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UNIVERSITÀ DI BOLOGNA
DIPARTIMENTO DI
SCIENZE MEDICHE E CHIRURGICHE

POLICLINICO DI
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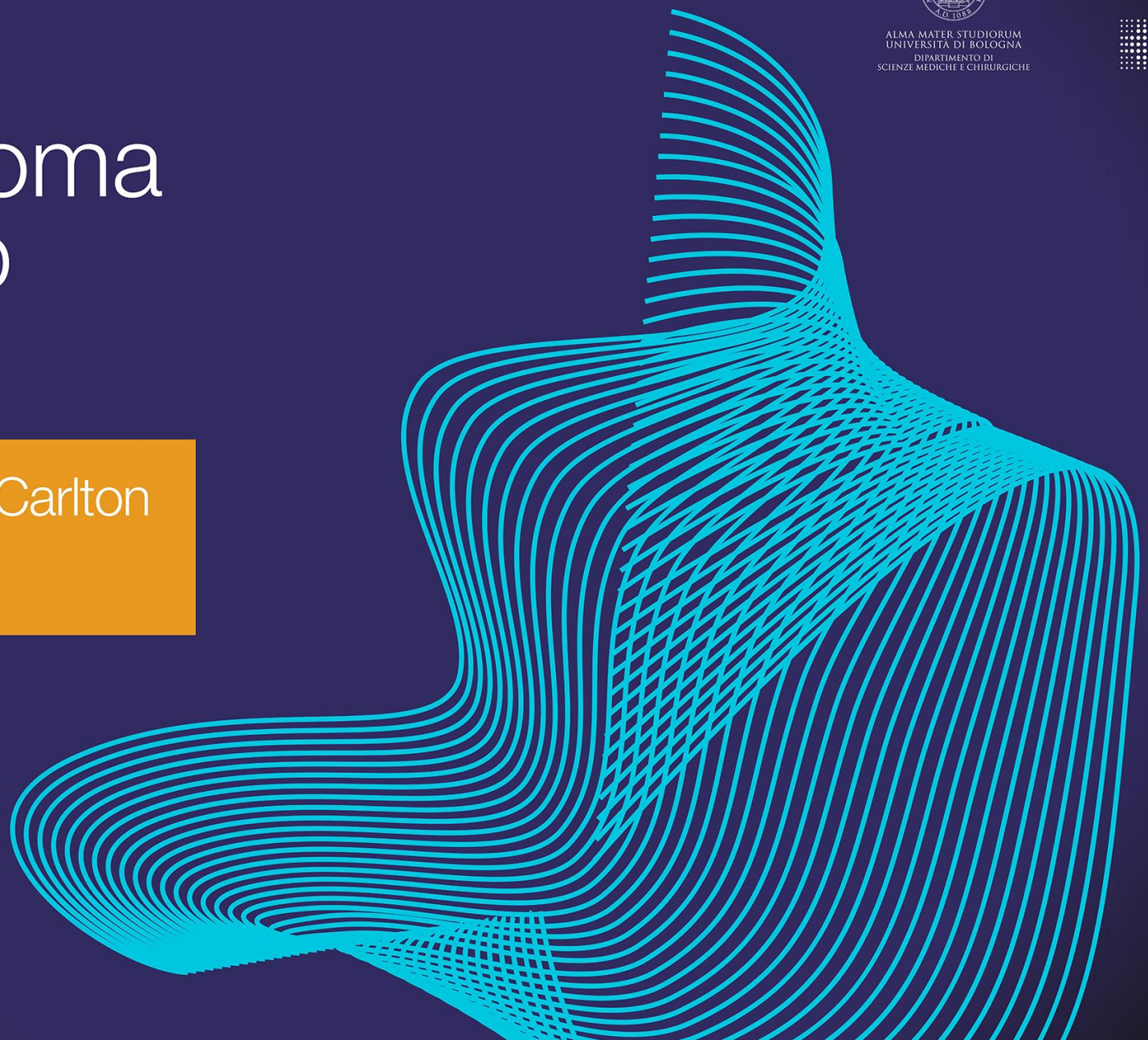
Aggressive Lymphoma Workshop



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Disclosures of Dr. Michael Wang

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Zilovertamab Vedotin in Mantle Cell Lymphoma

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Phase 1 Dose Escalation and Cohort Expansion Study of the Anti-ROR1 Antibody-Drug Conjugate Zilovertamab Vedotin (MK-2140) for the Treatment of Non-Hodgkin Lymphoma

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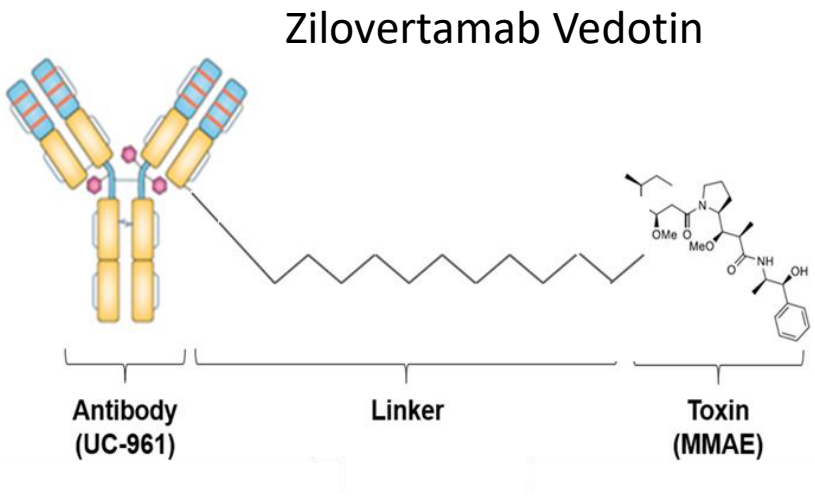
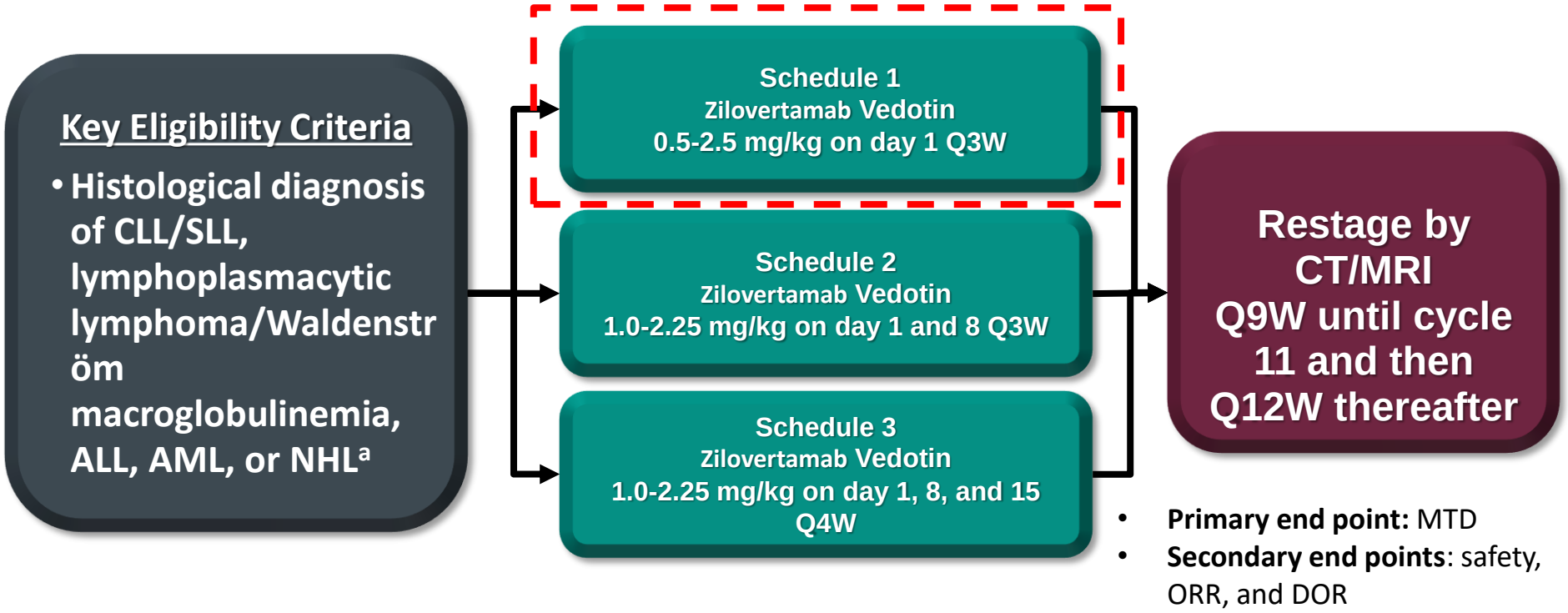
ROR1 and Zilovertamab Vedotin

- ROR1 is an oncofetal protein important for embryonic development
  - Physiologic expression disappears before birth[1]
  - Pathologic expression of ROR1 often reappears in aggressive hematologic and solid tumor cancers[2]
- ROR1 is present on the tumor cell surface and amenable to targeting with antibody-based therapeutics[1]
- Zilovertamab vedotin (MK-2140) is an ADC of:
  - The humanized monoclonal antibody, UC-961, with no normal tissue cross-reactivity
  - A cleavable linker and the anti-microtubule toxin, MMAE[3]
- Binding to tumor cell ROR1 causes rapid internalization and lysosomal trafficking to deliver MMAE



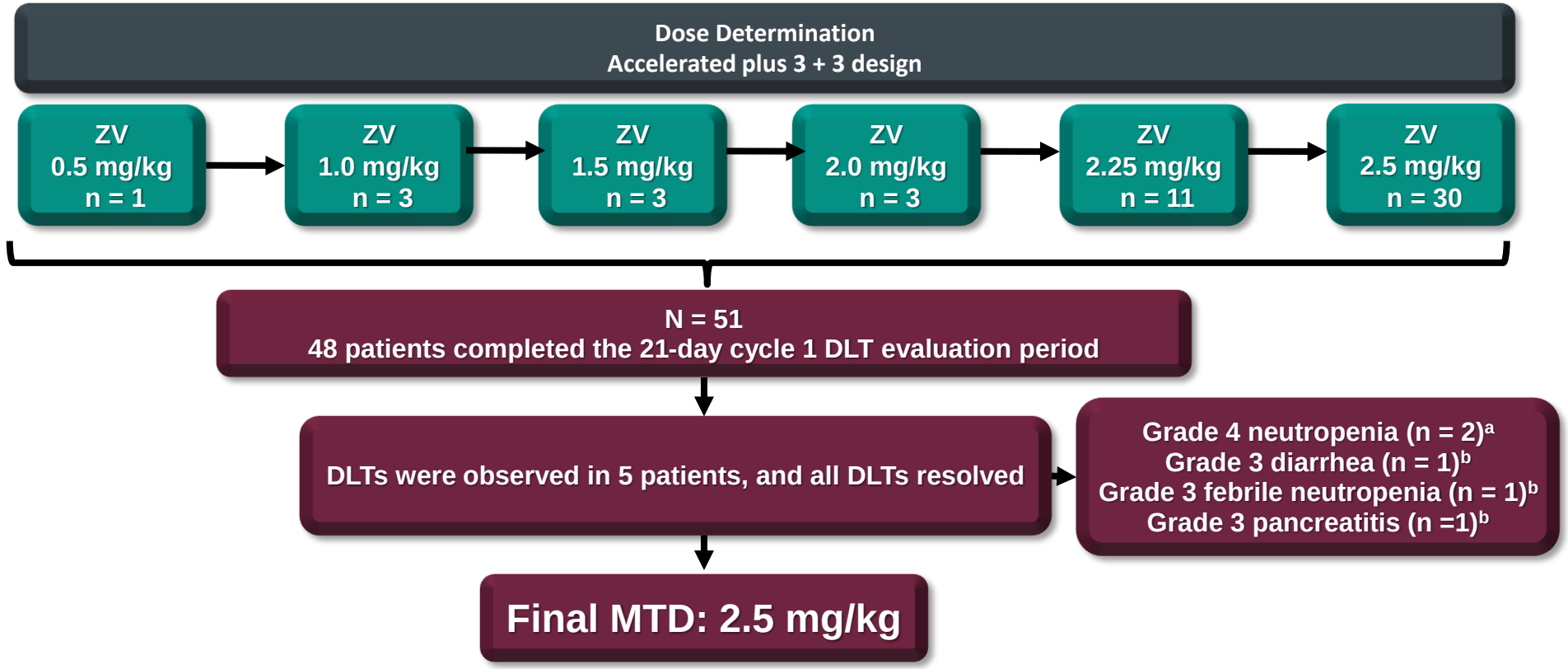
1. Borcherding N et al. *Protein Cell.* 2014;5:496-502; 2. Danesmanesh AH et al. *Leuk Lymphoma.* 2013;54:843-850.3. Vaisitti T et al. *Blood.* 2021;137:3365-3377.

Phase 1 First In-Human Dose Escalation Study (NCT03833180)



- [a]Mantle cell lymphoma, follicular lymphoma, marginal zone lymphoma, diffuse large B-cell lymphoma, Richter transformation, Burkitt lymphoma, and T-cell NHL.

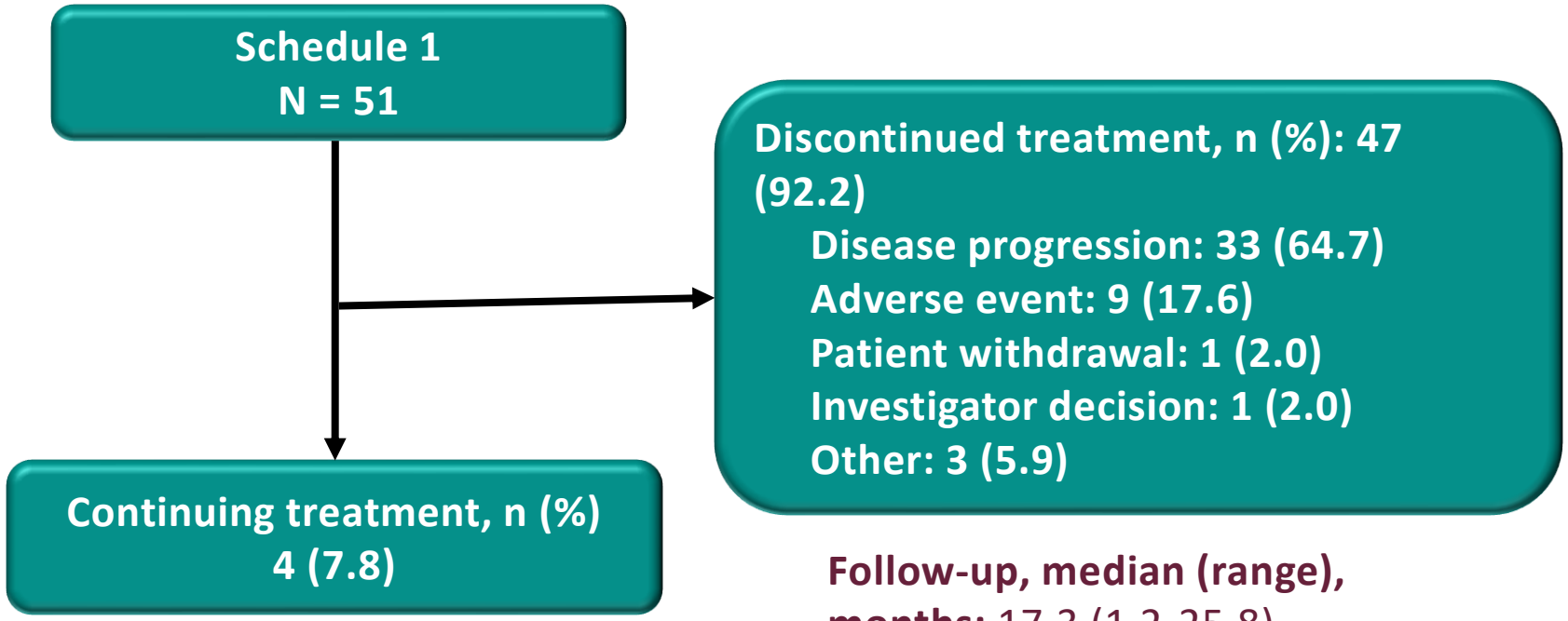
Schedule 1 Study Chronology



- a1 each for 2.25 mg/kg and 2.5 mg/kg; b2.5 mg/kg.

- Data cutoff: May 18, 2021 ■

Disposition (Schedule 1)



Follow-up, median (range), months: 17.3 (1.2-25.8)

- Data cutoff: May 18, 2021.

Baseline Demographics (Schedule 1)

n (%)	All Patients N = 51
Age, median (range), years	70 (44-91)
≥65 years	35 (68.6)
Male	28 (54.9)
Prior ASCT	4 (7.8)
Prior CAR-T or CAR-NK	15 (29.4)
DLBCL	7 (13.7)
MCL	6 (11.8)

n (%)	All Patients N = 51
Prior lines of therapy, median (range)	3 (1-19)
DLCBL	3 (1-7)
MCL	4 (1-9)
Patients with prior CAR-T/CAR-NK	4 (1-19)
Type of hematological malignancy	
NHL	41 (80.4)
DLBCL	13 (25.5)
MCL	17 (33.3)
RT	6 (11.8)
Other NHL[a]	5 (9.8)
Other diseases[b]	10 (19.6)

- [a]Includes FL (n = 3), MZL (n = 1), and mixed histology (n = 1). [b]Includes CLL/SLL (n = 7) and AML (n = 3).
- Data cutoff: May 18, 2021.

Any-Grade Adverse Events in ≥20% of Patients

Any-Grade AEs, n (%)	All Patients N = 51	
	All-Cause	Treatment-Related
Peripheral neuropathy[a]	25 (49.0)	24 (47.0)
Fatigue	23 (45.1)	19 (37.3)
Nausea	23 (45.1)	14 (27.5)
Diarrhea	19 (37.3)	11 (21.6)
Dizziness	19 (37.3)	9 (17.6)
Decreased neutrophil count	18 (35.3)	16 (31.4)

Any Grade AEs, n (%)	All Patients N = 51	
	All-Cause	Treatment-Related
Constipation	15 (29.4)	5 (9.8)
Myalgia	15 (29.4)	10 (19.6)
Pyrexia	14 (27.5)	4 (7.8)
Vomiting	12 (23.5)	5 (9.8)
Decreased appetite	12 (23.5)	9 (17.6)
Dyspnea	11 (21.6)	8 (15.7)

- [a]Includes the preferred terms peripheral sensory neuropathy, peripheral neuropathy, peripheral motor neuropathy, and peripheral sensorimotor neuropathy.
- Data cutoff: May 18, 2021.

AEs Leading to Permanent Study Discontinuation

AEs, n (%)	All Patients N = 51
	All-Cause
Peripheral neuropathy[a]	5 (9.8)
Presyncope	1 (2.0)
Sinus tachycardia	1 (2.0)
Fatigue	1 (2.0)
Pneumonia	1 (2.0)
Decreased neutrophil count	1 (2.0)
Myositis	1 (2.0)
Maculopapular rash	1 (2.0)

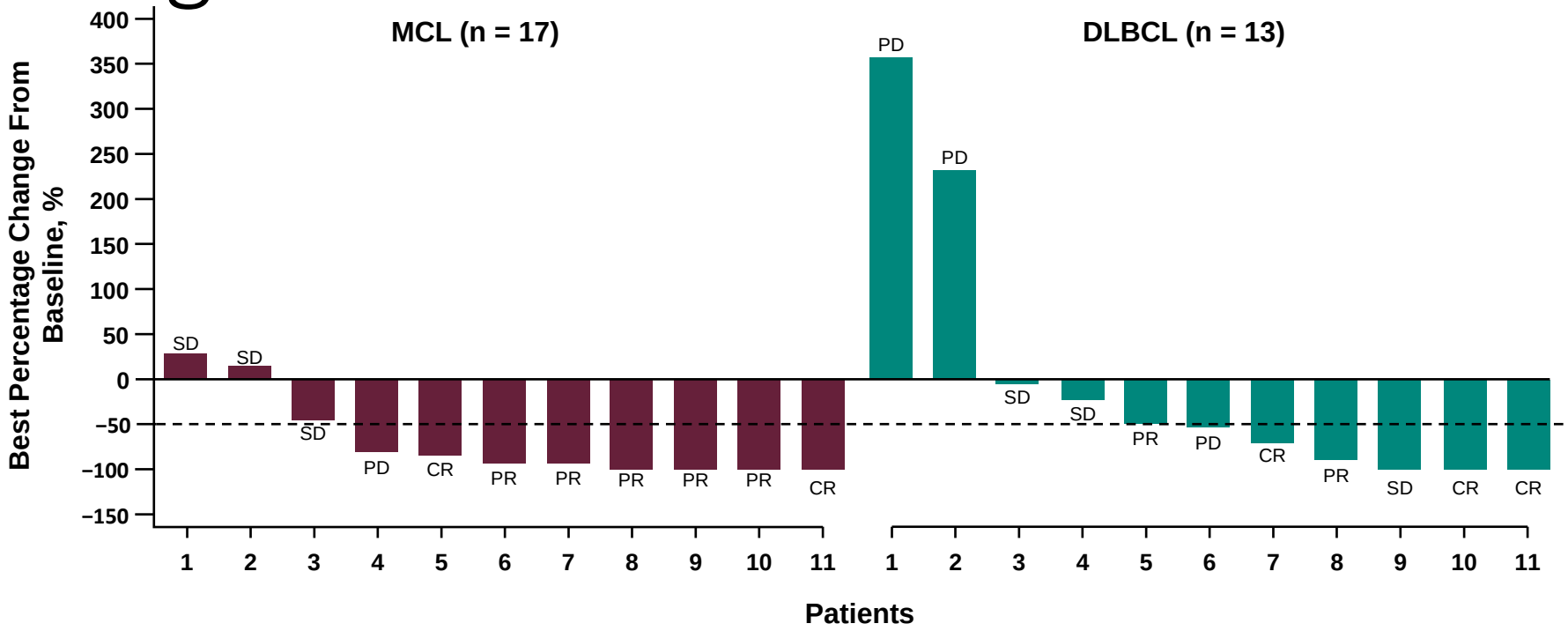
- [a]Includes the preferred terms peripheral sensory neuropathy, peripheral neuropathy, peripheral motor neuropathy, and peripheral sensorimotor neuropathy.
- Data cutoff: May 18, 2021.

Objective Response Rate

	All Patients[a] N = 51	DLBCL n = 13	MCL n = 17	Prior CAR-T or CAR-NK n = 15
ORR, % (95% CI)	33.3 (20.8-47.9)	38.5 (13.9-68.4)	52.9 (27.8-77.0)	40.0 (16.3-67.7)
BOR, n (%)				
CR	5 (9.8)	3 (23.1)	2 (11.8)	2 (13.3)
PR	12 (23.5)[b]	2 (15.4)	7 (41.2)	4 (26.7)

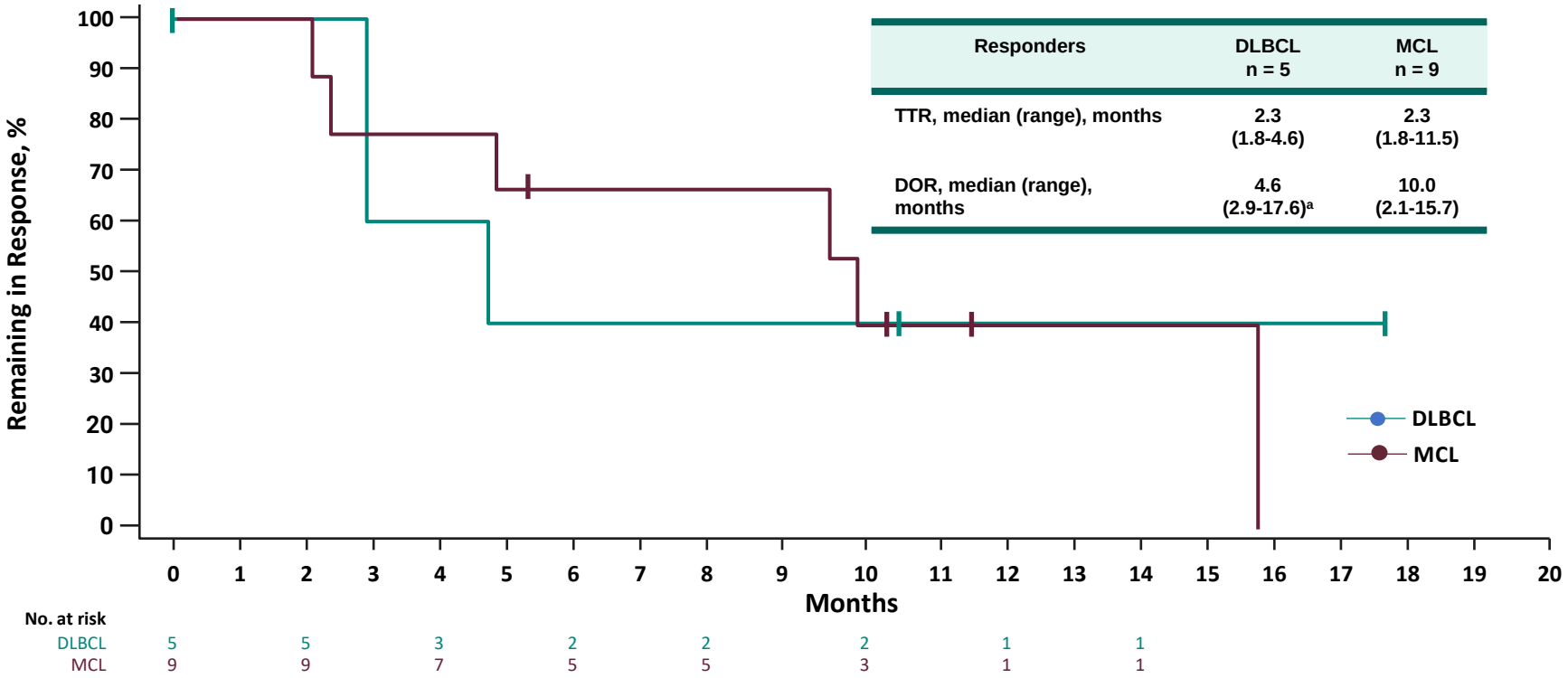
- [a]Patients with CLL/SLL and AML did not achieve a response. [b]At the time of data cutoff, 3 patients with RT experienced a partial response but only had 1 post-baseline assessment.
- Data cutoff: May 18, 2021.

Percent Change From Baseline in Target Lesions[a]



- [a]Only patients with evaluable postbaseline scans prior to subsequent anticancer therapy were included.
- Data cutoff: May 18, 2021.

Duration of Response[a]



Responders	DLBCL n = 5	MCL n = 9
TTR, median (range), months	2.3 (1.8-4.6)	2.3 (1.8-11.5)
DOR, median (range), months	4.6 (2.9-17.6)[a]	10.0 (2.1-15.7)

- [a]Maximum DOR represents a censored value.
- Data cutoff: May 18, 2021.

Summary and Conclusions

- The novel anti-ROR1 ADC zilovertamab vedotin was associated with a tolerable safety profile in schedule 1 of this study
  - Few dose-limiting toxicities observed up to the MTD of 2.5 mg/kg
  - The most common AEs were fatigue and neutropenia
  - GI AEs included nausea and diarrhea
  - The primary cumulative toxicity was peripheral neuropathy
  - No ROR-mediated toxicities (infusion reactions or tumor lysis syndrome) were observed

- Zilovertamab vedotin demonstrated clinical activity in patients with relapsed NHL
  - ORR was 38.5% for patients with DLBCL and 52.9% for patients with MCL
  - For patients who previously received CAR-T/CAR-NK, ORR was 40.0%

- Targeting the ROR1 pathway with zilovertamab vedotin is a promising therapeutic option for heavily pretreated patients with relapsed NHL

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