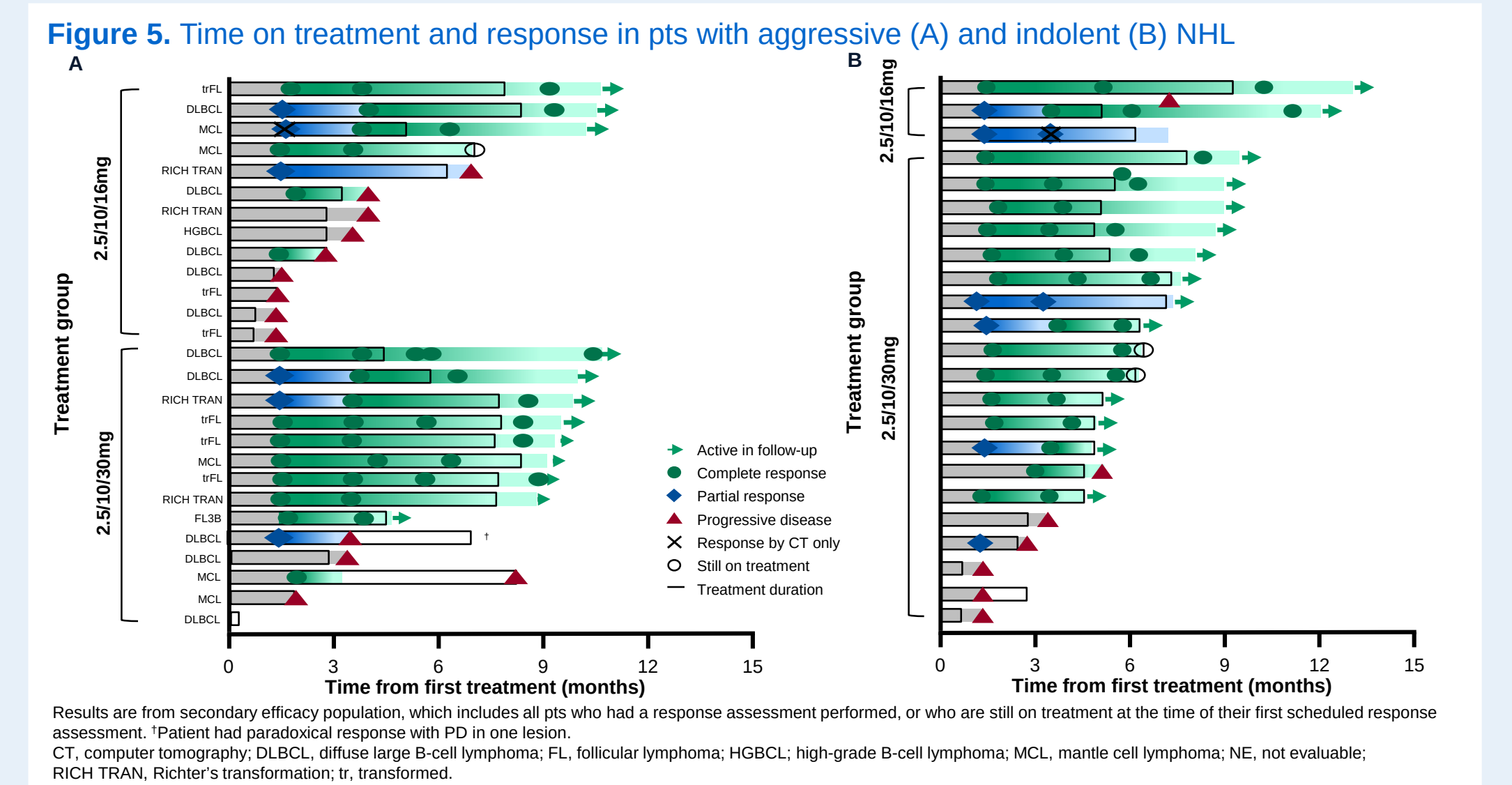
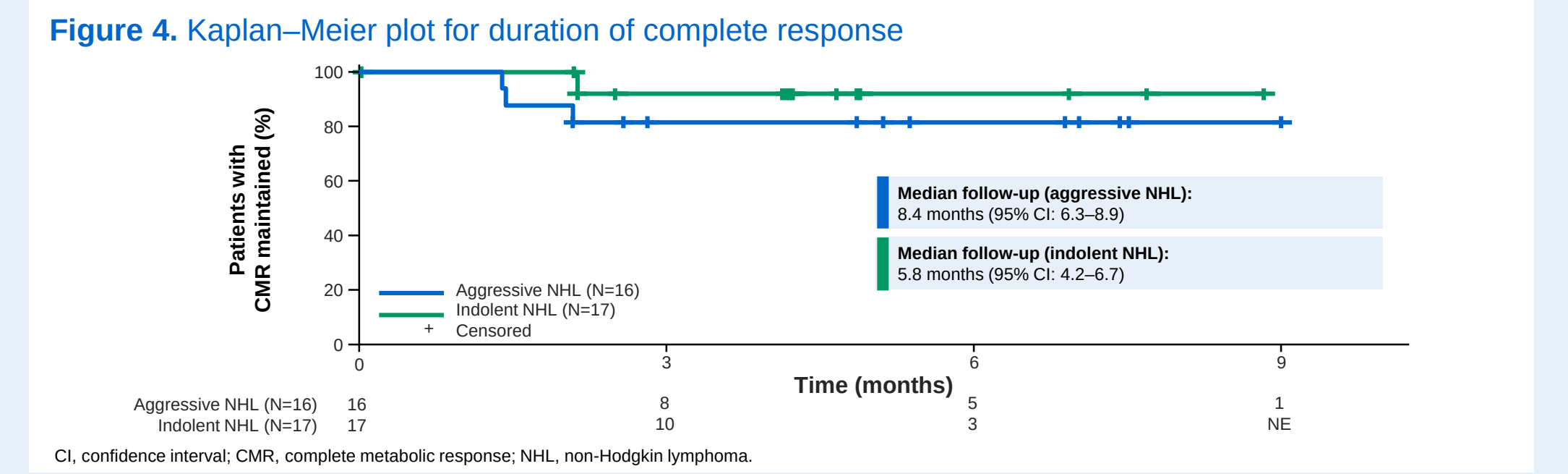
Glofitamab resulted in high response rates

- Response rates for aggressive and indolent NHL are shown in **Figure 2** and waterfall plots in **Figure 3**
 - For aggressive NHL, a trend of improved response was observed at the RP2D (2.5/10/30mg; N=14), with a complete metabolic response (CMR) rate of **71.4%**
 - 4/5 pts (**80%**) with mantle cell lymphoma achieved a CMR.



Most patients have ongoing responses

- Aggressive NHL:** 13/16 CMRs are ongoing, 8 CMRs lasting >3 months; 5 CMRs lasting >6 months.
- Indolent NHL:** 16/17 CMRs are ongoing, 10 CMRs lasting >3 months; 3 CMRs lasting >6 months.



Adverse events reported with glofitamab

- A summary of adverse events (AEs) is presented in **Table 2**.
- Commonly reported AEs were CRS⁴ (67.3%), neutropenia (42.3%), and pyrexia (38.5%) (**Figure 7**).
- CRS was mostly low grade and confined to cycles 1 and 2 (**Figure 6**).

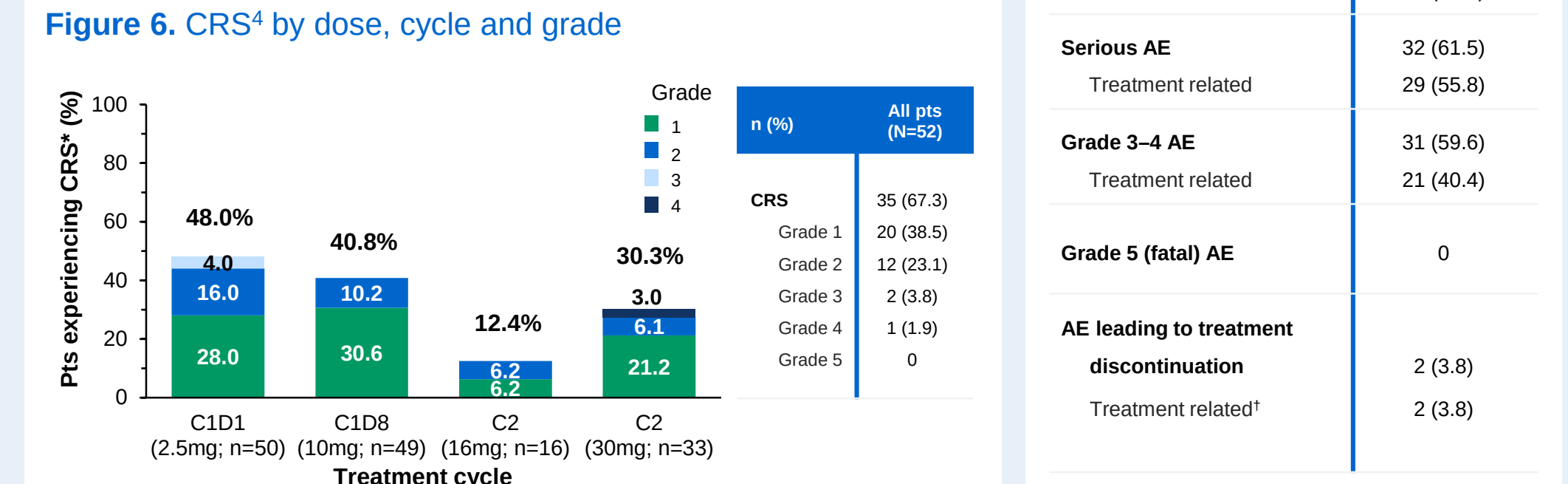
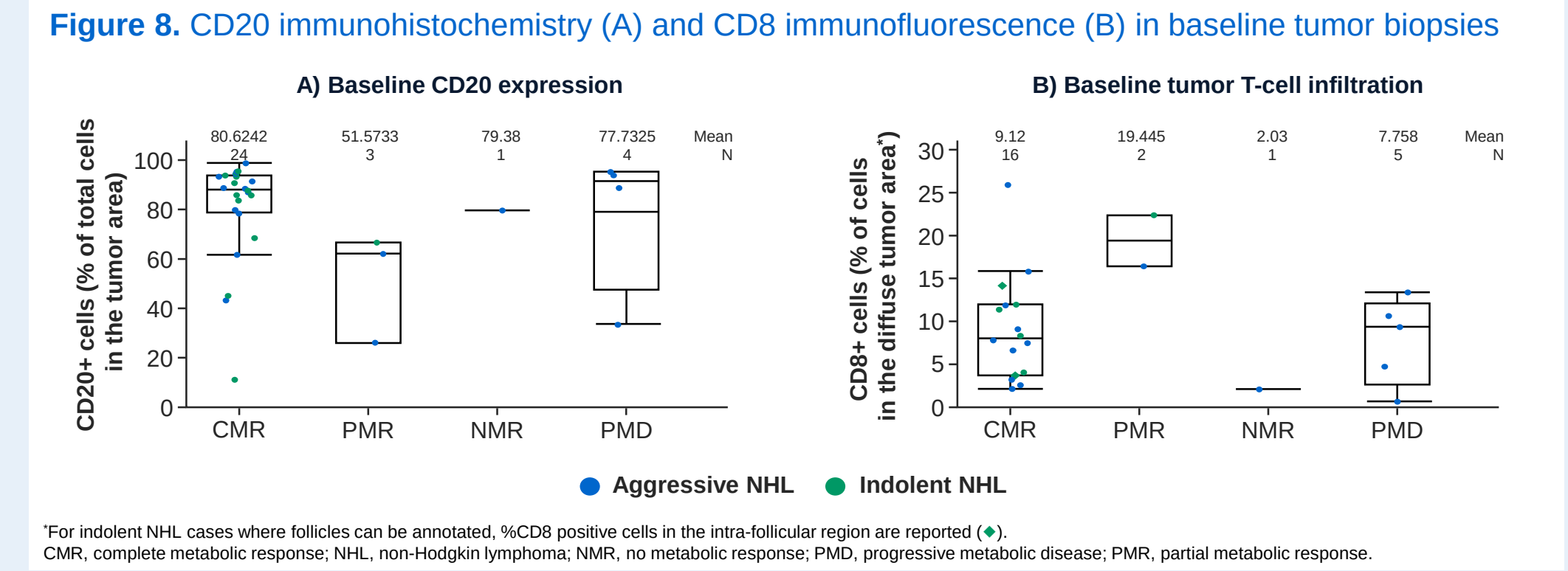


Table 2. Summary of AEs

n (%)	All patients (N=52)
Any AE	51 (98.1)
Treatment related	47 (90.4)
Serious AE	32 (61.5)
Treatment related	29 (55.8)
Grade 3–4 AE	31 (59.6)
Treatment related	21 (40.4)
Grade 5 (fatal) AE	0
AE leading to treatment discontinuation	2 (3.8)
Treatment related*	2 (3.8)

Glofitamab efficacy was observed across a range of CD20 expression levels and was independent of CD8 T-cell levels

- Immunohistochemistry/immunofluorescence analysis of baseline tumor biopsies revealed that clinical responses were achieved across a range of CD20 expression levels (n=32) and irrespective of the amount of tumor T-cell infiltration (n=24). No significant differences were found between response categories.



Conclusions and future directions

Updated glofitamab SUD data show high and durable response rates in pts with aggressive and indolent R/R NHL who have failed multiple lines of therapy.

Responses to glofitamab are achieved early and show durability after completion of the fixed treatment period.

Glofitamab SUD enabled the attainment of a 30mg target dose while CRS remains mainly low grade and confined to Cycle 1 and 2.

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References

1. Bacac M, et al. Clin Cancer Res 2018;24:4785–97.
2. Hutchings M, et al. J Clin Oncol 2021;39:1959–70.
3. Cheson BD, et al. J Clin Oncol 2014;32:3059–68.
4. Lee DW, et al. Biol Blood Marrow Transplant 2019;25:625–38.

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Disclosures

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