

Preliminary Results from the Phase 1 Clinical Study of DR-01, a Non-Fucosylated Anti-CD94-Targeting Antibody in Patients with Relapsed/Refractory Cytotoxic Lymphomas

Jasmine Zain, MD¹, Swaminathan P Iyer, MD², Enrica Marchi, MD, PhD³, Mitul Gandhi, MD⁴, Youn H. Kim, MD⁵, Michael S. Khodadoust, MD, PhD⁶, Jonathan E. Brammer⁷, Christina Poh, MD⁸, Pierluigi Porcu⁹, Kimberley Dilley, MD, MPH¹⁰, Wan-Jen Hong, MD¹⁰, Andrea Kantor¹⁰, Cathrine Leonowens, PhD¹⁰, Nenad Tomasevic, PhD¹⁰, H. Miles Prince, MD, MBBS¹¹ and Steven Horwitz, MD¹²

¹City of Hope, Duarte, CA; ²University of Texas MD Anderson Cancer Center, Houston, TX; ³University of Virginia Comprehensive Cancer Center, Charlottesville, VA; ⁴Next Oncology, Fairfax, VA; ⁵Stanford Cancer Center, Stanford, CA; ⁶Stanford Cancer Center, Palo Alto, CA; ⁷The Ohio State University Comprehensive Cancer Center, Columbus, OH; ⁸Fred Hutchinson Cancer Center, Seattle, WA; ⁹Jefferson Health, Philadelphia, PA; ¹⁰Dren Bio, Inc, Foster City, CA; ¹¹Epworth HealthCare and University of Melbourne, Melbourne, VIC, Australia; ¹²Memorial Sloan Kettering Cancer Center, New York, NY

INTRODUCTION

Cytotoxic Lymphomas (CTLs)

- Group of rare lymphoma subtypes characterized by cytotoxic cells expressing CD94
- Account for 25%-40% of mature NK/T-cell lymphomas (3%–6% of non-Hodgkin lymphoma)¹
- Patients with CTL have no established standard of care; few CTL patients are represented in randomized studies
- Outcomes in CTL patients are poor:
 - Median overall survival (mOS) < 1 year in newly diagnosed HSTCL, EATL and ENKTL patients²
 - mOS of only ~3 months in R/R ENKTL³
- Patients with CTLs have a high unmet need for safe and effective therapies

Figure 1. Cytotoxic Lymphoma Histologies

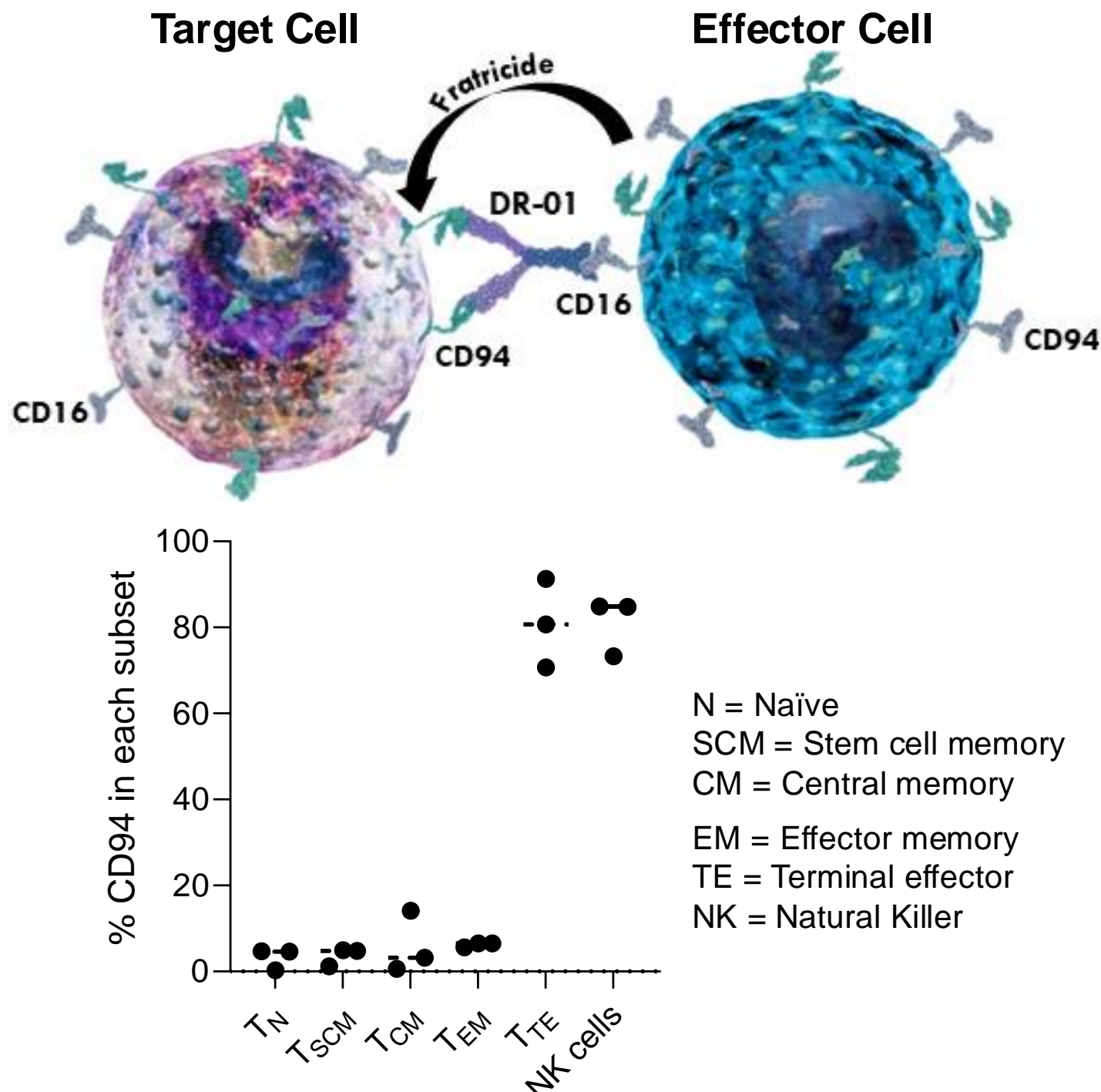
ENKTL, nasal type	ET-CTCL
EATL	ANKL
MEITL	HVLPD
HSTCL	PTCL-NOS*
SPTCL	Cutaneous PTCL-NOS*
PCyδTCL	

ANKL, aggressive NK leukemia; EATL, enteropathy-associated TCL; ENKTL, extranodal NK/TCL; ET-CTCL, epidermotropic cytotoxic TCL; HSTCL, hepatosplenic TCL; HVLPD, Hydroa vacciniforme-like lymphoproliferative disorder; MEITL, monomorphic epitheliotropic intestinal TCL; PCyδTCL, primary cutaneous γδTCL; PTCL-NOS, peripheral TCL, not otherwise specified; SPTCL, subcutaneous panniculitis-like TCL; TCL, T-cell lymphoma. *Some cases are cytotoxic.

DR-01

- Non-fucosylated human IgG antibody against CD94, a receptor selectively expressed on a subset of terminally differentiated and malignant cytotoxic T cells and NK cells
- Engages Fc-γ receptors, such as CD16a, and triggers antibody-dependent cellular cytotoxicity (ADCC) by effector cells or fratricide, resulting in rapid target cell depletion

Figure 2. CD94 Expression on CD8 T Cell Subsets in Healthy Donor Peripheral Blood Mononuclear Cells

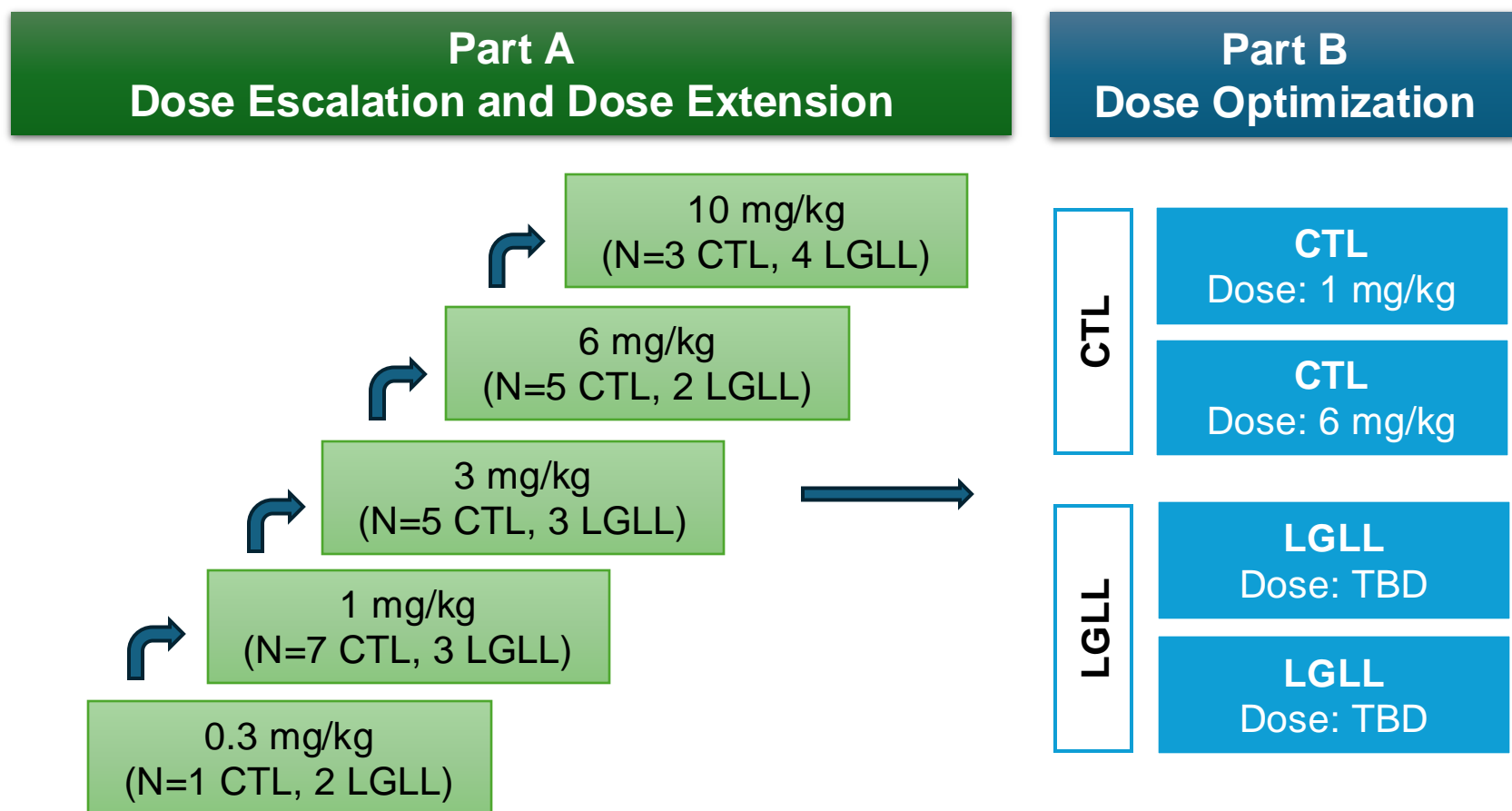


METHODS

Study Design and Objectives

- Phase 1/2, open-label dose-escalation/extension and optimization
- Primary: evaluate DR-01 safety and determine the optimized dose/regimen for DR-01
- Secondary: objective response rate (ORR), duration of response (DoR), DR-01 pharmacokinetic (PK) profile, and immunogenicity

Figure 3. Study Schema: First-in-Human Phase 1/2 Study for DR-01



Patients

- Relapsing/Refractory (R/R) CTL and large granular lymphocytic leukemia (LGLL)
- Adequate organ function
- Part A:
 - CTL: ≥2 prior lines of therapy, ECOG PS 0-1
 - LGLL: ≥1 prior line of therapy, ECOG PS 0-2
- Part B:
 - CTL: ≥1 prior line of therapy

Dosing

- Induction regimen for Cycle 1 (28 days)
 - Primary induction: 1st dose over D1-2, D15
 - Secondary induction: 1st dose over D1-2, D8, D15
 - Tertiary induction: 1st dose D1-5, D15
- Maintenance dose once every 28 days, following induction

RESULTS

Table 1. Baseline Demographics (Safety Population)

	0.3 mg/kg (n=3)	1 mg/kg (n=22)	3 mg/kg (n=8)	6 mg/kg (n=14)	10 mg/kg (n=3)	Total (N=54)
Age, median (range)	64 (53–75)	55 (19–76)	60 (46–71)	48 (26–81)	59 (23–86)	57 (19–86)
Male, n (%)	3 (100)	18 (82)	5 (62.5)	5 (36)	4 (57)	35 (65)
Race, n (%)						
White	2 (67)	14 (64)	7 (88)	6 (43)	5 (71)	34 (63)
Black or African Amer.	1 (33)	3 (14)	0	1 (7)	1 (14)	6 (11)
Asian	0	1 (5)	0	4 (29)	0	5 (9)
American Indian	0	1 (5)	0	0	0	1 (2)
Native Hawaiian	0	0	1 (13)	0	0	1 (2)
Other / Unknown	0	3 (14)	0	3 (21)	1 (14)	7 (13)
ECOG PS, n (%)						
0-1	3 (100)	22 (100)	8 (100)	14 (100)	5 (72)*	52 (96)*
2	0	0	0	0	1 (14)	1 (2)
Histology						
LGLL	2 (67)	3 (14)	3 (38)	2 (14)	4 (57)	14 (26)
CTL	1 (33)	19 (86)	5 (63)	12 (86)	3 (43)	40 (74)

54 patients (40 CTL and 14 LGLL) were safety evaluable (≥1 dose of DR-01) as of 23 Oct 2024
*ECOG Performance Status (PS) of 1 for 1 LGLL patient entered after data cut-off

Table 2. Baseline Characteristics: CTL Patients, Dose Escalation (Part A)

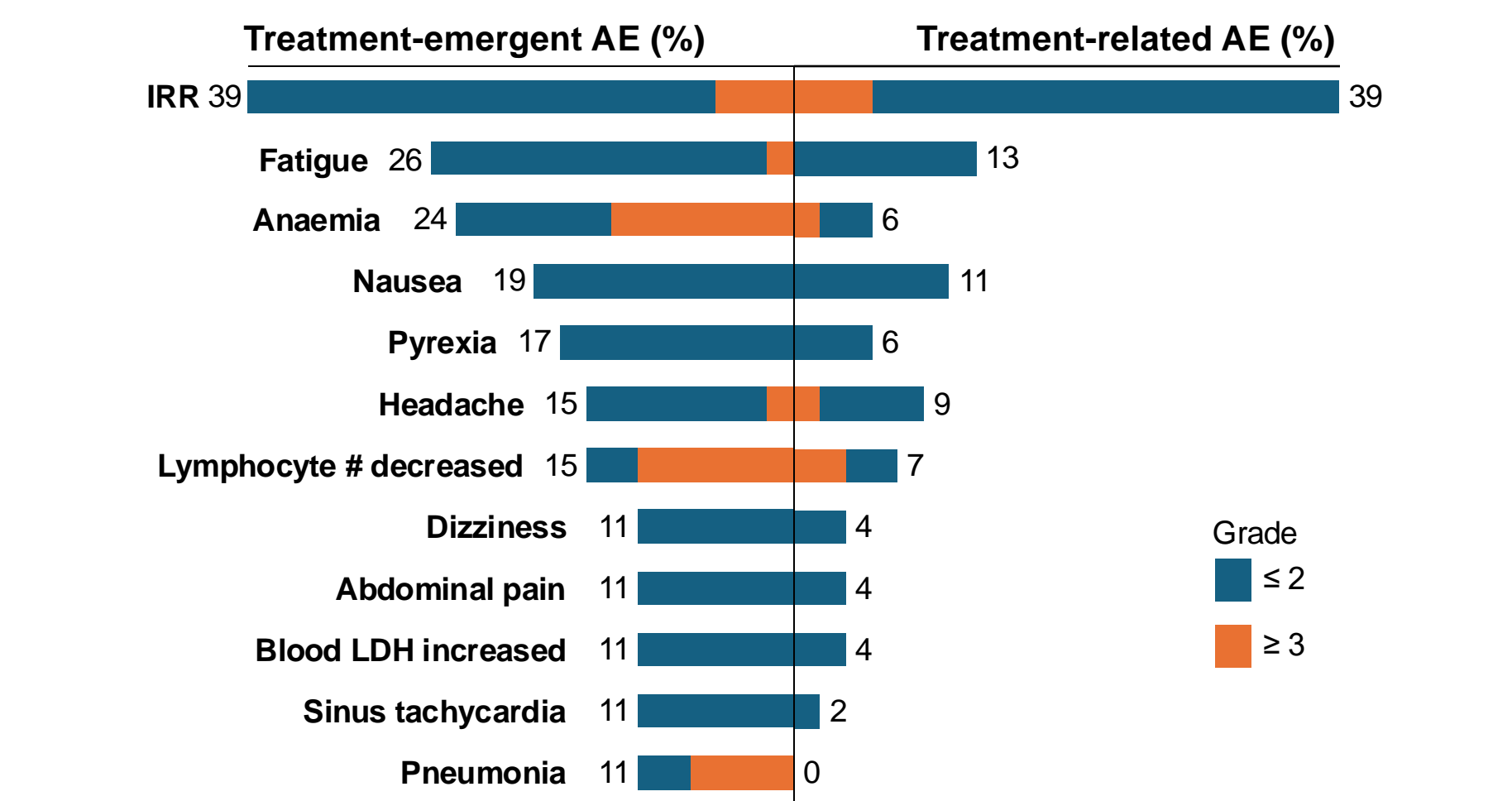
	0.3 mg/kg (n=1)	1 mg/kg (n=7)	3 mg/kg (n=5)	6 mg/kg (n=5)	10 mg/kg (n=3)	Total (N=21)
CTL histology, n (%)						
PCyδTCL	0	2 (29)	0	2 (40)	2 (67)	6 (29)
ET-CTCL	1 (100)	0	1 (20)	0	0	2 (10)
HSTCL	0	0	0	0	1 (33)	1 (5)
SPTCL	0	1 (14)	0	0	0	1 (5)
ENKTL	0	1 (14)	1 (20)	0	0	2 (10)
MEITL	0	0	1 (20)	1 (20)	0	2 (10)
PTCL-NOS & Other*	0	3 (43)	2 (40)	2 (40)	0	7 (33)
No. prior LoT, median (range)	8 (8–8)	5 (2–14)	5 (2–7)	3 (2–6)	4 (2–9)	4 (2–14)

Reason for discontinuation from last therapy, n (%)

Lack of response	1 (100)	4 (57)	1 (20)	2 (40)	2 (67)	10 (48)
Intolerance	0	0	1 (20)	2 (40)	0	3 (14)
Prior autologous or allogeneic HSCT, n (%)	0	1 (14)	3 (60)	0	0	4 (19)

LoT, lines of therapy; HSCT, hematopoietic stem cell transplant

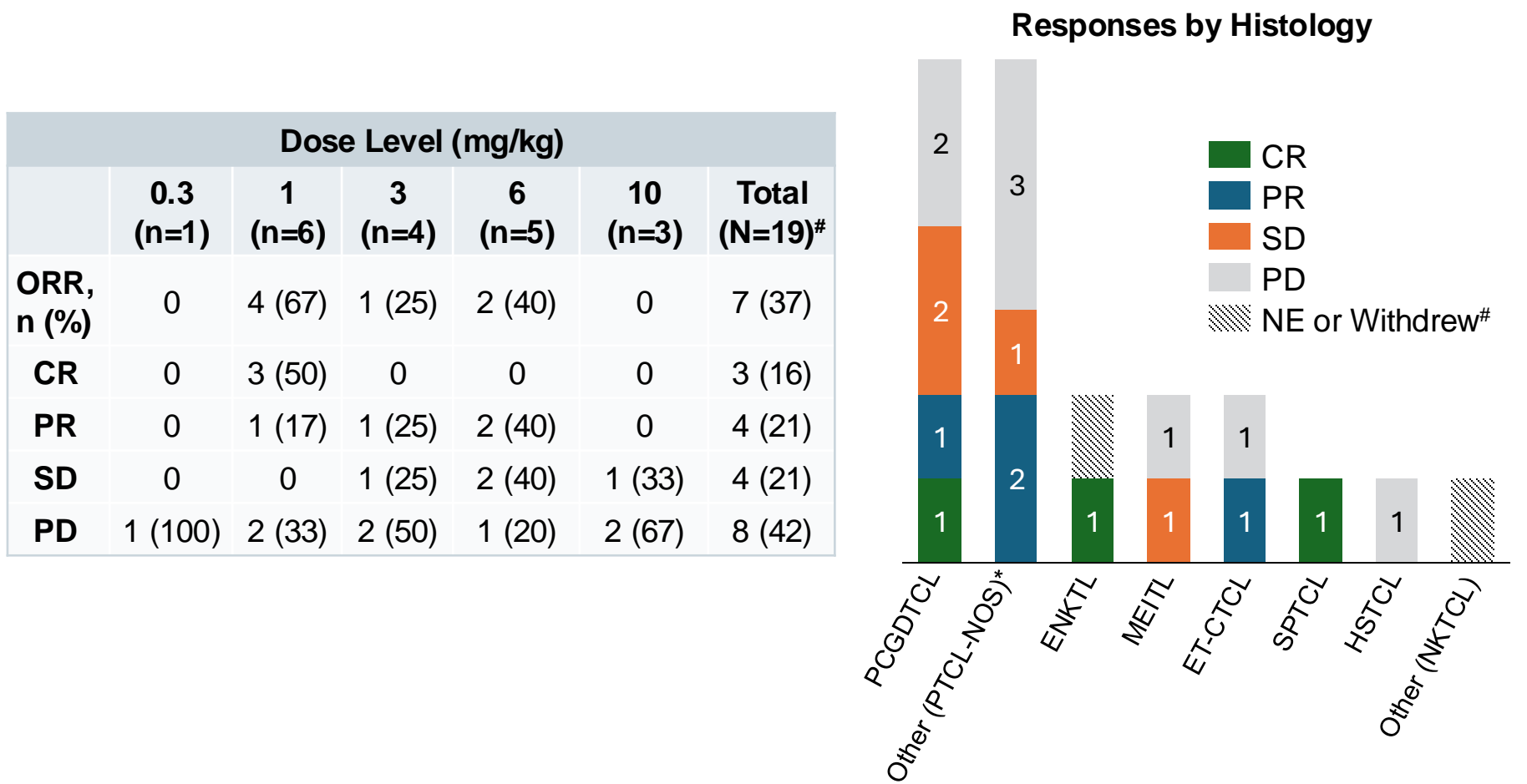
Figure 4. Most Common Adverse Events (AEs)



IRR, infusion-related reaction; LDH, lactate dehydrogenase.

- No dose-limiting toxicities (DLTs) were reported during dose escalation; the maximum tolerated dose (MTD) was not reached
- Infusion-related reactions (IRR) were the most common TEAE
- Majority of IRR events were Grade 1–2 and all events were manageable with mitigation strategies including standard pre-medications and splitting the initial dose
- Only 2/54 (4%) AEs of viral reactivation (Gr 1 CMV, Gr 1 HSV) were noted and continued on study. Other acquired viral infections (e.g. COVID-19) resolved as expected

Figure 5. Promising Response Rate, including CRs, in CTL Patients During Dose Escalation in Majority of Histologies

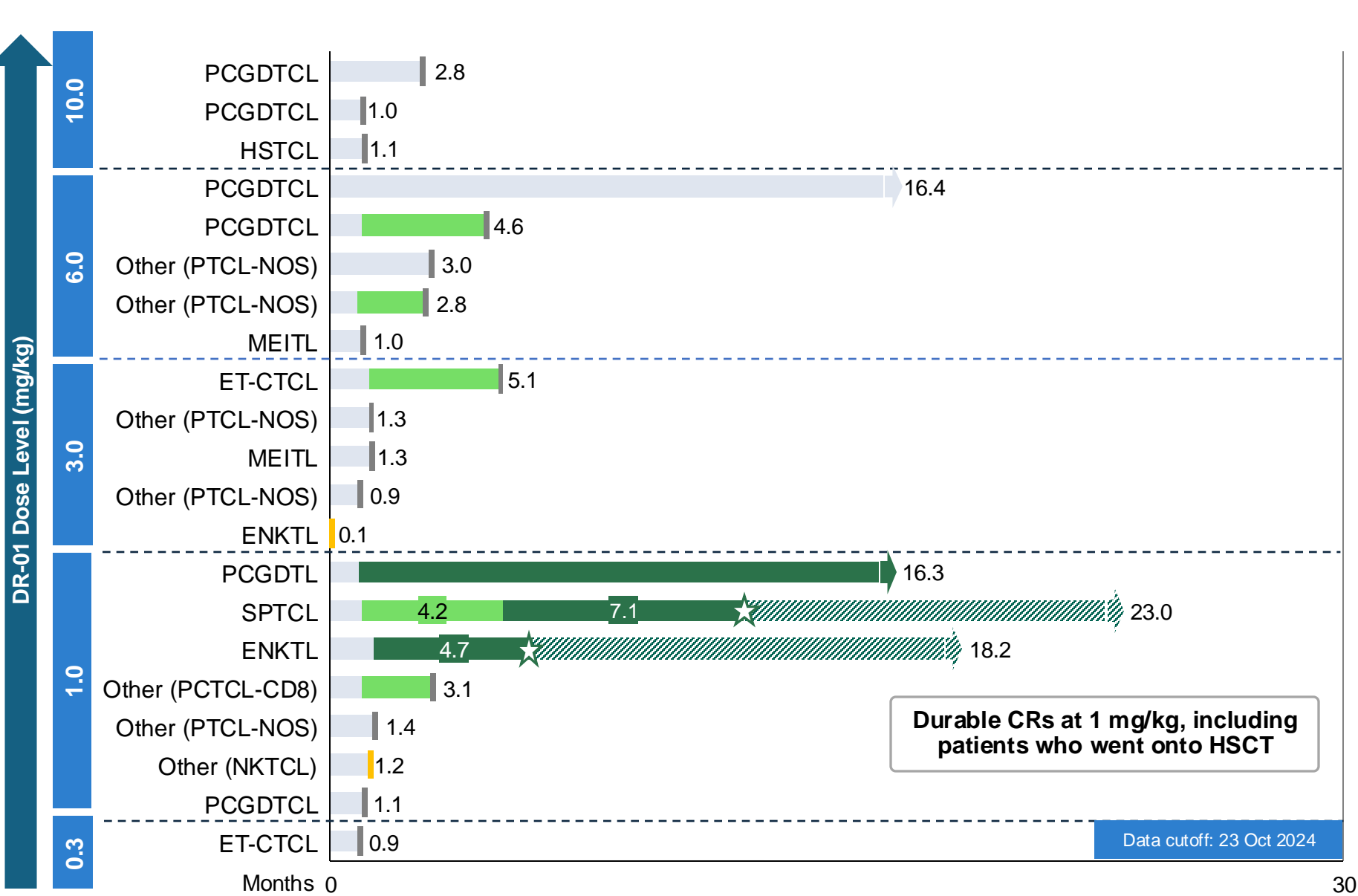


CR, complete response; NE, not evaluable; ORR, objective response rate; PR, partial response; PD, progressive disease; SD, stable disease.

*One unrelated AE withdrawal and one PI withdrawal without assessment.

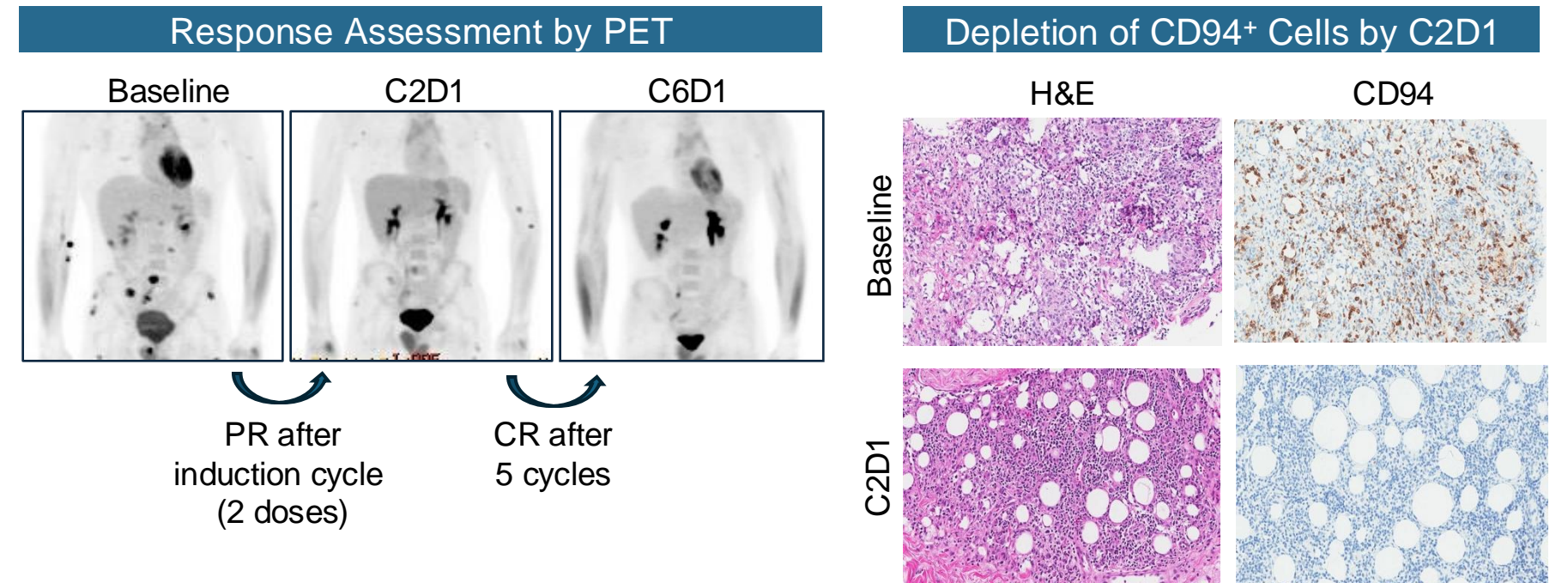
*includes cutaneous subtypes

Figure 6. Duration of DR-01 Treatment and Responses of CTL Patients on Dose Escalation



CR, complete response; PR, partial response; PD, progressive disease; SD, stable disease

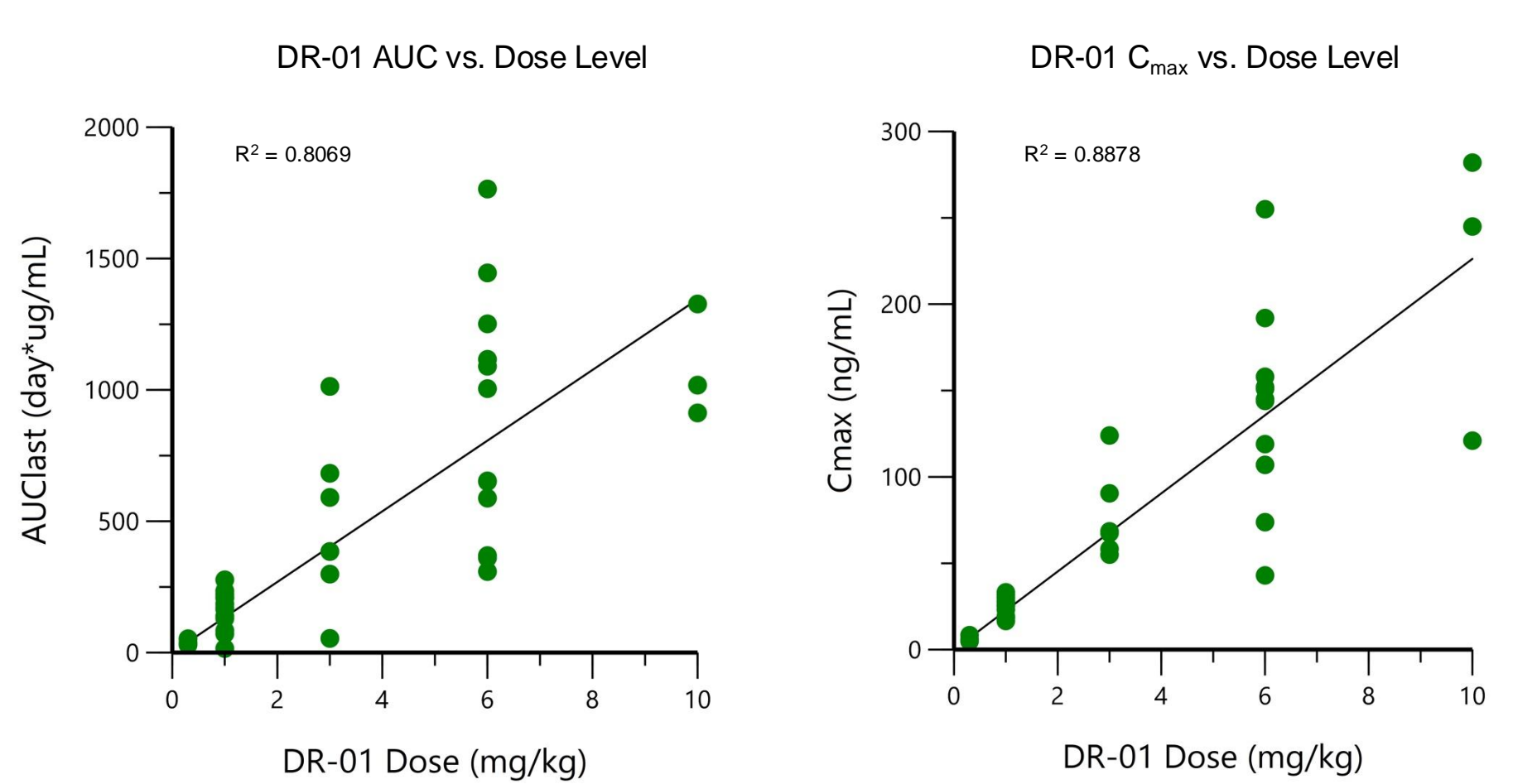
Figure 7. Case Study: R/R Subcutaneous Panniculitis-like TCL in CR



CR, complete response; PR, partial response

- 19-year-old male; received 4 prior lines of therapy, including corticosteroids, cyclosporine, methotrexate, and romidepsin
- Patient achieved PR after the first cycle; deepened to CR after 5 cycles
- After 14 cycles on DR-01, patient received allogeneic HSCT and remains in remission an additional 23 months later

Figure 8. Dose-Proportional PK and No Observed Immunogenicity



Symbols, individual C_{max} and AUC values (14-day dose interval from Days 15 to 28). Line, linear regression of the relationship between exposure and dose. AUC, area under the concentration-time curve; C_{max}, maximum observed concentration

- PK is linear and dose proportional within the dose range tested
- No exposure-response relationship was observed for either safety or efficacy endpoints
- Minimal clinically efficacious dose: 1 mg/kg
- No treatment-emergent anti-drug antibodies observed to date

CONCLUSIONS

- 54 R/R CTL and LGLL patients enrolled across dose levels ranging from 0.3–10 mg/kg; 21 CTL patients treated in Part A dose escalation
- No DLTs were observed during dose escalation and no MTD was reached
- IRR was the most common treatment-related AE, typically occurred after the first dose; was manageable with standard mitigation strategies
- Responses seen across multiple CTL histologies, including durable CRs at 1 mg/kg
- Preliminary clinical data demonstrate that DR-01 is safe and tolerable and has a favorable benefit/risk profile in a high unmet need population
- Expansion cohort in CTLs continues to enroll and dose escalation for LGLL is ongoing with responses observed

REFERENCES

- Leukemia and Lymphoma Society 2024
- Vose et al. *JCO* 2008
- Bellei M et al. *Haematologica* 2018