Golcadomide, a Potential, First-In-Class, Oral CELMoD™ Agent, Plus R-CHOP in Patients With Previously Untreated Aggressive B-Cell Lymphoma: 24-Month Efficacy Results

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ASH 2025, Presentation 476

Introduction

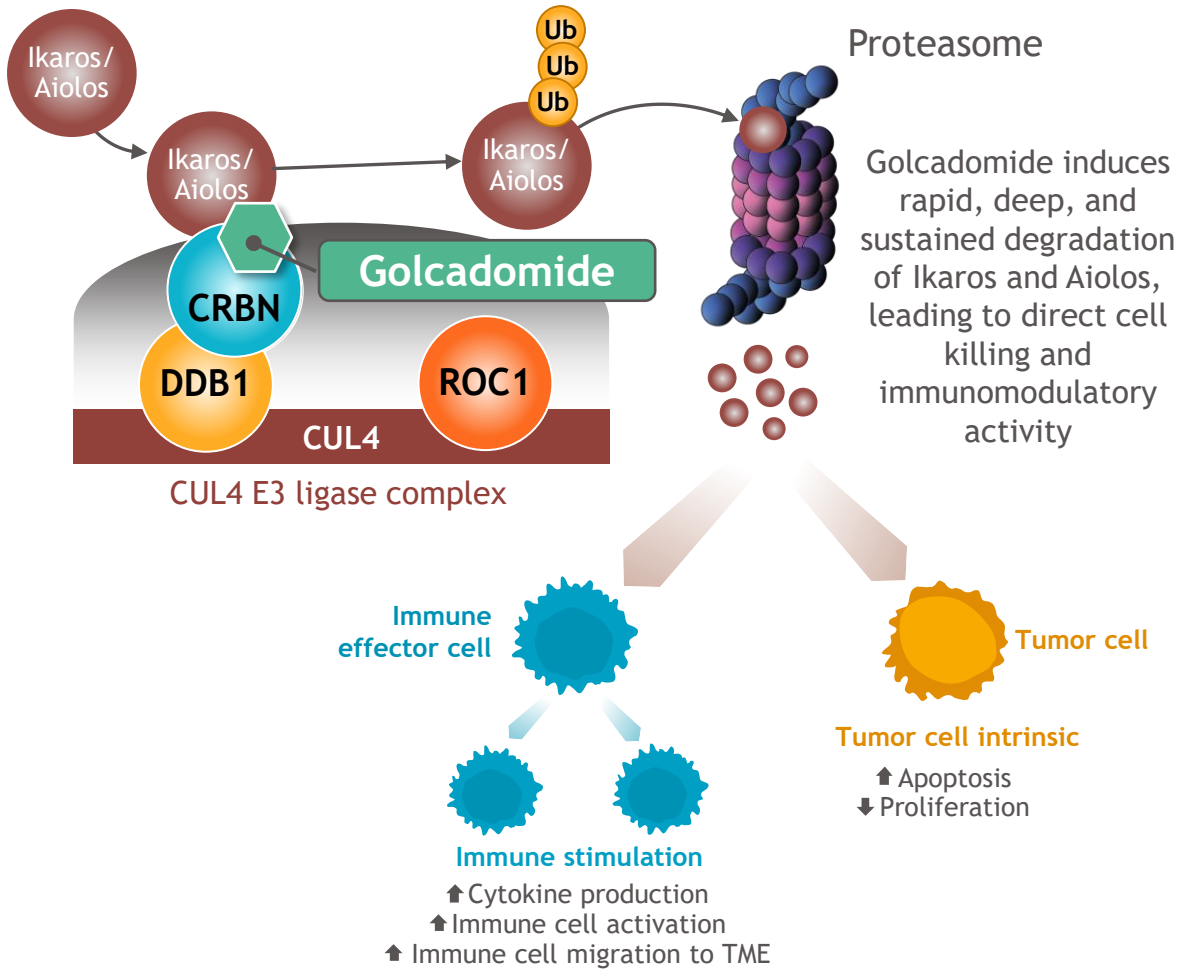
- LBCL is the most common aggressive lymphoma, with 30–40% of patients not cured by SOC regimens in the 1L setting[1]
- The International Prognostic Index is widely used to predict outcomes in 1L; however, it fails to identify a subset of patients with an inferior prognosis with the lower scores (IPI of 1 or 2)[2,3]
  - Patients with an IPI score of 1—2, who have high LDH (≥ 1.3 × ULN) and/or bulky disease (single lesion of ≥ 7 cm maximum diameter) were identified as a high-risk subset with similar progression rates to those of IPI 3 patients[2]
- Golcadomide is a potential, first-in-class, oral CELMoD agent designed for the treatment of lymphoma. It drives the active, closed conformation of cereblon to induce rapid and deep degradation of Ikaros and Aiolos, leading to direct cell killing and immunomodulatory activity[4]
- In the Phase 1b dose-escalation and dose-expansion trial CC-220-DLBCL-001 (NCT04884035) in 1L LBCL, golcadomide + R-CHOP has shown manageable safety and promising efficacy, with a 1-year PFS rate of 86% in patients with high-risk disease, and high rates of EOT CMR and MRD negativity[5,6]
- In this presentation, we report long-term efficacy results with a median follow-up of over 24 months

1L, first line; CMR, complete metabolic response; EOT, end of treatment; IPI, International Prognostic Index; LBCL, large B-cell lymphoma; LDH, lactate dehydrogenase; MRD, minimal residual disease; PFS, progression-free survival; R-CHOP, rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone; SOC, standard of care; ULN, upper limit of normal.

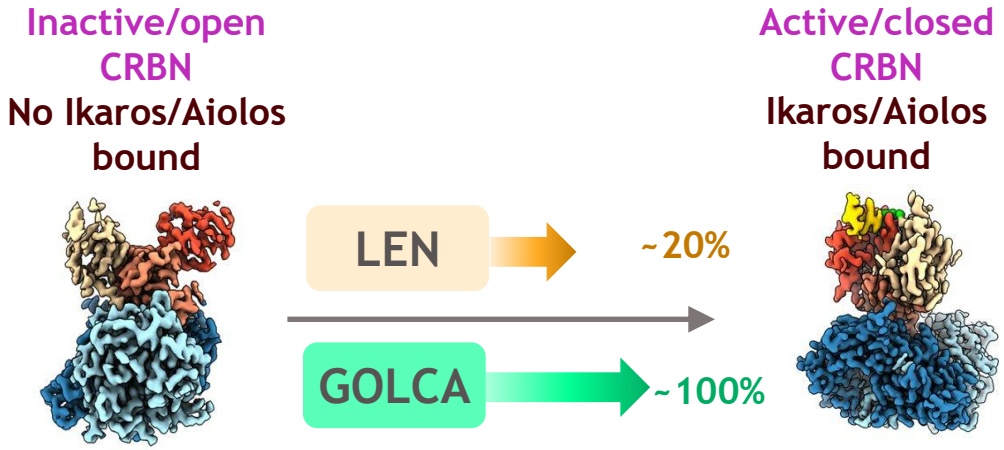
1. Duarte C & Kamdar M. Am Soc Clin Oncol Educ Book 2023;43:e390802; 2. Maurer MJ, et al. ASH 2023. Poster presentation 4512; 3. McMillan AK, et al. Ann Oncol 2020;31:1251—1259; 4. Mo Z, et al. Blood Cancer Discov 2025; doi:10.1158/2643-3230.BCD-25-0059. Online ahead of print; 5. Hoffmann MS, et al. EHA 2024. Abstract S235; 6. Amzallag A, et al. ASH 2024. Oral presentation 579.

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

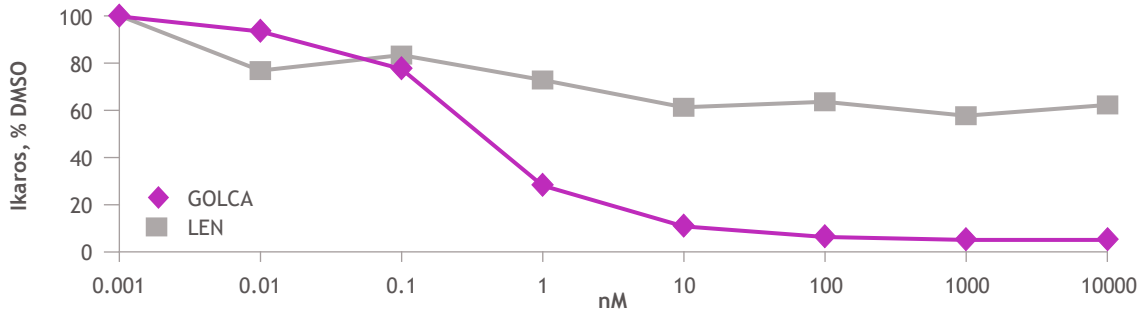
CRBN, cereblon; CUL4, cullin 4; DDB1, DNA damage-binding protein 1; GOLCA, golcadomide; LEN, lenalidomide; ROC1, regulator of cullins 1; TME, tumor microenvironment; TRP, tryptophan; Ub, ubiquitin.

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.

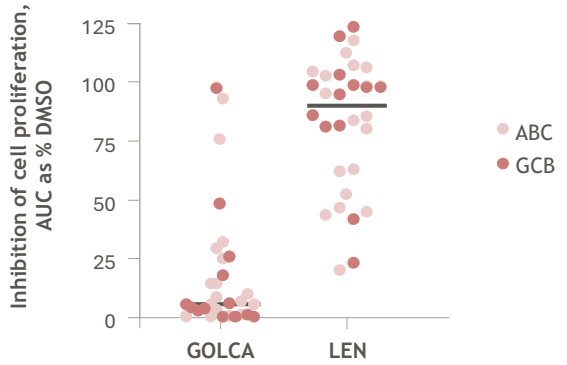
Nowakowski GS, et al. ASH 2025. Abstract 476.

Golcadomide has potent tumoricidal and immune stimulatory effects in lymphoma, with preferential tissue distribution

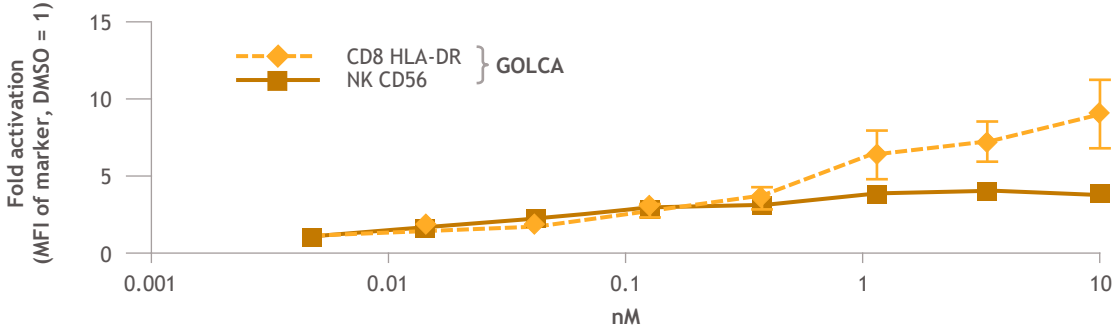
Potent Ikaros degradation[1,2]



Inhibits proliferation agnostic of COO[1]

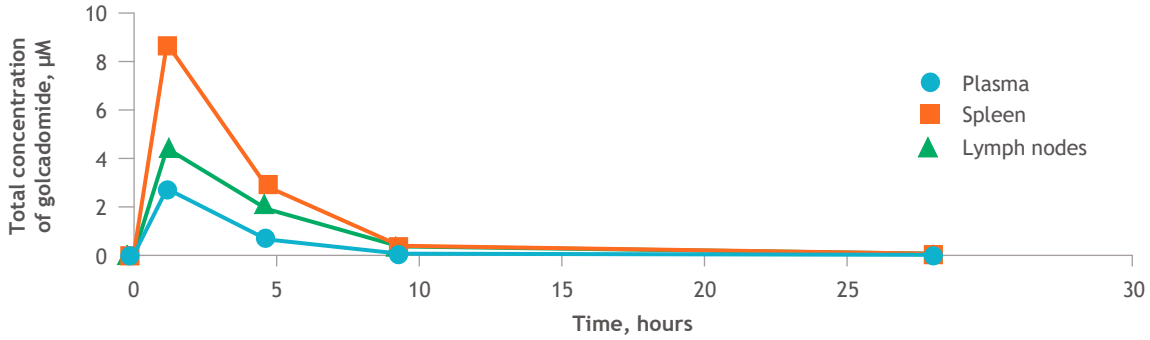


Stimulation of T and NK cells[1]



Distribution favors target organs[3]

Rat, 10 mg/kg PO dosing



ABC, activated B cell; AUC, area under the curve; CD, cluster of differentiation; COO, cell of origin; DMSO, dimethyl sulfoxide; GCB, germinal center B cell; GOLCA, golcadomide; HLA-DR, human leukocyte antigen DR isotype; LEN, lenalidomide; MFI, mean fluorescence intensity; NK, natural killer; PO, orally.

1. Thiebelmont C, et al. ASH 2022. Oral presentation 233; 2. Mo Z, et al. Blood Cancer Discov 2025; doi:10.1158/2643-3230.BCD-25-0059. Online ahead of print; 3. Bristol Myers Squibb. Data on file (BMS-REF-HEMA-0004).

Nowakowski GS, et al. ASH 2025. Abstract 476.

CC-220-DLBCL-001: An ongoing Phase 1b dose-escalation and dose-expansion trial of golcadomide + R-CHOP in untreated aggressive B-cell lymphoma[1,2]

Screening period

Key eligibility criteria

- Age ≥ 18 years
- Diagnosis of aggressive B-cell lymphoma[3,a]
- Measurable lesion ≥ 1.5 cm (by CT/MRI)
- Previously untreated
- ECOG performance status 0—2
- IPI score
  - Part 1: 0—5
  - Part 2: 2—5

Treatment period

Dose escalation (part 1)

Golcadomide + R-CHOP-21

- DL-1: Golcadomide 0.2 mg, D1—7
- DL1: Golcadomide 0.4 mg, D1—7
- DL2: Golcadomide 0.4 mg, D1—10[c]

R 1:1

Dose expansion (part 2)

- Golcadomide + R-CHOP-21 at RP2D-1
- Golcadomide + R-CHOP-21 at RP2D

ctDNA was collected at baseline, C2D1, C3D1, and EOT

Patients were treated for 6 cycles unless progressive disease or unacceptable toxicity occurred, patient withdrew from study, or physician decision led to discontinuation

Endpoints

1 Primary endpoints

- Part 1: MTD and RP2D
- Part 2: Safety[b] and tolerability at RP2D (DL1)

2 Secondary efficacy endpoints

- Best ORR, CMR rate, DOR, PFS, and OS

Exploratory efficacy endpoints

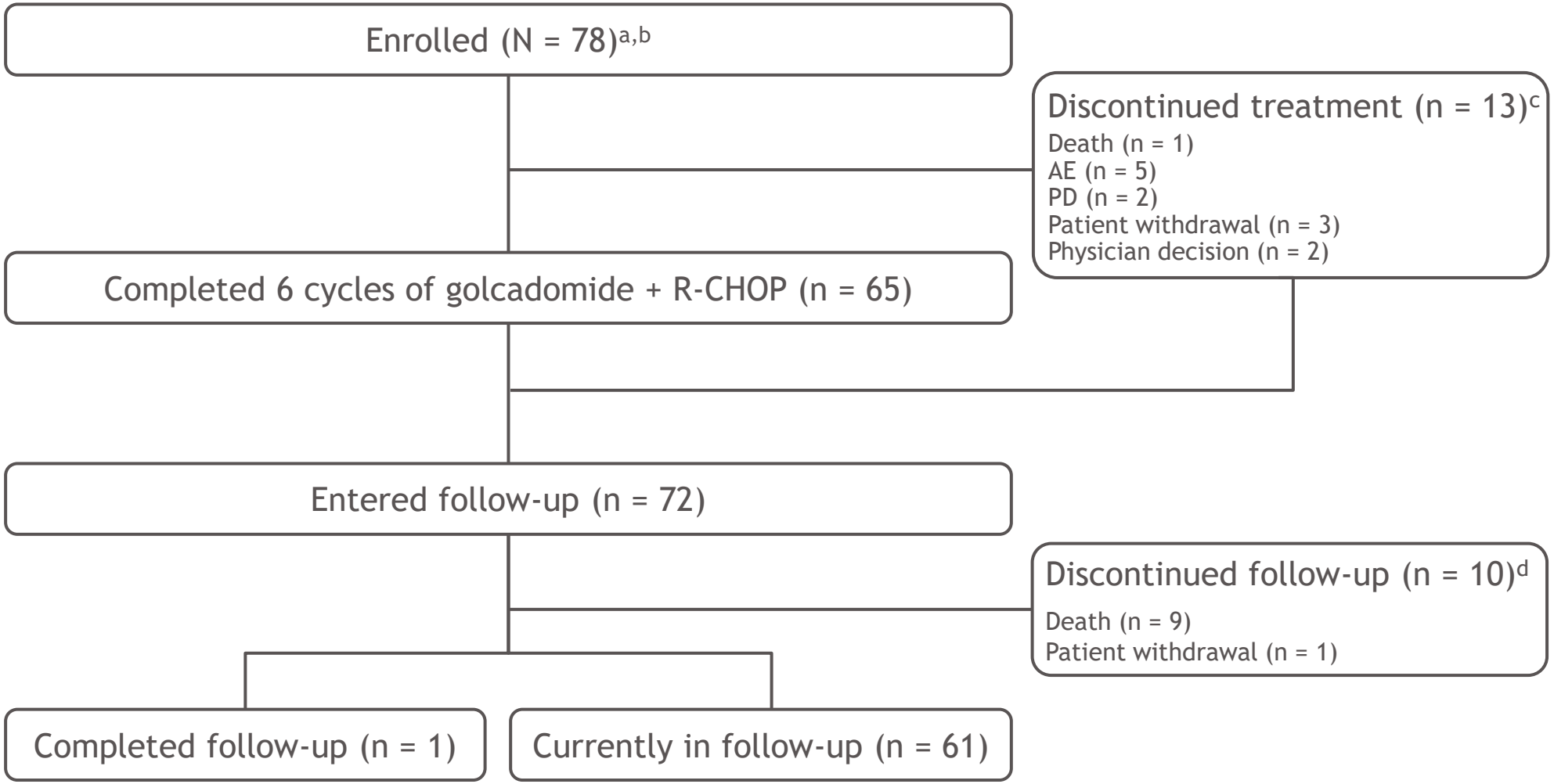
- PK, PD, and biomarkers

Data cutoff for efficacy: May 12, 2025. Data cutoff for safety: September 23, 2024. [a] Aggressive B-cell lymphoma defined according to WHO 2016 classification,[3] including DLBCL, high-grade BCL with *MYC* and *BCL2* and/or *BCL6* rearrangements, primary mediastinal BCL, primary cutaneous DLBCL—leg type, ALK-positive large BCL, EBV-positive DLBCL, and grade 3b FL; [b] Safety analysis population included all enrolled patients who received ≥ 1 dose of study drug; [c] Patients in DL2 met the dose-limiting toxicity threshold, and this dose was not continued in the expansion phase. ALK, anaplastic lymphoma kinase; C, cycle; CMR, complete metabolic response; CT, computed tomography; ctDNA, circulating tumor DNA; D, day; DL, dose level; DLBCL, diffuse large B-cell lymphoma; DOR, duration of response; EBV, Epstein-Barr virus; ECOG, Eastern Cooperative Oncology Group; EOT, end of treatment; FL, follicular lymphoma; IPI, International Prognostic Index; MRI, magnetic resonance imaging; MTD, maximum tolerated dose; ORR, overall response rate; OS, overall survival; PD, pharmacodynamics; PFS, progression-free survival; PK, pharmacokinetics; R, randomized; RP2D, recommended Phase 2 dose; R-CHOP, rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone; WHO, World Health Organization.

1. Hoffmann MS, et al. ASH 2023. Abstract 4459; 2. Hoffmann MS, et al. EHA 2024. Abstract S235; 3. Swerdlow SH, et al. Blood 2016;127:2375—2390.

Nowakowski GS, et al. ASH 2025. Abstract 476.

Patient disposition in study CC-220-DLBCL-001



Data cutoff: May 12, 2025.
[a] All enrolled patients received ≥ 1 dose of study therapy; [b] Median (range) number of golcadomide cycles was 6 (1—6) in the 0.2 mg D1—7 and 0.4 mg D1—7 cohorts; [c] Four and seven patients discontinued golcadomide 0.2 mg D1—7 and 0.4 mg D1—7, respectively; [d] Four patients in each cohort discontinued golcadomide 0.2 mg D1—7 and 0.4 mg D1—7.
AE, adverse event; PD, progressive disease; R-CHOP, rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone.

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Baseline characteristics were generally balanced between treatment arms

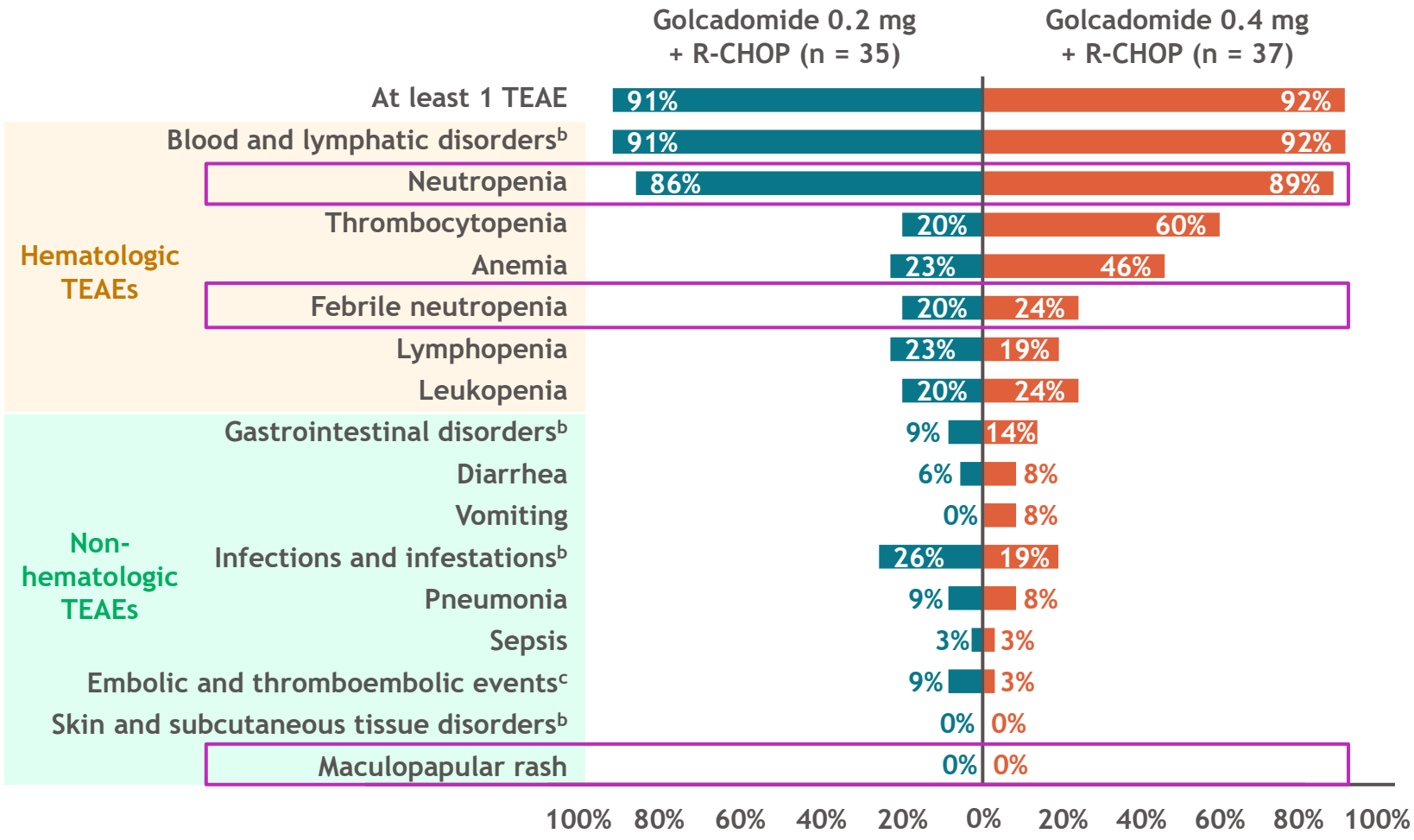
	Golcadomide 0.2 mg + R-CHOP[a] (n = 35)	Golcadomide 0.4 mg + R-CHOP[a] (n = 37)
Age, median (IQR), years	62.0 (52.0–69.0)	63.0 (53.0–69.0)
Female	12 (34)	20 (54)
IPI score at enrollment		
Low and low-intermediate risk (0–2)	11 (31)	11 (30)
Low-intermediate (1–2) risk with high-risk features[b]	6 (17)	5 (14)
High-intermediate risk (3)	17 (49)	16 (43)
High risk (4 or 5)	7 (20)	10 (27)
High-risk disease[c]	30 (86)	31 (84)
Hans COO[d]		
GCB	18 (51)	18 (49)
Non-GCB	12 (34)	12 (32)
Other[e]	5 (14)	7 (19)
Histology		
DLBCL NOS	27 (77)	32 (87)
Grade 3b FL	4 (11)	1 (3)
Double-hit lymphoma[f]	3 (9)	2 (5)
EBV-positive DLBCL NOS	1 (3)	0
ALK-positive LBCL	0	1 (3)
Elevated LDH	27 (77)	27 (73)
Extranodal involvement		
≤ 1 site	19 (54)	19 (51)
> 1 site	16 (46)	18 (49)

Data cutoff: May 12, 2025. Data are n (%) unless otherwise noted. [a] Includes patients who received the D1–7 schedule in dose escalation plus the RP2D in dose expansion; [b] Defined as IPI 1–2 with ≥ 1 lesion with a maximum diameter ≥ 7 cm and/or screening LDH ≥ 1.3 × ULN; [c] High-risk subgroup includes patients with IPI 3–5 disease or those with IPI 1–2 with ≥ 1 lesion with a maximum diameter ≥ 7 cm and/or screening LDH ≥ 1.3 × ULN; [d] Determined by immunohistochemistry; [e] Includes not done or unknown; [f] High-grade BCL with *MYC* and *BCL2* and/or *BCL6* rearrangements. ALK, anaplastic lymphoma kinase; BCL, B-cell lymphoma; COO, cell of origin; D, day; DLBCL, diffuse large B-cell lymphoma; EBV, Epstein-Barr virus; FL, follicular lymphoma; GCB, germinal center B cell; IPI, International Prognostic Index; IQR, interquartile range; LBCL, large B-cell lymphoma; LDH, lactate dehydrogenase; NOS, not otherwise specified; R-CHOP, rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone; RP2D, recommended Phase 2 dose; ULN, upper limit of normal.

Nowakowski GS, et al. ASH 2025. Abstract 476.

Grade 3/4 TEAEs were mainly hematologic; non-hematologic TEAEs were infrequent and mostly low grade

Grade 3/4 TEAEs[a]



Median relative dose intensity

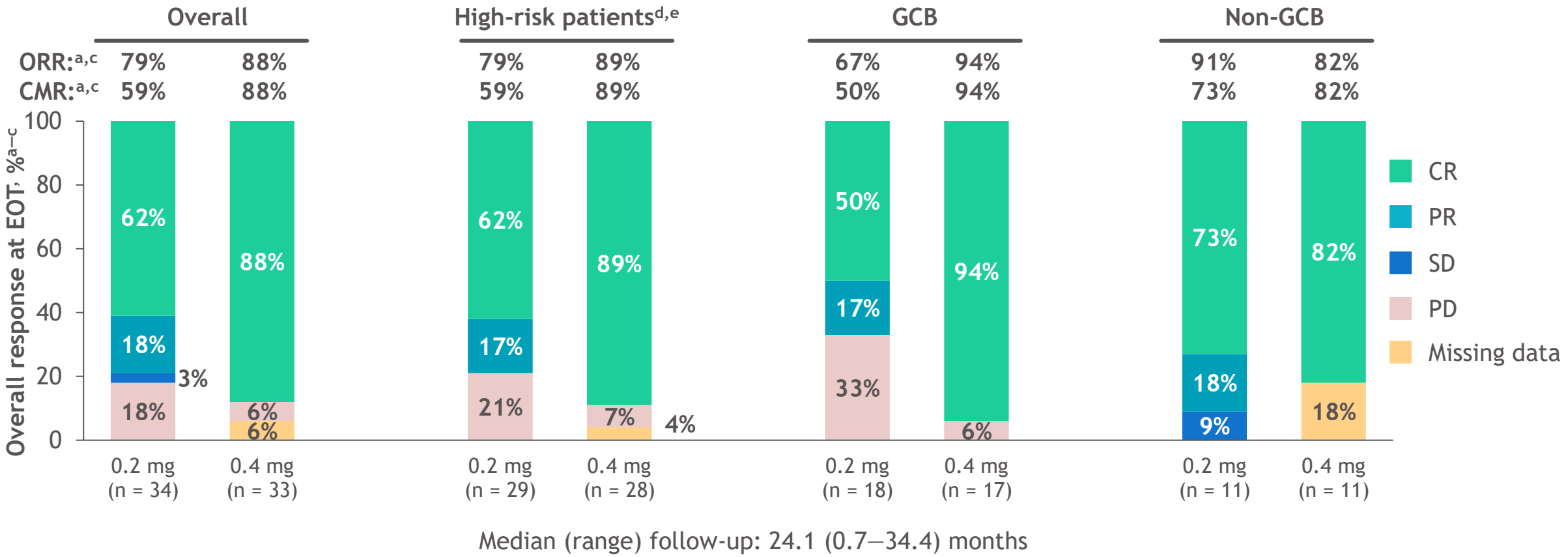
	Golcadomide 0.2 mg (n = 35)	Golcadomide 0.4 mg (n = 37)
Golcadomide, %	98	97
Cyclophosphamide, %	98	99
Doxorubicin, %	99	99
Vincristine, %	93	99

The addition of golcadomide 0.4 mg to R-CHOP did not compromise delivery (≥ 97% dose intensity of CHO)

Data cutoff: September 23, 2024. Data cutoff for relative dose intensity: May 12, 2025. [a] System organ classes with events occurring in 10% of the overall population are shown. Additional clinically relevant TEAEs have been included. System organ class and preferred terms are coded using the 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; [b] System organ class term; [c] From different system organ classes and includes the terms pulmonary embolism, deep vein thrombosis, superficial vein thrombosis, jugular vein thrombosis, and venous thrombosis limb. R-CHOP, rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone; TEAE, treatment-emergent adverse event.

Nowakowski GS, et al. ASH 2025. Abstract 476.

Golcadomide 0.4 mg + R-CHOP resulted in high complete response rates



Median (range) follow-up: 24.1 (0.7–34.4) months

High complete response rates at EOT were consistent across the overall and high-risk populations and irrespective of cell of origin

Data cutoff: May 12, 2025. [a] The efficacy-evaluable population included all enrolled patients who received ≥ 1 dose of study drug, had a baseline efficacy assessment, and had ≥ 1 valid post-baseline tumor assessment or discontinued treatment due to PD or study disease–related death; [b] Percentages may not sum to 100% due to rounding; [c] Response assessment based on the 2014 IWG Response Criteria for Lymphoma (Cheson BD, et al. J Clin Oncol 2014;32:3059–3068); [d] Includes patients with IPI 3–5 or high-risk IPI 1–2 disease (defined as IPI 1–2 with screening LDH ≥ 1.3 × ULN or any lesion with maximum diameter ≥ 7 cm); [e] One patient in the 0.4 mg D1–7 cohort was part of the high-risk population with LDH > 1.3 × ULN and achieved a CMR at EOT; however, they were not included in this subset due to a missing unit of LDH measurement. CMR, complete metabolic response; CR, complete response; EOT, end of treatment; GCB, germinal center B cell; IPI, International Prognostic Index; IWG, International Working Group; LDH, lactate dehydrogenase; ORR, overall response rate; PD, progressive disease; PR, partial response; R-CHOP, rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone; SD, stable disease; ULN, upper limit of normal.

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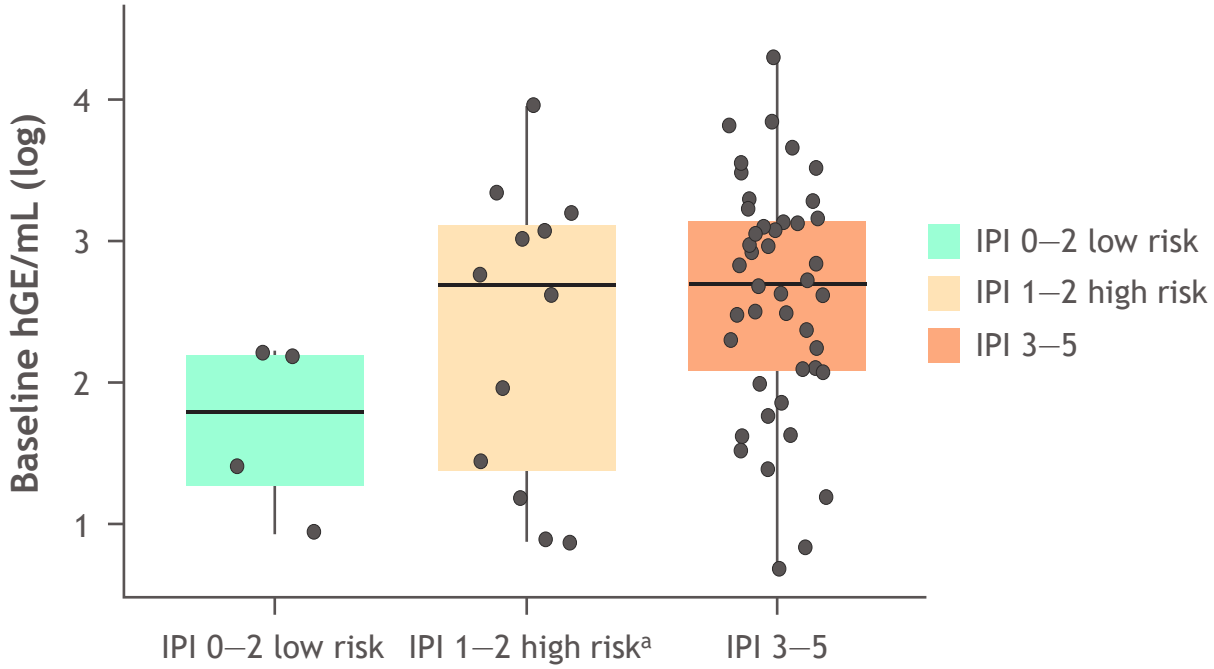
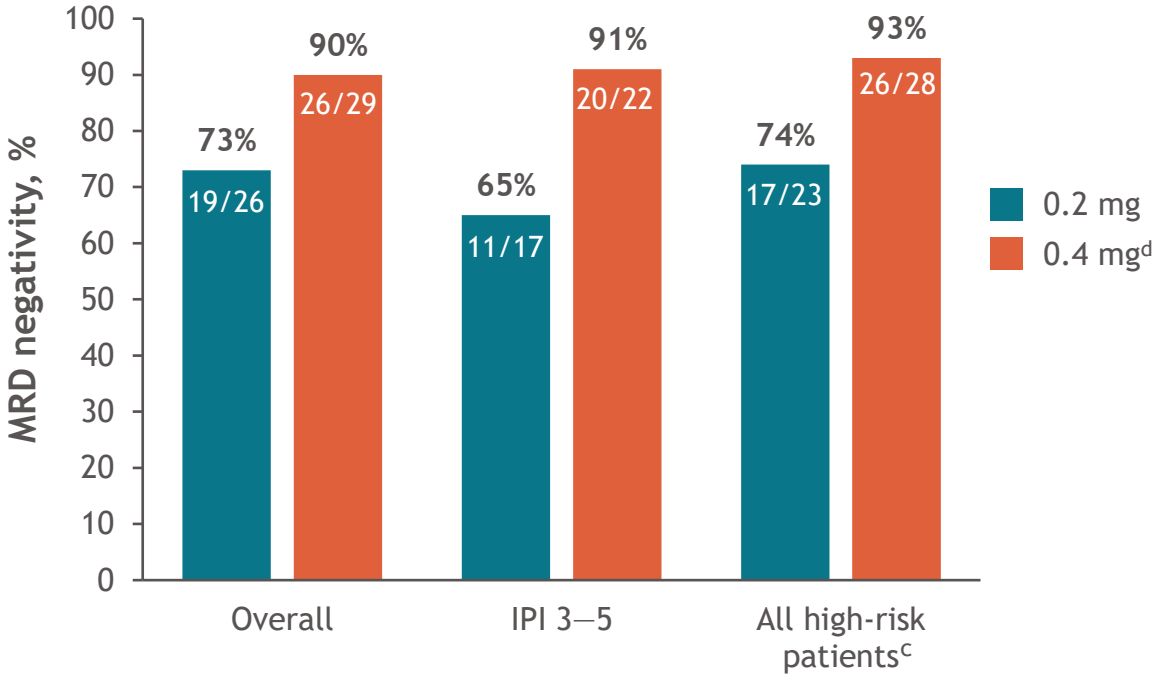
Golcadomide 0.4 mg + R-CHOP achieved MRD negativity in 90% of patients

Baseline ctDNA levels by IPI and clinical risk



Baseline ctDNA levels in patients with high-risk IPI 1—2 disease were similar to those in patients with IPI 3—5

EOT MRD negativity using PhasED-Seq in the overall and high-risk populations[b]



MRD negativity rates at EOT were higher with golcadomide 0.4 mg + R-CHOP (≥ 90% in the overall and high-risk populations)

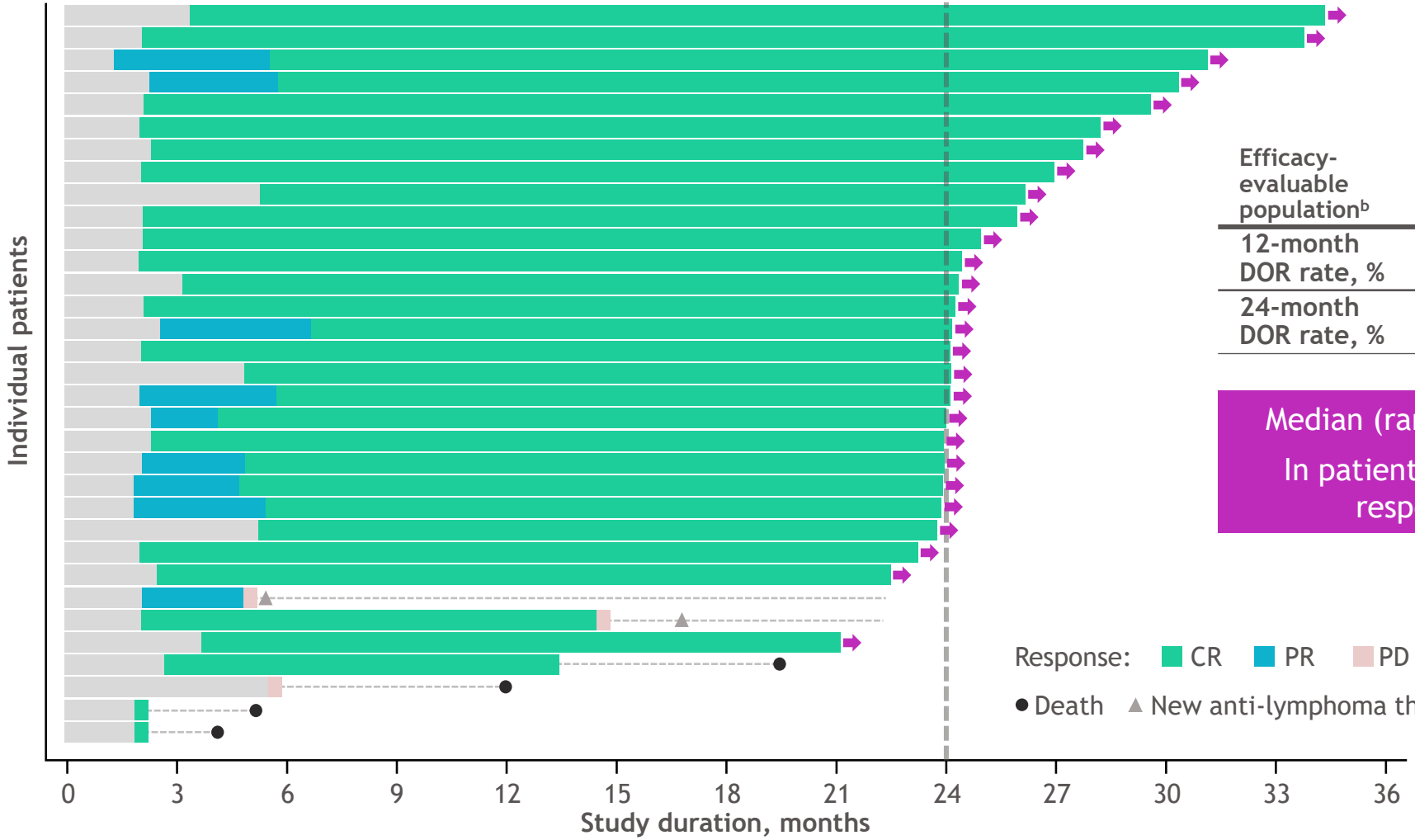
[a] IPI 1—2 with ≥ 1 lesion with a maximum diameter ≥ 7 cm and/or screening LDH ≥ 1.3 × ULN; [b] Denominators represent the number of patients with available ctDNA; [c] Combined high-risk population includes IPI 3—5 and IPI 1—2 patients with either elevated LDH or bulky disease; [d] Pooled cohort included patients in the 0.4 mg D1—7 and 0.4 mg D1—10 groups who had comparable exposure to golcadomide (no patient completed the 10-day schedule). ctDNA, circulating tumor DNA; EOT, end of treatment; hGE, haploid genome equivalents; IPI, International Prognostic Index; LDH, lactate dehydrogenase; MRD, minimal residual disease; PhasED-Seq, phased variant enrichment and detection sequencing; R-CHOP, rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone; ULN, upper limit of normal. Amzallag A, et al. ASH 2024. Oral presentation 579.

Nowakowski GS, et al. ASH 2025. Abstract 476.

Golcadomide 0.4 mg + R-CHOP resulted in a high rate of durable remissions in the overall and high-risk populations at a median follow-up of 24 months

Treatment response with golcadomide 0.4 mg + R-CHOP[a]

Efficacy-evaluable population (n = 33)



Efficacy-evaluable population[b]	Overall population		Patients with high-risk disease	
	0.2 mg (n = 34)	0.4 mg (n = 33)	0.2 mg (n = 29)	0.4 mg (n = 28)
12-month DOR rate, %	78	97	74	96
24-month DOR rate, %	75	93	70	92

Median (range) follow-up: 24.1 (0.7—34.4) months

In patients treated with golcadomide + R-CHOP, response occurred early in treatment

Data cutoff: May 12, 2025. [a] One patient was excluded from the efficacy-evaluable population due to ineligibility (Burkitt lymphoma); [b] Efficacy-evaluable population included all enrolled patients who received ≥ 1 dose of study drug, had a baseline efficacy assessment, and had ≥ 1 valid post-baseline tumor assessment or discontinued treatment due to PD or study disease—related death.

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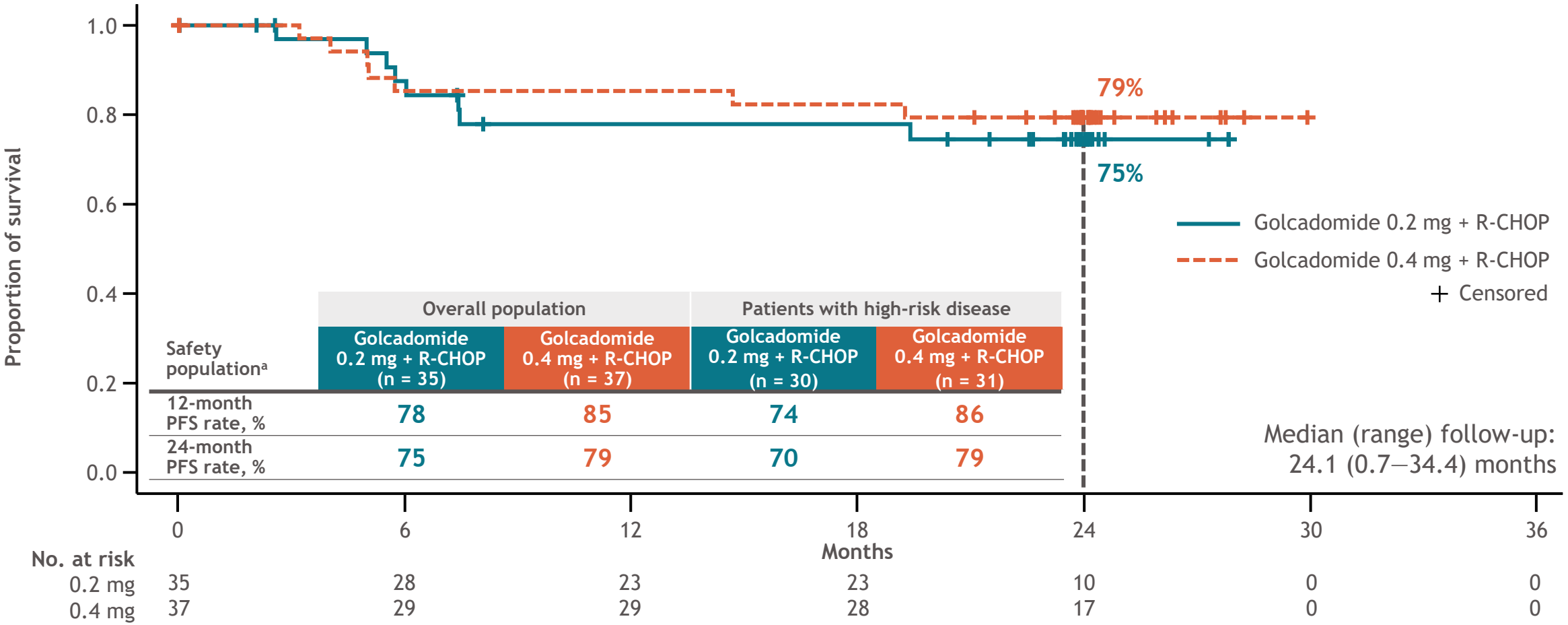
Golcadomide 0.4 mg + R-CHOP showed a 24-month PFS rate of 79% in the overall and high-risk populations



Safety population[a]	Overall population		Patients with high-risk disease	
	Golcadomide 0.2 mg + R-CHOP (n = 35)	Golcadomide 0.4 mg + R-CHOP (n = 37)	Golcadomide 0.2 mg + R-CHOP (n = 30)	Golcadomide 0.4 mg + R-CHOP (n = 31)
12-month PFS rate, %	78	85	74	86
24-month PFS rate, %	75	79	70	79

- As expected, most events occurred within the first 12 months; only one PD event with golcadomide 0.4 mg + R-CHOP occurred between months 12 and 24
- In the pooled 0.4 mg D1—7 and D1—10 schedules with comparable exposure, 24-month PFS rate was 82% in both the overall (n = 43) and high-risk (n = 35) populations[b]

Data cutoff: May 12, 2025.
[a] Safety analysis population included all enrolled patients who received ≥ 1 dose of study drug; [b] Pooled cohort included patients in the 0.4 mg D1—7 and 0.4 mg D1—10 groups who had comparable exposure to golcadomide (no patient completed the 10-day schedule). D, day; PD, progressive disease; PFS, progression-free survival; R-CHOP, rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone.

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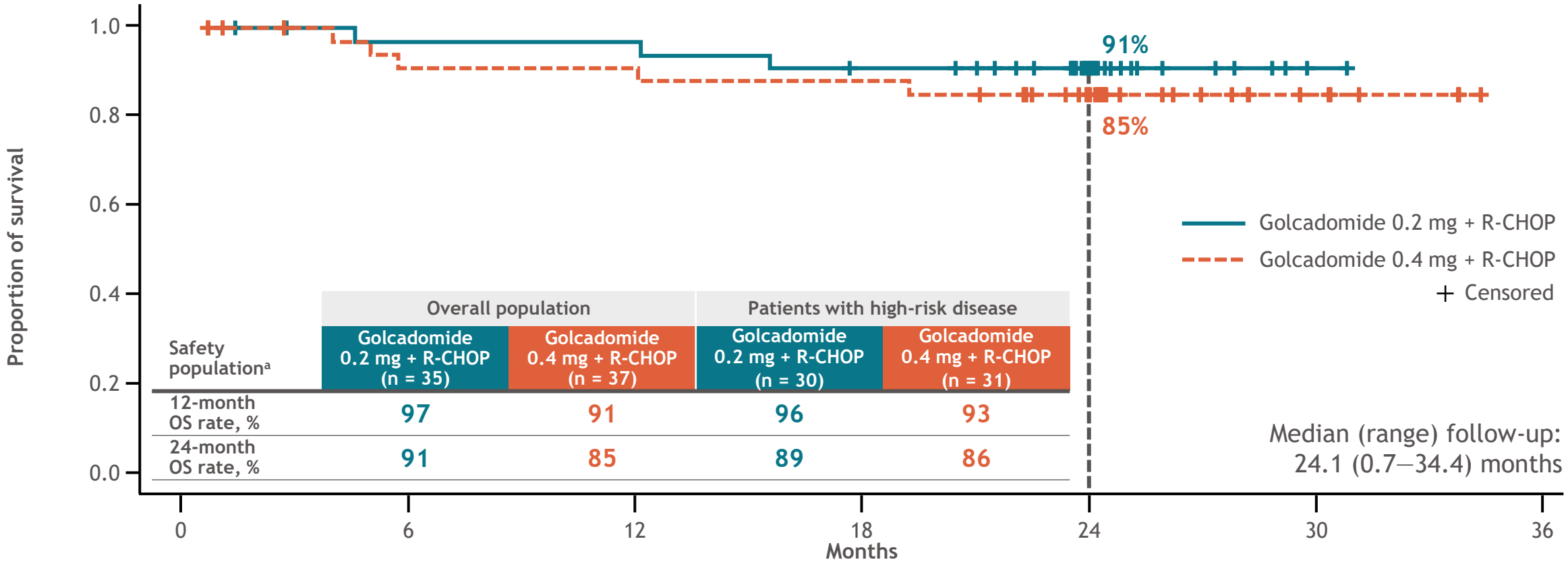
Golcadomide 0.4 mg + R-CHOP 24-month OS rate was consistent in the overall and high-risk populations



Safety population[a]	Overall population		Patients with high-risk disease	
	Golcadomide 0.2 mg + R-CHOP (n = 35)	Golcadomide 0.4 mg + R-CHOP (n = 37)	Golcadomide 0.2 mg + R-CHOP (n = 30)	Golcadomide 0.4 mg + R-CHOP (n = 31)
12-month OS rate, %	97	91	96	93
24-month OS rate, %	91	85	89	86

	No. of patients	No. of events	Censored	Median	Survival (95% CI)
0.2 mg	35	3	32	NA	(NA, NA)
0.4 mg	37	5	32	NA	(NA, NA)

Deaths due to progressive disease: Three at 0.2 mg dose and two at 0.4 mg dose. Deaths due to AEs: None at 0.2 mg dose and two at 0.4 mg (one out-of-hospital cardiac arrest and one COVID-19). Cause of death was missing for one patient at 0.4 mg dose who died off treatment.

Data cutoff: May 12, 2025.
[a] Safety analysis population included all enrolled patients who received ≥ 1 dose of study drug.
AE, adverse event; NA, not available; OS, overall survival; R-CHOP, rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone.

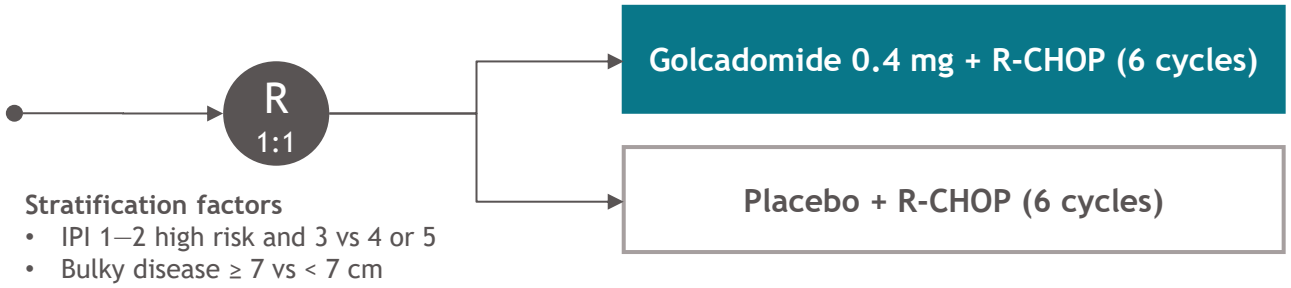
Nowakowski GS, et al. ASH 2025. Abstract 476.

Conclusions

- The long-term follow-up data for golcadomide + R-CHOP demonstrated impressive efficacy with a predictable and manageable safety profile, with no new safety signals observed
  - TEAEs were similar to historical R-CHOP and primarily hematologic (91%); non-hematologic AEs were infrequent and mostly low grade
  - Combining golcadomide with R-CHOP did not compromise delivery of chemotherapy (≥ 97% dose intensity)
- At a median follow-up of 24 months, golcadomide 0.4 mg + R-CHOP demonstrated durable responses and a promising 24-month PFS rate of 79% across the overall and high-risk populations
  - Patients achieved high rates of durable CMRs (88%) and MRD negativity (90%) irrespective of cell of origin
- These long-term follow-up data support the potential of oral golcadomide 0.4 mg + R-CHOP to cure more newly diagnosed patients with high-risk LBCL and the ongoing Phase 3 GOLSEEK-1 trial in high-risk 1L LBCL (NCT06356129)

GOLSEEK-1 trial design[1]

Key eligibility criteria
- Previously untreated LBCL (WHO 2022 classification[2,a])
- IPI score of 1—2 high risk or 3—5
- Age 18—80 years
- Measurable disease per Lugano response criteria



Primary endpoint
- PFS by investigator

Key secondary endpoints
- OS
- EFS by investigator
- CMR by IRAC
- MRD negativity at EOT

[a] Includes DLBCL (including GCB and ABC types or not specified), high-grade BCL (including *MYC* and *BCL2* rearrangements or not specified), T-cell/histiocyte-rich LBCL, and Epstein–Barr virus—positive DLBCL.

1. Vassilakopoulos TP, et al. ASH 2025. Poster 3704; 2. Alaggio R, et al. Leukemia 2022;36:1720—1748.

Nowakowski GS, et al. ASH 2025. Abstract 476.

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