Odronextamab

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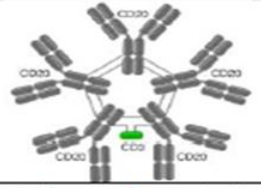
Disclosure

- I have the following relevant financial relationships to disclose:

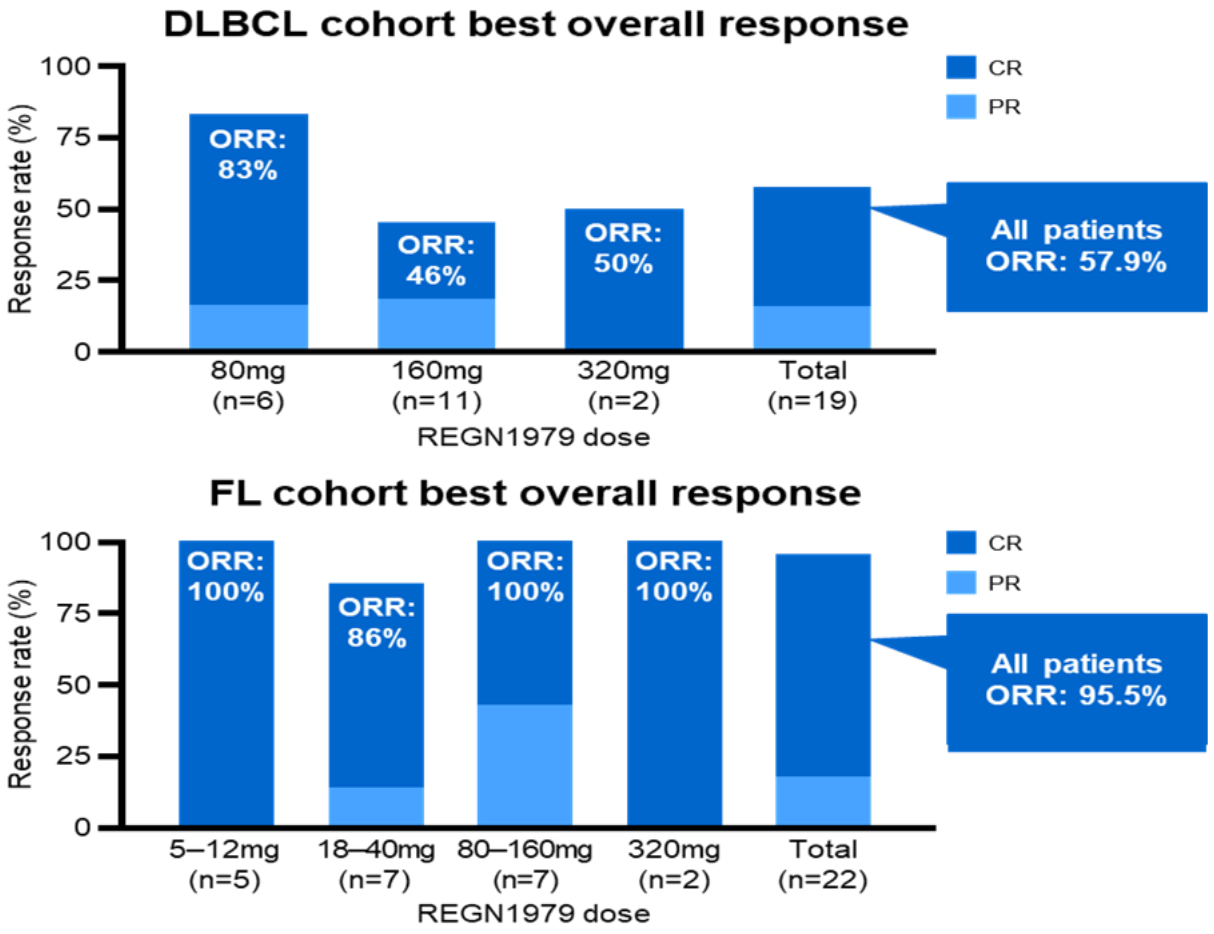
- Grant/Research support from: Sanofi, Beigene, Boryong, Roche, Kyowa-Kirin, Donga

CD20xCD3

Product name	Schematic depiction	Format	Technology	CD20:CD3 ratio	CD3 clone	CD20 clone	Fc silencing mutations*
Mosunetuzumab[18]		IgG1	Knobs-into-holes (different Fabs)	1:1	UCHT1v9 (CD3δε)	2H7 (type 1 epitope, identical to rituximab)	N297G (No FcγR binding)
Glofitamab[15]		IgG1	Head-to-tail fusion	2:1	SP34-der.(CD3ε)	By-L1(type 2 epitope, identical to obinutuzumab)	IgG1-P329G-LALA (No FcγR binding)
Epcoritamab[16]		IgG1	Controlled Fab-arm exchange	1:1	huCACAO (SP34-der.)(CD3ε)	7D8 (type 1 epitope, shared by ofatumomab)	L234F,L235E,D265A (No FcγR,C1q binding)
Odronexamab[17]		IgG4	Heavy chains with different affinity	1:1	REG1250 (CD3δε)	3B9-10 (type 1 epitope, shared by ofatumomab)	Modified IgG4 (No FcγRIII binding)
Plamotamab[90]		IgG1	Fab-Fc x scFv-Fc	1:1	α-CD3_H1.30 (SP34-der.)(CD3ε)	C2B8_H1_L1 (type 1 epitope, shared by rituximab)	G236R, L328R (No FcγR binding)
IgM 2323[19]		IgM	IgM + modified J chain	10:1	Not reported	Not reported	No

Felchi L et al Blood 2022

Odronextamab : ELM-1

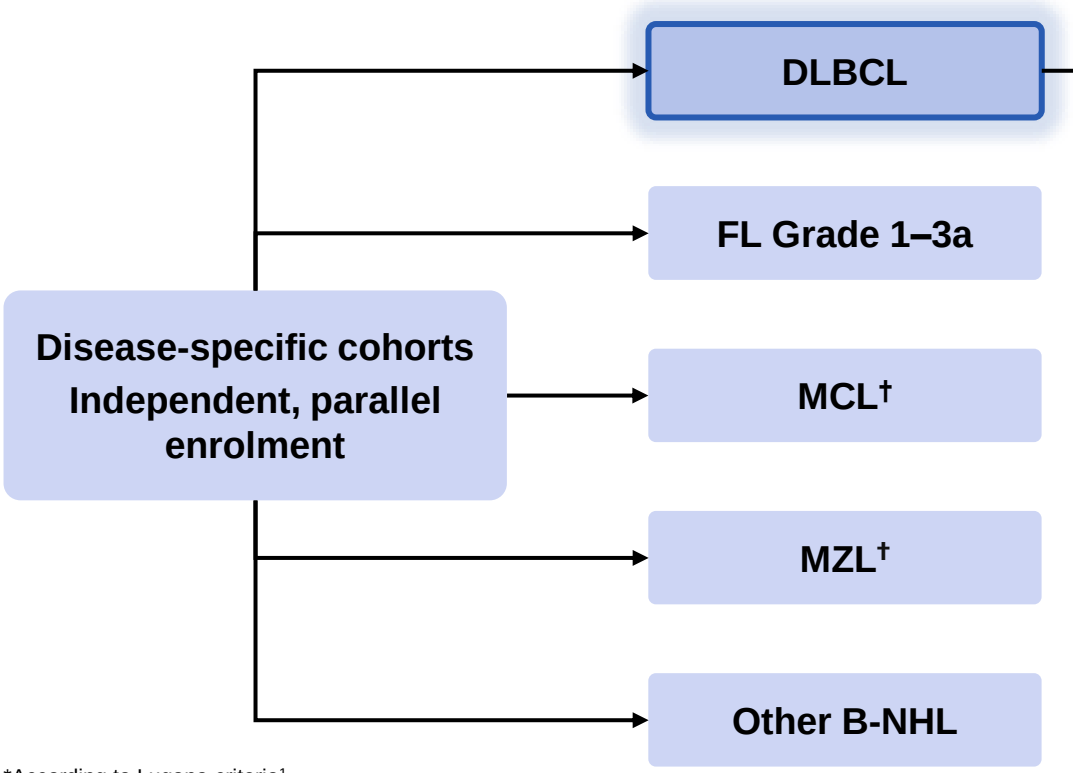


Grade 3/4 AEs, %	N=110
Anaemia	21.8%
Hypophosphataemia	19.1%
Neutropenia	19.1%
Lymphopenia	19.1%
Thrombocytopenia	13.6%
CRS	6.4%

Bannerji R, et al. ASH 2019; abstr #762

ELM-2 study design – DLBCL cohort

- Phase 2, open-label, multi-cohort, multicenter study of odronextamab monotherapy for patients with R/R B-NHL (NCT03888105)
  - R/R FL cohort results presented at ASH 2022: oral presentation #949



Key eligibility criteria

- DLBCL per WHO 2016 classification
- ECOG PS 0 or 1
- Refractory to or relapsed after ≥2 prior lines of therapy, including an anti-CD20 antibody and an alkylator

Primary endpoint

- ORR* by ICR

Key secondary endpoints

- ORR* by local investigator
- CR, DOR, PFS, and OS
- Safety and tolerability

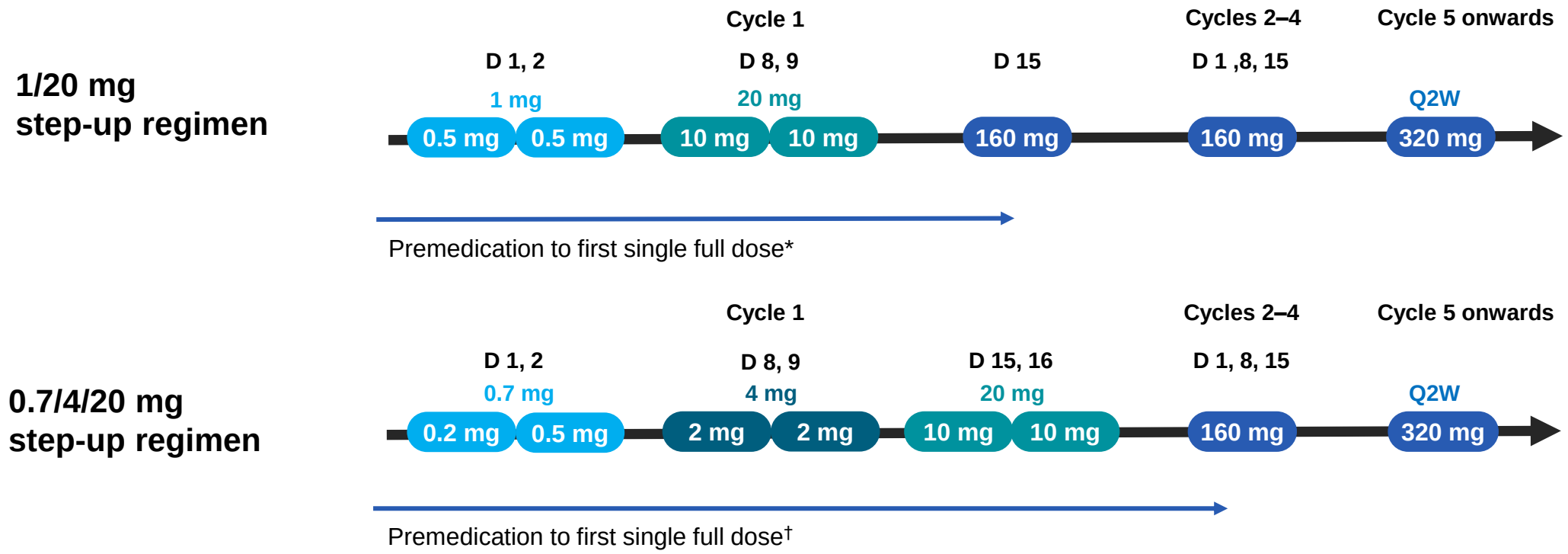
Odronextamab administration:

- IV, 21-day cycles
- Cycle 1 Step-up
- Cycles 2-4 160mg Days 1, 8,15
- Cycle 5 onwards 320mg Q2W
- Treatment until disease progression

*According to Lugano criteria[1]
†New enrolment is currently paused.
B-NHL, B-cell non-Hodgkin's lymphoma; CD, cluster of differentiation; CR, complete response; DLBCL, diffuse large B-cell lymphoma; DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance score; FL, follicular lymphoma; ICR, independent central review; IV, intravenous; MCL, mantle cell lymphoma; MZL, marginal zone lymphoma; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; Q2W, every 2 weeks; R/R, relapsed/refractory; WHO, World Health Organization.
1. Cheson BD, et al. *J Clin Oncol*. 2014;32(27):3059–3068.

Cycle 1 step-up regimen optimized to mitigate the risk for cytokine release syndrome

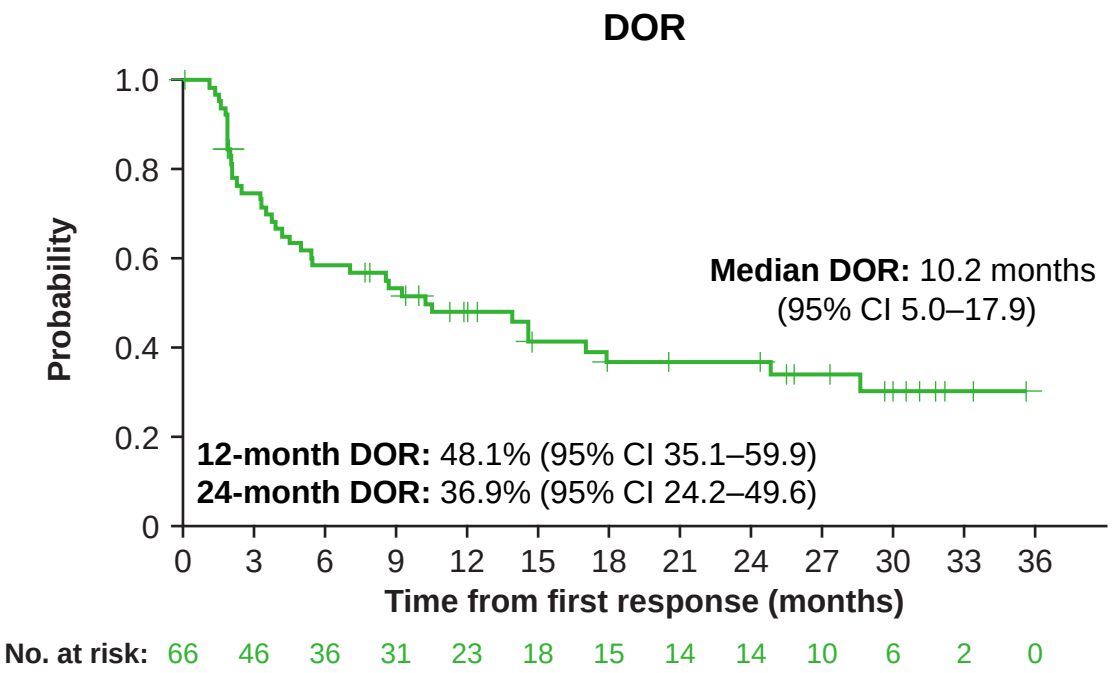
- The study initiated with a Cycle 1 step up regimen of 1/20 mg
- This was modified to 0.7/4/20 mg during Cycle 1 to further mitigate the risk of CRS

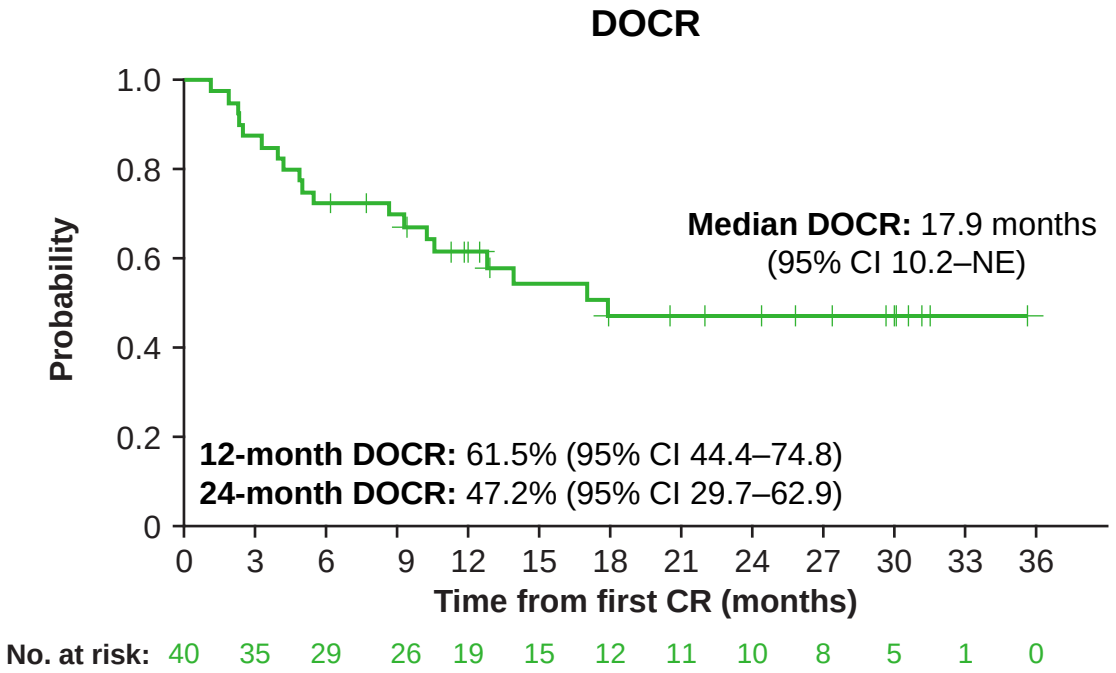


Updated guidelines for tocilizumab and steroids introduced with 0.7/4/20 mg regimen.
*20 mg IV dexamethasone 1 to 3 hours prior to each split or initial single infusion. †10 mg dexamethasone orally 12 to 24 hours prior to the first split infusion. On each day of split or single infusion: dexamethasone 20 mg IV 1 to 3 hours before infusion; diphenhydramine 25 mg IV or orally and acetaminophen 650 mg orally 30 to 60 minutes before infusion.
CRS, cytokine release syndrome; D, day; IV, intravenous; Q2W, every 2 weeks.

ELM-2: Efficacy analysis

- Median duration of follow-up for efficacy: 29.9 months (95% CI 20.4–32.6)
- **N=127: ORR* 52.0%, CR 31.5%**





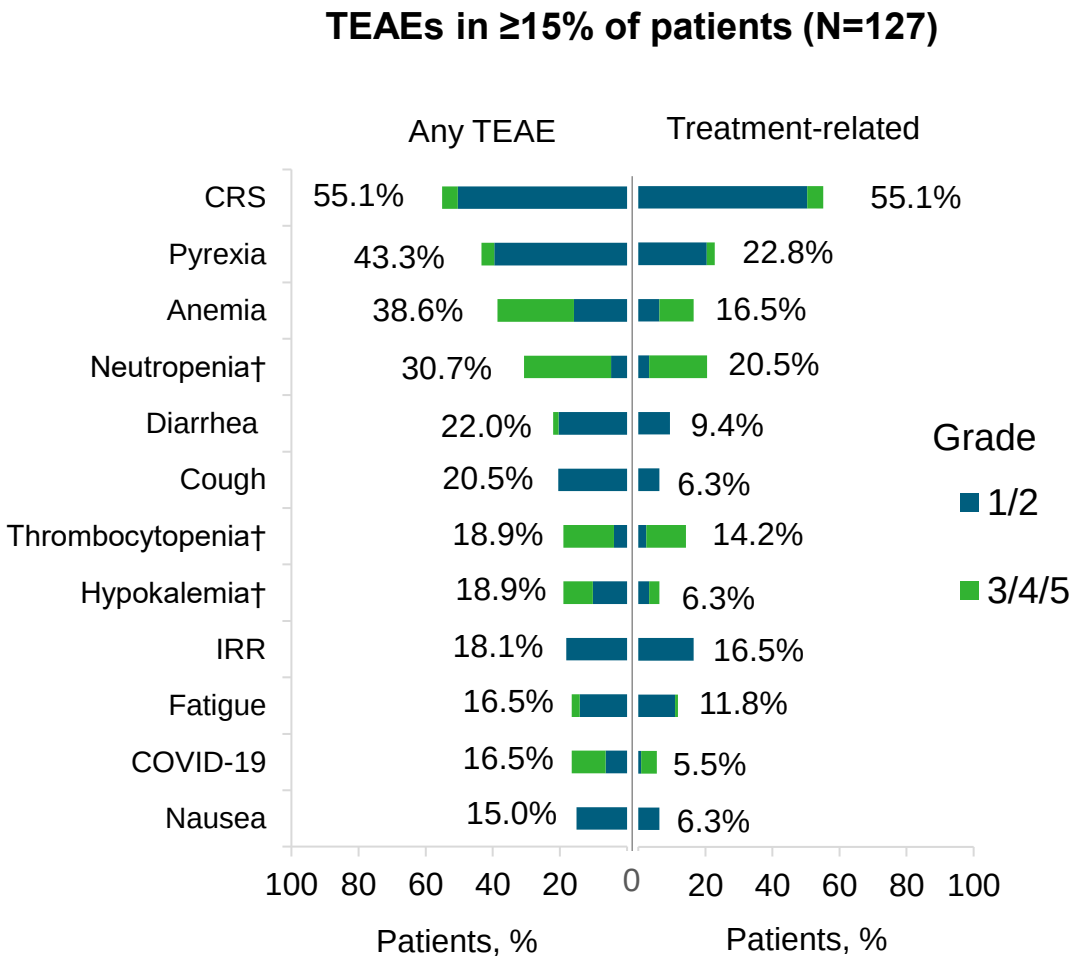
- Response data were consistent in post-CAR T patients from the ELM-1 study:
  - ASH 2023 poster presentation 4461, December 11, 2023, 18:00–20:00 PST

Data cut-off date: August 18, 2023. Efficacy per independent central review. *CRs + PRs.
CAR T, chimeric antigen receptor T cell; CI, confidence interval; CR, complete response; DOCR, duration of complete response; DOR, duration of response; NE, not evaluable; ORR, objective response rate; PR, partial response.

ELM-2 safety: Consistent with previous reports

TEAEs, n (%)	N=127* Any event	Treatment related
Any TEAE	126 (99.2)	111 (87.4)
Grade ≥3 TEAE	107 (84.3)	68 (53.5)
Serious TEAE	82 (64.6)	62 (48.8)
TEAE leading to interruption	92 (72.4)	67 (52.8)
TEAE leading to dose reduction	4 (3.1)	4 (3.1)
TEAE leading to discontinuation	17 (13.4)	12 (9.4)
TEAE leading to death (Grade 5)	20 (15.7)	5 (3.9)

- **Treatment-related Grade 5 events:** COVID-19, pneumonia, cytomegalovirus infection reactivation + pneumonia cytomegaloviral, *Pneumocystis jirovecii* pneumonia, pseudomonal sepsis (n=1 each)



Data cut-off date: August 18, 2023. AEs per NCI-CTCAE v5.0, CRS per Lee 2014/2019 criteria[1,2]. *0.7/4/20 mg (n=60) and 1/20 mg (n=67) Cycle 1 step-up regimen. †Composite term.
CRS, cytokine release syndrome; IRR, infusion-related reaction; NCI-CTCAE, National Cancer Institute's Common Terminology Criteria for Adverse Events; TEAE, treatment-emergent adverse event.
1. Lee DW, et al. *Blood*. 2014;124(2):188–95; 2. Lee DW, et al. *Biol Blood Marrow Transplant*. 2019;25(4):625–38.

#65

Odronextamab Plus Chemotherapy in Patients with Previously Untreated Diffuse Large B-Cell Lymphoma (DLBCL): First Results from Part 1 of the Phase 3 OLYMPIA-3 Study

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ClinicalTrials.gov ID: NCT06091865

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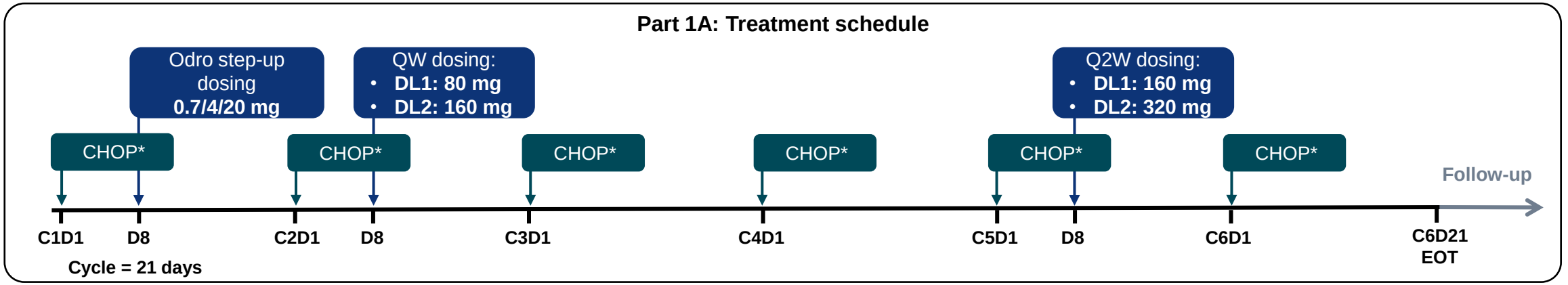
Presented at the 67th American Society of Hematology (ASH) Congress, December 6–9, 2025, Orlando, FL, USA

OLYMPIA-3 Part 1A (dose escalation): Study design

- OLYMPIA-3: Phase 3, randomized, open-label, multicenter study of Odro-CHOP vs R-CHOP for previously untreated DLBCL
  - The study comprises Part 1A (dose escalation of Odro-CHOP), Part 1B (dose optimization), and Part 2 (randomization: Odro-CHOP vs R-CHOP)



Key eligibility criteria for Part 1A

- Age ≥18 years
- Previously untreated CD20+ DLBCL NOS or HGBL (WHO 2016[1])
  - R/R DLBCL permitted
- ECOG PS ≤2
- Adequate organ function
- No CNS lymphoma
- ≥1 high-risk feature, including:
  - IPI score 3–5; non-GCB cell of origin (IPI score ≥2); or HGBL with *MYC*, *BCL-2*, and/or *BCL-6* rearrangements (IPI score ≥2)

Endpoints

Primary
- DLT incidence
- TEAEs

Secondary
- ORR (per local investigator; Lugano criteria[2])
- CR rate
- DOR

Exploratory
- Biomarkers
- Immunophenotyping

- Anti-infection prophylaxis, including IVIg supplementation and antivirals, was recommended
- PJP prophylaxis was mandated
- CMV infection was assessed by blood PCR at screening, C4D1, and as clinically warranted†

*Dosing as follows: cyclophosphamide (750 mg/m^2), vincristine (1.4 mg/m^2), and doxorubicin (50 mg/m^2) given IV on D1 of each cycle, and prednisone/prednisolone (100 mg) given orally on D1–5 of each cycle. †If CMV DNA is detected, continue weekly monitoring until viral load decreases, then every 2 weeks until 2 consecutive undetectable results. C, Cycle; CHOP, cyclophosphamide, doxorubicin, vincristine, prednisone/prednisolone; CMV, cytomegalovirus; CNS, central nervous system; CR, complete response; D, Day; DL, dose level; DLBCL, diffuse large B-cell lymphoma; DLT, dose-limiting toxicity; DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; EOT, end of treatment; GCB, germinal center B-cell; HGBL, high-grade B-cell lymphoma; Ig, immunoglobin; IPI, International Prognostic Index; IV, intravenous; NOS, not otherwise specified; Odro, odronextamab; ORR, objective response rate; PCR, polymerase chain reaction; PJP, *Pneumocystis jirovecii* pneumonia; QW, once weekly; Q2W, once every 2 weeks; R, rituximab; R/R, relapsed/refractory; TEAE, treatment-emergent adverse event; WHO, World Health Organization.

1. Swerdlow SH, et al. *Blood* 2016;127(20):2375–90; 2. Cheson BD, et al. *J Clin Oncol* 2014;32(27):3059–68.

OLYMPIA-3 Part 1A: Baseline demographics and disease characteristics

Baseline demographics and disease characteristics*		DL1: 80 mg (n=9)	DL2: 160 mg (n=13)	Total Part 1A (N=22)
Median age (range), years		55.0 (30–81)	71.0 (24–78)	66.0 (24–81)
Age, years, n (%)	<65	6 (67)	5 (38)	11 (50)
	≥65 to <75	0	4 (31)	4 (18)
	≥75	3 (33)	4 (31)	7 (32)
Male / female, n (%)		6 (67) / 3 (33)	5 (38) / 8 (62)	11 (50) / 11 (50)
Race, n (%)	White	9 (100)	7 (54)	16 (73)
	Asian	0	3 (23)	3 (14)
	Missing	0	3 (23)	3 (14)
ECOG PS, n (%)	0	2 (22)	7 (54)	9 (40)
	1	5 (56)	5 (38)	10 (45)
	2	2 (22)	1 (8)	3 (14)
Cell of origin, n (%)	GCB	6 (67)	2 (15)	8 (36)
	Non-GCB	3 (33)	10 (77)	13 (59)
	Unclassified	0	1 (8)	1 (5)
DLBCL subtype, n (%)	De novo	9 (100)	9 (100)	22 (100)
IPI score, n (%)	1	1 (11)	0	1 (5)
	2	3 (33)	4 (31)	7 (32)
	3	3 (33)	5 (38)	8 (36)
	4–5	2 (22)	4 (31)	6 (27)
Lugano stage at study entry,† n (%)	I–II	1 (11)	0	1 (5)
	III–IV	8 (89)	13 (100)	21 (95)
Longest lesion diameter, n (%)	<10 cm	8 (89)	12 (92)	20 (91)
	≥10 cm	1 (11)	1 (8)	2 (9)

Data cut-off date: Aug 19, 2025. *Gender and disability data were not collected per protocol; †Confirmed by the medical director at study entry.
DL, dose level; DLBCL, diffuse large B-cell lymphoma; ECOG PS, Eastern Cooperative Oncology Group performance status; GCB, germinal center B-cell-like; IPI, International Prognostic Index.

OLYMPIA-3 Part 1A: Patient disposition and treatment exposure

Disposition, n (%)	DL1: 80 mg (n=9)	DL2: 160 mg (n=13)
Completed Cycle 1	7 (77.8)	13 (100.0)
Completed Cycle 6	7 (77.8)	11 (84.6)
Discontinued early	2 (22.2)*	2 (15.4)†
Physician decision	2 (22.2)	2 (15.4)

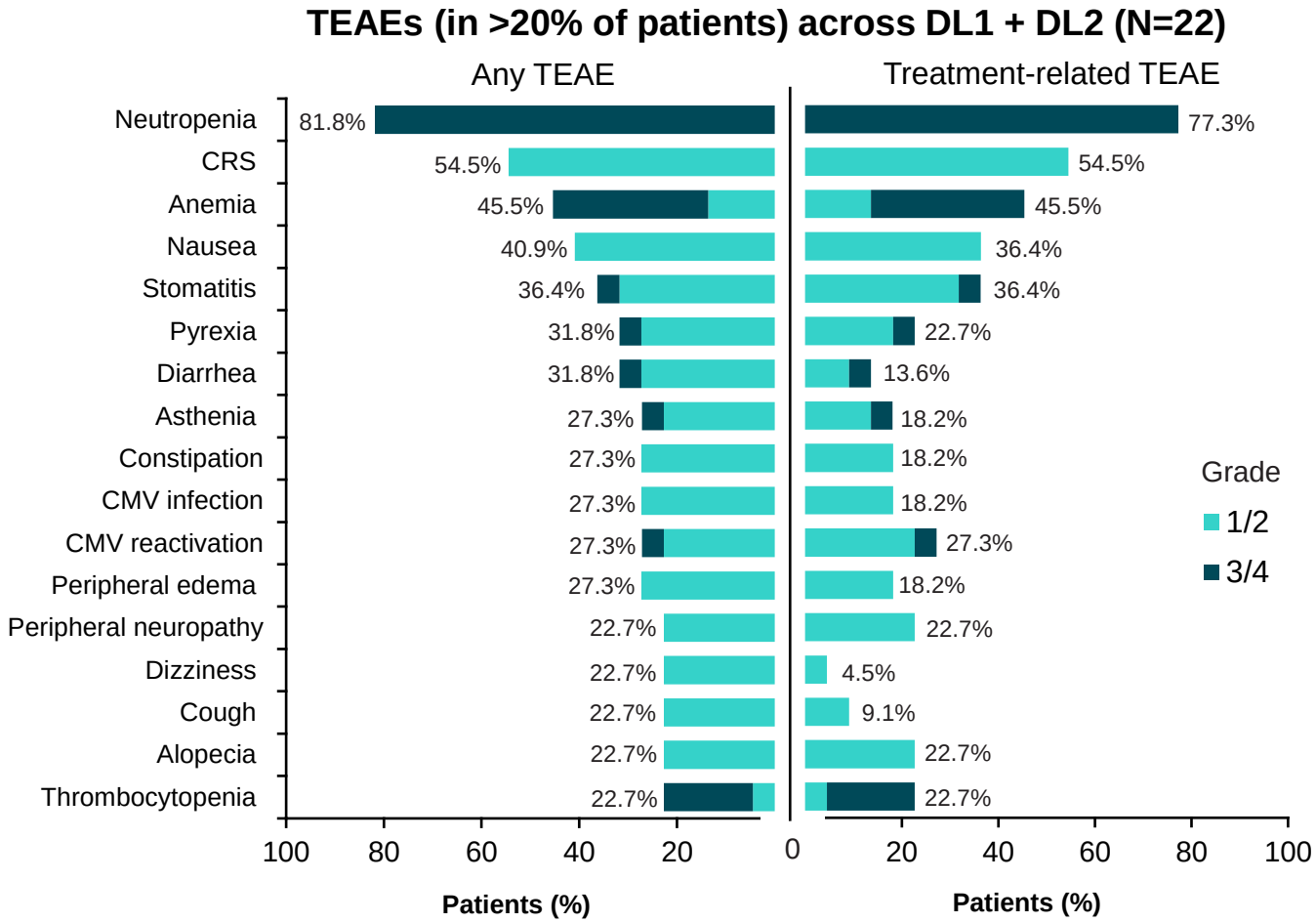
Median relative dose intensity‡, %	Odronextamab	Cyclophosphamide	Doxorubicin	Vincristine	Prednisone/ prednisolone
DL1: 80 mg (n=9¶)	87	84	84	79	89
DL2: 160 mg (n=13)	77	78	78	79	85

Data cutoff date: Aug 19, 2025.
*Myocardial infarction occurred on C1D6 in both patients, leading to physician decision to discontinue treatment before the first Odro administration; †Physician decision to prematurely end treatment in one patient at C5D8 and in the other patient at C6D14; ‡Relative dose intensity = 100% × actual dose intensity / protocol planned dose intensity, where protocol planned dose intensity = protocol planned cumulative dose / protocol planned duration of treatment exposure; ¶n=9 for CHOP dosing, and n=7 for Odro dosing as two patients discontinued treatment prematurely before Odro administration.
CHOP, cyclophosphamide, doxorubicin, vincristine, prednisone/prednisolone; DL, dose level; Odro, odronextamab.

OLYMPIA-3 Part 1A Safety: Safety summary and most common TEAEs

n (%)	DL1: 80 mg (n=9)	DL2: 160 mg (n=13)
Any TEAE	9 (100.0)	13 (100.0)
Grade ≥3 TEAE	9 (100.0)	13 (100.0)
Serious TEAE	7 (77.8)	12 (92.3)
TEAE leading to treatment interruption/delay	6 (66.7)	11 (84.6)
TEAE leading to dose reduction of Odro	0	1 (7.7)
TEAE leading to dose reduction of CHOP	1 (11.1)	5 (38.5)
TEAE leading to treatment discontinuation	1 (11.1)	1 (7.7)
TEAE leading to death (Grade 5)	0	1 (7.7)*

- No DLTs reported

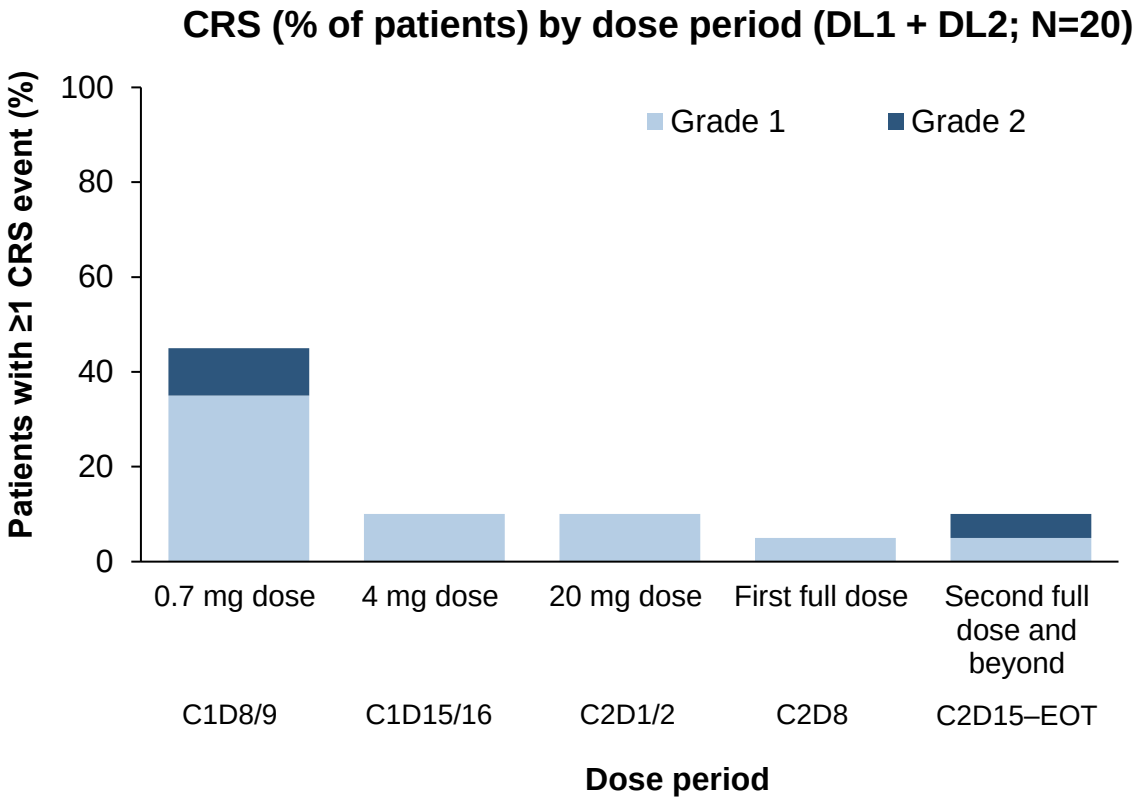


Data cut-off date: Aug 19, 2025. Adverse events were graded per National Cancer Institute Common Terminology Criteria for Adverse Events v5.0,[1] except CRS, which was graded per Lee DW, et al. 2019.[2]
*Death due to cardiac arrest following completion of Odro-CHOP treatment, and not considered treatment-related. CHOP, cyclophosphamide, doxorubicin, vincristine, prednisone/prednisolone; CRS, cytokine release syndrome; CMV, cytomegalovirus; DL, dose level; DLT, dose-limiting toxicity; Odro, odronextamab; PCR, polymerase chain reaction; TEAE, treatment-emergent adverse event.

1. NCI. Common Terminology Criteria for Adverse Events (CTCAE) Version 5.0. https://ctep.cancer.gov/protocoldevelopment/electronic_applications/docs/ctcae_v5_quick_reference_5x7.pdf (accessed Sept 5, 2025);
2. Lee DW, et al. *Biol Blood Marrow Transplant* 2019;25(4):625–38.

OLYMPIA-3 Part 1A Safety: Cytokine release syndrome

CRS*	Total Part 1A (N=22)
Any grade, n (%)	12 (54.5)
Grade 1	9 (40.9)
Grade 2	3 (13.6)
Grade ≥3	0
Median time to CRS onset (range), hours	9.0 (5.1, 60.2)
Median CRS duration (range), hours	3.8 (-19.3, 9.6)
Systemic steroids for CRS management, n (%)	4 (18.2)
Tocilizumab for CRS management, n (%)	6 (27.3)



- CRS mostly occurred during step-up dosing
- **No ICANS or TLS events were reported**

Data cut-off date: Aug 19, 2025.
*CRS graded per Lee DW, et al. 2019;[1]
C, cycle; CRS, cytokine release syndrome; D, day; DL, dose level; EOT, end of treatment; ICANS, immune effector cell-associated neurotoxicity syndrome; TEAE, treatment-emergent adverse event; TLS, tumor lysis syndrome.
1. Lee DW, et al. *Biol Blood Marrow Transplant* 2019;25(4):625–38.

OLYMPIA-3 Part 1A Safety: Infections

Infections,* n (%)	DL1: 80 mg (n=9)	DL2: 160 mg (n=13)	Total Part 1A (N=22)
Any grade†	6 (66.7)	12 (92.3)	18 (81.8)
Grade 1	1 (11.1)	2 (15.4)	3 (13.6)
Grade 2	3 (33.3)	3 (23.1)	6 (27.3)
Grade 3	2 (22.2)	5 (38.5)	7 (31.8)
Grade 4	0	2 (15.4)	2 (9.1)
Grade 5	0	0	0
Opportunistic infection‡	2 (22.2)	9 (69.2)	11 (50.0)
Grade ≥3	0	1 (7.7)	1 (4.5)

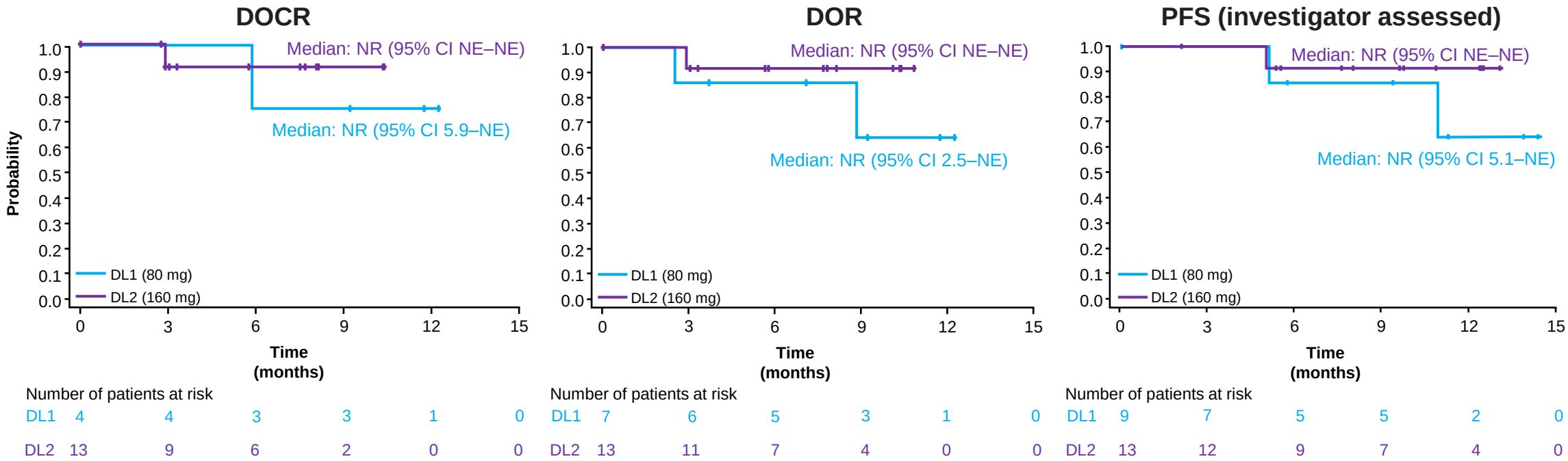
- Most commonly reported infections (PT) overall (any grade): CMV infection, CMV reactivation (both 27%), COVID-19, and oral candidiasis (both 18%)
  - CMV was assessed by blood PCR at screening, C4D1, and as clinically warranted. CMV infection was reported in 11 patients, 9 (82%) of whom had asymptomatic viremia

Data cut-off date: Aug 19, 2025. *Graded per NCI Common Terminology Criteria for Adverse Events v5.0;[1] †Grade 1: asymptomatic/mild with no intervention indicated. Grade 2: Intervention indicated, even if TEAE is asymptomatic. Grade 3: Medically significant with hospitalization indicated (e.g., IV treatment). Grade 4: Life-threatening, and requiring urgent intervention. ‡Defined by narrow SMQ (MedDRA version 28.0).
C, cycle; CMV, cytomegalovirus; D, day; DL, dose level; MeDRA, Medical Dictionary for Regulatory Activities; IV, intravenous; NCI, National Cancer Institute; PCR, polymerase chain reaction; PT, preferred term; SMQ, standardized MeDRA query; TEAE, treatment-emergent adverse event.
1. NCI. Common Terminology Criteria for Adverse Events (CTCAE) Version 5.0. https://ctep.cancer.gov/protocoldevelopment/electronic_applications/docs/ctcae_v5_quick_reference_5x7.pdf (accessed Sept 5, 2025);
2. Medical Dictionary for Regulatory Activities (MedDRA), version 28.0; International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH); 2025.

OLYMPIA-3 Part 1A Efficacy: 100% CR rate with Odro 160 mg + CHOP

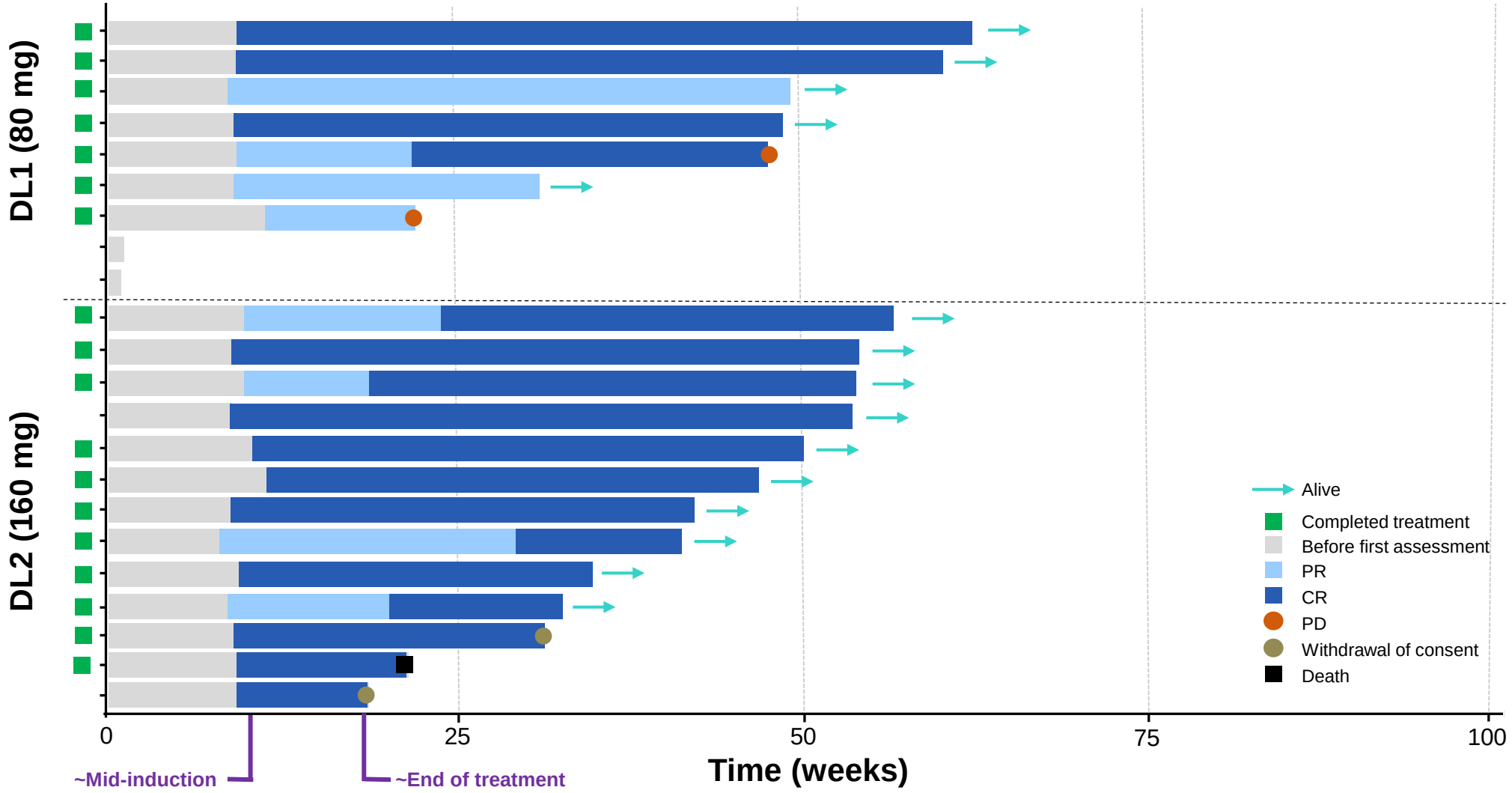
Response*, n (%)		DL1: 80 mg (n=9)	DL2: 160 mg (n=13)
Mid-induction	ORR	7 (78)	13 (100)
	CR	3 (33)	9 (69)
Overall	ORR	7 (78)	13 (100)
	CR	4 (44)	13 (100)

- Median duration of follow-up†:
  - DL1: 9.2 months (95% CI 3.7–NE)
  - DL2: 7.8 months (95% CI 3.1–10.3)



Data cut-off date: Aug 19, 2025.
*Investigator assessed according to the Lugano classification response criteria 2014 by PET-CT.[1] †Median duration of follow-up based on reverse Kaplan-Meier DOR.
CHOP, cyclophosphamide, doxorubicin, vincristine, prednisone/prednisolone; CI, confidence interval; CR, complete response; DL, dose level; DOCR, duration of complete response; DOR, duration of response; NE, not evaluable; NR, not reached; Odro, odronextamab; ORR, objective response rate; PET-CT, positron emission tomography-computed tomography; PFS, progression free survival.
1. Cheson BD, et al. *J Clin Oncol* 2014;32(27):3059–68.

OLYMPIA-3 Part 1A Efficacy: Swimmer plot



Data cut-off date: Aug 19, 2025.
CR, complete response; DL, dose level; PD, progressive disease; PR, partial response.

OLYMPIA-3 Part 1A: Key takeaways

- **In Part 1A of the Phase 3 OLYMPIA-3 study, the safety profile of fixed duration (six cycles) Odro-CHOP treatment was generally manageable in patients with previously untreated DLBCL with high-risk features, with no new safety signals compared with previous reports[1]**
  - Most patients completed six cycles of Odro-CHOP at both dose levels
  - Few dose reductions of odronextamab and no permanent treatment discontinuations due to TEAEs related to odronextamab
  - No clinically important differences in safety between dose levels
- **Preliminary efficacy of Odro-CHOP was encouraging**
  - Higher CR/ORR by mid-induction and at end of treatment with DL2 160 mg QW
  - 100% CR rate with the DL2 160 mg QW
  - CRs appeared durable, with median DOCR and median PFS not reached
- **Data from Part 1A of OLYMPIA-3 suggest that when combining odronextamab with CHOP in previously untreated patients with DLBCL, rituximab was not required to achieve deep and durable responses**
- **DL2 Odro 160 mg + CHOP was selected for further investigation in OLYMPIA-3**

CHOP, cyclophosphamide, doxorubicin, vincristine, prednisone/prednisolone; CR, complete response; DLBCL, diffuse large B-cell lymphoma; DOCR, duration of complete response; Odro, odronextamab; ORR, objective response rate; PFS, progression-free survival; QW, once weekly; TEAE, treatment-emergent adverse event.

1. Kim TM, et al. *Nat Cancer* 2025;6(3):528–39.

Trial in Progress: Phase 1 Trial Evaluating the Safety and Tolerability of Odronextamab in Combination with Cemiplimab in Relapsed/Refractory Aggressive B-Cell Non-Hodgkin Lymphoma

Cecilia Carpio1, Manjusha Namuduri2, Nazia Iqbal2, Dishan Liu2, Nickolas Sophos2, Min Zhu2, Ayesha Sabir2, Jurriaan Brouwer-Visser2, Brouwer-Visser2, Aafia Chaudhry2, Hesham Mohamed2, Alejandro Martín García-Sancho3

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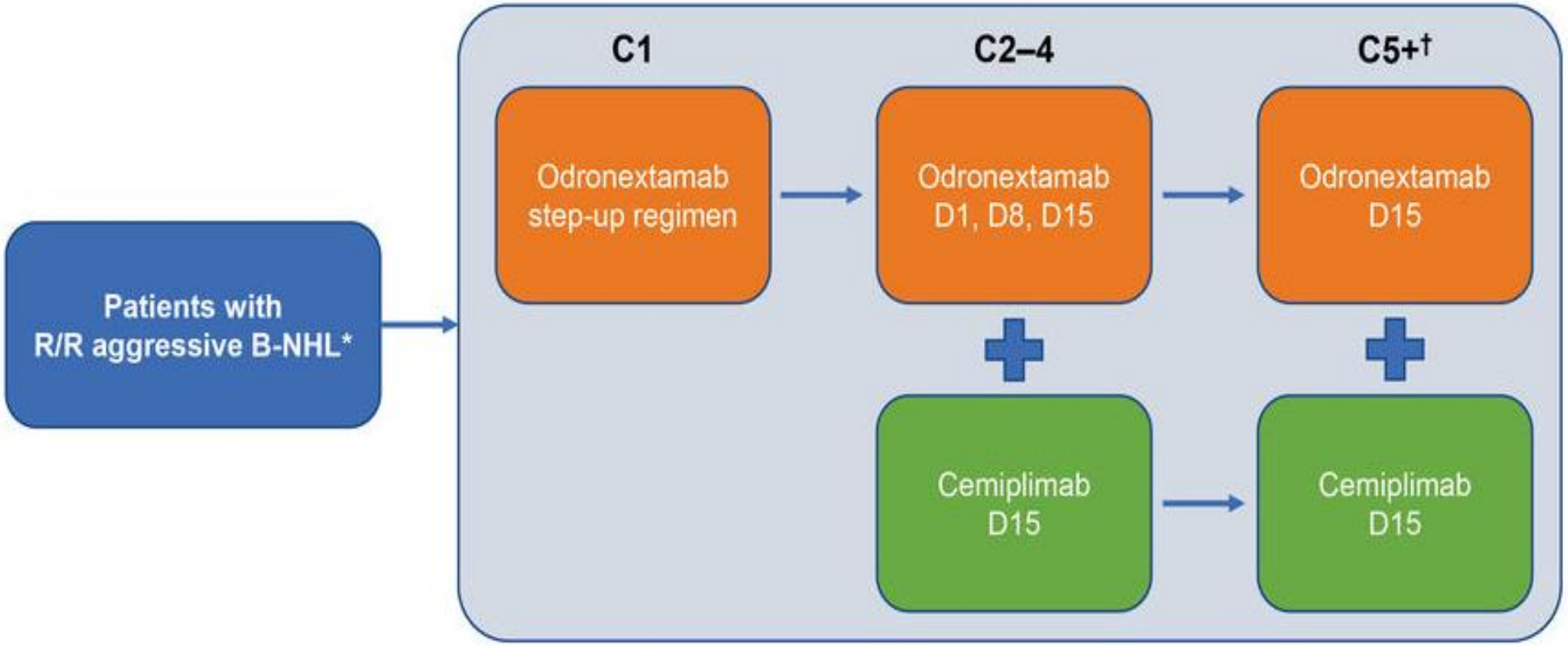
Treatment Schedule and Dosing Schema

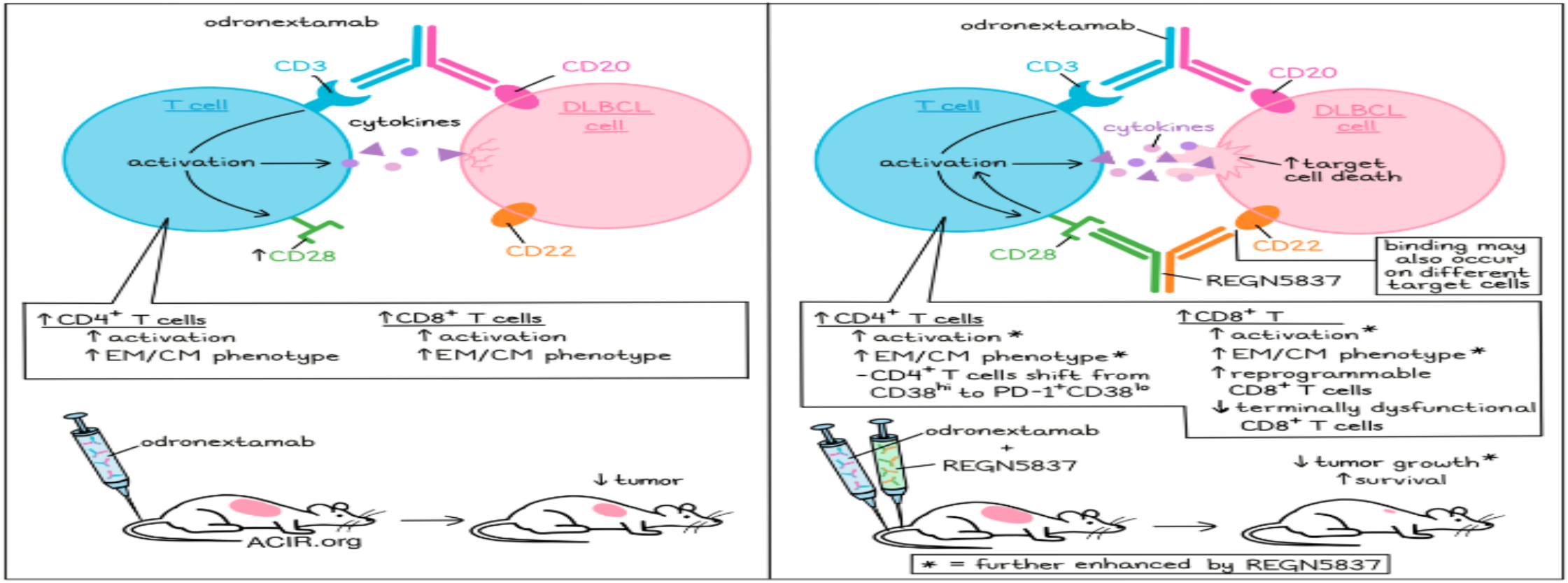


Treatment continues until disease progression or treatment discontinuation.

- Odronextamab administered IV in 21-day cycles; step-up dosing in C1 to mitigate cytokine release syndrome risk.
- Cemiplimab (IV) starts at C2D15 at specified dose level (DL1-DL7).
- At end of dose escalation, a regimen will be selected for further investigation in dose expansion phase.

Recruiting

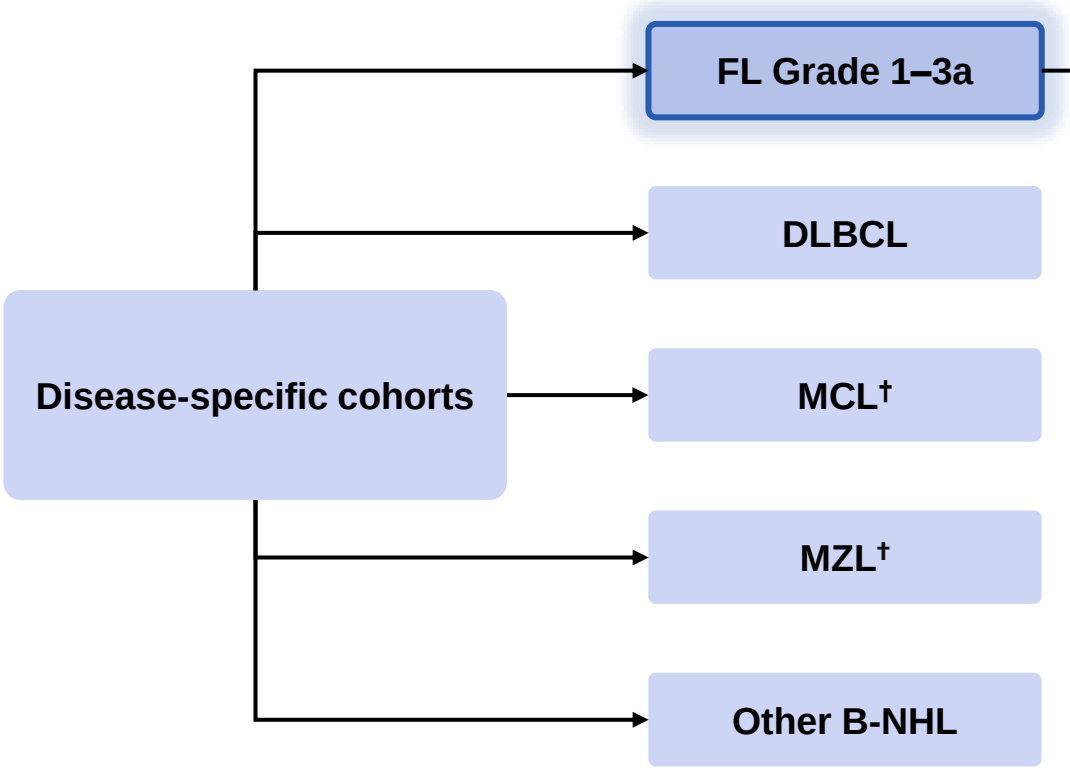
A Trial to Study if REGN5837 in Combination With Odronextamab is Safe for Adult Participants With Aggressive B-cell Non-Hodgkin Lymphomas (ATHENA-1)



Sci Transl Med. 2022 Nov 9;14(670):eabn1082

ELM-2 study design – FL cohort

- ELM-2 Phase 2, open-label, multi-cohort, multicenter study of odronextamab monotherapy for patients with R/R B-NHL (NCT03888105)
  - R/R DLBCL cohort results also presented at ASH 2022: oral presentation #444



Key eligibility criteria

- FL grades 1–3a
- ECOG PS 0 or 1
- Refractory to or relapsed after ≥2 prior lines of therapy, including an anti-CD20 antibody and an alkylator

Primary endpoint

- ORR* by ICR

Key secondary endpoints

- ORR* by local investigator
- CR, DOR, PFS, and OS
- Safety and tolerability

Odronextamab administration:
IV, 21-day cycles

- Cycle 1 Step-up
- Cycles 2–4 80mg Days 1, 8,15
- Cycle 5 onwards 160mg Q2W
- Treatment until disease progression

*According to Lugano criteria[1]
†New enrolment is currently paused.
B-NHL, B-cell non-Hodgkin's lymphoma; CD, cluster of differentiation; CR, complete response; DLBCL, diffuse large B-cell lymphoma; DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance score; FL, follicular lymphoma; ICR, independent central review; IV, intravenous; MCL, mantle cell lymphoma; MZL, marginal zone lymphoma; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; R/R, relapsed/refractory; Q2W, every 2 weeks.

1. Cheson BD, et al. *J Clin Oncol*. 2014;32(27):3059–3068.

Study design and methods

- ELM-2: Phase 2, open-label, multicohort, multicenter study of odronextamab monotherapy for patients with R/R B-cell non-Hodgkin lymphoma
- Measures taken to facilitate diverse and inclusive enrollment: diverse trial sites, translated consents for under-represented populations, extended screening windows for patients with access restraints, broad eligibility criteria to include patients with controlled HIV, hepatitis B and C, and lower thresholds for those with compromised organ function
- A prespecified interim analysis was performed when 80 patients with FL had completed ≥12 months of follow-up

ELM-2 study design – FL cohort

Key eligibility criteria

- FL Grade 1–3a*
- ECOG PS 0 or 1
- Refractory to or relapsed after ≥2 prior lines of therapy, including an anti-CD20 antibody and an alkylator

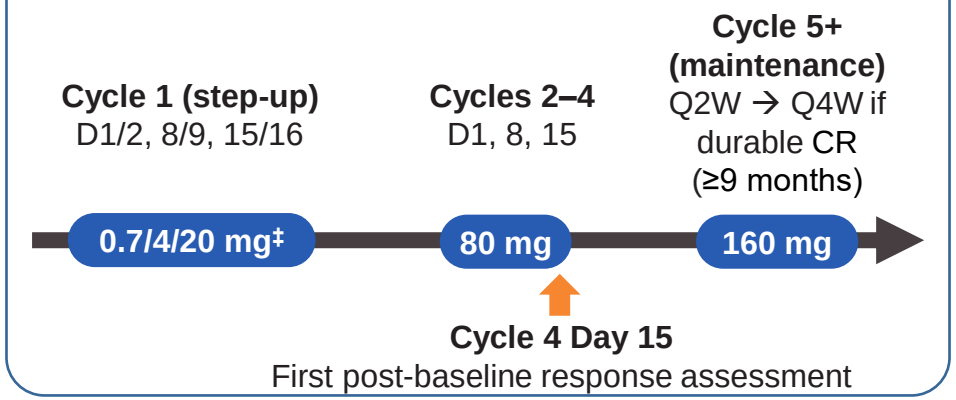
Primary endpoint: ORR† by ICR

Secondary endpoints:

- ORR† by local investigator
- CR†, DOR†, PFS†, and OS
- Safety and tolerability
- Patient-reported outcomes

Key exploratory endpoint: MRD

Odronextamab administration (IV, 21-day cycles):



*Per WHO 2017 classification[1]; †According to Lugano criteria[2]; ‡The study initiated with a Cycle 1 step-up regimen of 1/20 mg. This was modified to 0.7/4/20 mg to further mitigate the risk of CRS. Premedication administered during Cycle 1 step up included dexamethasone, diphenhydramine, and acetaminophen.

1. Swerdlow SH, et al. *WHO Classification of Tumours of Haematopoietic and Lymphoid Tissues, Fourth Edition.* Geneva, Switzerland: IARC Press; 2017; 2. Cheson BD, et al. *J Clin Oncol*. 2014;32(27):3059–68.

CD, cluster of differentiation; CR, complete response; CRS, cytokine release syndrome; D, day; DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; FL, follicular lymphoma; HIV, human immunodeficiency virus; ICR, independent central review; IV, intravenous; MRD, minimal residual disease; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; QXW, once every X weeks; R/R, relapsed/refractory; WHO, World Health Organization.

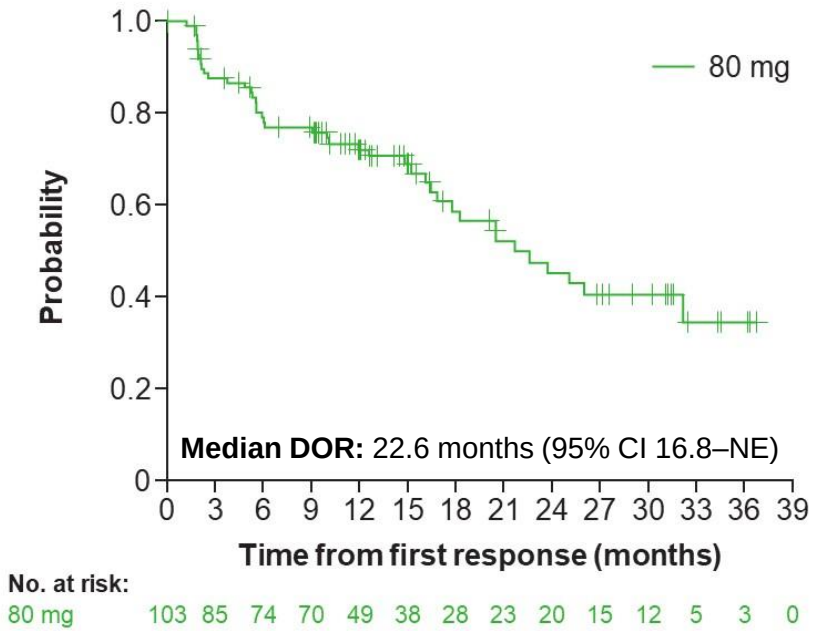
Efficacy: Best overall response, DOR and DOCR

- Median duration of follow-up for efficacy: 17.7 months (95% CI 15.0–27.8)
  - An estimated 81.8% of patients had ≥12 months of follow-up
- Odronextamab demonstrated high CR rates that were durable
  - 91.3% of responders were complete responders
  - 75.8% of patients with CR maintained response at 12 months

Best overall response (ICR)

n (%)	N=128
ORR*	**103 (80.5);** 95% CI 72.5–86.9
CR	**94 (73.4)**

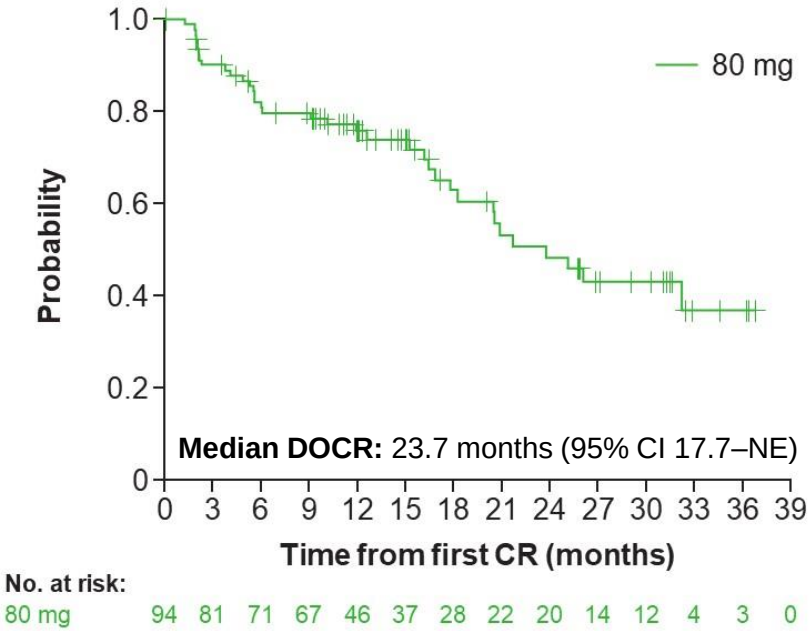
DOR (ICR)



Median DOR: 22.6 months (95% CI 16.8–NE)

12-month DOR: 72.3% (95% CI 61.9–80.2)
24-month DOR: 45.5% (95% CI 32.2–57.9)

DOCR (ICR)



Median DOCR: 23.7 months (95% CI 17.7–NE)

12-month DOCR: 75.8% (95% CI 65.2–83.5)
24-month DOCR: 48.5% (95% CI 34.2–61.3)

Data cut-off date: August 18, 2023.
*CRs + PRs.
CI, confidence interval; CR, complete response; DOCR, duration of complete response; DOR, duration of response; ICR, independent central review; NE, not estimable; ORR, objective response rate; PR, partial response.

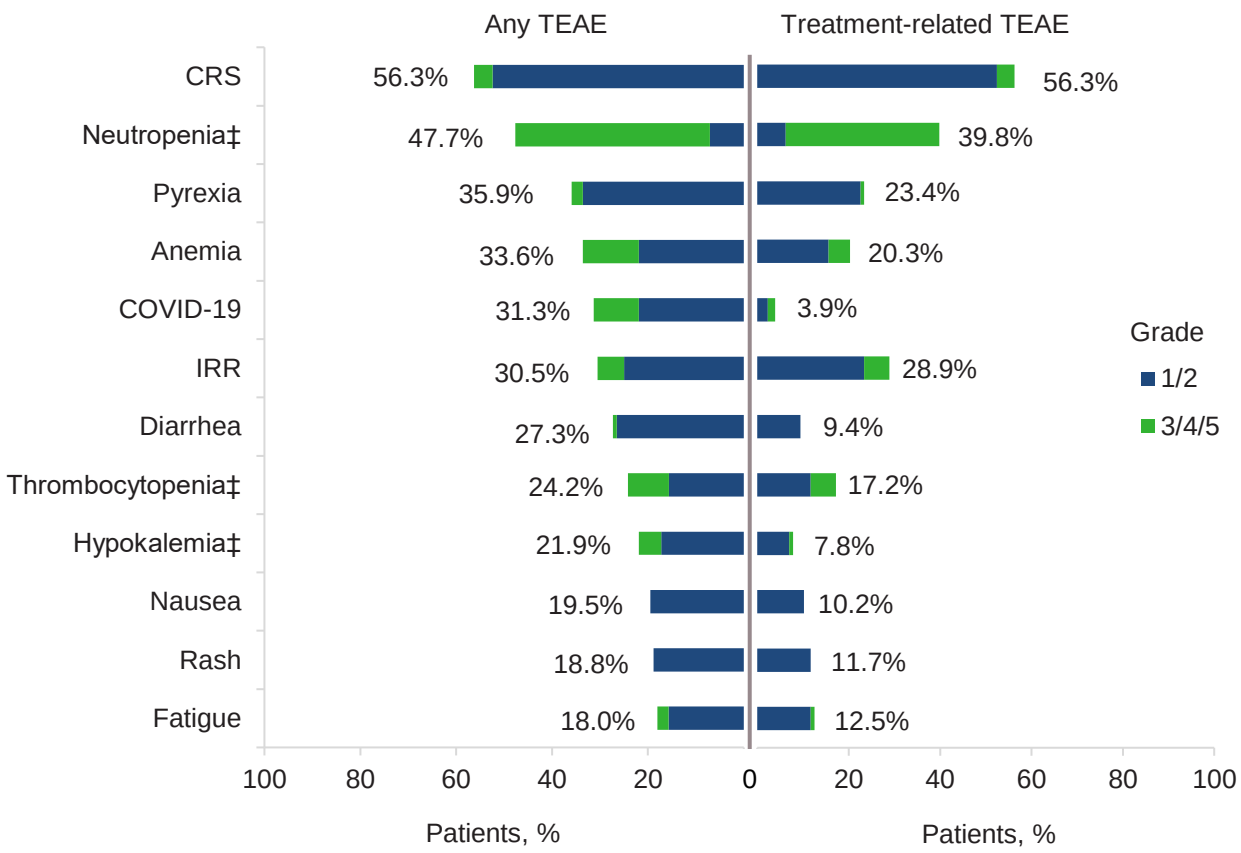
Safety: TEAEs

TEAEs

n (%)	N=128*	
	Any event	Treatment related
Any TEAE	128 (100)	118 (92.2)
Grade ≥3 TEAE	109 (85.2)	80 (62.5)
Serious AE	87 (68.0)	57 (44.5)
TEAE leading to treatment interruption/delay	106 (82.8)	79 (61.7)
TEAE leading to dose reduction	12 (9.4)	12 (9.4)
TEAE leading to treatment discontinuation	20 (15.6)	10 (7.8)
TEAE leading to death (Grade 5)	19 (14.8)	4 (3.1)†

- Safety was generally consistent with previous reports

TEAEs in ≥15% of patients (N=128)



Data cut-off date: August 18, 2023.
AEs per NCI-CTCAE v5.0, CRS per Lee 2014/2019 criteria[1,2]. *0.7/4/20 mg (n=60) and 1/20 mg (n=68) Cycle 1 step-up regimen. †Pneumonia, PML, pneumonia pseudomonal, and COVID-19 pneumonia + systemic mycosis (each, n=1). ‡Composite term.
1. Lee DW, et al. *Blood*. 2014;124(2):188–95. 2. Lee DW, et al. *Biol Blood Marrow Transplant*. 2019;25(4):625–38.
AE, adverse event; ALT, alanine aminotransferase; CRS, cytokine release syndrome; IRR, infusion-related reaction; NCI-CTCAE, National Cancer Institute Common Terminology Criteria for Adverse Events; PML, progressive multifocal leukoencephalopathy; TEAE, treatment-emergent adverse event.

Poster number
5381

Odronextamab (Odro) Plus Lenalidomide (+ Len) in Patients with Relapsed/Refractory (R/R) Follicular Lymphoma (FL): First Results from Part 1 (Safety Lead-In) of the Phase 3 OLYMPIA-5 Study

Umberto Vitolo,[1] Lalita Norasetthada,[2] Jae-Cheol Jo,[3] Biyi Shen,[4] Dina M. Flink,[4] Min Zhu,[4] Soujanya Chandrasekharan,[4] Jingxiao Chen,[4] Jurriaan Brouwer-Visser,[4] Aafia Chaudhry,[4] Hesham Mohamed,[4] Sabela Bobillo-Varela,[4] Catherine Thieblemont[5]

[1]Candiolo Cancer Institute, FPO-IRCCS, Candiolo, Turin, Italy; [2]Chiang Mai University, Chiang Mai, Thailand; [3]Ulsan University Hospital, Ulsan, South Korea; [4]Regeneron Pharmaceuticals, Inc., Tarrytown, NY, USA; [5]Université Paris Cité, Assistance Publique-Hôpitaux de Paris, Hôpital Saint-Louis, Hemato-oncology, Paris, France

ClinicalTrials.gov ID: NCT06149286

Presented at the 67th American Society of Hematology (ASH) Annual Meeting and Exposition, December 6–9, 2025, Orlando, FL, USA

OLYMPIA-5 is a randomized, open-label, multicenter study of Odro + Len in patients with R/R FL or MZL after ≥1 prior LOT

Key eligibility criteria

- Age ≥18 years
- FL Grade 1–3a or MZL (nodal, splenic, or extranodal)
- R/R after ≥1 prior line of systemic therapy
- ECOG PS ≤2
- Adequate organ function
- No CNS lymphoma or relevant CNS pathology
- No prior use of lenalidomide or a CD20×CD3 bispecific antibody in the past 6 months

Part 1: Dose selection and safety lead-in

R/R FL or MZL

Odro + Len

12 cycles

Endpoints

Primary

- DLT incidence*
- TEAEs (incidence and severity)

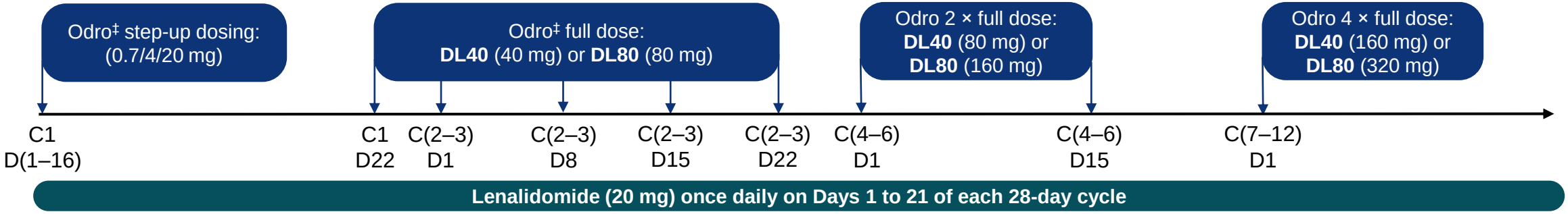
Selected secondary

- PK and immunogenicity
- Investigator-assessed ORR, CR rate, and DOR†

Exploratory

- Immunophenotyping

Odronextamab (IV) and lenalidomide (oral) administration (28-day cycles)



*DLTs assessed during the DLT observation period (35 days or at least two full doses of odronextamab and at least one dose of lenalidomide); †Assessed according to the Lugano classification response criteria by PET-CT;[1] ‡Dexamethasone (or equivalent) premedication was required for step-up doses and the first full weekly dose, then reduced or omitted if further infusions were tolerated without CRS.

CNS, central nervous system; C, cycle; CR, complete response; CRS, cytokine release syndrome; D, day; DL, dose level; DLT, dose-limiting toxicity; DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; FL, follicular lymphoma; IV, intravenous; Len, lenalidomide; LOT, line of therapy; MZL, marginal zone lymphoma; Odro, odronextamab; ORR, objective response rate; PET-CT, positron emission tomography-computed tomography; PK, pharmacokinetics; R/R, relapsed/refractory; TEAE, treatment-emergent adverse event.

1. Cheson BD, et al. *J Clin Oncol* 2014;32(27):3059–68.

Baseline demographics and disease characteristics of the Part 1 FL population by dose level

Demographics and disease characteristics*		DL40 (n=6)	DL80 (n=26)
Median age (range), years		48.5 (35–74)	60.0 (40–80)
Age, years, %	<65 / ≥65 to <75 / ≥75	66.7 / 33.3 / 0	65.4 / 19.2 / 15.4
Male, %		33.3	46.2
Race, %	White	0	50.0
	Asian	100	19.2
	Not reported	0	30.8
ECOG PS, %	0 / 1	50.0 / 50.0	57.7 / 42.3
Bulky disease, %		16.7	19.2
FL grade, %	1	50.0	15.4
	2	16.7	30.8
	1–2	0	30.8
	3a	33.3	23.1
FLIPI risk score, %	0–1 / 2 / 3–5	33.3 / 33.3 / 33.3	34.6 / 34.6 / 30.8
Lugano stage III–IV,†[1] %	III–IV	66.7	73.1
POD24, %		0	3.8
Median number of prior lines of therapy (range)		1.5 (1–7)	1 (1–5)
Refractory to last line of therapy, %		33.3	42.3

- Treatment was ongoing in 15.6% of patients in the FL cohort (**Suppl. Table 1**)
- The median duration of treatment exposure was 47.9 weeks in the DL40 group and 43.1 weeks in the DL80 group (**Suppl. Table 1**)
- Exposures to odronextamab were similar with or without co-administration of lenalidomide[2] (**Suppl. Figure 1**)

Data cut-off date: September 17, 2025. *Gender and disability data were not collected per protocol; †Confirmed by medical director at study entry.
DL, dose level; ECOG PS, Eastern Cooperative Oncology Group performance status; FL, follicular lymphoma; FLIPI, Follicular Lymphoma International Prognostic Index; POD24, progression of disease or relapse within 2 years of frontline therapy.
1. Cheson BD, et al. *J Clin Oncol* 2014;32(27):3059–68; 2. Kim TM, et al. *Ann Oncol* 2024;35(11):1039–47.

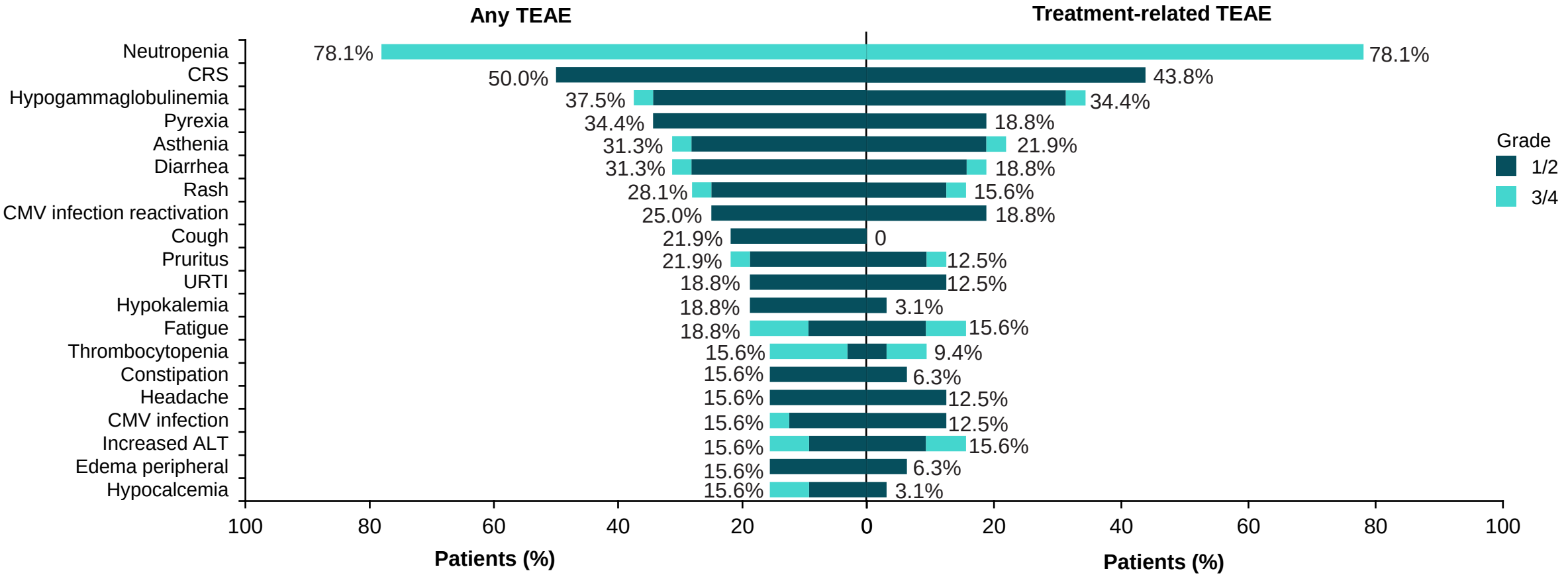
Odronextamab DL80 had a generally manageable safety profile in combination with lenalidomide

n (%)	DL40 (n=6)		DL80 (n=26)		Part 1 total (N=32)	
	Any event	Treatment related	Any event	Treatment related	Any event	Treatment related
Any TEAE	6 (100)	6 (100)	26 (100)	25 (96.2)	32 (100)	31 (96.9)
Grade ≥3 TEAE	4 (66.7)	4 (66.7)	25 (96.2)	23 (88.5)	29 (90.6)	27 (84.4)
Serious TEAE	2 (33.3)	1 (16.7)	14 (53.8)	9 (34.6)	16 (50.0)	10 (31.3)
TEAE leading to treatment interruption/delay	4 (66.7)	4 (66.7)	24 (92.3)	23 (88.5)	28 (87.5)	27 (84.4)
TEAE leading to dose reduction (Odro)	1 (16.7)	1 (16.7)	0	0	1 (3.1)	1 (3.1)
TEAE leading to dose reduction (Len)	3 (50.0)	3 (50.0)	9 (34.6)	9 (34.6)	12 (37.5)	12 (37.5)
TEAE leading to treatment discontinuation	0	0	4 (15.4)	4 (15.4)	4 (12.5)	4 (12.5)
TEAE leading to death (Grade 5)*	1 (16.7)	0	1 (3.8)	0	2 (6.3)	0

- No DLTs were recorded during the observation period
- The TEAEs leading to treatment discontinuation (by SOC) were infections and infestations (6.3%, CMV infection, pneumonia, and sepsis), nervous system disorders (6.3%, hemorrhagic stroke, and neuromyopathy), and skin and subcutaneous disorders (3.1%, rash)†

Data cut-off date: September 17, 2025.
Adverse events graded per NCI Common Terminology Criteria for Adverse Events v5.0,[1] except CRS and ICANS, which were graded per Lee DW, et al. 2019.[2] *TEAEs leading to death were influenza (DL40) and hemorrhagic stroke (DL80); †Patients may have experienced more than one TEAE leading to treatment discontinuation.
DL, dose level; DLT, dose-limiting toxicity; CMV, cytomegalovirus; CRS, cytokine release syndrome; ICANS, immune cell-associated neurotoxicity syndrome; Len, lenalidomide; NCI, National Cancer Institute; Odro, odronextamab; SOC, System Organ Class; TEAE, treatment-emergent adverse event.
1. NCI. Common Terminology Criteria for Adverse Events (CTCAE) Version 5.0. https://ctep.cancer.gov/protocoldevelopment/electronic_applications/docs/ctcae_v5_quick_reference_5x7.pdf (accessed Oct 14, 2025);
2. Lee DW, et al. *Biol Blood Marrow Transplant* 2019;25(4):625–38.

TEAEs observed in >15% of patients treated with Odro + Len



- The safety profile in the DL40 and DL80 groups is shown in **Suppl. Figure 2**

Data cut-off date: September 17, 2025.
Adverse events graded per NCI Common Terminology Criteria for Adverse Events v5.0,[1] except CRS and ICANS, which were graded per Lee DW, et al. 2019.[2]
ALT, alanine transaminase; CRS, cytokine release syndrome; CMV, cytomegalovirus; DL, dose level; ICANS, immune effector cell-associated neurotoxicity syndrome; Len, lenalidomide; NCI, National Cancer Institute; Odro, odronextamab; URTI, upper respiratory tract infection; TEAE, treatment-emergent adverse event.

1. NCI. Common Terminology Criteria for Adverse Events (CTCAE) Version 5.0. https://ctep.cancer.gov/protocoldevelopment/electronic_applications/docs/ctcae_v5_quick_reference_5x7.pdf (accessed Oct 14, 2025);
2. Lee DW, et al. *Biol Blood Marrow Transplant* 2019;25(4):625–38.

All CRS events were low grade

CRS		DL40 (n=6)	DL80 (n=26)	Part 1 total (N=32)
Any grade, n (%)		2 (33.3)	14 (53.8)	16 (50.0)
Grade 1		2 (33.3)	9 (34.6)	11 (34.4)
Grade 2		0	5 (19.2)	5 (15.6)
Grade ≥3		0	0	0
Median time to CRS onset (range), hours		12.5 (5.2–19.8)	11.0 (6.3–64.9)	11.0 (5.2–64.9)
Median CRS duration (range), hours		5.2 (5.2–5.2)	7.2 (1.0–43.1)	5.2 (1.0–43.1)
CRS management, n (%)	Systemic steroids	2 (33.3)	1 (3.8)	3 (9.4)
	Tocilizumab	1 (16.7)	6 (23.1)	7 (21.9)
	Steroids or tocilizumab	2 (33.3)	6 (23.1)	8 (25.0)

- A single ICANS event of Grade 3 severity occurred in the DL80 group
- No TLS was reported

Data cut-off date: September 17, 2025.
CRS and ICANS were graded per Lee DW, et al. 2019.[1]
CRS, cytokine release syndrome; DL, dose level; ICANS, immune effector cell-associated neurotoxicity syndrome; TLS, tumor lysis syndrome.
1. Lee DW, et al. *Biol Blood Marrow Transplant* 2019;25(4):625–38.

Infections were mostly low grade and generally manageable in the DL80 group

Infections,* n (%)	DL40 (n=6)	DL80 (n=26)
Any grade†	5 (83.3)	20 (76.9)
Grade 1	2 (33.3)	1 (3.8)
Grade 2	1 (16.7)	14 (53.8)
Grade 3	1 (16.7)	1 (3.8)
Grade 4	0	4 (15.4)
Grade 5‡	1 (16.7)	0
Opportunistic infection§	4 (66.7)	12 (46.2)
Grade 3	0	2 (7.7)
Grade ≥4	0	0

- Most common infections were CMV infection reactivation (DL40, 33.3%; DL80, 23.1%),
  CMV infection (DL40, 0; DL80, 23.1%), and
  URTI (DL40, 0; DL80, 23.1%)
  - Two patients (33.3%) had asymptomatic CMV viremia in the DL40 group, and one patient (3.8%) had CMV reactivation with viremia and CMV infection in the DL80 group
- Grade 3 opportunistic infections were CMV infection and pneumonia fungal infection (both occurred in the DL80 group)
- Ten patients required inpatient hospitalization due to infections (DL40, n=2; DL80, n=8)

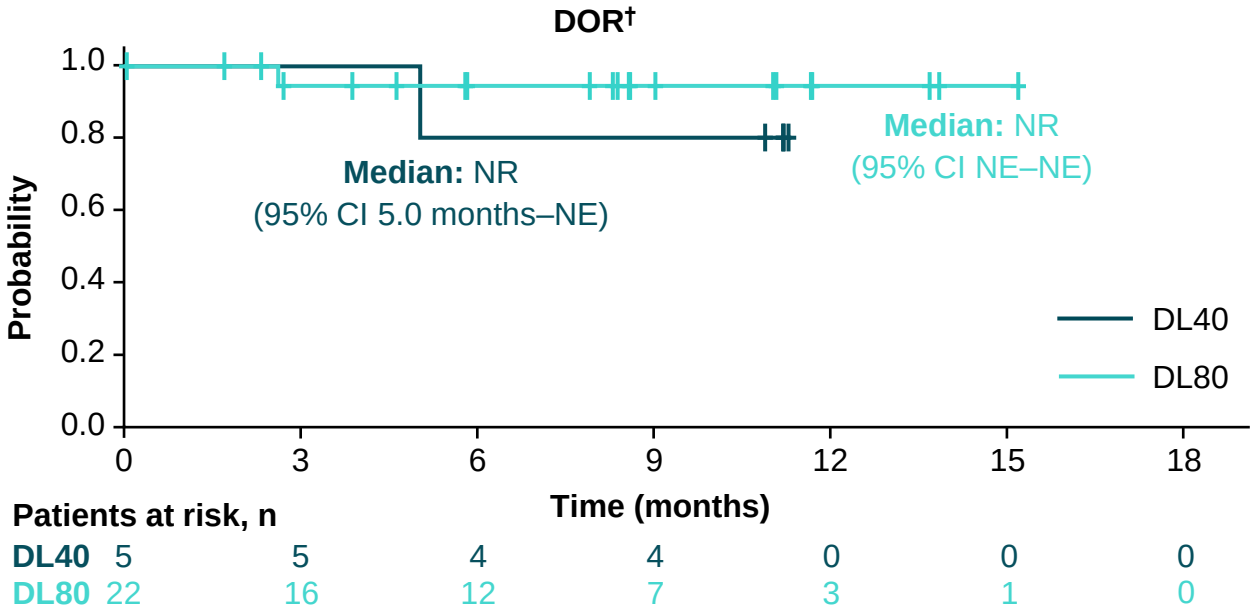
Data cut-off date: September 17, 2025.
*Graded per NCI Common Terminology Criteria for Adverse Events v5.0;[1] †Any-grade infections leading to treatment discontinuation were Grade 2 CMV infection and *Stenotrophomonas* infection in one patient, plus Grade 4 sepsis and Grade 2 pneumonia in another patient from the DL80 group; ‡One patient in DL40 experienced Grade 5 influenza virus; §Defined by narrow SMQ (MedDRA version 28.0).[2]
CMV, cytomegalovirus; DL, dose level; MedDRA, Medical Dictionary for Regulatory Activities; NCI, National Cancer Institute; SMQ, Standardized MedDRA Query; URTI, upper respiratory tract infection.
1. NCI. Common Terminology Criteria for Adverse Events (CTCAE) Version 5.0. https://ctep.cancer.gov/protocoldevelopment/electronic_applications/docs/ctcae_v5_quick_reference_5x7.pdf (accessed Oct 14, 2025);
2. Medical Dictionary for Regulatory Activities (MedDRA), version 28.0; International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH); 2024.

Responses were durable in the DL80 group

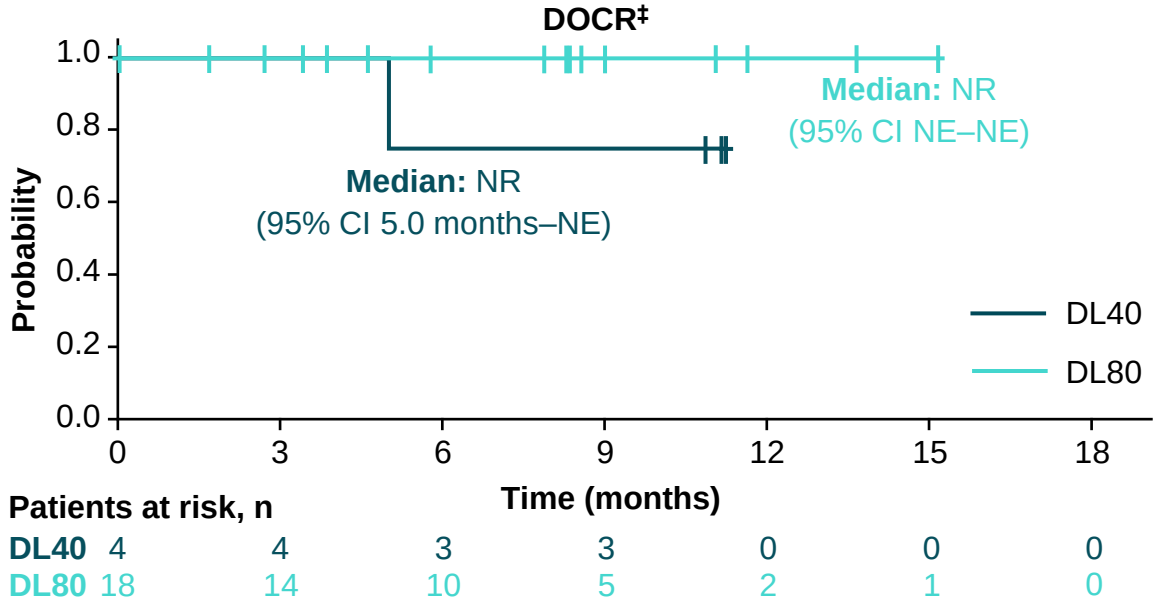
Response rates

n (%)	DL40 (n=6)	DL80 (n=26)
ORR*	5 (83.3)	22 (84.6)
CR rate	4 (66.7)	18 (69.2)

- Median follow-up duration:
  - DL40: 13.7 months (95% CI 0.0–NE)
  - DL80: 11.1 months (95% CI 6.7–11.6)
- At the first response assessment (~12 weeks), 4/5 (80.0%) patients in the DL40 group and 15/25 (60.0%) patients in the DL80 group had achieved a CR (**Suppl. Figure 3**)



	DL40 (n=5)	DL80 (n=22)
9-month DOR rate, % (95% CI)	80.0 (20.4–96.9)	94.4 (66.6–99.2)



	DL40 (n=4)	DL80 (n=18)
9-month DOCR rate, % (95% CI)	75.0 (12.8–96.1)	100 (100–100)

Data cut-off date: September 17, 2025. *CRs + PRs. Assessed according to the Lugano classification response criteria by PET-CT;[1] †Based on patients with a CR or PR; ‡Based on patients with a CR.
CI, confidence interval; CR, complete response; DL, dose level; DOCR, duration of complete response; DOR, duration of response; NE, not evaluable; NR, not reported; PET-CT, positron emission tomography-computed tomography; ORR, objective response rate; PR, partial response.

1. Cheson BD, et al. *J Clin Oncol* 2014;32(27):3059–68.

Key takeaways

- **In Part 1 of the Phase 3 OLYMPIA-5 study, the safety profile of Odro + Len at DL80 was generally manageable in the FL cohort, with no new safety signals reported[1]**
  - All CRS events were Grade 1 or Grade 2
  - One Grade 3 ICANS event in DL80 and no TLS events were reported
  - Grade ≥3 infections occurred in 19.2% of patients in DL80
- **Preliminary efficacy in the DL80 group was encouraging**
  - ORR was 84.6%
  - Median DOR was not reached
- **Biomarker data were mostly consistent with odronextamab monotherapy[1]**
  - Rapid and robust activation of CD8+ T cells; B cells rapidly depleted with odronextamab treatment
  - Compared with odronextamab monotherapy,[1] serum IL-6 levels were similar but C2D1 IFN-γ levels were elevated
- **OLYMPIA-5 Part 2 enrollment is underway with odronextamab 80 mg as the selected dose**

C, cycle; CRS, cytokine release syndrome; D, day; DL, dose level; DOR, duration of response; FL, follicular lymphoma; ICANS, immune effector cell-associated neurotoxicity syndrome; IFN-γ, interferon-gamma; IL, interleukin; Len, lenalidomide; Odro, odronextamab; ORR, objective response rate; TLS, tumor lysis syndrome.

1. Kim TM, et al. *Ann Oncol* 2024;35(11):1039–47.

ASH 2025

OLYMPIA-2

Odronextamab Plus Chemotherapy in Previously Untreated Follicular Lymphoma:
A Phase 3, Open-Label, Randomized Trial

Abstract #3600

Poster Session 623

Sunday, December 7, 2025

6:00 - 8:00 PM

West Halls B3-B4, Orlando, FL

PB2275 TRIAL IN PROGRESS: PHASE 3 TRIAL EVALUATING THE EFFICACY AND SAFETY OF ODRONEXTAMAB PLUS CHEMOTHERAPY VERSUS RITUXIMAB PLUS CHEMOTHERAPY IN PREVIOUSLY UNTREATED FOLLICULAR LYMPHOMA (OLYMPIA-2)

Topic: 18. Indolent and mantle-cell non-Hodgkin lymphoma – Clinical

Silvana Novelli*[1], Ashish Risal[2], Manjusha Namuduri[2], Jingxian Cai[2], Melanie Ufkin[2], Min Zhu[2], Sushmita Mukherjee[2], Jurriaan Brouwer-Visser[2], Aafia Chaudhry[2], Hesham Mohamed[2], Srikanth Ambati[2], Elżbieta Iskierka-Jażdżewska[3]

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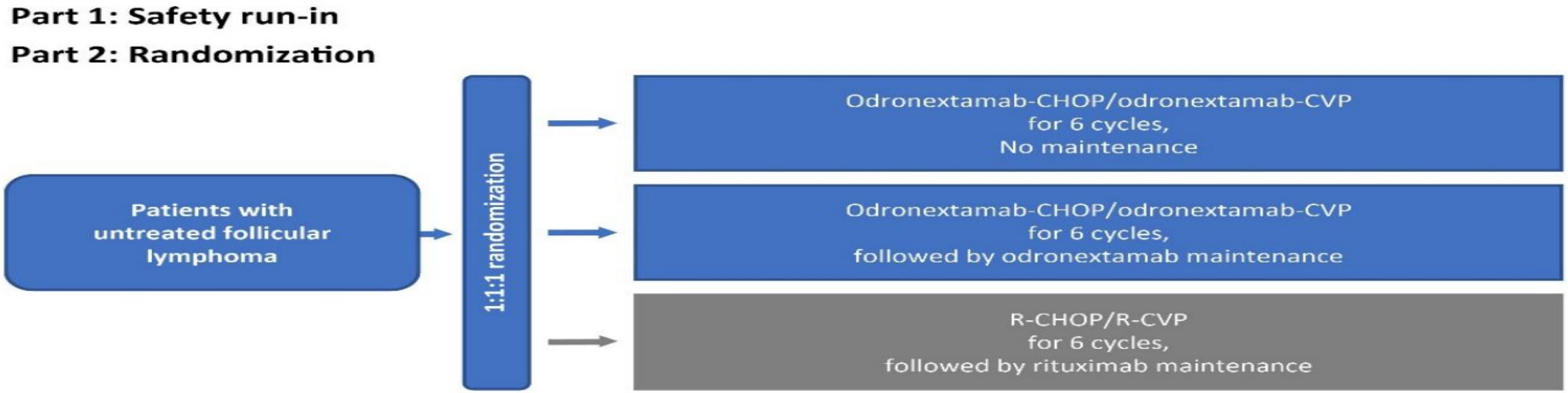

CHOP, cyclophosphamide, doxorubicin, vincristine, prednisone; CVP, cyclophosphamide, vincristine, prednisone; R, rituximab.

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