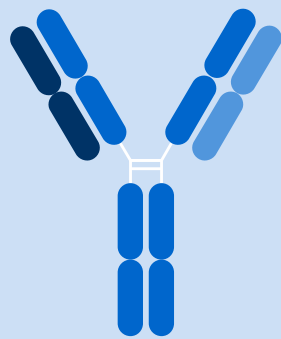


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The combination of M and Pola demonstrated increased efficacy compared to either agent alone in pre-clinical studies.



M-Pola has a manageable safety profile in R/R B-NHL with no Grade ≥ 2 cytokine release syndrome (CRS) observed.

M-Pola was assessed in poor-risk pt populations such as those who have failed prior chimeric antigen receptor T-cell (CAR-T) therapy and/or refractory disease.



M-Pola demonstrates promising efficacy in pts with R/R NHL with predominantly aggressive histologies.

- There is a continued need for the development of safe and effective therapies in the R/R NHL setting.
- Mosunetuzumab (M), a full-length, humanized, IgG1 bispecific antibody targeting CD20 and CD3, has shown promising efficacy and safety as monotherapy for R/R B-NHL (NCT02500407).¹
- The combination of M with the anti-CD79b antibody-drug conjugate, Pola, demonstrated increased efficacy compared to either agent alone, showing synergistic anti-lymphoma activity in the WSU-DLCL2 xenograft model (**Figure 1**). These data supported a Phase Ib/II, open-label, multicenter trial of M-Pola for R/R B-NHL.

- Pts with R/R follicular lymphoma (FL, Grade [Gr] 1–3a) or aggressive NHL (aNHL), including *de novo* diffuse large B-cell lymphoma (DLBCL), transformed FL (trFL) and FL Gr 3b (FL3b), received M-Pola as per dosing schedule outlined in **Figure 2**.
- Exclusion criteria included: CD20-directed bispecific antibodies, immunochemotherapy (within 4 weeks of first dose of study treatment) or radiotherapy (within 2 weeks of first dose of study treatment).

GO40516 (NCT03671018):
M-Pola

- Step-up doses of M in Cycle 1 (C1) day (D) 1, 8 and 15 to mitigate CRS.²
- C1D15 dose of M given on D1 from C2 onwards.
- Pola (1.8mg/kg) given on D1 of each 21-day cycle for six cycles.
- Response rates are based on the Lugano criteria.³
- Primary endpoint: to determine the RP2D.
- Biomarkers were evaluated using whole blood flow cytometry, a plasma cytokine ELISA, and ex-vivo single-cell cytokine assay of PBMC.

M-Pola dosing schedule^a

Dose finding (R/R B-NHL)
1mg / 2mg / C1 D15 target dose (9, 20, 40 or 60/30mg)

D1 D8 D15 D1 D1

M M M M M

Pola Pola Pola

Cycle 1 **Cycle 2** ... **Cycle 6**

21 days

In pts achieving CR, mosunetuzumab is continued for eight cycles; in pts achieving PR or SD, M is continued for a total of 17 cycles.

For the biomarker analyses, blood samples were obtained at various timepoints before and during administration of M-Pola.

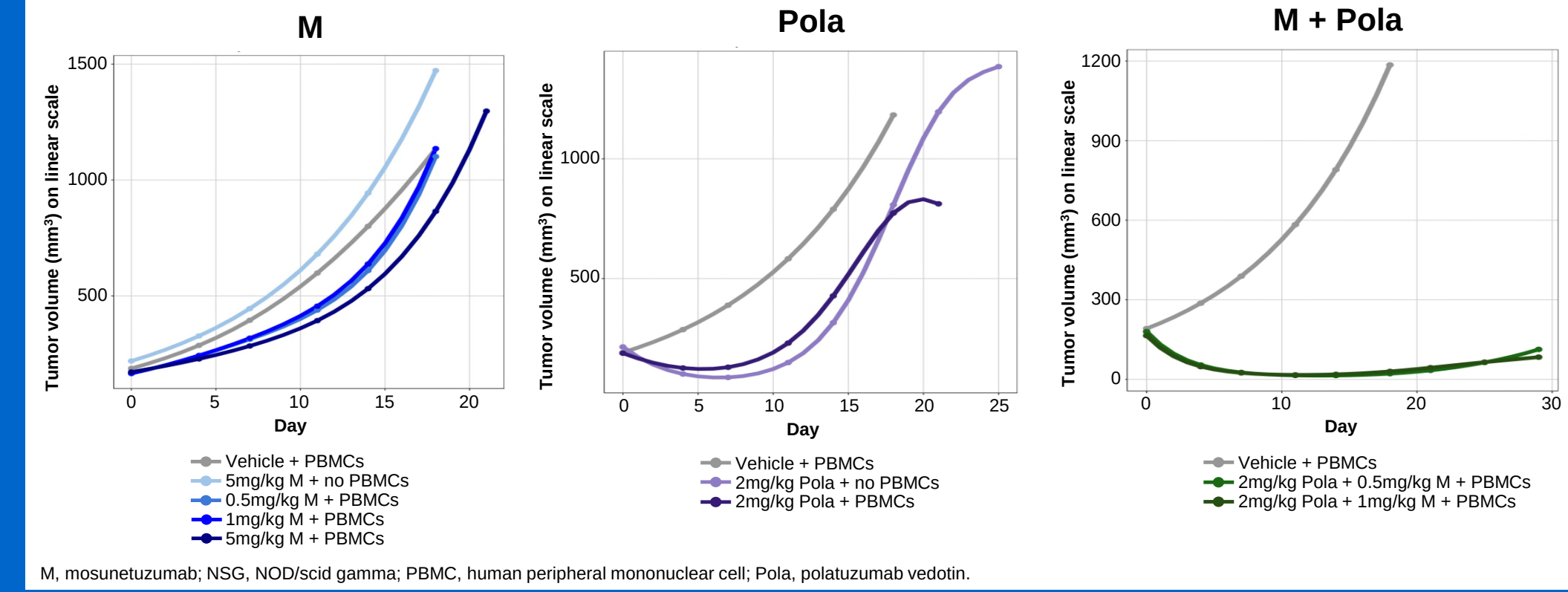
Pre-remediation with steroids (20mg IV dexamethasone or 80mg IV methylprednisolone) required C1-2 and optional C3+.

- As of 15th March 2021, 22 pts had received M-Pola (**Table 1**) (M target doses: 9mg, n=7; 20mg, n=3; 40mg, n=6; 60mg [with D1 dose of 30mg from C3 onwards], n=6).
- Median follow-up duration was 13.5 (0.7–27.5) months.

Characteristic	R/R B-NHL 1mg / 2mg / C1 D15 target dose (N=22)
Median age, years (range)	70 (38–81)
Male, n (%)	11 (50)
NHL subtype, n (%)	
DLBCL	12 (55)
FL 3b	3 (14)
trFL	4 (18)
FL 1–3a	3 (14)
ECOG PS 0–1 at baseline, n (%)	22 (100)
Ann Arbor Stage, n (%)	
II	3 (14)
III	9 (41)
IV	9 (41)
IPI score, n (%)	
2	4 (18)
3–5	8 (36)
Median prior therapies, n (range)	3 (1–10)
Prior CAR-T, n (%)	7 (32)
Refractory to last prior therapy,* n (%)	18 (82)
Refractory to last prior anti-CD20 therapy,* n (%)	20 (91)

Defined as not achieving a response (partial response or CR) or progressing within 56 months of applicable treatment.

Figure 1. *In vivo* synergistic activity of M-Pola in a preclinical xenograft model. The activity of M and Pola were evaluated as single agents or in combination, with or without the presence of human PBMCs, in human WSU-DLCL2 lymphoma in NSG mice



- **Table 2** a summary of adverse events (AEs). Most frequent treatment-related AEs were neutropenia and nausea (40.9%), followed by fatigue and diarrhea (36.4%).
- One dose-limiting toxicity (Gr 3 new onset atrial fibrillation) was observed in the 40mg cohort; maximum tolerated dose was not exceeded.
- Two (9.1%) Gr 5 AEs (not including progressive disease) occurred: sudden cardiac death (n=1), and respiratory failure (n=1); none deemed treatment related by investigator.
- AEs of special interest (**Table 3**):
 - CRS events were all Gr 1 and occurred during C1 step-up dosing, all after M initial dose; median time to first CRS onset was 2 days (range: 1–3)
 - All CRS events resolved without tocilizumab, intensive care unit admission, or vasopressors
 - CRS signs/symptoms consisted of pyrexia (n=2; 9.1%), and chills (n=1, 4.5%).

Summary of AEs, n (%)		R/R B-NHL All cohorts (N=22)	
Any AE	22 (100.0)	CRS*	2 (9.1)
Treatment-related	19 (86.4)	Gr 1	2 (9.1)
Serious AE	8 (36.4)	Gr ≥2	0
		Infections	7 (31.8)
Treatment-related	5 (22.7)	Gr 1–2	5 (22.7)
Gr 3–4 AE	11 (50.0)	Gr ≥3	2 (9.1)
		Neuropathy peripheral	9 (40.9)
Treatment-related	11 (50.0)	Gr 1–2	6 (27.3)
Gr 5 (fatal) AE	2 (9.1)	Gr ≥3	3 (13.6)
		Neutropenia	12 (54.5)
Treatment-related	0	Gr 1–2	3 (13.6)
AE leading to dose modification	8 (36.4)	Gr ≥3	9 (40.9)
		Febrile neutropenia	0
AE leading to treatment discontinuation	3 (13.6)		

*Defined by ASTCT 2019 criteria⁴. AE, adverse events; ASTCT, American Society for Transplantation and Cellular Therapy; B-NHL, B-cell non-Hodgkin's lymphoma; CRS, cytokine release syndrome; Gr, grade; pts, patients; R/R relapsed/refractory.

Pts with ≥ 1 AE, <i>n</i> (%)	R/R B-NHL All cohorts (N=22)
CRS*	2 (9.1)
Gr 1	2 (9.1)
Gr ≥ 2	0
Infections	7 (31.8)
Gr 1–2	5 (22.7)
Gr ≥ 3	2 (9.1)
Neuropathy peripheral	9 (40.9)
Gr 1–2	6 (27.3)
Gr ≥ 3	3 (13.6)
Neutropenia	12 (54.5)
Gr 1–2	3 (13.6)
Gr ≥ 3	9 (40.9)
Febrile neutropenia	0

Response, n (%)	All pts (N=22)	aNHL pts (n=19)	Post-CAR-T pts (n=7)	FL 1-3a pts (n=3)
BOR	15 (68.2)	12 (63.2)	4 (57.1)	3 (100)
CR	12 (54.5)	9 (47.4)	2 (28.6)	3 (100)

aNHL, aggressive NHL; BOR, best overall response; CAR-T, chimeric antigen receptor T-cell; CR, complete response; FL, follicular lymphoma; pts, patients

Best % change in SPD

Time on initial treatment (weeks)

Best response with or without PET

de novo DLBCL FL 3b trFL FL (striped bars indicate double-hit)

SD PD SD SD PR CR PD CR CR CR CR CR CR CR CR PR CR PR CR

Lesion measurements were missing for 2 patients.
CR, complete response; PD, progressive disease; PET, positron-emission tomography; PR, partial response; SD, stable disease; SPD, sum of the product of greatest diameter.

*The C1D15 and C2D1 dose was 60mg; D1 dose was 30mg from C3 onwards. C, cycle; D, day.

- T-cell activation, marked by the induction of plasma IFN- γ and the increase in the CD69+ in CD4 and CD8 cells, was observed after M plus Pola (**Figures 5 and 6**):
 - Findings are consistent with those observed after single-agent M in R/R NHL patients,⁵ and they do not seem to be affected by Pola given prior to M on C1D1.
- No significant association was observed between clinical response and these markers in this limited number of patients.

[illegible]

C, cycle; CR, complete response; D, day; EOI, 30 minutes after the end of Pola infusion; 2H EOI, 2 hours after the end of mosunetuzumab infusion; PD, partial disease; PR, partial response; PRE, predose.

The Phase II expansion cohort in R/R DLBCL is ongoing, with **no mandatory hospitalization**.

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Disclosures

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