# Golcadomide, a Potential, First-In-Class, Oral CELMoD™ Agent, ± Rituximab in Patients With Relapsed/Refractory Diffuse Large B-Cell Lymphoma: Phase 1/2 Study Extended Follow-Up Results

Marc S. Hoffmann,[1] Julio Chavez,[2] Jason R. Westin,[3] Judit Mészáros Jørgensen,[4] Javier Munoz,[5] Cecilia Carpio Segura,[6] Guilherme Fleury Perini,[7] Emmanuel Bachy,[8] Victoria Campbell,[9] Caroline Riley,[10] Franck Morschhauser,[11] Daniel Morillo,[12] Alev Akyol,[13] Berengere de Moucheron,[14] Michael Pourdehnad,[15] Akshay Sudhindra,[13] Soraya Carrancio,[16] Jessica Voetsch,[17] Gang Yang,[18] Serena Perna,[13] Jean-Marie Michot[19]

[1]The University of Kansas Medical Center, Kansas City, KS, USA; [2]Moffitt Cancer Center, Tampa, FL, USA; [3]The University of Texas MD Anderson Cancer Center, Houston, TX, USA; [4]Aarhus University Hospital, Aarhus, Denmark; [5]Mayo Clinic, Phoenix, AZ, USA; [6]University Hospital Vall d'Hebron, Experimental Hematology, Vall d'Hebron Institute of Oncology (VHIO), Barcelona, Spain; [7]Hospital Israelita Albert Einstein, São Paulo, Brazil; [8]Lyon Sud Hospital, Lyon, France; [9]NHS Lothian - Western General Hospital, Edinburgh, Scotland; [10]Rigshospitalet University Hospital, Copenhagen, Denmark; [11]University of Lille, Centre Hospitalier Universitaire de Lille, Lille, France; [12]START Madrid - FJD Early Phase Unit, Fundación Jiménez Díaz University Hospital, Madrid, Spain; [13]Late Clinical Development, Hematology/Oncology and Cell Therapy, Bristol Myers Squibb, Madison, NJ, USA; [14]Center for Innovation and Translational Research Europe (CITRE), Bristol Myers Squibb, Seville, Spain; [15]Early Clinical Development, Hematology/Oncology and Cell Therapy, Bristol Myers Squibb, San Francisco, CA, USA; [16]Oncogenesis (ONC) Thematic Research Center (TRC), Bristol Myers Squibb, San Diego, CA, USA; [17]Translational Informatics and Predictive Sciences, Bristol Myers Squibb, Lawrenceville, NJ, USA; [18]Global Biometrics & Data Sciences, Bristol Myers Squibb, Madison, NJ, USA; [19]Gustave Roussy Institute of Cancer, Département d'Innovation Thérapeutique et d'Essais Précoces (DITEP), Villejuif, France

# Introduction

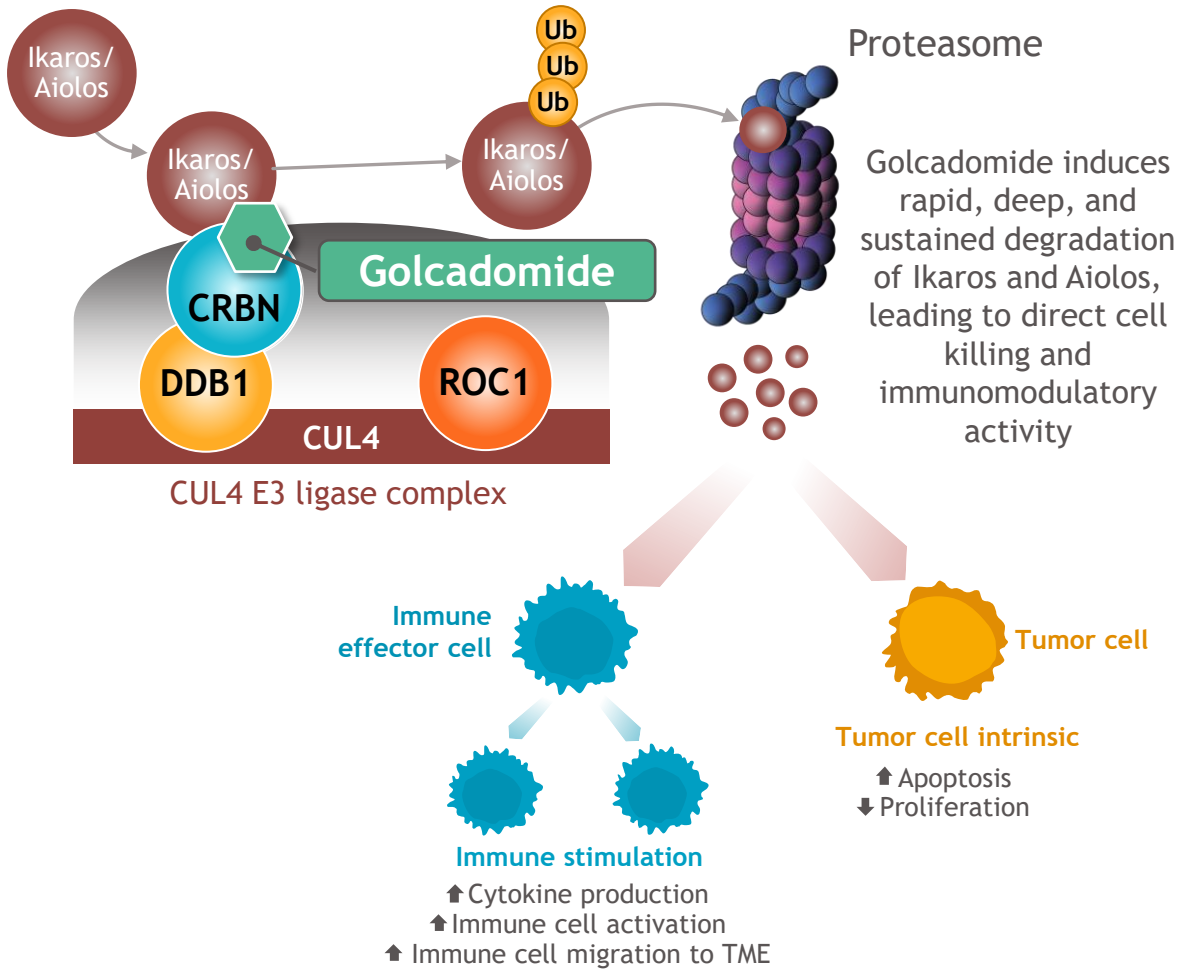
- Approximately 30–40% of patients with DLBCL will experience relapse after initial treatment with standard-of-care chemo-immunotherapy[1]
- Effective treatment options are limited for patients who experience first-line treatment failure, particularly for those with R/R disease who have failed or are unable to receive T-cell—redirecting therapy[2,3]
- Golcadomide is a potential, first-in-class, oral CELMoD agent designed for the treatment of lymphoma. It drives the closed, active conformation of cereblon to induce rapid, deep, and sustained degradation of Ikaros and Aiolos, leading to direct cell killing (agnostic of COO) and immunomodulatory activity[4]
- In a two-part, multicenter, first-in-human Phase 1/2 study (CC-99282-NHL-001; NCT03930953), golcadomide was well tolerated and effective in patients with R/R DLBCL[5]
- Here, we provide longer follow-up results with golcadomide + rituximab in patients with R/R DLBCL from Part B of the Phase 1/2 CC-99282-NHL-001 trial

CAR, chimeric antigen receptor; COO, cell of origin; DLBCL, diffuse large B-cell lymphoma; R/R, relapsed/refractory.

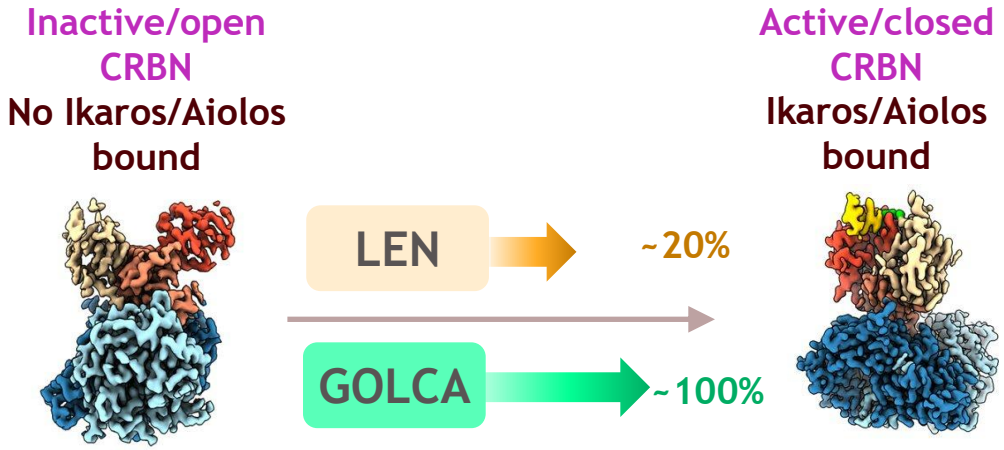
1. Kurz KS, et al. Cancers (Basel) 2023;15(8):2285; 2. Ip A, et al. Adv Ther 2024;41:1226—1244; 3. Sehn LH, at al. N Engl J Med 2021;384(9):842—858; 4. Mo Z, et al. Blood Cancer Discov 2025; doi:10.1158/2643-3230.BCD-25-0059. Online ahead of print; 5. Bachy E, at al. ICML 2025. Oral presentation 148.

# Golcadomide is a potential, first-in-class, oral CELMoD agent for the treatment of lymphoma[1,2]

## Mechanism of action[1,3,4]




## Allosteric regulation of CRBN[1]




- The distinct binding of golcadomide outside of the tri-TRP pocket induces the complete conversion to the active, closed conformation of cereblon vs LEN (~100% vs ~20%), leading to deeper and more rapid degradation of Ikaros/Aiolos compared with LEN
- Golcadomide deeply penetrates lymphoid tissue, an optimal feature for the treatment of lymphoma

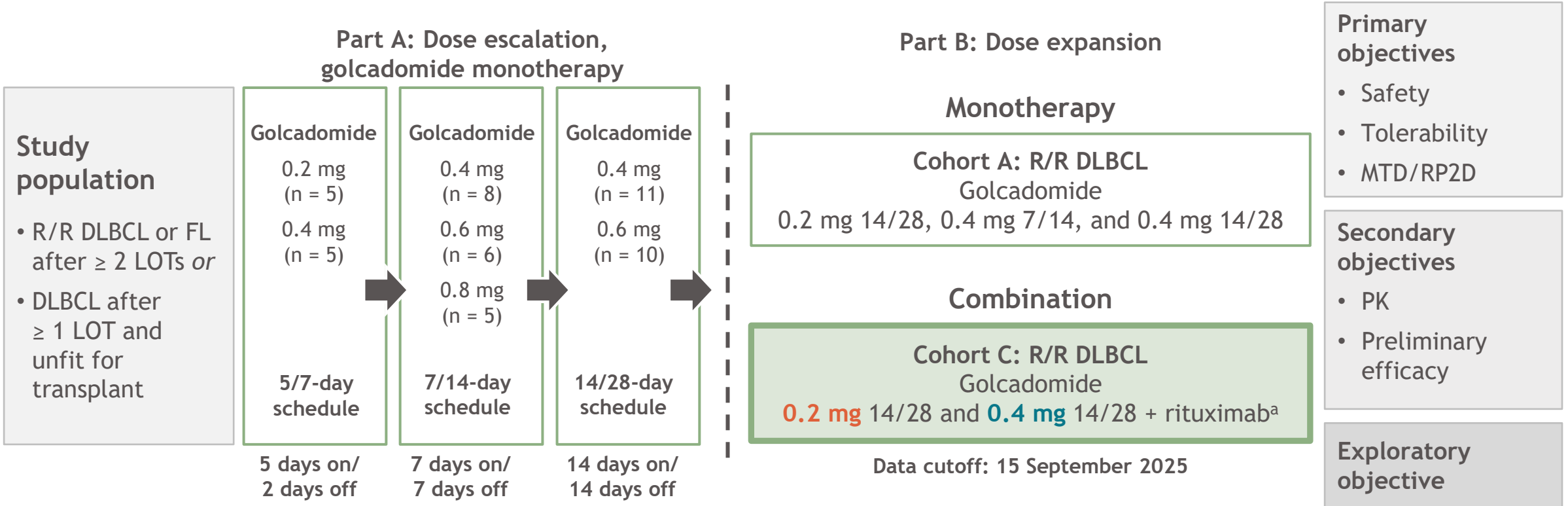
CRBN, cereblon; CUL4, cullin 4; DDB1, DNA damage-binding protein 1; GOLCA, golcadomide; LEN, lenalidomide; ROC1, regulator of cullins; TME; tumor microenvironment; TRP, tryptophan; Ub, ubiquitin.

1. Mo Z, et al. Blood Cancer Discov 2025; doi: 10.1158/2643-3230.BCD-25-0059. Online ahead of print; 2. Amzallag A, et al. ASH 2024. Oral presentation 579; 3. Carrancio S, et al. ASH 2024. Poster presentation 3104; 4. Nakayama Y, et al. ASH 2024. Poster presentation 1617.



Hoffmann MS, et al. ASH 2025. Abstract 479.

# CC-99282-NHL-001: A two-part, multicenter, Phase 1/2 study of golcadomide as monotherapy and in combination with rituximab in patients with R/R NHL




- Total duration of treatment with golcadomide was up to 2 years
- PD changes in immune populations and Ikaros/Aiolos degradation were monitored by flow cytometry
- ctDNA was analyzed by CAPP-Seq, and BL biopsies were profiled by RNA-Seq

[a] Rituximab dosing was 375 mg/m$^2$ IV on Days 1, 8, 15, and 22 of Cycle 1 and Day 1 of Cycles 2–5.
BL, baseline; CAPP-Seq, cancer personalized profiling by deep sequencing; ctDNA, circulating tumor DNA; DLBCL, diffuse large B-cell lymphoma; FL, follicular lymphoma; IV, intravenously; LOT, line of therapy; MTD, maximum tolerated dose; NHL, non-Hodgkin lymphoma; PD, pharmacodynamics; PK, pharmacokinetics; R/R, relapsed/refractory; RNA-Seq, RNA sequencing; RP2D, recommended Phase 2 dose.

Hoffmann MS, et al. ASH 2025. Abstract 479.

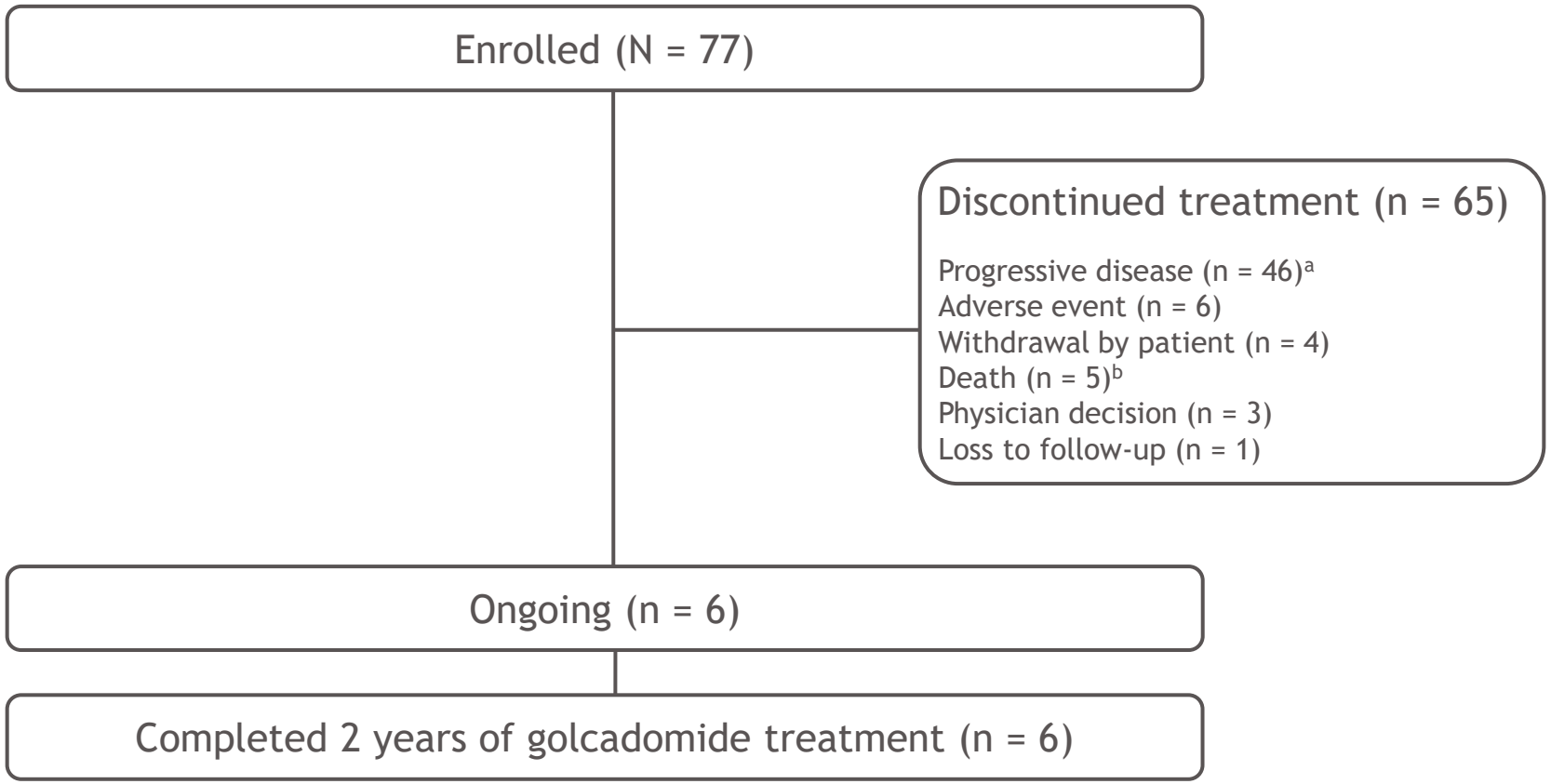
# Cohort C consisted of a heavily pretreated R/R DLBCL patient population

| Characteristic | Part B Cohort C | |
|---|---|---|
| | Golcadomide 0.2 mg + RTX (n = 39) | Golcadomide 0.4 mg + RTX (n = 38) |
| **Age, median (range), years** | 65.0 (20–86) | 68.5 (21–78) |
| **Sex, male, n (%)** | 24 (62) | 24 (63) |
| **Diagnosis, n (%)** | | |
| DLBCL | 39 (100) | 37 (97) |
| Double-hit[a]/triple-hit[b] positive | 6 (15) | 13 (34) |
| Grade 3b FL | 0 | 1 (3) |
| Stage III–IV | 30 (77) | 31 (82) |
| **Hans COO, n (%)[c]** | | |
| GCB | 11 (28) | 7 (18) |
| Non-GCB | 4 (10) | 3 (8) |
| Other[d] | 24 (62) | 27 (71) |
| **ECOG PS, n (%)** | | |
| 0 | 12 (31) | 16 (42) |
| 1 | 24 (62) | 17 (45) |
| 2 | 3 (8) | 5 (13) |
| **Treatment history** | | |
| Median prior LOTs (range), No. | 4 (1–11) | 4.5 (1–11) |
| Prior stem cell transplant, n (%) | 4 (10) | 7 (18) |
| Prior T-cell–redirecting therapy, n (%)[e] | 26 (67) | 22 (58) |
| Prior lenalidomide treatment, n (%) | 10 (26) | 10 (26) |
| **Best response to last regimen, n (%)** | | |
| Refractory | 19 (49) | 15 (39) |
| CR or PR | 12 (31) | 15 (39) |
| Unknown | 8 (21) | 8 (21) |

Data cutoff: 15 September 2025. Data are from the safety population (n = 77).
[a] Double hit is defined as a positive case of MYC + BCL2 or MYC + BCL6 determined by FISH; [b] Triple hit is defined as a positive case of MYC + BCL2 + BCL6 determined by FISH; [c] Determined by immunohistochemistry; [d] Other includes not done, unknown, or missing; [e] CAR T and/or bispecific antibody treatment. BCL, B-cell lymphoma; CAR, chimeric antigen receptor; COO, cell of origin; CR, complete response; DLBCL, diffuse large B-cell lymphoma; ECOG PS, Eastern Cooperative Oncology Group performance status; FISH, fluorescence in situ hybridization; FL, follicular lymphoma; GCB, germinal center B cell; LOT, line of therapy; PR, partial response; RTX, rituximab.

Hoffmann MS, et al. ASH 2025. Abstract 479.

# Patient disposition in Cohort C



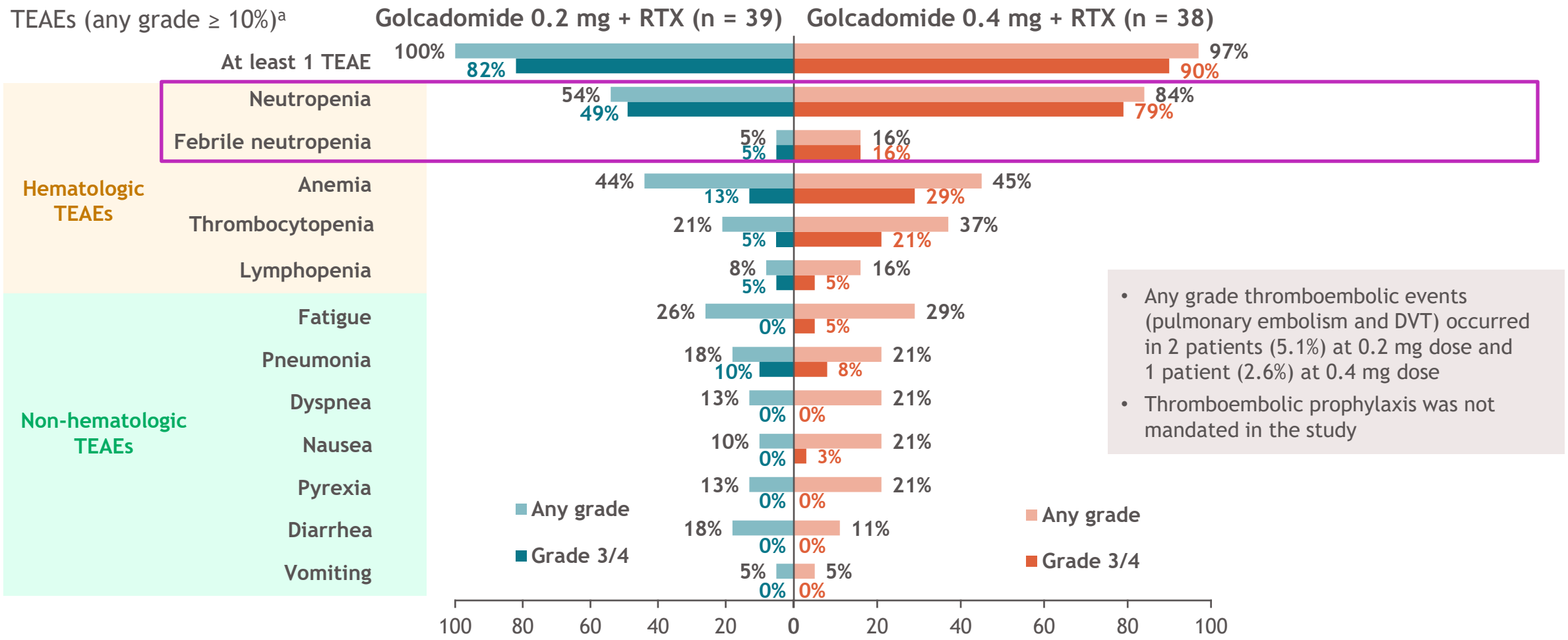

Median follow-up was 7.13 (range, 0.3—37.5) months (ITT population)

Data cutoff: 15 September 2025.
[a] Progressive disease is inclusive of symptomatic deterioration, disease relapse, and lack of efficacy; [b] Includes deaths due tubulointerstitial nephritis (n=1), pneumonia (n = 1), septic shock (n = 1) and general physical health deterioration (n=2). Only pneumonia was assessed as related to study drug.
ITT, intention to treat.



Hoffmann MS, et al. ASH 2025. Abstract 479.

# TEAEs were mainly hematologic, and non-hematologic TEAEs were infrequent and mostly low grade




- Any grade thromboembolic events (pulmonary embolism and DVT) occurred in 2 patients (5.1%) at 0.2 mg dose and 1 patient (2.6%) at 0.4 mg dose
- Thromboembolic prophylaxis was not mandated in the study

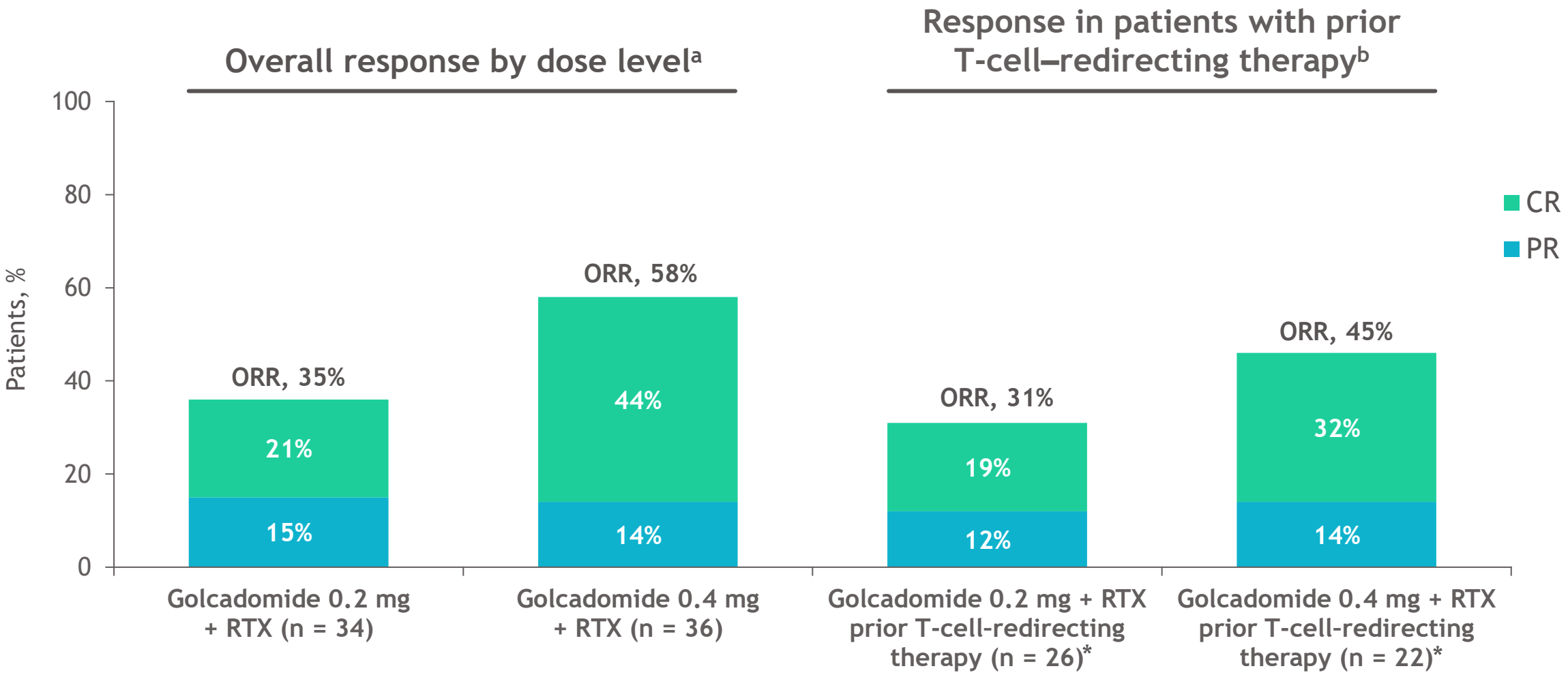
- One case of Grade 5 pneumonia was considered related to study treatment (golcadomide 0.2 mg + RTX)

Data cutoff: 15 September 2025.

[a] System organ classes with events occurring in 10% of the overall population are shown. Additional clinically relevant TEAEs have also been included. System organ class and preferred terms coded using Medical Dictionary for Regulatory Activities version 27.0 or higher. TEAEs were graded according to the National Cancer Institute Common Terminology Criteria for Adverse Events version 5.0. DVT, deep vein thrombosis; RTX, rituximab; TEAE, treatment-emergent adverse event.

Hoffmann MS, et al. ASH 2025. Abstract 479.

# Golcadomide 0.4 mg + RTX achieves a high ORR and CRR in a heavily pretreated patient population, including patients with prior T-cell–redirecting therapy



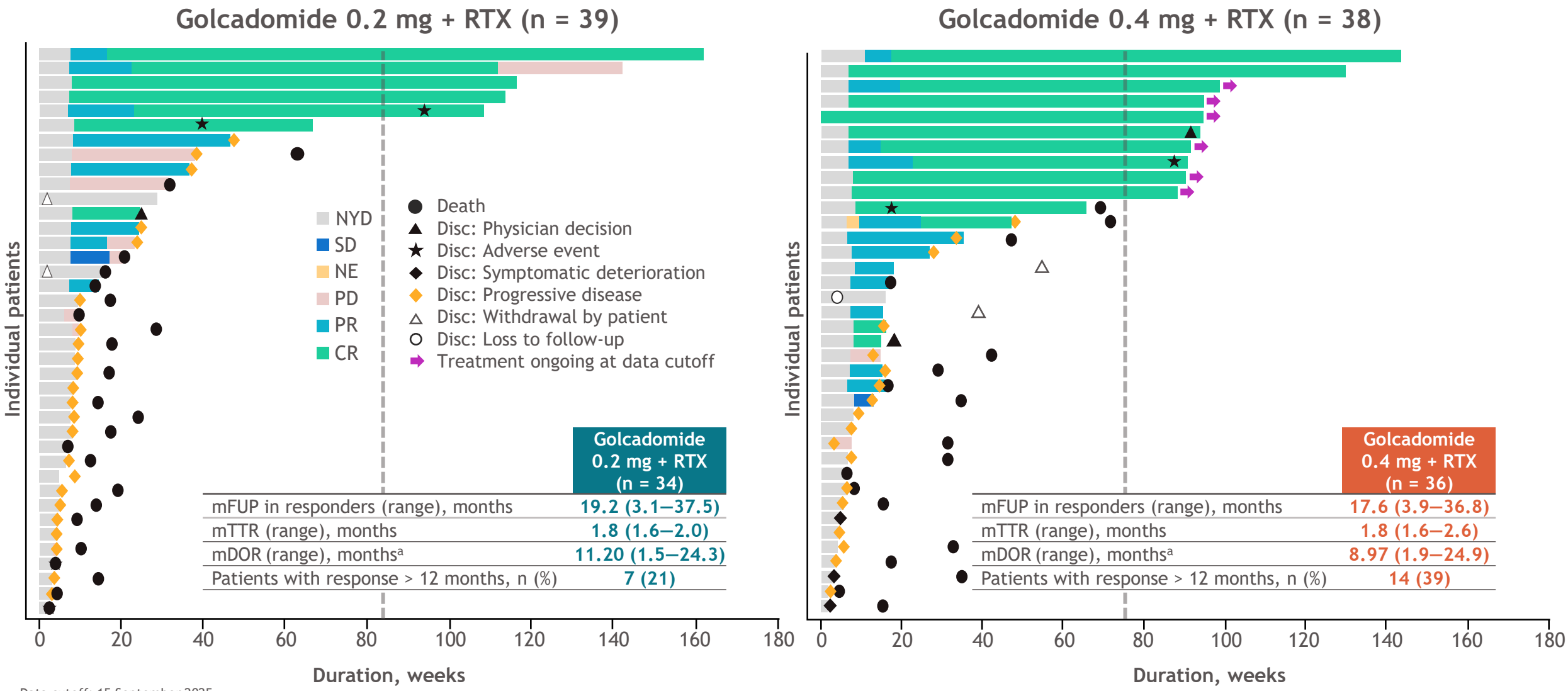

Data cutoff: 15 September 2025.

[a] Efficacy-evaluable population consisting of patients who completed ≥ 1 cycle of golcadomide (taking ≥ 75% of assigned doses) and having a baseline and ≥ 1 postbaseline tumor assessment.; [b] CAR T and/or bispecific antibody treatment.

*11 and 14 patients had both CAR-T and bispecifics in the 0.2mg and 0.4mg, respectively; CAR, chimeric antigen receptor; CR, complete response; CRR, complete response rate; ORR, overall response rate; PR, partial response; RTX, rituximab.

Hoffmann MS, et al. ASH 2025. Abstract 479.

# Golcadomide 0.4 mg + RTX demonstrated durable remissions




| | Golcadomide 0.2 mg + RTX (n = 34) | Golcadomide 0.4 mg + RTX (n = 36) |
|---|---|---|
| mFUP in responders (range), months | 19.2 (3.1–37.5) | 17.6 (3.9–36.8) |
| mTTR (range), months | 1.8 (1.6–2.0) | 1.8 (1.6–2.6) |
| mDOR (range), months[a] | 11.20 (1.5–24.3) | 8.97 (1.9–24.9) |
| Patients with response > 12 months, n (%) | 7 (21) | 14 (39) |

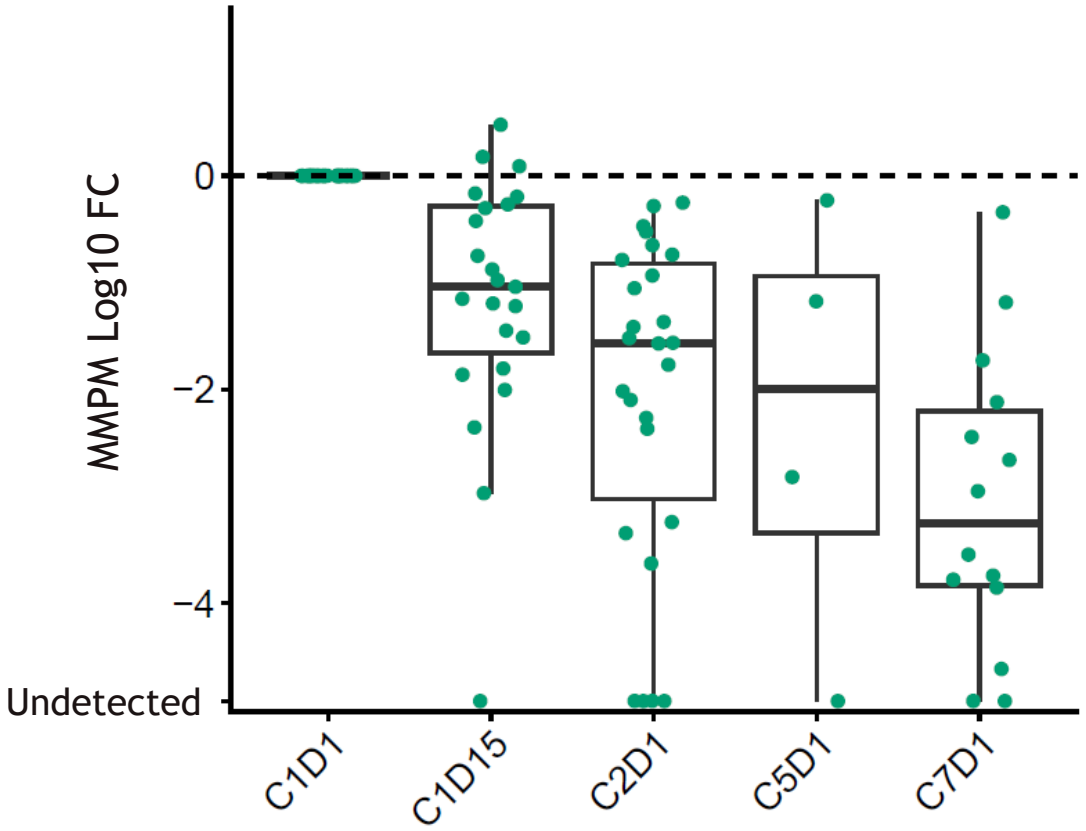
Data cutoff: 15 September 2025.

[a] Duration of response is measured from the time measurement criteria are first met for CR/CRu or PR (whichever is first recorded) until the first date at which PD or death is objectively documented, whichever comes first. If no PD or death, then patients are censored and calculated as the last tumor assessment date - first recorded date of CR/CRu/PR + 1. Based on responders only. CR, complete response; CRu, complete response unconfirmed; Disc, discontinued; mDOR, median duration of response; mFUP, median follow-up; mTTR, median time to response; NE, not evaluable; NYD, not yet determined; PD, progressive disease; PR, partial response; RTX, rituximab; SD, stable disease.

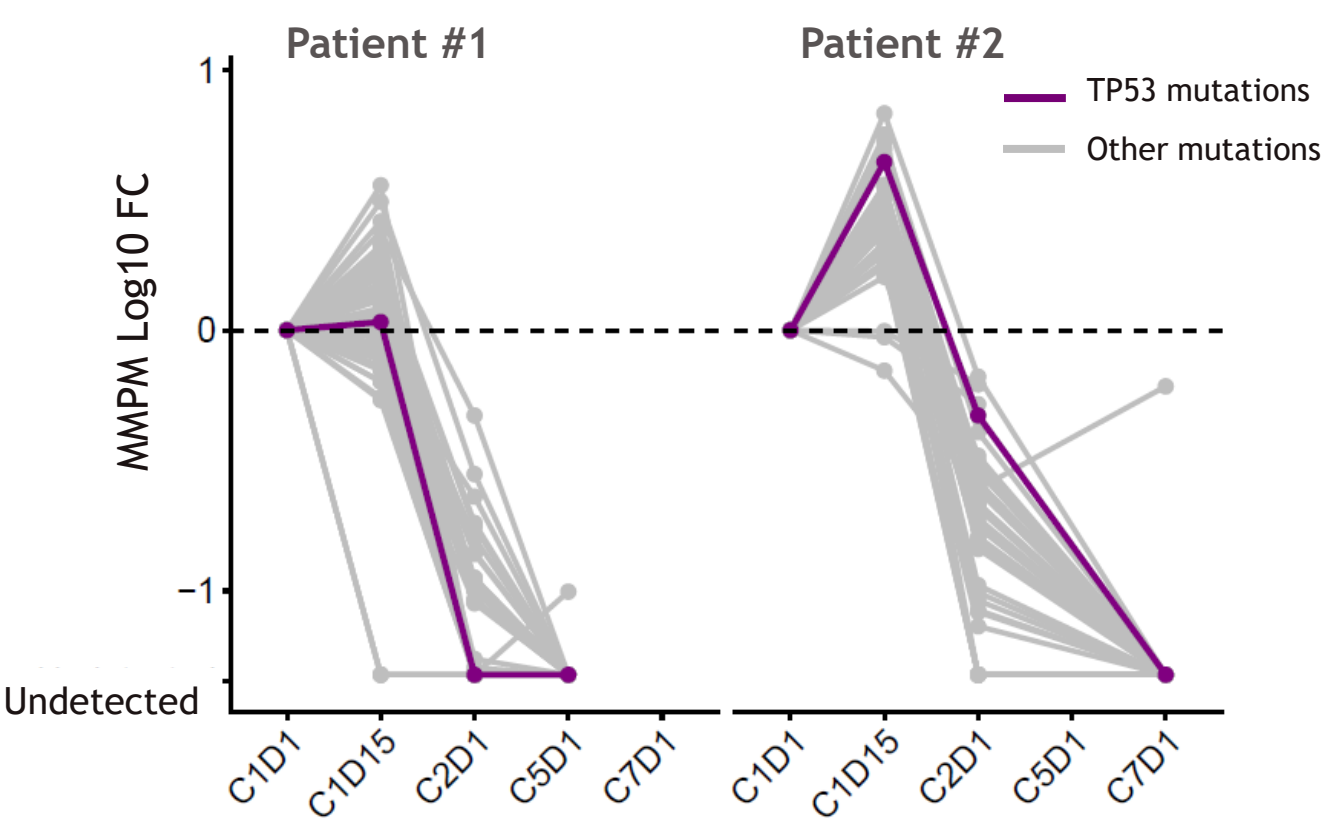
Hoffmann MS, et al. ASH 2025. Abstract 479.

# Golcadomide + RTX resulted in early, deep reductions in ctDNA including in high-risk TP53 mutations

## Change in ctDNA level across doses*




## Change in single mutant variants




ctDNA reduction continues to deepen over time, inducing MRD negativity[a] in ~30% of CRs

Variant analysis demonstrates molecular clearance of TP53 mutants in CRs

[a] Undetectable ctDNA ($1 \times 10^{-4}$ threshold) by CAPP-Seq assay. *Select patients. C1D1, cycle 1 day 1; CRs, complete responders; ctDNA, circulating tumor DNA; MRD, minimal residual disease; RTX, rituximab; MMPM, mutant molecules per mL.

Hoffmann MS, et al. ASH 2025. Abstract 479.

# Conclusions

- Golcadomide + rituximab continued to demonstrate a predictable and manageable safety profile, similar to that reported previously; no new safety signals were observed with longer follow-up
  - TEAEs were mainly hematologic, with low rates of non-hematologic toxicity
- Golcadomide + rituximab showed promising efficacy in heavily pre-treated patients with R/R DLBCL; durable responses were observed, including in those with prior T-cell–redirecting therapy
  - Golcadomide 0.4 mg + rituximab resulted in an ORR of 58% and a CRR of 44%, vs an ORR of 35% and a CRR of 21% with golcadomide 0.2 mg + rituximab
  - With a median follow-up of 17.6 months among responders, durable remissions of > 12 months were observed in 14 patients (39%) with golcadomide 0.4 mg + rituximab
- Golcadomide + rituximab resulted in early, deep reductions in ctDNA including in the 2 patients with high-risk TP53 mutations
- These data continue to support the ongoing development of golcadomide for patients with NHL, including the Phase 3 GOLSEEK-1 study in previously untreated, high-risk LBCL (NCT06356129)[1] and the newly initiated Phase 3 GOLSEEK-4 study in 2L+ FL (NCT06911502)[2]

CRR, complete response rate; DLBCL, diffuse large B-cell lymphoma; FL, follicular lymphoma; MRD, minimal residual disease; NHL, non-Hodgkin lymphoma; ORR, overall response rate; R/R, relapsed/refractory; RTX, rituximab;TEAE, treatment emergent adverse event. 1. Vassilakopoulos TP, et al. ASH 2025. Poster 3704; 2. Hawkes E, et al. EHA 2025. Abstract PB3190.

# Acknowledgments


- The patients and their families who are making the study possible
- The clinical study teams who participated
- The study was supported by Bristol Myers Squibb
- All authors contributed to and approved the presentation
- Writing and editorial assistance were provided by Lindsay Faure, MSc, and Joel Schwartz-Moretti, PhD, of Nucleus Global, an Inizio company, and funded by Bristol Myers Squibb