ALMA MATER STUDIORUM
UNIVERSITÀ DI BOLOGNA
DIPARTIMENTO DI
SCIENZE MEDICHE E CHIRURGICHE

POLICLINICO DI
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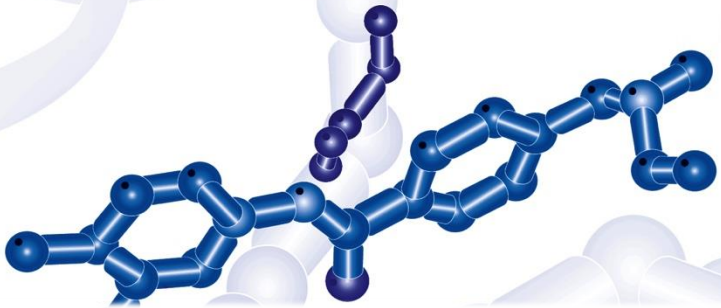
New Drugs in Hematology



CC99282 / golcadomide
Session non-Hodgkin lymphoma

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Disclosures of jean-marie Michot

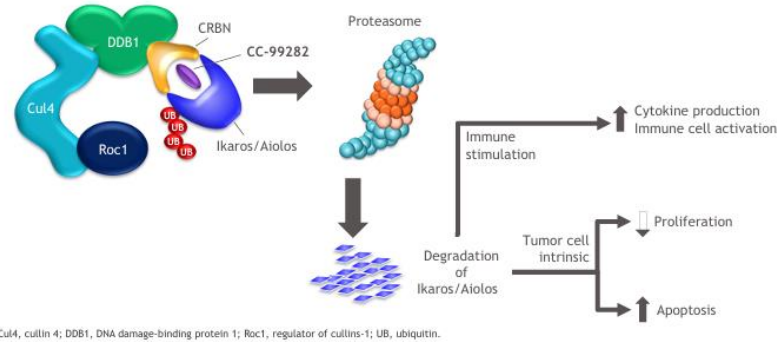
Company name	Research support	Employee	Consultant	Stockholder	Speakers bureau	Advisory board	Other
Regeneron						x	
Boehringer Ingelheim			x				
Amgen							x
Ideogen							x
Beigene							x

CC99282 / golcadomide in non-hodgkin lymphoma

- MOA
- Preclinical data
- P1/2 R/R DLBCL
- P1/2 R/R FL
- Trials in progress
- Conclusion & discussion

CC99282/ golcadomide fully activates CRBN, driving superior **Ikaros/Aiolos degradation** vs len.

Figure 2. Schematic of CC-99282 mechanism of action (MOA)[7-9]



Cul4, cullin 4; DDB1, DNA damage-binding protein 1; Roc1, regulator of cullins-1; UB, ubiquitin.

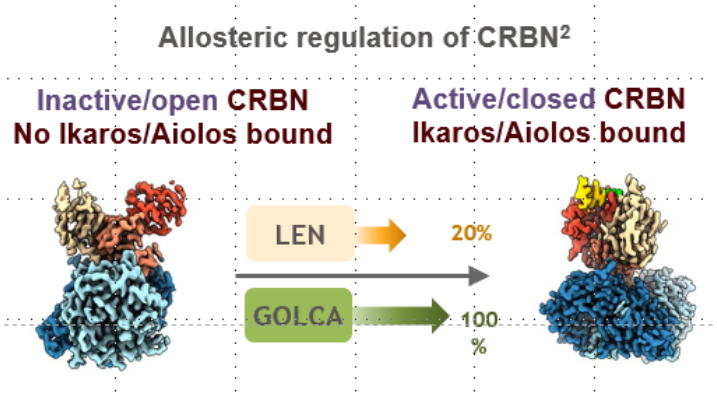
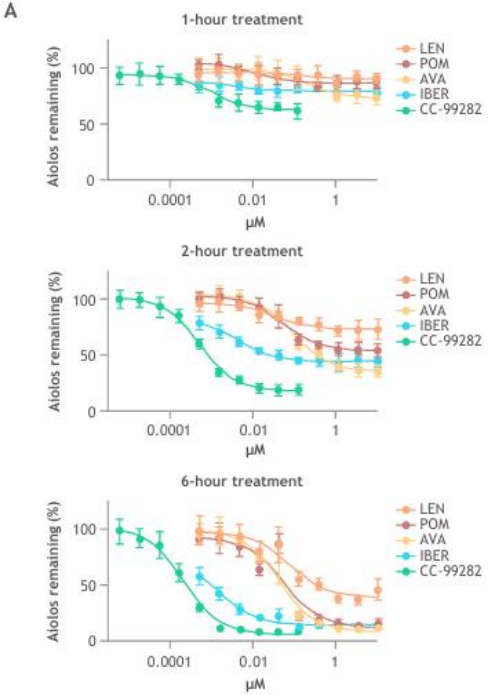


Figure 1. CC-99282 inhibits proliferation of DLBCL cells, while inducing apoptosis



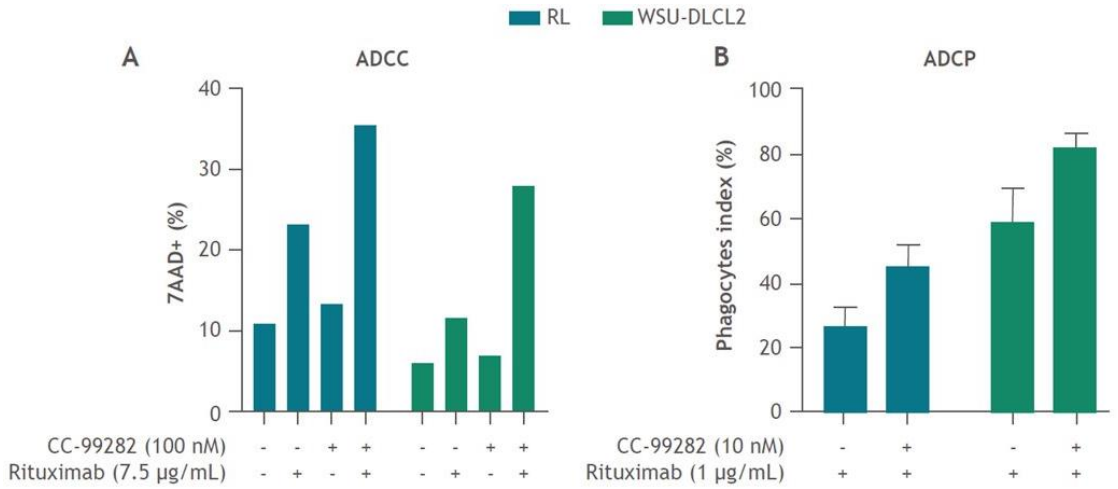
B

	LEN	AVA	IBER	CC-99282
Karpas-422	1,194	471.5	399.1	42.28
SU-DHL16	1,232	884.5	631.2	177.8
HT	983.9	716.7	691	480.7
ULA	229.9	22.25	13.62	1.74
WSU-DLCL2	984.6	607.1	914.5	58.85
SU-DHL-5	807.6	91.2	97.14	1.607
SU-DHL-10	978.5	231.5	238.3	2.13
DB	1,030	1,225	1,118	974.3
SU-DHL-4	978.6	807.2	684.3	259.3
VAL	414.2	135.3	16.27	12.07
Farage	588.6	107.4	75.21	14.74
OCI-LY-3	951.7	925.8	928.3	927.3
OCI-LY-1	811.5	390	249.7	54.46
SU-DHL-6	947.6	629.6	692.8	26.72
OCI-LY-7	855.9	320.1	286.3	37.19
U2940	623.2	303.9	95.01	66.82
U2932	1,044	514.1	252.4	142.6
U2932*	1,027	397.1	365.5	142.9
OCI-LY-18	433.1	64.9	3.417	1.659
SU-DHL-2	463.1	91.68	7.82	3.608
SU-DHL-1	198.5	46.1	47.39	33.14
WILL-2	616.7	123.7	595	67.88
U2946	1,070	330.2	80.05	53.36
RC-K8	629.8	212.9	121.1	85.41
SU-DHL-8	1,124	1,180	701.4	54.95
NU-DUL-1	1,174	496.3	648.5	98.4
RIVA	798.5	632	267.3	292.8
ROS-50	1,062	971.1	812.6	755.3
WILL-1	836.9	586.3	586.3	320
U2904	445.8	506.8	209.2	248.4
NU-DHL-1	521.1	154.4	427.8	9,284
TMD8	851.1	183.9	171.5	5,615
(Follicular L) RL	992.3	354.7	278.8	184.4

Rationale for CC99282/golcadomide + anti-CD20 combinations

Rituximab combination

ADCC + ADCP



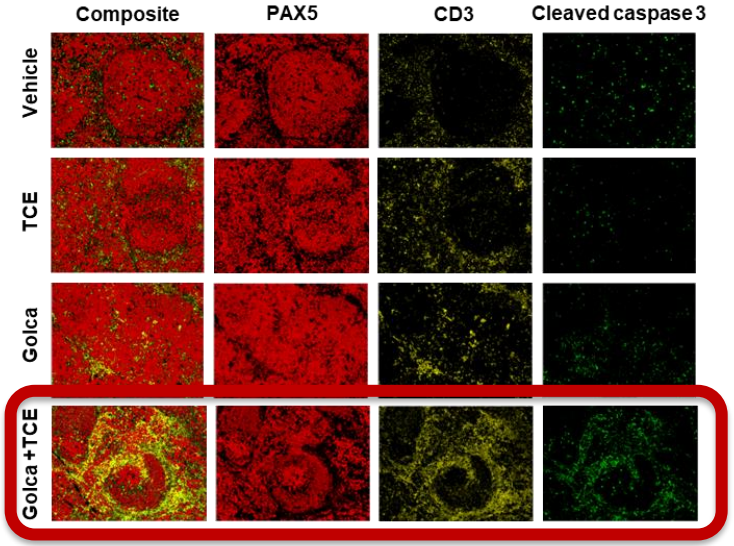
ADCC — Antibody-Dependent Cellular Cytotoxicity

ADCP — Antibody-Dependent Cellular Phagocytosis

In vivo xenograft

TCE combination

Golcadomide + TCE increases immune infiltrate and cell killing over TCE mono

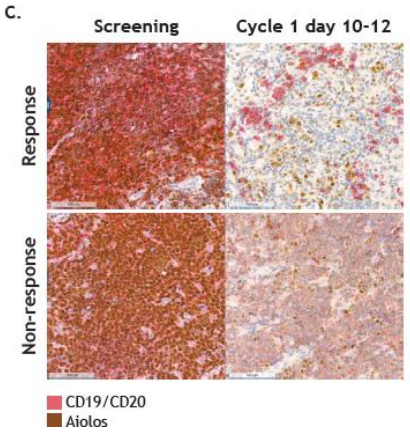


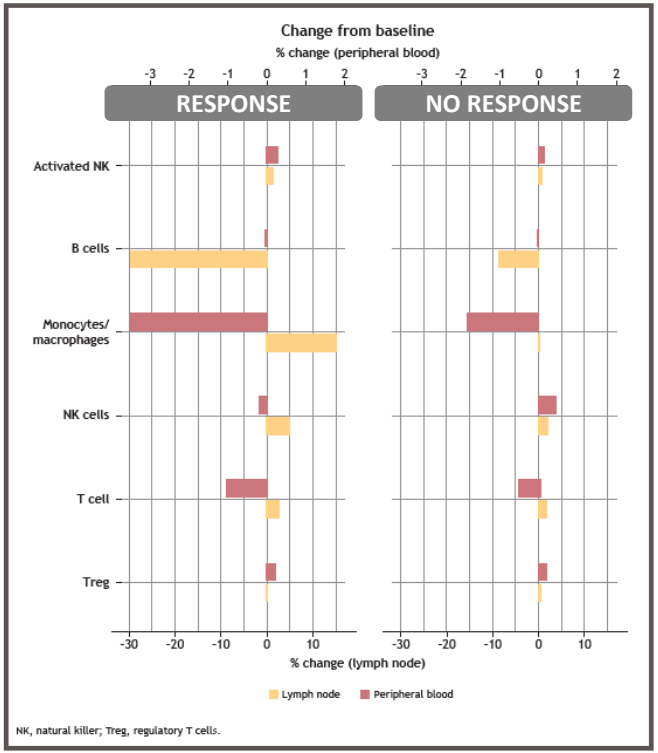
Syngeneic lymphoma model Eμ-myc/hCRBN cells injected into hCRBN mice

CC-99282-NHL-001 DLBCL biomarker cohort

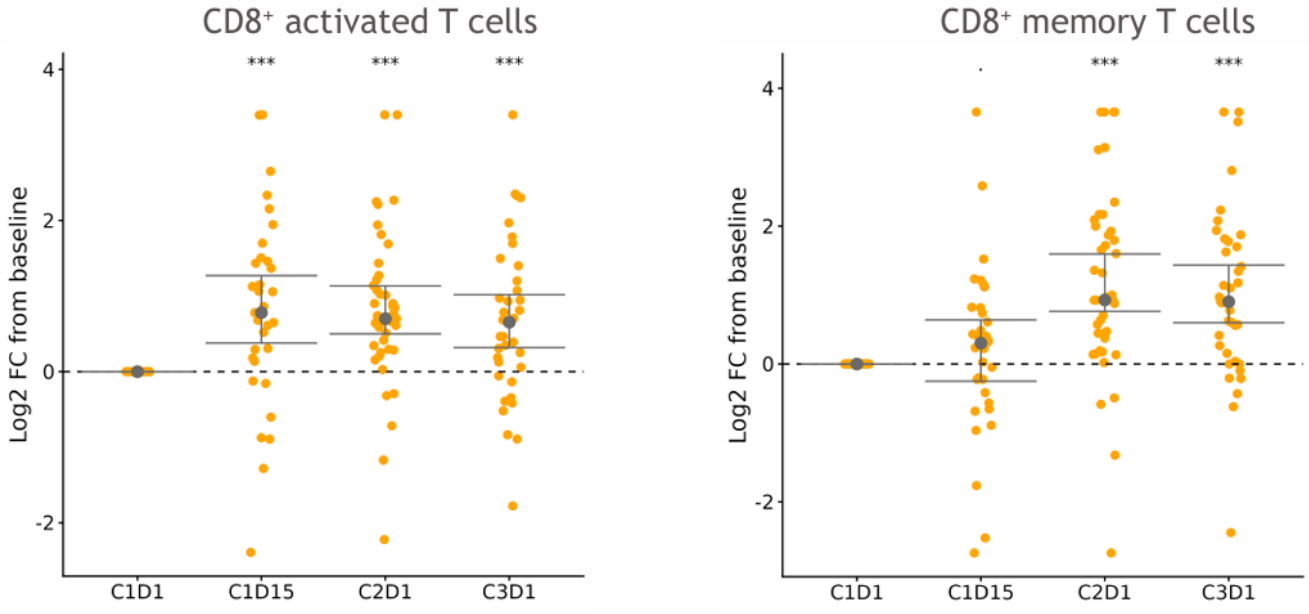
- Most B cells in biopsies from patients with DLBCL **had a high expression of Aiolos**, which was reduced or eliminated on treatment
- The degree of aiolos/Ikaros degradation is not predictive to the response status

- **Changes in immune populations** were more evident in patients responding to golcadomide treatment





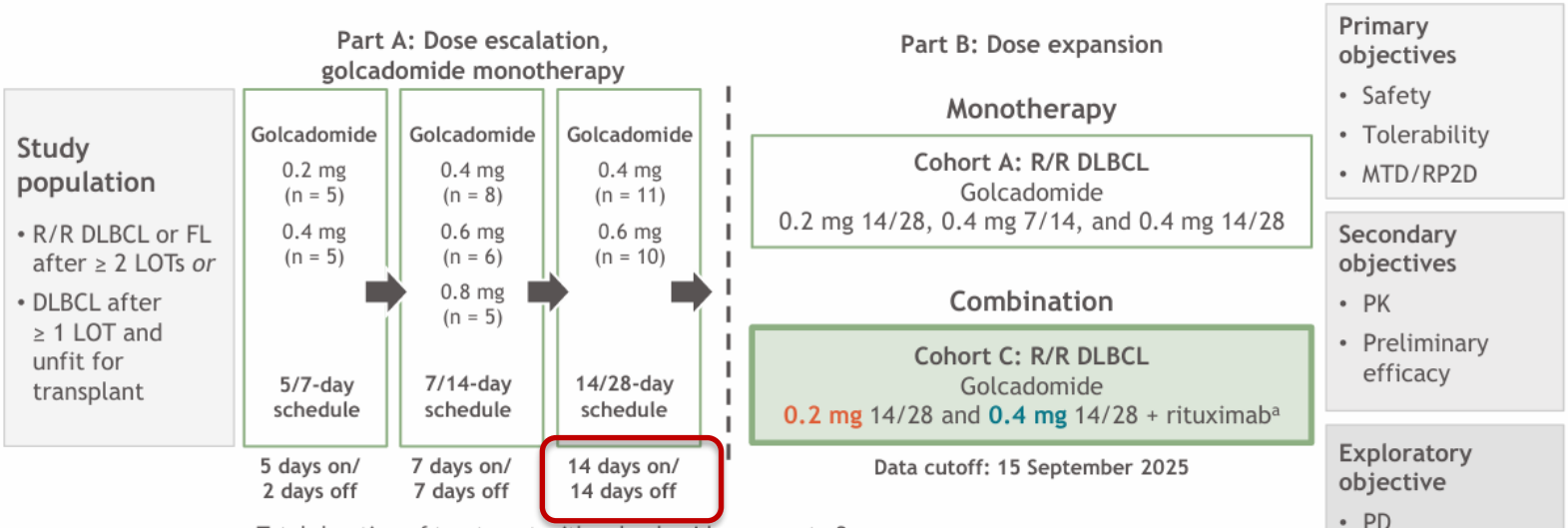
Peripheral T-cell subsets were activated within 2 weeks of golcadomide + RTX treatment



Immunophenotyping confirmed significant immune activation early during treatment, as indicated by increase in CD8⁺ activated T cells and CD8⁺ memory T cells

C. cycle; D. day; FC. fold change; RTX. rituximab.

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/m² 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.

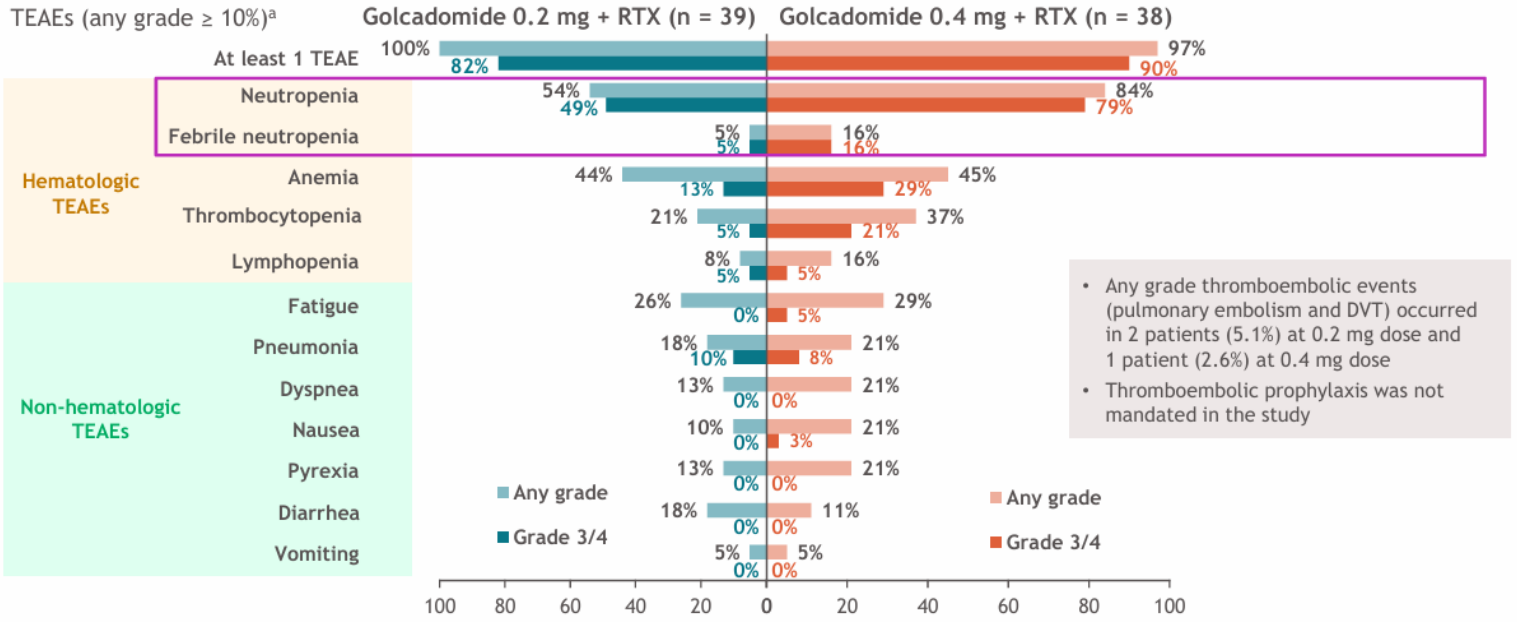
Cohort C consisted of a heavily pretreated R/R DLBCL patient population (n=77 pts)

Characteristic	Part B Cohort C: Golcadomide 0.2 mg + RTX (n = 39)	Part B Cohort C: 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.

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

Cohort C: R/R DLBCL



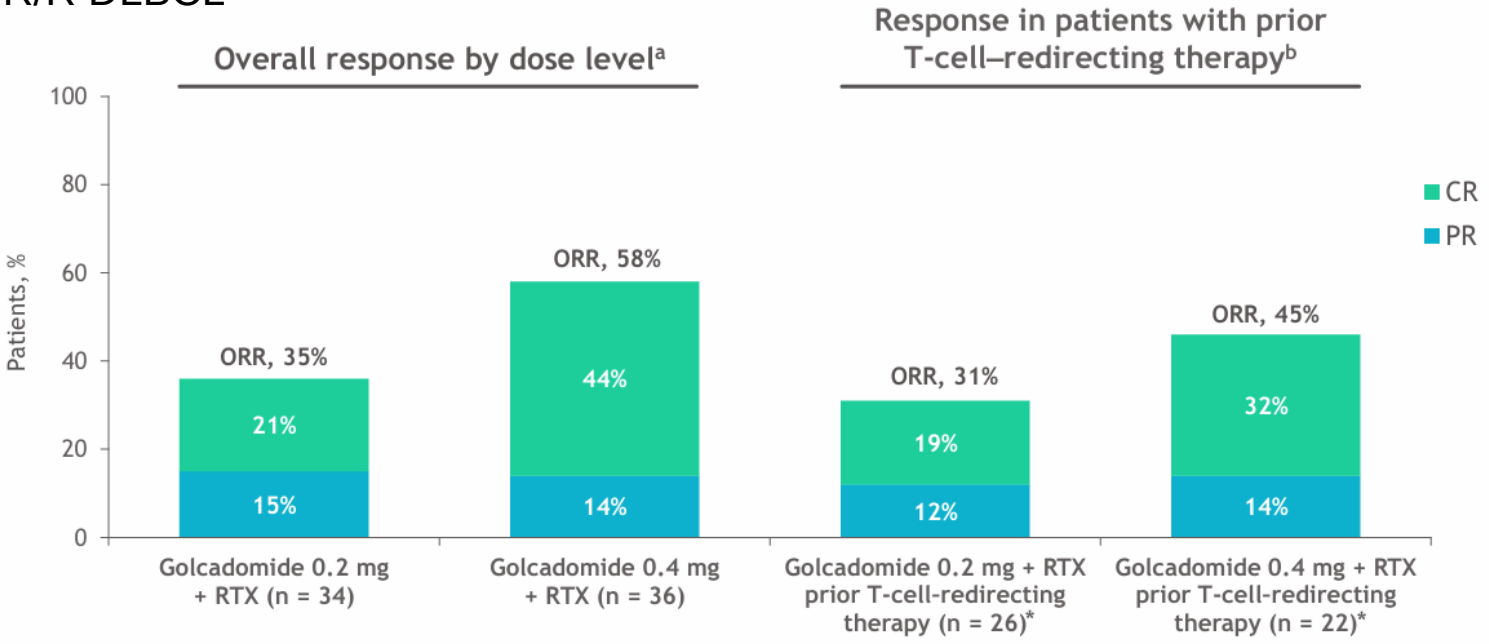
- Any grade thromboembolic events (pulmonary embolism and DVT) occurred in 2 patients (5.1%) at 0.2 mg dose and 1 patient (2.6%) at 0.4 mg dose
- Thromboembolic prophylaxis was not mandated in the study

- 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.

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

Cohort C: R/R DLBCL

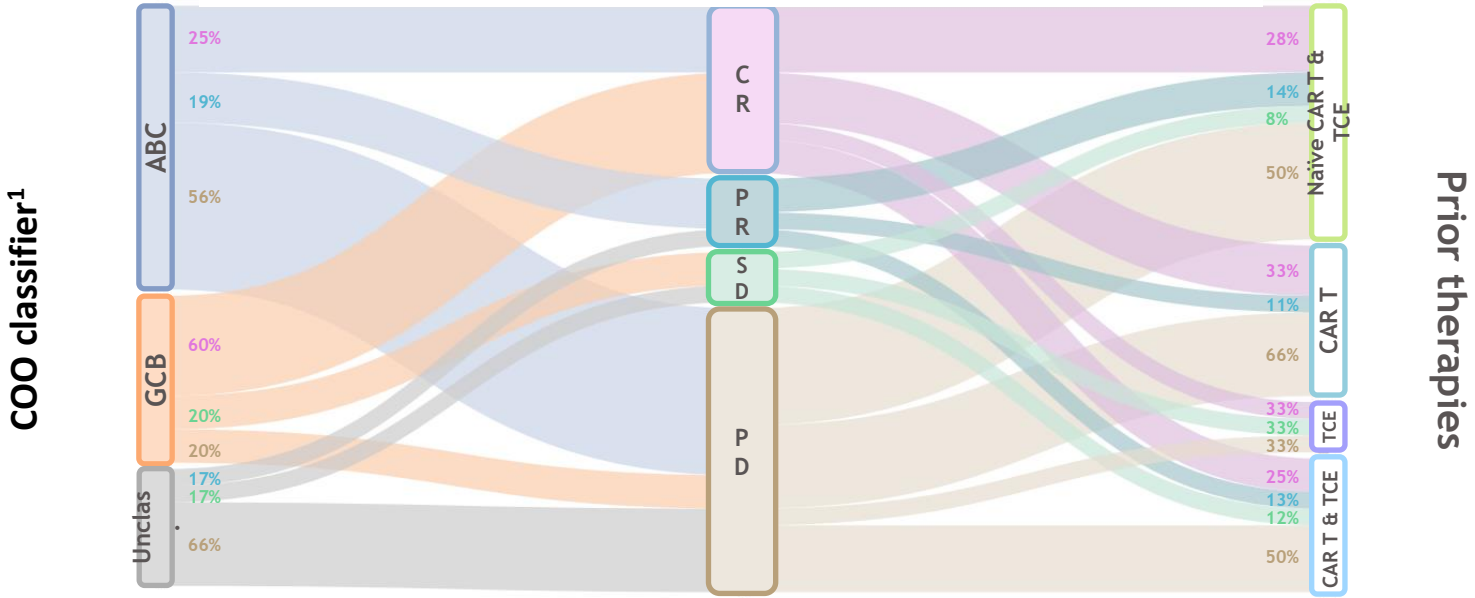


Data cutoff: 15 September 2025.
[a] Efficacy-evaluable population consisting of patients who completed ≥ 1 cycle of golcadomide (taking ≥ 75% of assigned doses) and having a baseline and ≥ 1 postbaseline tumor assessment.; [b] CAR T and/or bispecific antibody treatment.
*11 and 14 patients had both CAR-T 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.

Treatment response was independent of cell of origin and prior therapies

Golcadomide 0.2mg/0.4mg + RTX

Cohort C: R/R DLBCL



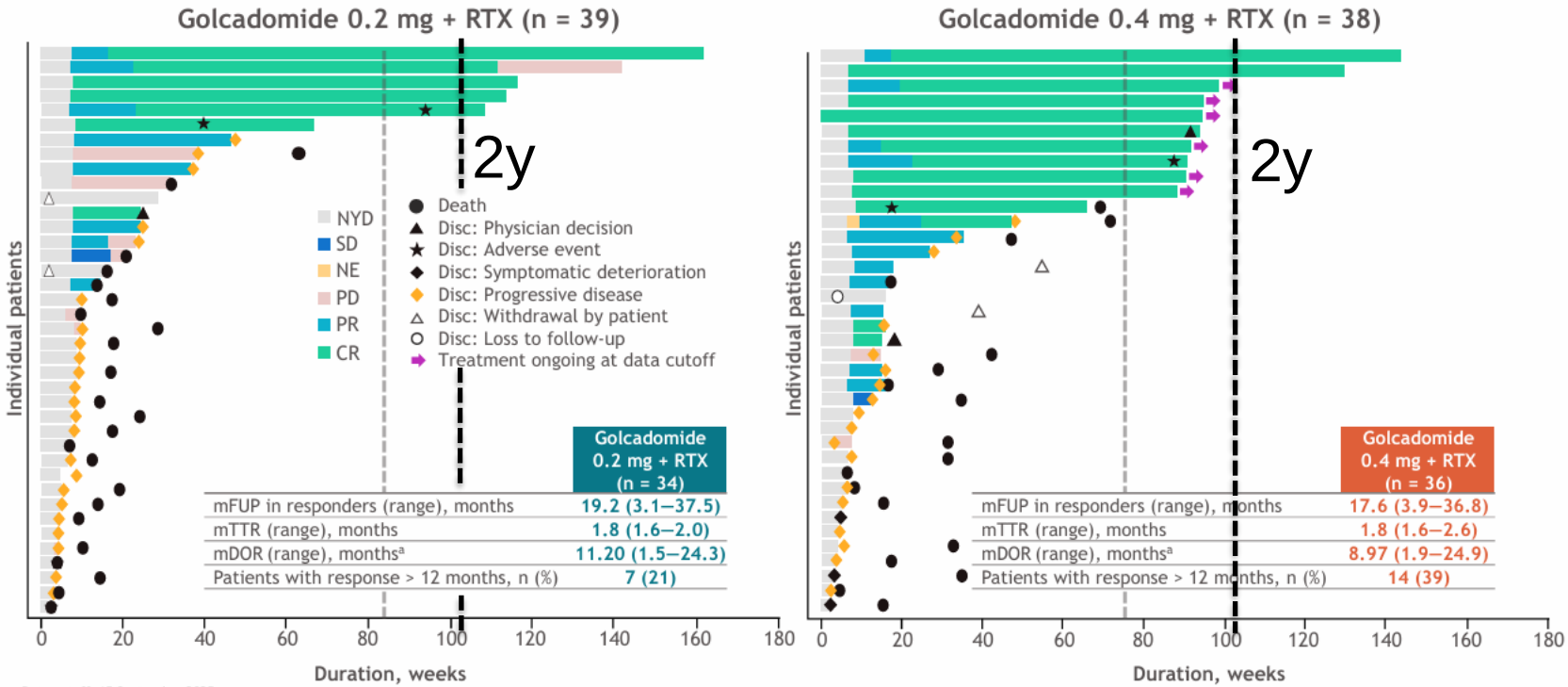
- Objective response was similar between ABC and GCB subgroups treated with Golcadomide + RTX
- Response to Golcadomide was observed in patients previously treated with CAR T cell therapy and/or T-cell engagers

Michot JM, ASH 2024, cohort C results

Screening formalin-fixed, paraffin-embedded tumor biopsies were used for RNA isolation and RNA exome sequencing (50 M 50 bp PE). RNA-sequencing data generated from screening biopsies of 88 patients dosed with GOLCA alone or in combination with RTX was used to classify patients according to COO[1]. 1. Reddy A, et al. *Cell* 2017;171:481–494.

Golcadomide 0.4 mg + RTX demonstrated durable remissions

Cohort C: R/R DLBCL

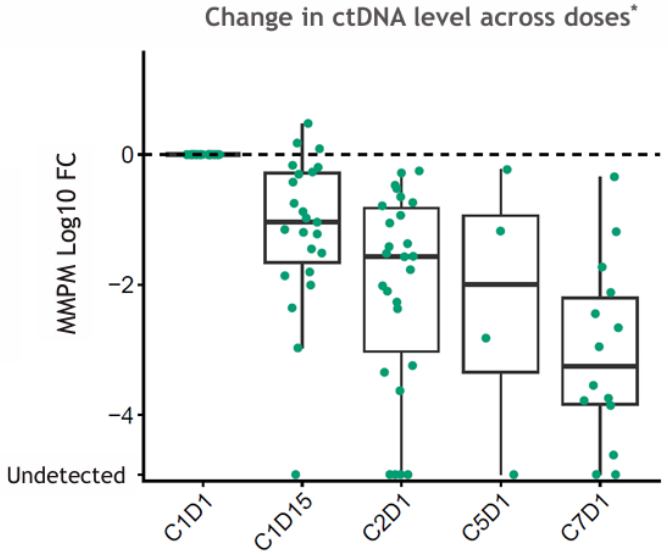


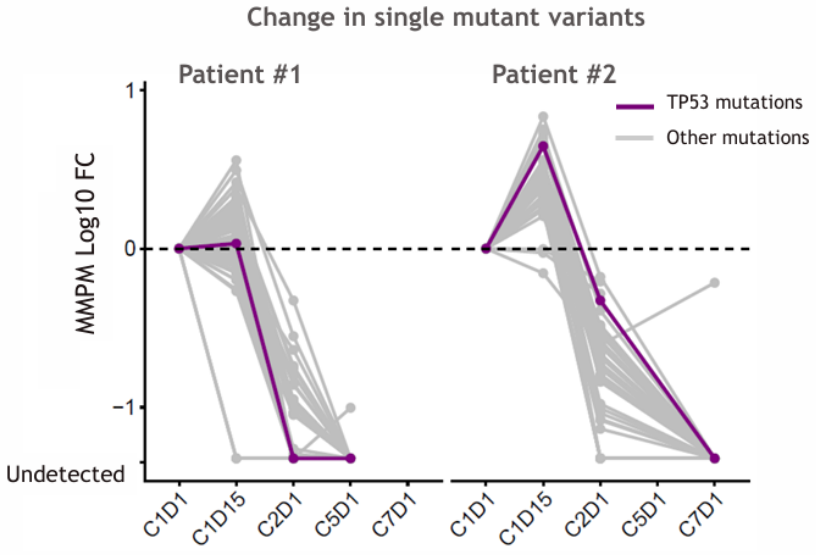
Data cutoff: 15 September 2025.

[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.

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

CC99282NHL001 study, cohort C: R/R DLBCL





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 (1x10^{-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.

CRS summary and management

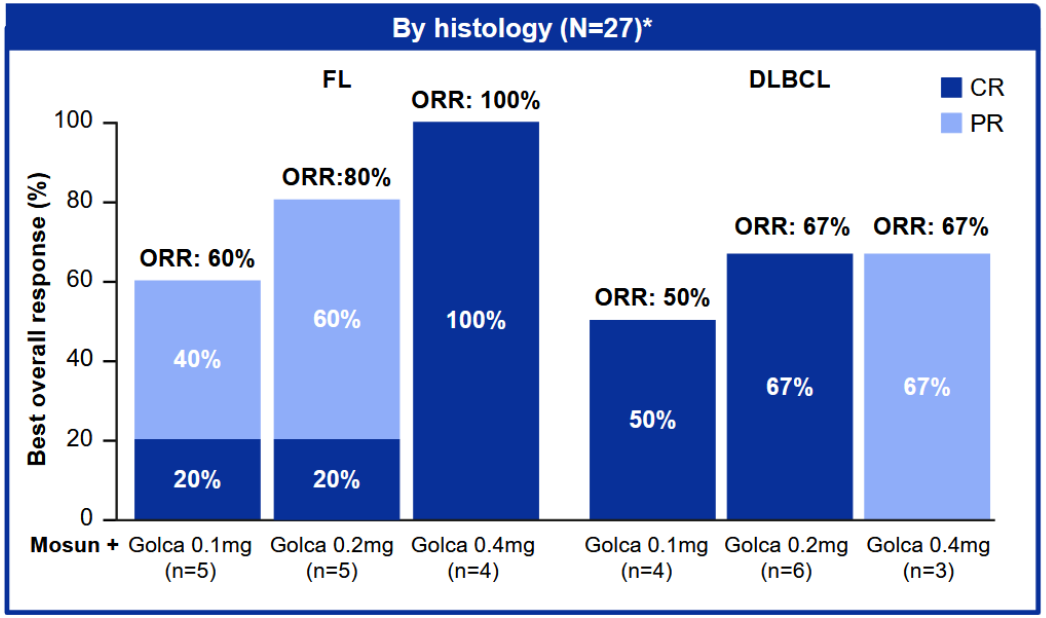
n (%) unless otherwise stated	Mosun + Golca			Glofit + Golca		
	All patients (N=35)	Golca initiation C1 (n=11)	Golca initiation C2 (n=24)	All patients (N=12)	Golca initiation C2 (n=5)	Golca initiation C3 (n=7)
CRS* by ASTCT criteria[1]						
Any grade	15 (42.9)	5 (45.5)	10 (41.7)	4 (33.3)	1 (20.0)	3 (42.9)
Grade 1	10 (28.6)	4 (36.4)	6 (25.0)	2 (16.7)	1 (20.0)	1 (14.3)
Grade 2	5 (14.3)	1 (9.1)	4 (16.7)	2 (16.7)	0	2 (28.6)
Grade 3	0	0	0	0	0	0
Median time since recent dose of Mosun/Glofit, days (range)	1 (0–4)	1 (0–2)	1 (0–4)	1 (0–1)	1 (0–1)	1 (0–1)
Median CRS duration, days (range)	4 (1–9)	1.8 (1–3)	5 (1–9)	3 (2–4)	2 (2–2)	2.5 (2–4)
CRS management						
Corticosteroids	4 (11.4)	1 (9.1)	3 (12.5)	2 (16.7)	0	2 (28.6)
Tocilizumab	5 (14.3)	1 (9.1)	4 (16.7)	3 (25.0)	0	3 (42.9)
Low-flow oxygen	2 (5.7)	1 (9.1)	1 (4.2)	1 (14.3)	0	1 (14.3)
Fluids	3 (8.6)	0	3 (12.5)	0	0	0

All CRS events were low grade and resolved

*No CRS events led to treatment discontinuation.

1. Lee DW, et al. Biol Blood Marrow Transplant 2019;25:625–38.

Best overall response in Arm 1: Mosun + Golca

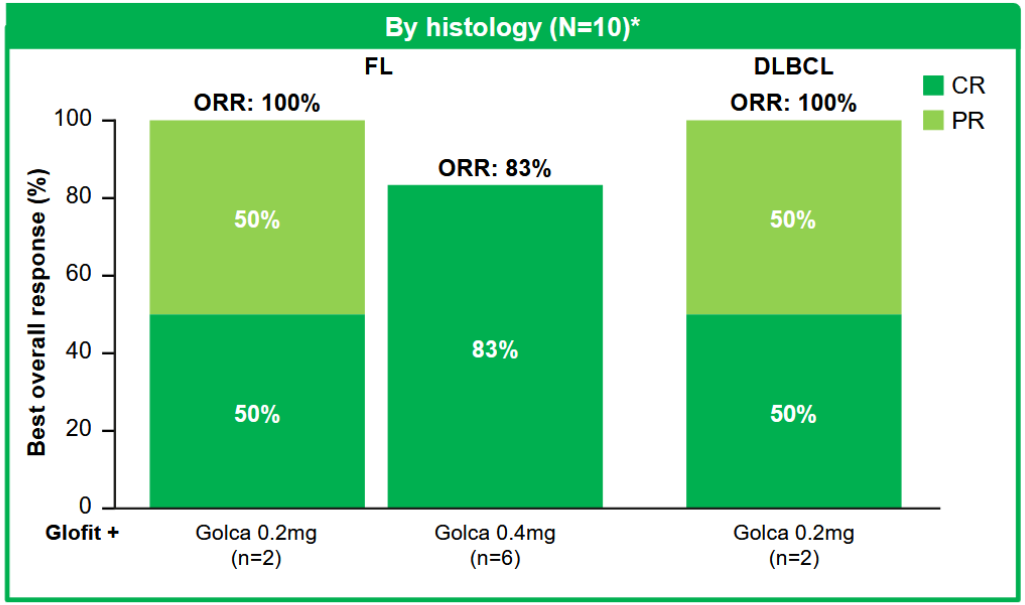


- Median time to first response for all patients (N=27)*: 2.6 months (range: 2–4)
- Response in patients who received prior CAR T-cell therapy (n=8):
  - Overall, 5 patients achieved a CR
    - Two patients had FL and one achieved CR
    - Six patients had DLBCL and four achieved a CR

High response rates were observed in patients with FL and DLBCL including those who received prior CAR T-cell therapy

*Efficacy-evaluable population. PR, partial response.

Best overall response in Arm 2: Glofit + Golca



- Median time to first response for all patients (N=10)*: 1.9 months (range: 1–3)
- All four patients who received prior CAR T-cell therapy had a response:
  - Overall, 3 patients achieved a CR, and one had a PR
    - Two patients had FL and achieved a CR
    - Two patients had DLBCL; one achieved CR and one had a PR

High response rates were observed across FL and DLBCL subtypes

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

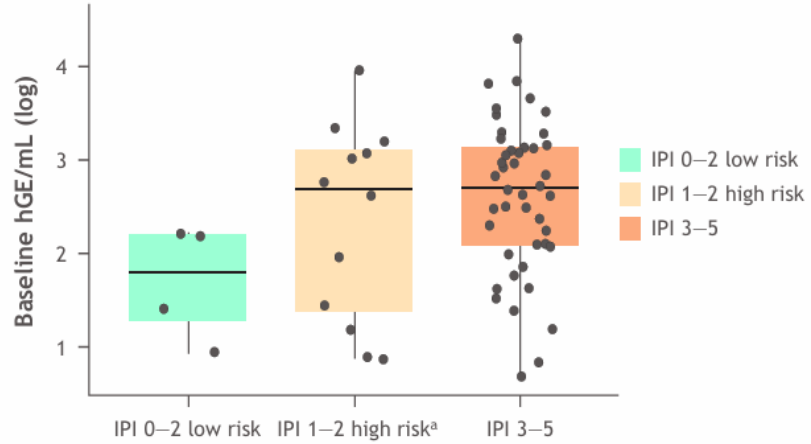
- PK, PD, and biomarkers

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.

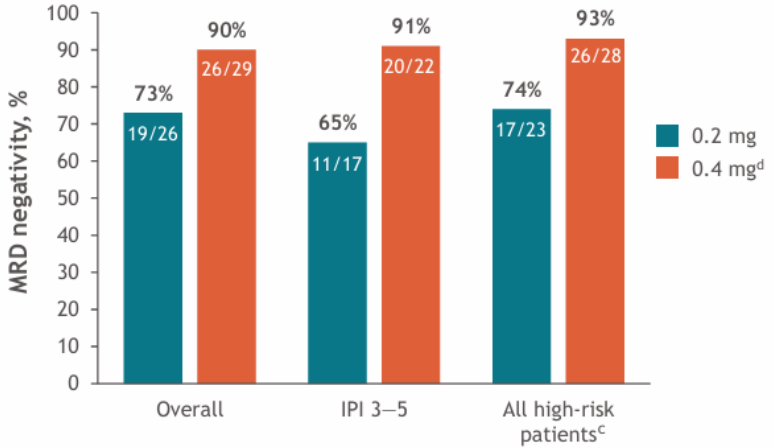
Golcadomide 0.4 mg + R-CHOP achieved MRD negativity in 90% of patients

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

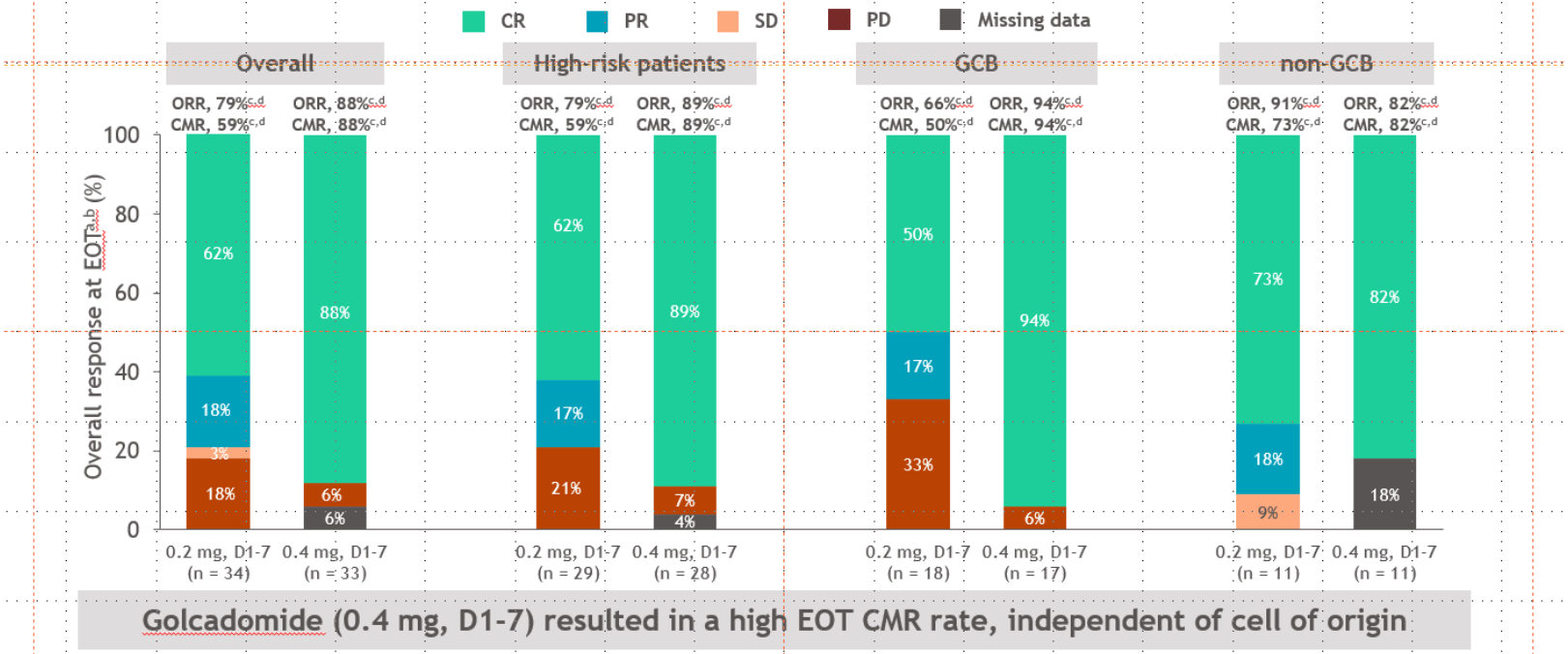
EOT MRD negativity using PhasED-Seq in the overall and high-risk populations[b]



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.

Figure 2. Phase 1b study (NCT04884035): high response rates with golcadomide plus R-CHOP in patients with aggressive BCL



Golcadomide (0.4 mg, D1-7) resulted in a high EOT CMR rate, independent of cell of origin

[a] The efficacy-evaluable population included all enrolled patients who received one or more doses of the study drug, had a baseline efficacy assessment, and had one or more post-baseline tumor assessments or discontinued treatment due to PD or study disease-related death; [b] Percentages may not sum to 100% due to rounding; [c] ORR and CMR were analyzed in patients with disease response after EOT; [d] Responses were according to Lugano 2014 criteria for DLBCL.[10] BCL, B-cell lymphoma; CMR, complete metabolic response; CR, complete response; D, day; DLBCL, diffuse large B-cell lymphoma; EOT, end of treatment; GCB, germinal center B-cell; ORR, overall response rate; PD, progressive disease; PR, partial response; R-CHOP, rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone; SD, stable disease. Figure from reference 1: Nowakowski G, et al. ASH 2025; Oral presentation (abstract 476).

Key Figure B. Overview of the global double-blind Phase 3 GOLSEEK-1 study (NCT06356129; CA073-1020)

Patients
N ≈ 850

Key eligibility criteria

- Age 18–80 years
- Previously untreated LBCL by WHO 2022 classification[a]
- Ann Arbor stage II–IV disease
- IPI score
  - ≥ 3
  - 1 or 2 with LDH > 1.3 × ULN and/or bulky disease[b]
- Measurable disease by Lugano classification[c]
- No other lymphoma subtypes
- No lymphoma involvement in CNS

R 1:1

Golcadomide + R-CHOP
× 6 cycles
(golcadomide 0.4 mg days 1-7 of each 21-day cycle)

Placebo + R-CHOP
× 6 cycles
(placebo; days 1-7 of each 21-day cycle)

Stratified by:
- **IPI score**
  - IPI 1-2 (with risk factors) + IPI 3
  - IPI 4-5
- **Bulky disease**
  - ≥ 7
  - < 7 cm

Primary endpoint

- PFS by investigator based on Lugano Response Criteria[1]

Key secondary endpoints

- PFS (non-high-grade BCL)
- OS
- EFS by investigator
- CMR by IRAC
- MRD-negativity rate (PhaseED-Seq)

Other (select) secondary endpoints

- PFS by IRAC
- OR by investigator
- CMR by investigator
- DOR
- HRQoL
- Safety

Study duration: ≤ 67 months

[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; Epstein-Barr virus-positive DLBCL; b Single lesion of ≥ 7 cm; c One or more FDG-avid lesion for FDG-avid subtype and one bi-dimensionally measurable (> 1.5 cm in longest diameter) disease, by CT or MRI.10 ABC, activated B cell; BCL, B-cell lymphoma. CMR, complete metabolic rate; CNS, central nervous system; CT, computed tomography; DLBCL, diffuse large B-cell lymphoma; DOR, duration of response; EFS, event-free survival; FDG, fluorodeoxyglucose; GCB, germinal center B cell; HRQoL, health-related quality of life; IPI, International Prognostic Index; IRAC, Independent Radiology Adjudication Committee; LBCL, large B-cell lymphoma; LDH, lactate dehydrogenase; MRD, minimal residual disease; MRI, magnetic resonance imaging; OR, overall response; OS, overall survival; PFS, progression-free survival; R-CHOP, rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone; ULN, upper limit of normal; WHO, World Health Organization. 1. Cheson BD, et al. J Clin Oncol 2014;32:3059–3068.

Cohort D consisted of a heavily pretreated R/R FL patient population

CC99282-NHL001 study (60 pts)

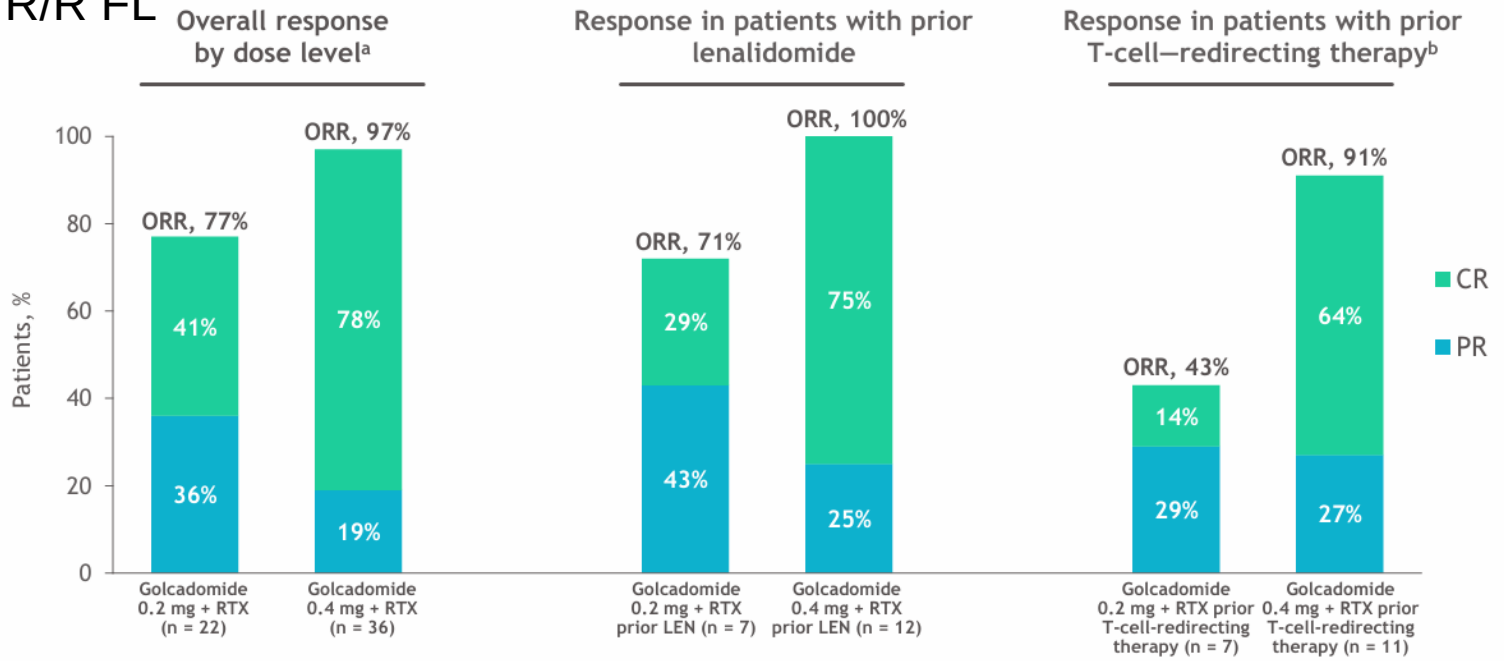
Characteristic	Part B Cohort D: Golcadomide 0.2 mg + RTX (n = 22)	Part B Cohort D: Golcadomide 0.4 mg + RTX (n = 38)
Age, median (range), years	55 (33–83)	63.5 (38–82)
Sex, male, n (%)	10 (46)	20 (53)
Diagnosis, n (%)		
FL Stage III–IV	22 (100)	37 (97)
Time from initial diagnosis to first dose, median (range), months	60 (15–203)	59 (10–420)
ECOG PS, n (%)		
0	10 (46)	18 (47)
1	11 (50)	20 (53)
2	1 (5)	0
Treatment history		
Median prior LOTs (range), No.	3 (1–9)	3 (1–12)
Prior T-cell-redirecting therapy (CAR T and/or bispecific antibodies), n (%)	6 (27)	11 (29)
Prior lenalidomide treatment, n (%)	7 (32)	12 (32)
Best response to last regimen, n (%)		
Refractory	7 (32)	12 (32)
CR or PR	12 (55)	19 (50)
Unknown	3 (14)	7 (18)

Data cutoff: 15 September 2025.

CAR, chimeric antigen receptor; CR, complete response; ECOG PS, Eastern Cooperative Oncology Group performance status; FL, follicular lymphoma; LOT, line of therapy; No, number; PR, partial response; R/R, relapsed/refractory; RTX, rituximab.

Golcadomide + RTX achieved a high ORR and CRR in a heavily pretreated patient population, including patients with prior LEN and/or T-cell–redirecting therapy

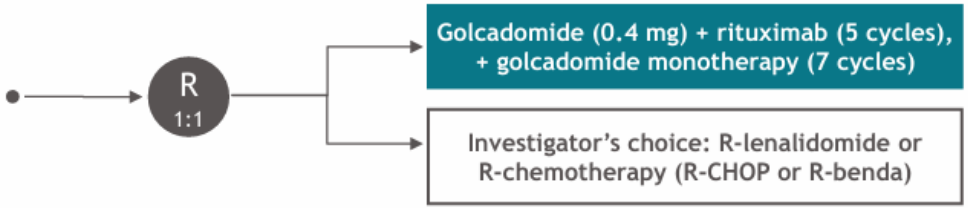
cohort D: R/R FL



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.
CAR, chimeric antigen receptor; CR., complete response; CRR, complete response rate; LEN, lenalidomide; ORR, overall response rate; PR, partial response; RTX, rituximab.

GOLSEEK-4 study design[1]

Key eligibility criteria
- Age ≥ 18 years
- Histologically confirmed Grade 1-3a FL/classical FL
- R/R FL: ≥ 1 line of therapy, including an anti-CD20 mAb + alkylating agent



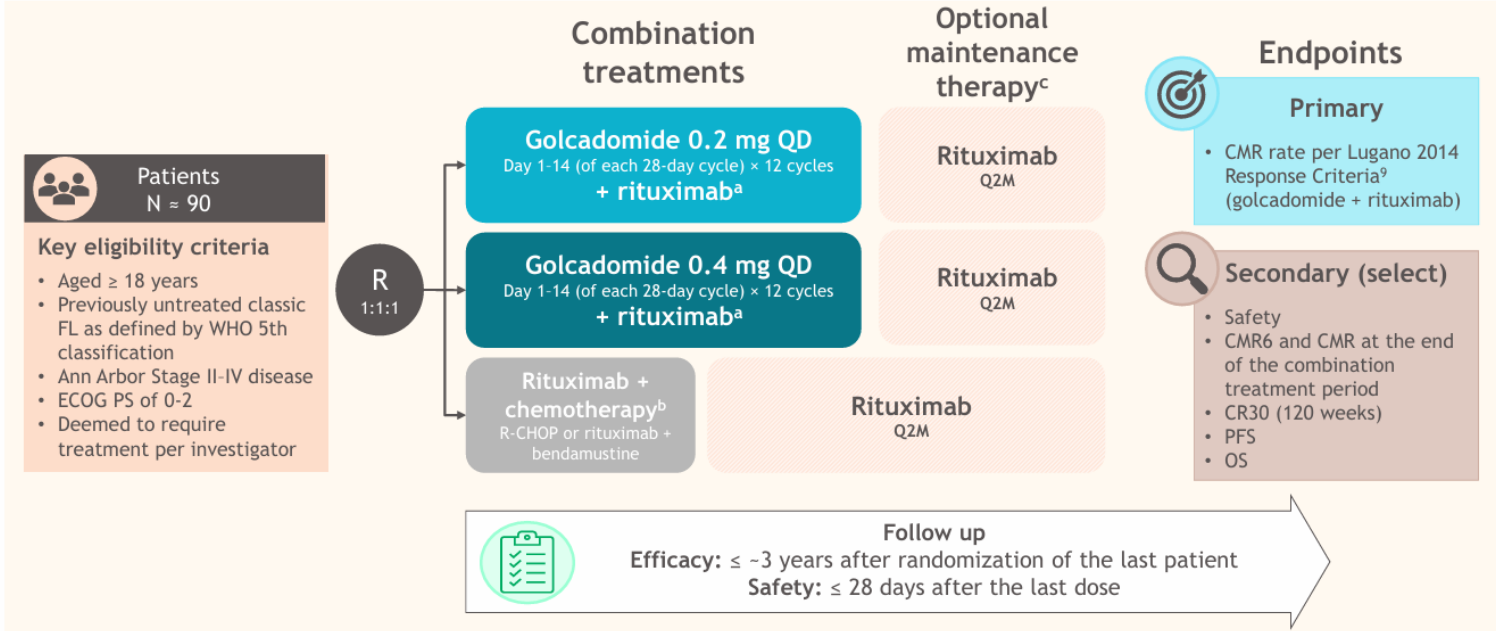
Primary endpoint
- PFS by IRAC

Key secondary endpoints
- ORR per IRAC
- OS

2L+, second line plus; CR, complete response; CRR, complete response rate; ctDNA, circulating tumor DNA; FL, follicular lymphoma; IRAC, Independent Radiology Adjudication Committee; LEN lenalidomide; mAb, monoclonal antibody; ORR, overall response rate; OS, overall survival; PFS, progression-free survival; R, randomized; R/R, relapsed/refractory.

1. Hawkes E, et al. ASH 2025. Abstract 3615.

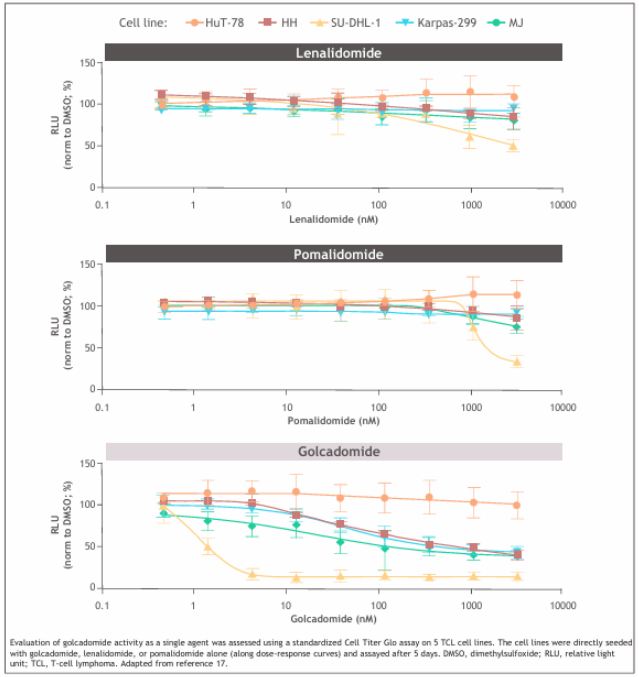
Key Figure B. Overview of the phase 2 GOLSEEK-2 study (NCT06425302)



[a]Rituximab administered on day 1, 8, 15, and 22 of cycle 1, and day 1 of each cycle from cycles 2-12. [b]Investigator's choice of chemotherapy includes 6 cycles of R-CHOP plus 2 additional cycles of rituximab, or 6 cycles of rituximab + bendamustine. [c]Optional rituximab maintenance every 2 months for patients who achieve a PR or better after completion of study treatment; ≤ 1 year maintenance for patients in golcadomide arms, and ≤ 1.5 years in the rituximab-chemotherapy arm.
CMR, complete metabolic response; CMR6, rate of complete metabolic responses at 6 months from randomization; CR30, rate of complete responses at 30 months; FL, follicular lymphoma; OS, overall survival; PFS, progression-free survival; PR, partial response; PS, performance status; Q2M, every 2 months; QD, once daily; R, randomized; R-CHOP, rituximab, cyclophosphamide, doxorubicin, vincristine, prednisone; WHO, World Health Organization.

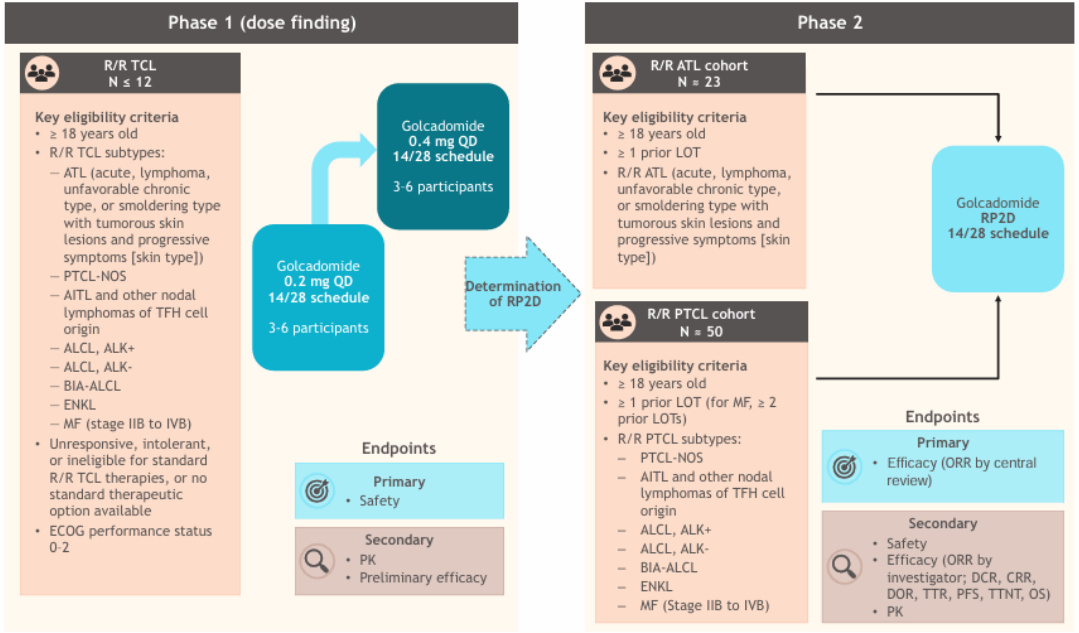
Golcadomide, a potential first-in-class, oral, Ikaros/Aiolos-degrading CELMoD agent for R/R T-cell lymphomas –design of the phase 1/2 GOLSEEK-3 study

Figure 1. TCL cell lines are sensitive to golcadomide[17]



Evaluation of golcadomide activity as a single agent was assessed using a standardized Cell Titer Glo assay on 5 TCL cell lines. The cell lines were directly seeded with golcadomide, lenalidomide, or pomalidomide alone (along dose-response curves) and assayed after 5 days. DMSO, dimethylsulfoxide; RLU, relative light unit; TCL, T-cell lymphoma. Adapted from reference 17.

Key Figure B. Overview of the GOLSEEK-3 study (NCT06035497)



14/28, 14 days on, 14 days off; AITL, angioimmunoblastic T-cell lymphoma; ALCL, anaplastic large cell lymphoma; ALK+, anaplastic lymphoma kinase-positive; ALK-, anaplastic lymphoma kinase-negative; ATL, adult T cell leukemia/lymphoma; BIA-ALCL, breast implant-associated ALCL; CRR, complete response rate; DCR, disease control rate; DOR, duration of response; ENKL, extranodal NK/T-cell lymphoma/nasal type; LOT, line of therapy; MF, mycosis fungoides; NOS, not otherwise specified; ORR, overall response rate; PFS, progression-free survival; PK, pharmacokinetics; PTCL, peripheral T-cell lymphoma; PTCL-NOS, peripheral T-cell lymphoma not otherwise specified; QD, once daily; RP2D, recommended phase 2 dose; R/R, relapsed and/or refractory; TCL, T cell lymphoma; TFH, T follicular helper; TTNT, time to next treatment; TTR, time to response

- CC992/2/golcadomide continue to demonstrate meaningful activity across different types of NHL (DOR; high CR/PR ratio)
  ➔ *longer FU require to see the potential curative effect in pts*

- Phases 3 in progress in L1 LBCL (golseek-1) and 2L+ FL (golseek-4)

- Attractive preclinical CD20 combination data (synergy with anti-CD20 agents)
  ➔ *potentially extended to other BCR targeted therapies (CD19/CD22/CD79?)*

- Need for continuation of investigations on potential biomarkers (MOA/MOR)
  ➔ *ikaros/aiolos protein, molecular aspects, cereblon complex*

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