9th POSTGRADUATE
Lymphoma
Conference

TCL New Agents

Swami iyer

MD Anderson Cancer Center

Florence,
March 20-21, 2025

Hotel Brunelleschi

President:
P.L. Zinzani

Disclosures

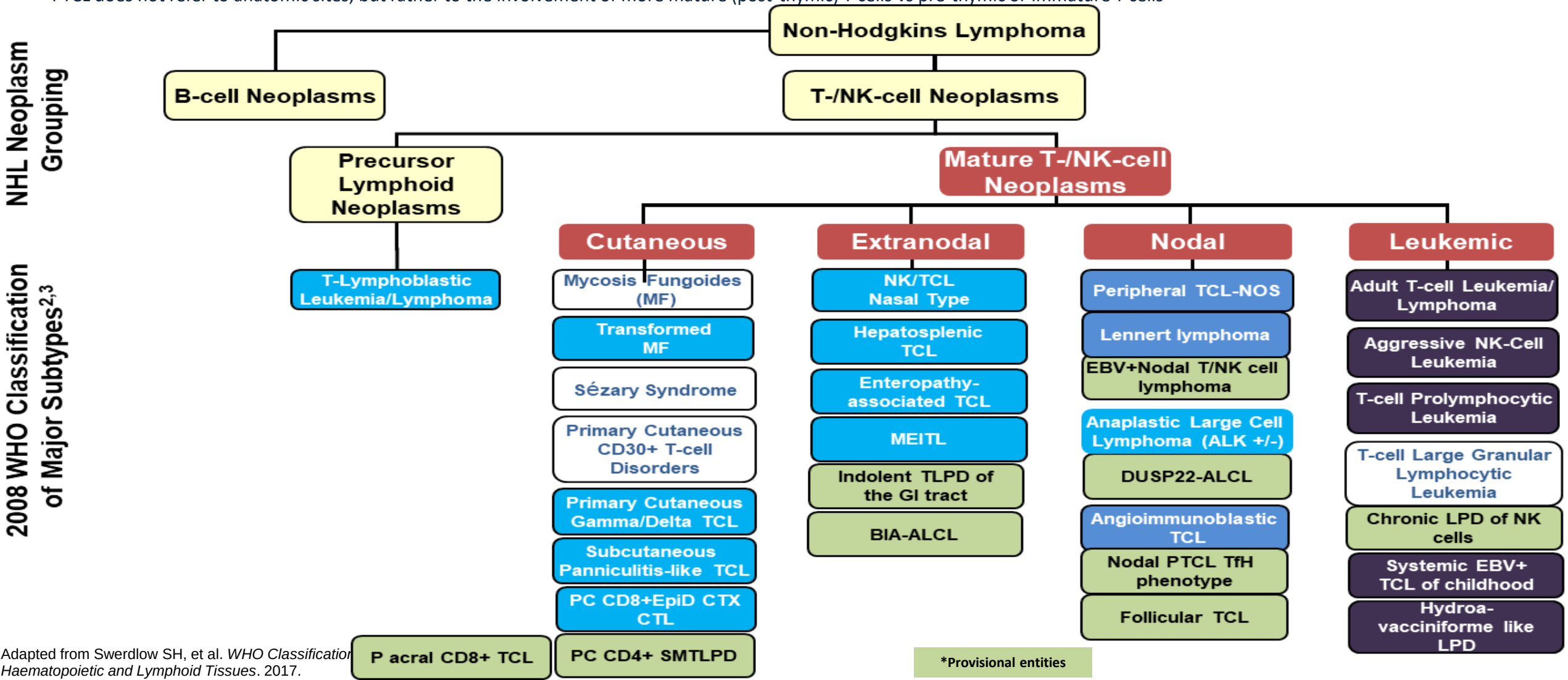
Company name	Research support	Employee	Consultant	Stockholder	Speakers bureau	Advisory board	Other
CRISPR	✓					✓	
MERCK	✓						
SEAGEN/PFIZER	✓					✓	
YINGLI	✓					✓	
ACROTECH	✓					✓	
INNATE	✓						
TRILLIUM/Pfizer	✓						
ASTRA ZENECA	✓						
ONO	✓						
LEGEND	✓						
SALARIUS			✓				
SECURA BIO						✓	
ELECTRA						✓	
DREN-BIO	✓					✓	
IMPaRT.AI				✓			Co-Founder
Sanofi			✓				

Classification of Peripheral T-cell Lymphoma (PTCL)

THE UNIVERSITY OF TEXAS MD Anderson Cancer Center
Making Cancer History®

PTCL is a heterogeneous group of aggressive mature T-/NK-cell lymphomas

PTCL does not refer to anatomic sites, but rather to the involvement of more mature (post-thymic) T cells vs pre-thymic or immature T cells[1]



Adapted from Swerdlow SH, et al. *WHO Classification Haematopoietic and Lymphoid Tissues*. 2017.

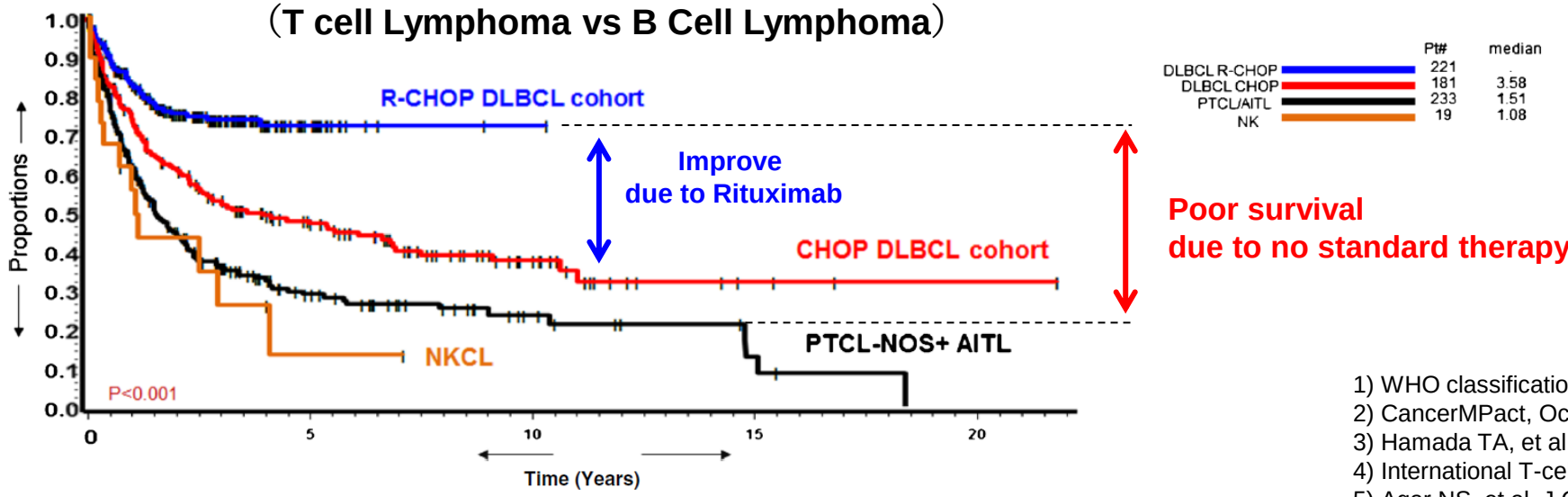
PTCL Prognostic Characteristics

THE UNIVERSITY OF TEXAS MD Anderson Cancer Center
Making Cancer History®

Major subtype of T-cell Lymphoma[1] (WHO classification 2008)	Number of newly diagnosed Pts in 2018 [2]			5yr OS [4] [5] (%)
	US	EU	Japan	
PTCL (Peripheral T-cell lymphoma) **PTCL-NOS** (PTCL not otherwise specified) **AITL** (Angioimmunoblastic T-cell lymphoma) **ALK (+) ALCL** (Anaplastic large-cell lymphoma) **ALK (-) ALCL**	3,683	3,033	2,340	32 32 70 49
CTCL (Cutaneous T-cell lymphoma) **MF** (Mycosis fungoides) **SS** (Sezary syndrome)	3,466	1,798	278 [3]	18～37*

n.d.: No data * Advance stage

Overall survival
(T cell Lymphoma vs B Cell Lymphoma)



Poor survival
due to no standard therapy

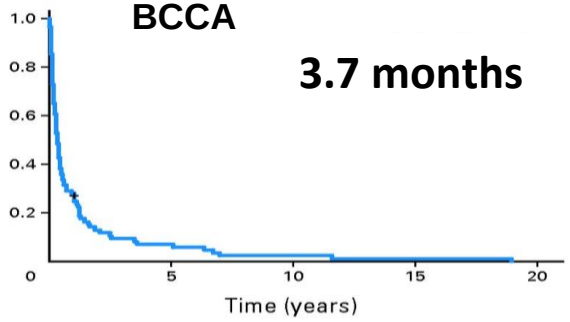
1) WHO classification of haematopoietic and Lymphoid Tissues. 2008.
2) CancerMPact, Oct, 3, 2019.
3) Hamada TA, et al, Nationwide survey on cutaneous lymphomas. 2008
4) International T-cell Lymphoma project, J Clin Oncol.2008.
5) Agar NS, et al, J Clin Oncol. 2010.
6) Lone W, et al, Current Hematologic Malignancy Reports. 2018.

Progression Free Survival: Relapsed/Refractory PTCL

THE UNIVERSITY OF TEXAS MD Anderson Cancer Center
Making Cancer History®

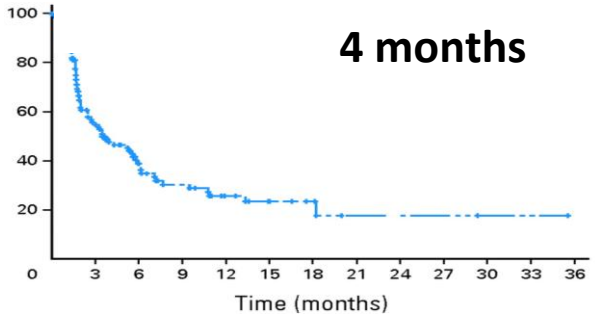
BCCA

3.7 months



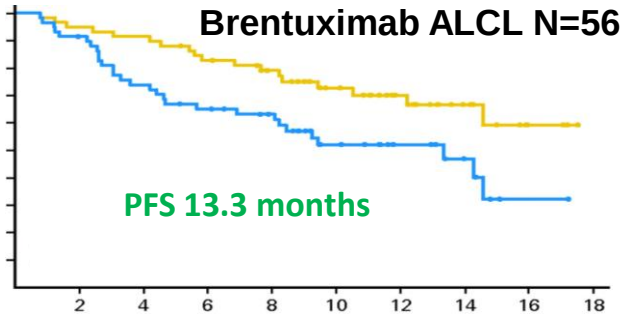
Romidepsin N=130

4 months



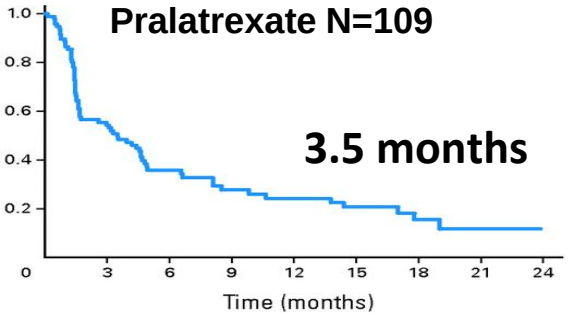
Brentuximab ALCL N=56

PFS 13.3 months



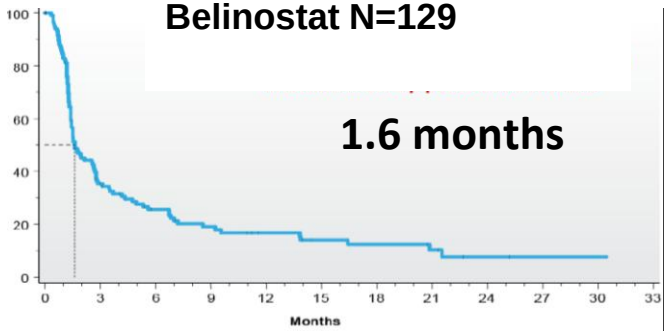
Pralatrexate N=109

3.5 months



Belinostat N=129

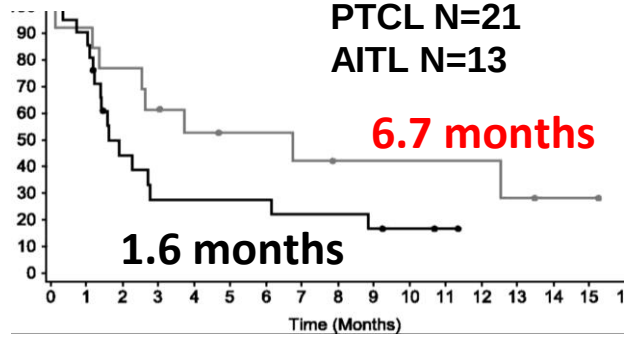
1.6 months



Brentuximab
PTCL N=21
AITL N=13

6.7 months

1.6 months

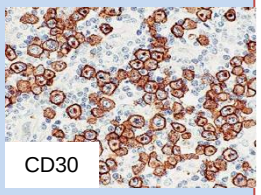


Mak V et al. JCO 2013;31:1970-1976, O'Connor OA, et al. *J Clin Oncol*. 2011;29:1182-1189,Coiffier B, et al. *J Clin Oncol*. 2012;30 :631-636, O'Connor OA et al ASCO 2013, Pro B, et al. J Clin Oncol. 2012;30:2190-2196, Horwitz S M et al. Blood 2014;123:3095-3100

CD30 as the predictive marker in TCL

THE UNIVERSITY OF TEXAS MD Anderson Cancer Center
Making Cancer History®

CD30+ Histologies:
PTCL-NOS
AITL (?)
ALK- ALCL
ALK + ALCL



BV + CHP
CHOEP

CR or PR → Complete Rx → CR or PR → ASCT

No response or PD → Rx as r/r PTCL

No response or PD → Rx as r/r PTCL

CD30

PTCL

Salvage therapy/
Clinical trials

PTCL Histologies:
PTCL-NOS
AITL (?)

CHOP
CHOEP

No response or PD → Rx as r/r PTCL

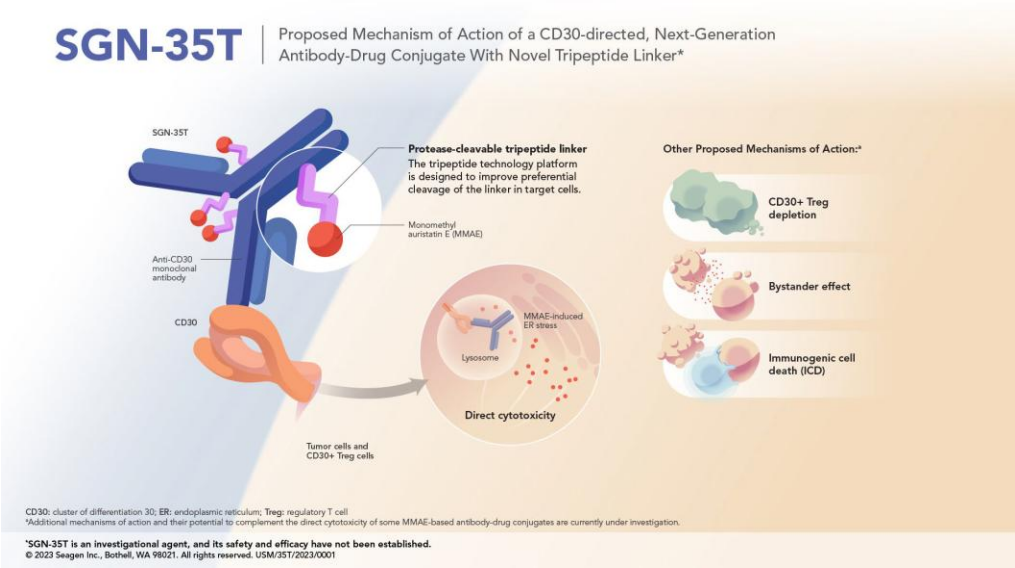
CR or PR → Complete Rx → No response or PD → Rx as r/r PTCL

CR or PR → ASCT

NexGen CD30: ADC and DuoBody

THE UNIVERSITY OF TEXAS MD Anderson Cancer Center
Making Cancer History®

SGN-35 T: Tripeptide linker



SGN-35C

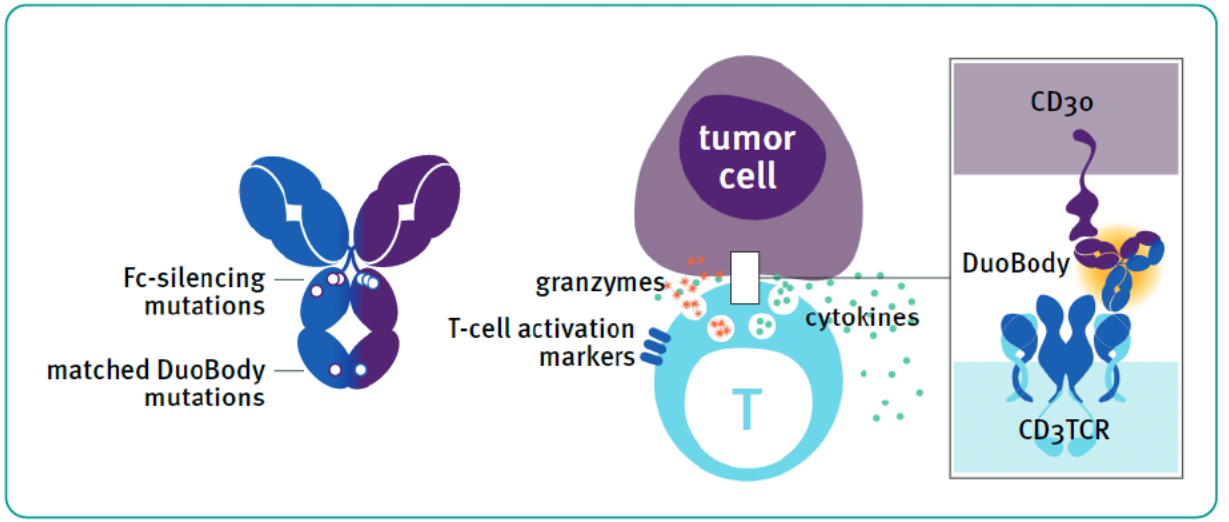
Novel camptothecin payload

GEN3017 (DuoBody®-CD3xCD30)

Mechanism of Action

- Bispecific Fc-silenced IgG1antibody obtained by controlled Fab-arm exchange of a humanized CD3e and a human CD30 monoclonal antibody

- Leads to crosslinking of T cells with CD30-expressing (CD30+) tumor cells resulting in T-cell–mediated killing of the malignant cells

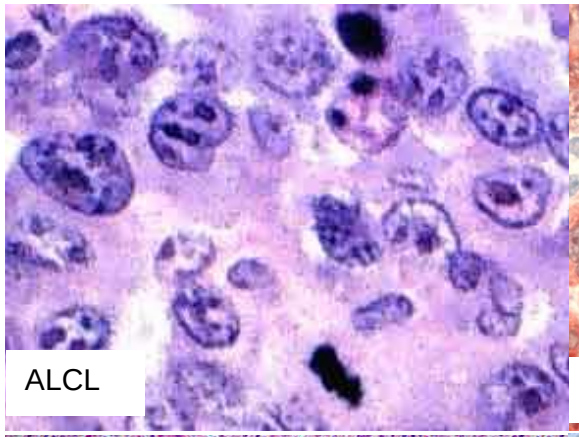


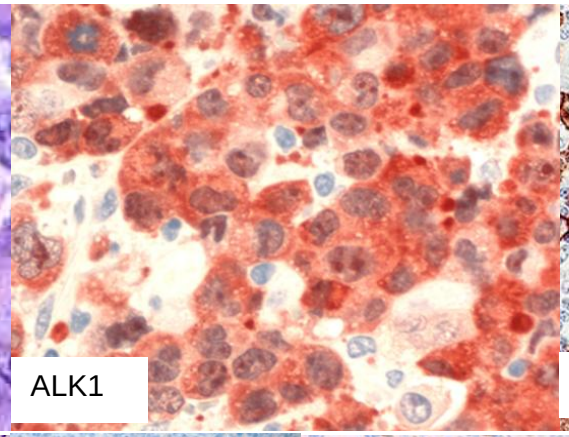
ALCL, anaplastic large-cell lymphoma; Fc, fragment crystallizable; HL, Hodgkins lymphoma; IgG1, immunoglobulin G. Oostindie, S, et al. Poster presented at the 64th ASH Annual Meeting, December 10-13, 2022.

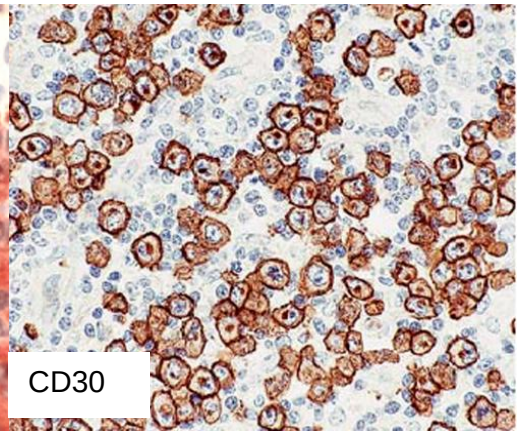
Pathology- basis for diagnosis, prognosis in PTCL

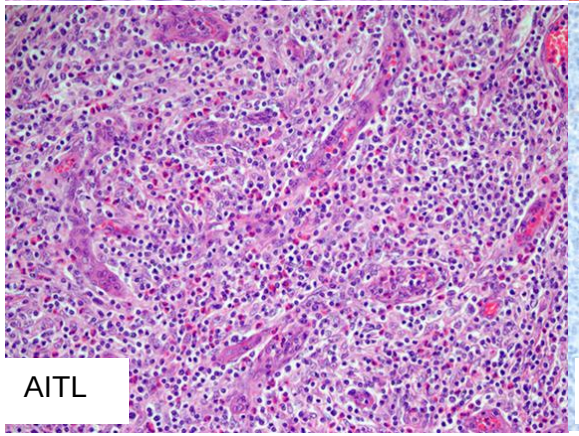
THE UNIVERSITY OF TEXAS MD Anderson Cancer Center
Making Cancer History®

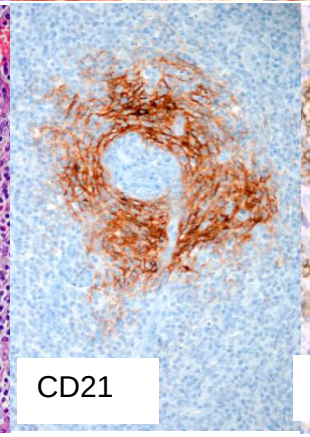
- Approximately 30-50% of PTCL cases are incorrectly diagnosed with conventional diagnostic techniques[1]
- Immunophenotypic analysis in conjunction with cellular morphology, analysis of lymph node architecture, and molecular genetic assays

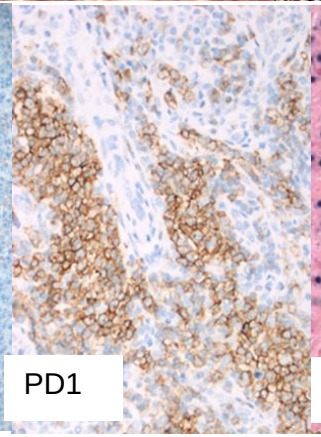

ALCL

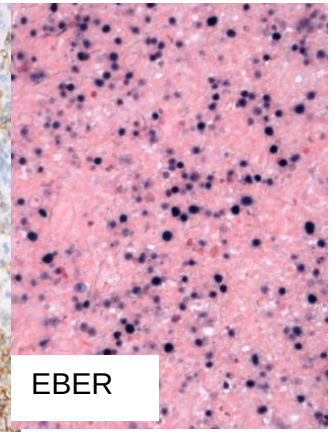

ALK1

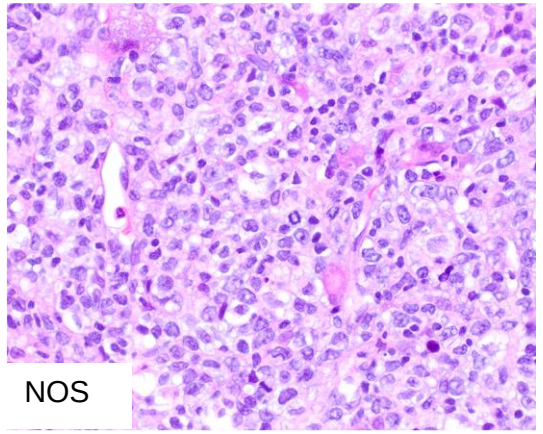

CD30


AITL


CD21


PD1

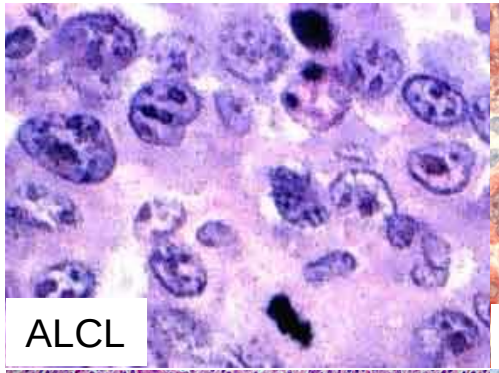

EBER

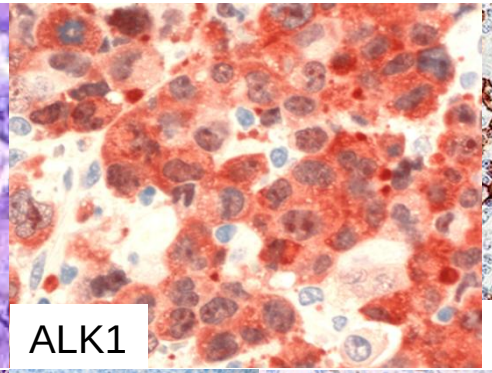

NOS

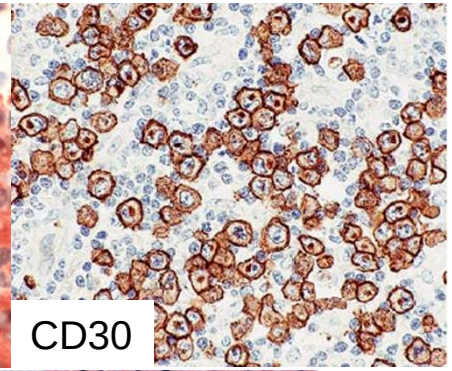
1. Armitage J, et al. *J Clin Oncol*. 2008;26:4124–4130.
2. Warnke RA, et al. Am J Clin Pathol. 2007;127:511–527 .
3. Swerdlow SH, et al. *WHO Classification of Tumours of Haematopoietic and Lymphoid Tissues*. 2008
4. Kocjan G. J Clin Pathol. 2005;58:561–567.

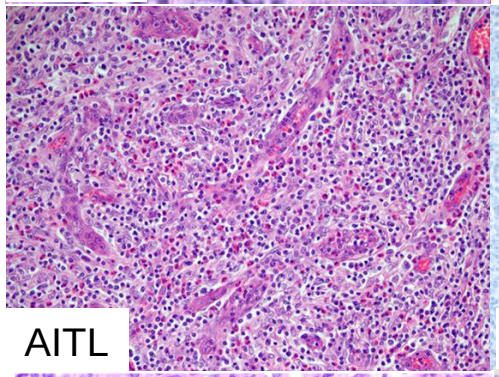
COO based Diagnosis in PTCL

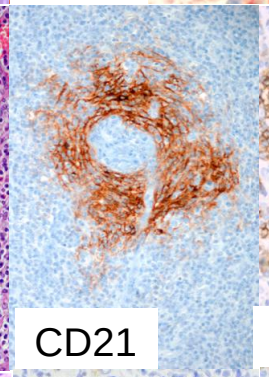
THE UNIVERSITY OF TEXAS MD Anderson Cancer Center
Making Cancer History®

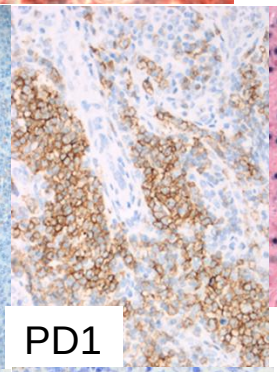

ALCL

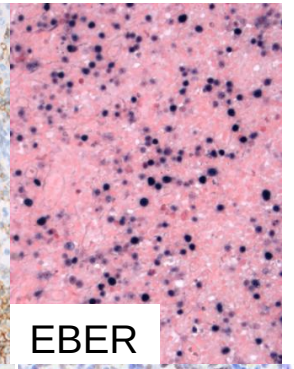

ALK1

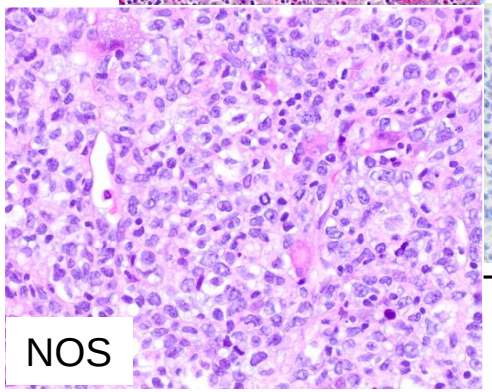

CD30

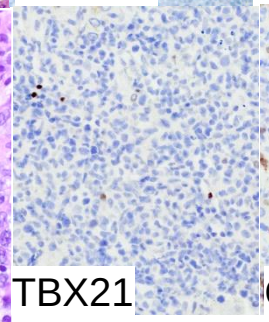

AITL

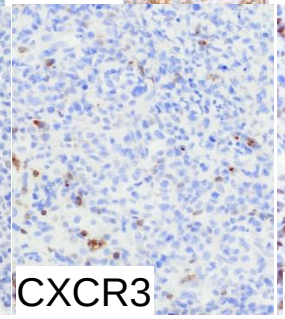

CD21

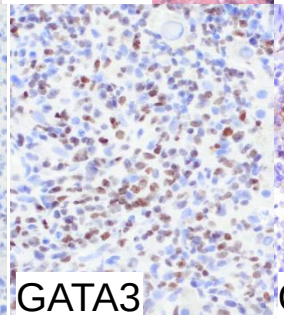

PD1

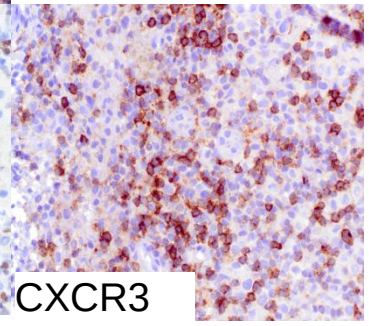

EBER

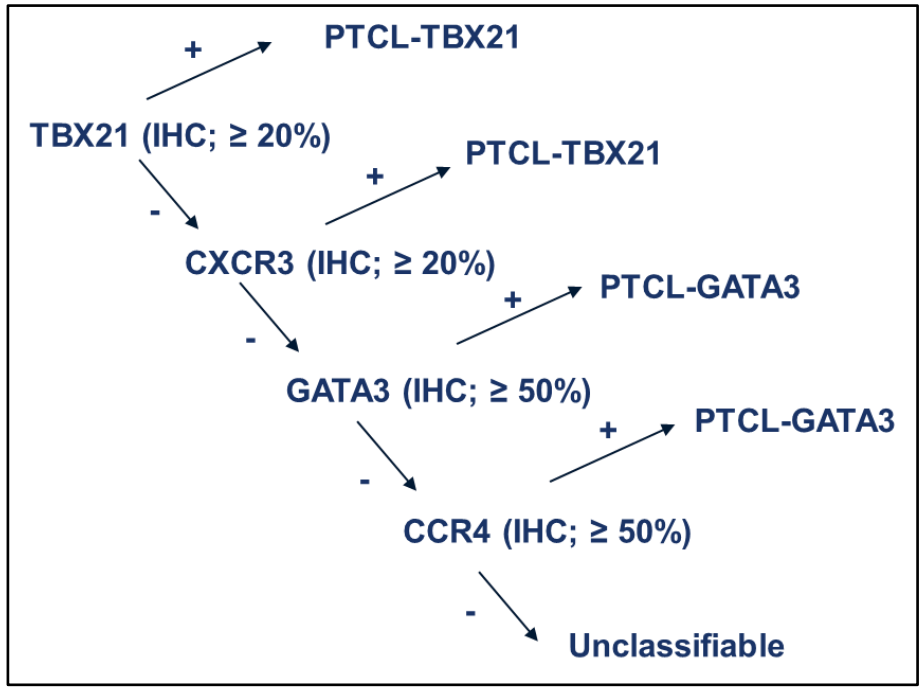

NOS


TBX21


CXCR3


GATA3


CXCR3



Vega F, EXABS-TCL-052.2020

THE UNIVERSITY OF TEXAS
MD Anderson Cancer Center
Making Cancer History®

- HOW CAN WE HARNESS THE ADVANCES IN BIOLOGY?

Emerging themes in T cell Lymphomas

THE UNIVERSITY OF TEXAS MD Anderson Cancer Center
Making Cancer History®

- Epigenetic targeting of Tfh
- Targeting dysregulated pathways: JAK/STAT, PI3K, EZH1/2, ITK
- Targeting cytotoxic, gamma-delta and NK subtypes
- Immunotherapy: checkpoint blockade and cellular
- Pan SIRP inhibitor for LA-HLH

Emerging themes in T cell Lymphomas

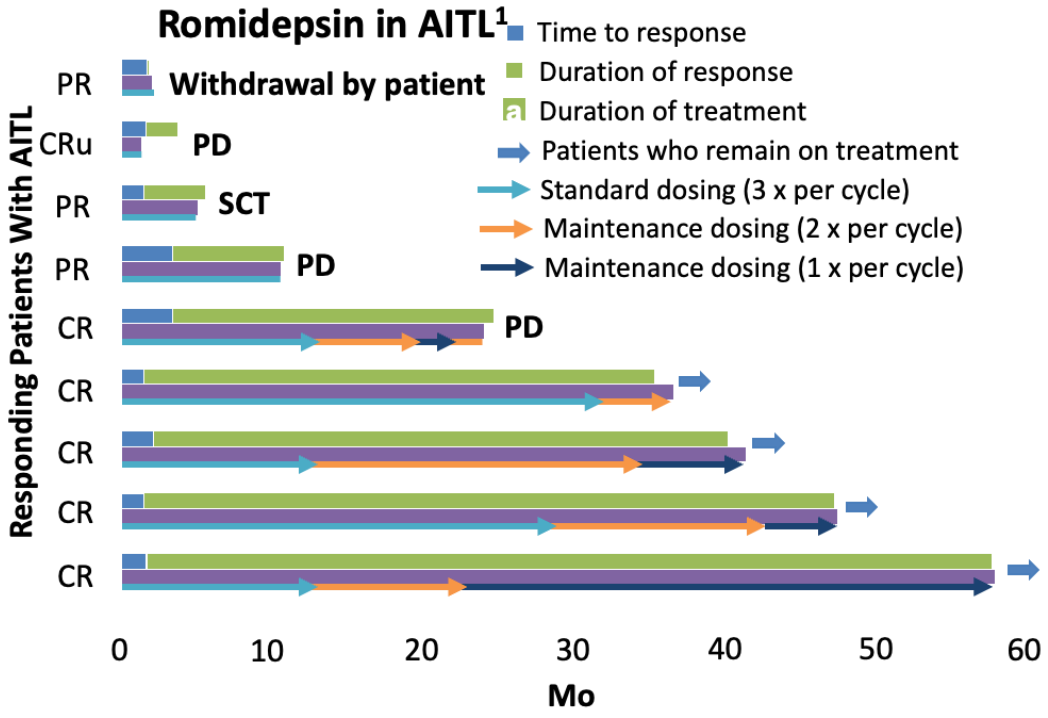
THE UNIVERSITY OF TEXAS MD Anderson Cancer Center
Making Cancer History®

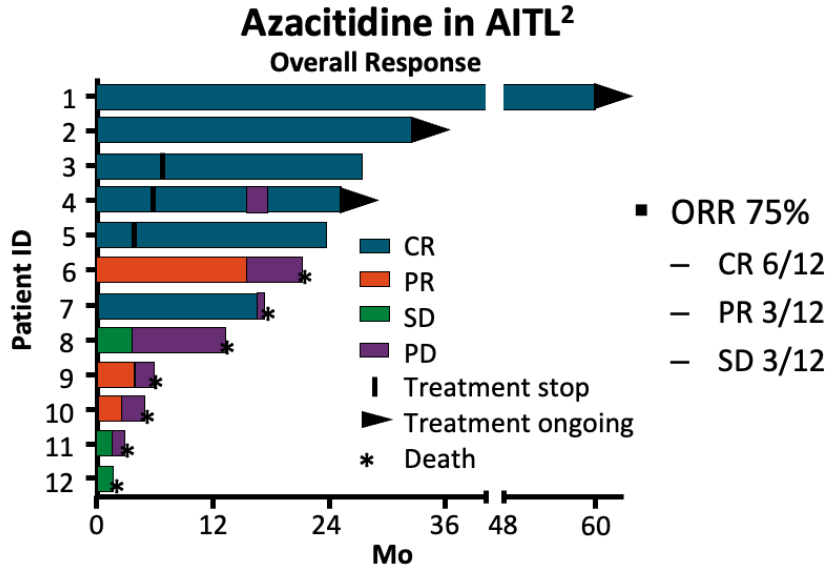
- Epigenetic targeting of Tfh
- Targeting dysregulated pathways: JAK/STAT, PI3K, EZH1/2
- Targeting cytotoxic, gamma-delta and NK subtypes
- Immunotherapy: checkpoint blockade and cellular

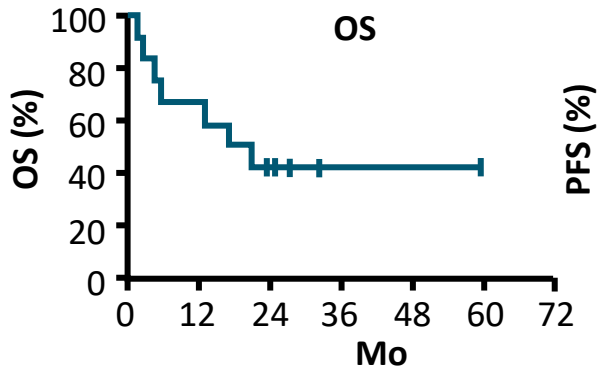
Nodal Lymphomas with TFH Phenotype: Role of Epigenetic Modifiers

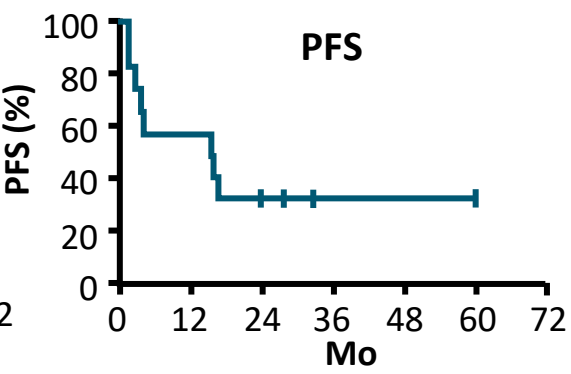
THE UNIVERSITY OF TEXAS MD Anderson Cancer Center
Making Cancer History®

n=114	Nodal lymphomas of TFH cell origin (TFH-PTCL)				
	AITL	Other TFH-PTCL		PTCL-NOS	
		TFH-like PTCL	F-PTCL*		
Mutations (%)					
TET2	31/64 (48%)	7/11 (64%)	3/4 (75%)	4/24 (17%)	p<0.001
DNMT3A	19/64 (30%)	1/10 (10%)	1/4 (25%)	1/24 (4%)	p<0.05
IDH2	22/66 (33%)	1/11 (10%)	0/5 (0%)	0/23 (0%)	p<0.001
RHOA (G17V)	42/72 (58%)	8/14 (57%)	3/5 (60%)	0/23 (0%)	p<0.001





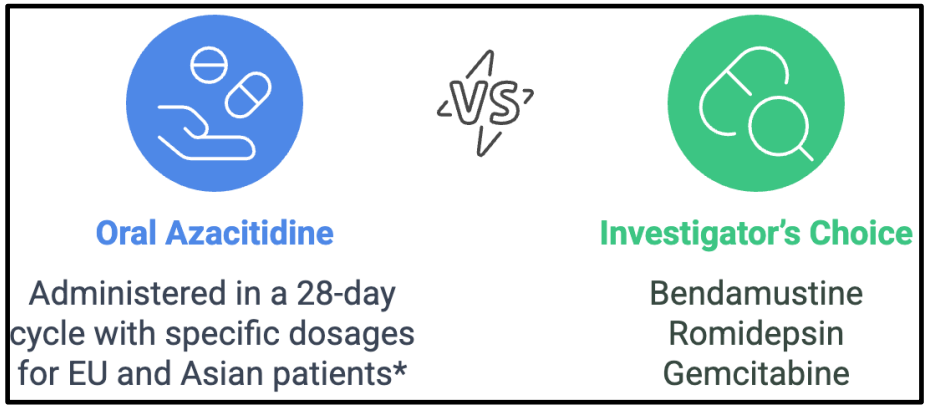




1. Pro. Hematol Oncol. 2017;35:914. 2. Lemonnier. Blood. 2018;132:2305.

ORACLE: Phase III study baseline characteristics

THE UNIVERSITY OF TEXAS MD Anderson Cancer Center
Making Cancer History®

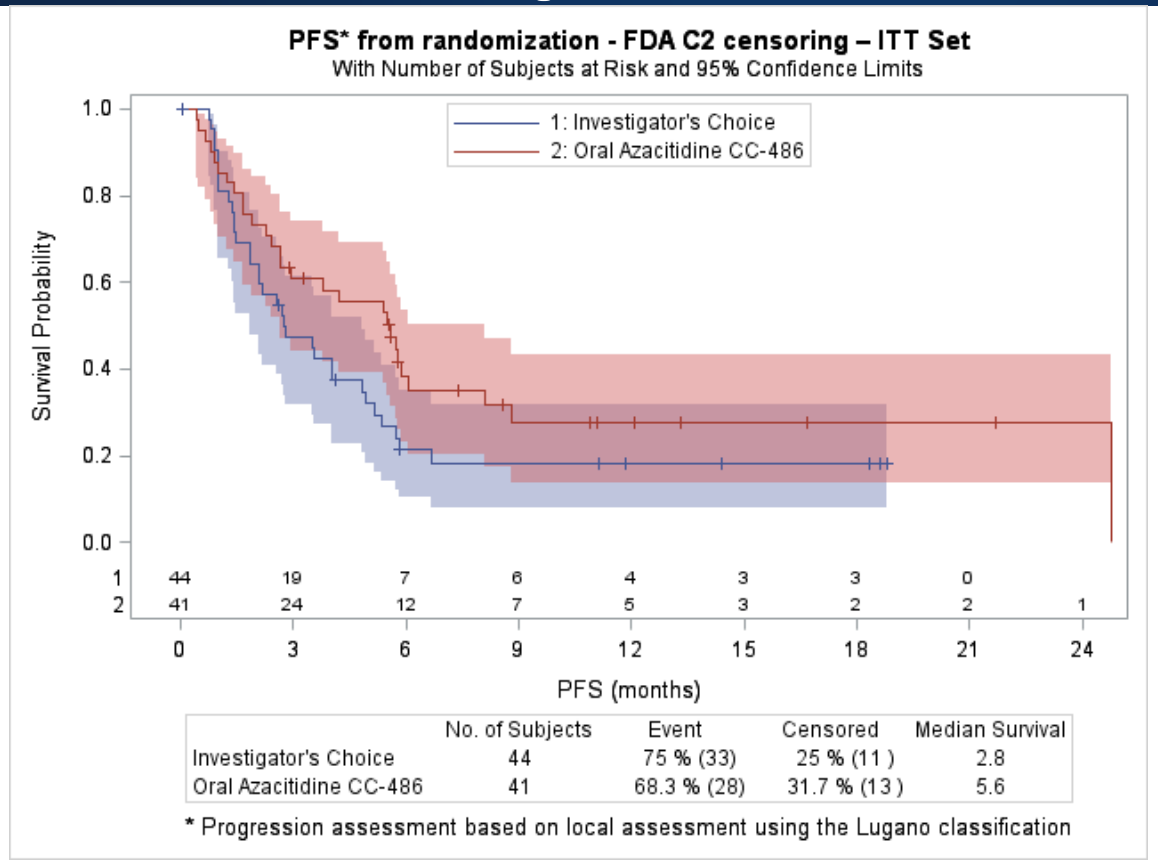


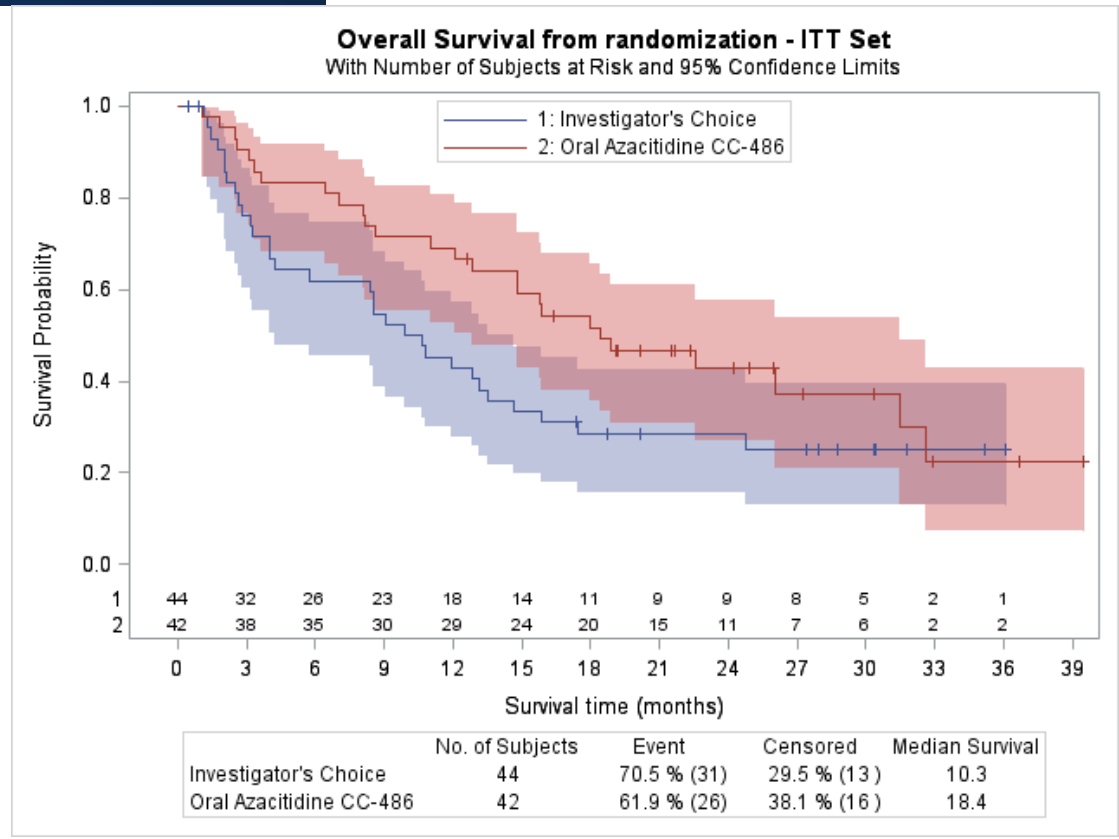
	Azacitidine CC486	Investigator treatment choice	romidepsin	Bendamustine	gemcitabine
N	42	44	4	16	24
median age (IQR)	70.5 (65-77)	68 (58.5-73.5)	68.5 (62.5-71.5)	63.5 (53-68)	72 (64-78)
Sex male	22 (52%)	28 (64%)	3 (75%)	10 (62.5%)	15 (62.5%)
ECOG 2-3	11 (26%)	9 (20%)	0 (0%)	4 (25%)	5 (20%)
Bone marrow involvement	12/37 (32%)	17/40 (42,5%)	1/4 (25%)	8/16 (50%)	8/20 (40%)
Associated MDS/CMML	0	1 (2%)	0	0	1 (4%)
IPI 4-5	13/42 (31%)	14/42 (33%)	0/4	5/15 (33%)	9/23 (39%)
Previous line number					
1-2 vs ≥3	34 (81%) vs 8 (19%)	37 (84%) vs 7(16%)	4 (100%) vs 0 (0%)	14 (88%) vs 2 (12%)	19 (79%) vs 5 (21%)
1	24 (57%)	14 (32%)	4 (100%)	3 (19%)	7 (29%)
2	10 (24%)	23 (52%)	0 (0%)	11 (69%)	12 (50%)
refractory patients	20 (48%)	28 (64%)	1 (25%)	13 (80%)	14 (58%)

Dupuis J et al, ASH 2022 #959

ORACLE – did not meet primary endpoint PFS but OS

THE UNIVERSITY OF TEXAS MD Anderson Cancer Center
Making Cancer History®





	CC-486	Investigator's choice
median	5.6 months	2.8 months
95% CI	2.7 - 8.1 months	1.9 - 4.8 months
	P=0.0421	>p=0.025

	CC-486	Investigator's choice
median	18.4 months	10.3 months
95% CI	12.9 – 31.5 months	4.2 – 13.5 months
	P=0.0166*	

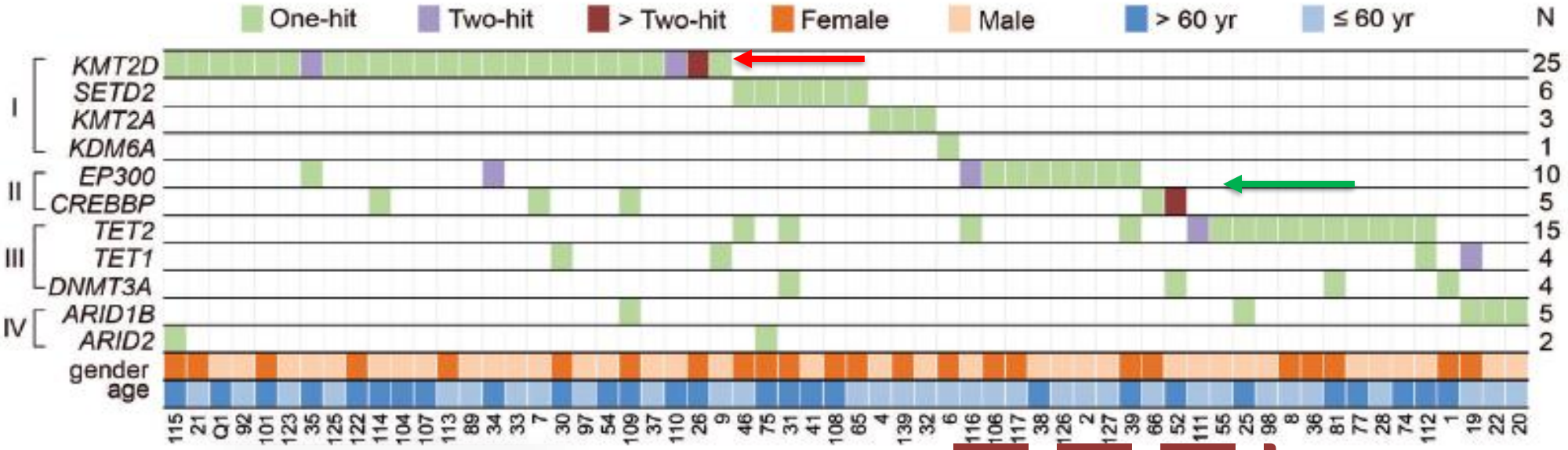
Dupuis J et al, ASH 2022 #959

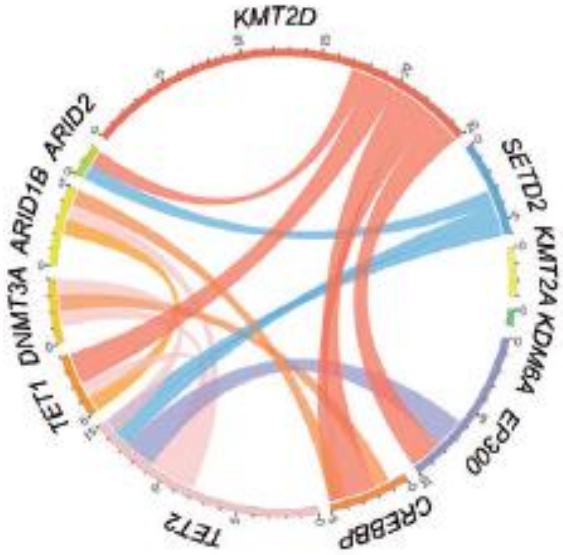
* Descriptive p value

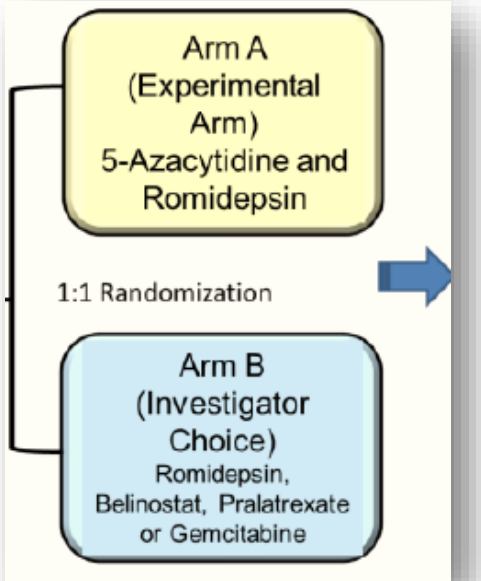
Histone modifier gene mutations in peripheral T-cell lymphoma, not otherwise specified.

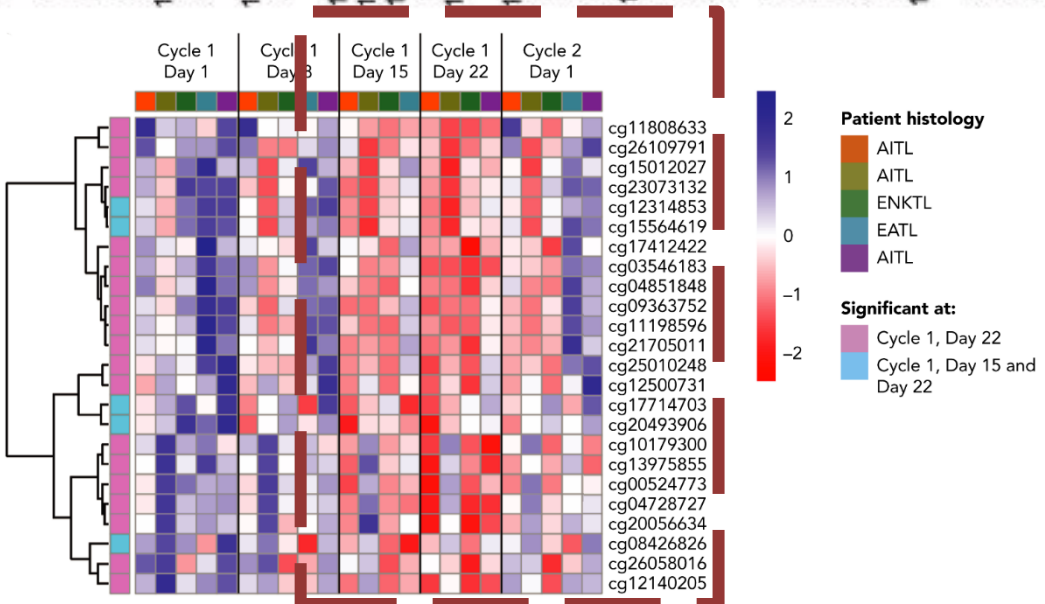
THE UNIVERSITY OF TEXAS MD Anderson Cancer Center
Making Cancer History®

- histone methylation
- histone acetylation
- DNA methylation
- chromatin remodeler









Ji MM et al. Haematologica 2018;103(4):679-687;

Emerging themes in T cell Lymphomas

THE UNIVERSITY OF TEXAS MD Anderson Cancer Center
Making Cancer History®

- Targeting dysregulated pathways: JAK/STAT, PI3K, EZH1/2, ITK

Golidocitinib: Study Design

THE UNIVERSITY OF TEXAS MD Anderson Cancer Center
Making Cancer History®

Key eligibility criteria

Patients with r/r PTCLs

- PTCLs diagnosed locally
- Had relapsed from or been refractory/intolerant to prior systemic therapy[1]
- Measurable disease
- Age ≥ 18 y (for Korean ≥ 19 y)
- ECOG PS ≤ 2
- Adequate bone marrow reserve and organ/system functions

Golidocitinib 150 mg QD[2]

1 cycle = 21 days

Tumor assessment

Day 1 of Cycle 3, and then every 3 cycles until disease progression or withdrawal from the study

Primary endpoint: IRC assessed ORR based on CT images per Lugano 2014 criteria

Secondary endpoints: other efficacy endpoints, e.g., IRC assessed CRR, DoR PFS and TTR, investigator assessed ORR, CRR, DoR, PFS, TTR and safety

1. Eligible patients must have relapsed from or been refractory/intolerant to prior systemic therapy(ies) for PTCLs and now require further treatment. In patients with CD30 positive ALCL, the prior systemic treatment should include CD30-targeted therapy (brentuximab vedotin).

2. Golidocitinib is administered orally at the recommended phase 2 dose (150 mg QD) on a 21-day dosing cycle until disease progression, intolerance or other discontinuation criteria are met.

Abbreviations: ALCL, anaplastic large-cell lymphoma; CD, cluster of differentiation; CT, computed tomography; CRR, complete response rate; DoR, duration of response; ECOG PS, Eastern Cooperative Oncology Group Performance Status; IRC, independent review committee; ORR, objective response rate; PFS, progression free survival; PTCL, peripheral T cell lymphoma; QD, once daily; r/r, relapsed/refractory; TTR, time to response.

Demographics and Baseline Characteristics

THE UNIVERSITY OF TEXAS MD Anderson Cancer Center
Making Cancer History®

Demographics & Characteristics	n = 104
Median age, y (range)	58 (20 - 78)
Female/Male, n (%)	37 (35.6)/67 (64.4)
ECOG PS, n (%)	
0/≥1	46 (44.2)/58 (55.8)
Median lines of prior systemic therapies (range)	2 (1 - 3)
Types of prior systemic therapies, n (%)	
Chemotherapy	104 (100.0)
Pralatrexate	1 (1.0)
Mitoxantrone liposome	3 (2.9)
HDAC inhibitor	50 (48.1)
Brentuximab vedotin	13 (12.5)
ALK inhibitor	1 (1.0)
Prior autologous HSCT, n (%)	2 (1.9)
Bone marrow involvement at baseline, n (%)	20 (19.2)
LDH elevation at baseline, n (%)	52 (50.0)

Demographics & Characteristics	n = 104
Histology subtypes by central review, n (%)	
PTCL, NOS	51 (49.0)
AITL	16 (15.4)
ALCL	11 (10.6)
NK/TCL	4 (3.8)
Others*	9 (8.7)
Central confirmed non-PTCL	4 (3.8)
Unable to confirm	9 (8.7)

Data cut-off date: August 31, 2023

- Between Feb 26, 2021 to Oct 12, 2022, a total of 104 subjects with r/r PTCLs were enrolled.
- All subjects received at least one dose of golidocitinib at 150 mg QD.

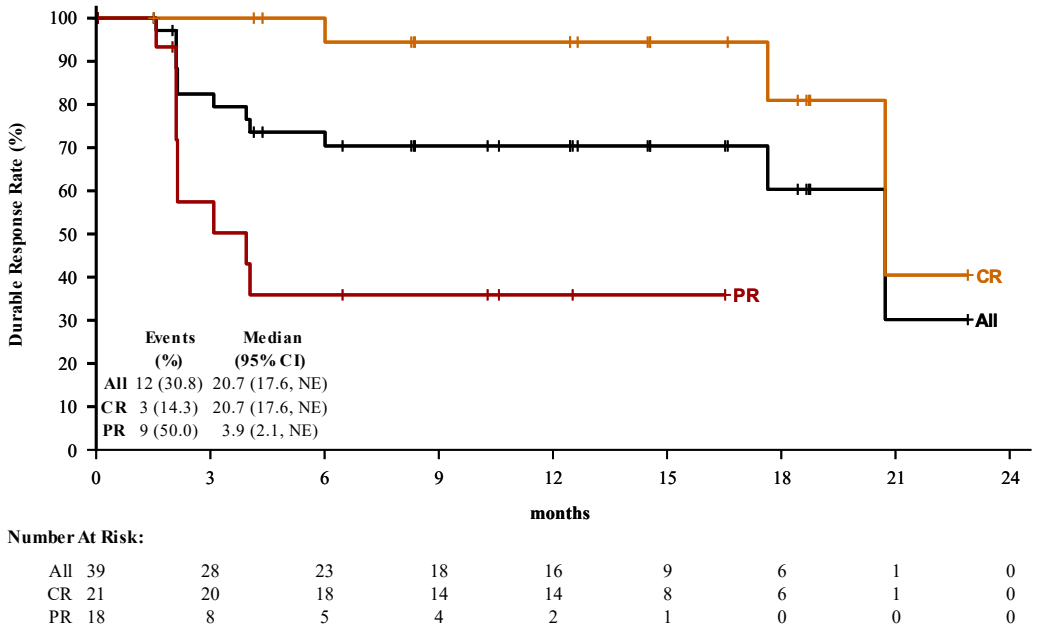
Note: * 'Others' including 1 centrally diagnosed as T cell prolymphocytic leukemia and 8 centrally diagnosed as PTCLs with unconfirmable histology subtypes.
Abbreviations: AITL, angioimmunoblastic T cell lymphoma; ALCL, anaplastic large-cell lymphoma; ALK, anaplastic lymphoma kinase; ECOG PS, Eastern Cooperative Oncology Group Performance Status; HDAC, histone deacetylase; HSCT, hematopoietic stem cell transplant; LDH, lactate dehydrogenase; NK/TCL, natural-killer/T cell lymphoma; PTCL, NOS, peripheral T cell lymphoma, not otherwise specified; r/r, relapsed/refractory; QD, once daily.

Tumor Response

THE UNIVERSITY OF TEXAS MD Anderson Cancer Center
Making Cancer History®

Tumor Response	n = 88	
	By IRC	By Investigator
ORR, n (%)	39 (44.3)	35 (39.8)
Overall response, n (%)		
Complete response	21 (23.9)	10 (11.4)
Partial response	18 (20.5)	25 (28.4)
Stable disease	17 (19.3)	15 (17.0)
Progressive disease	20 (22.7)	26 (29.5)
Not evaluable	12 (13.6)	12 (13.6)

DOR-IRC Assessment

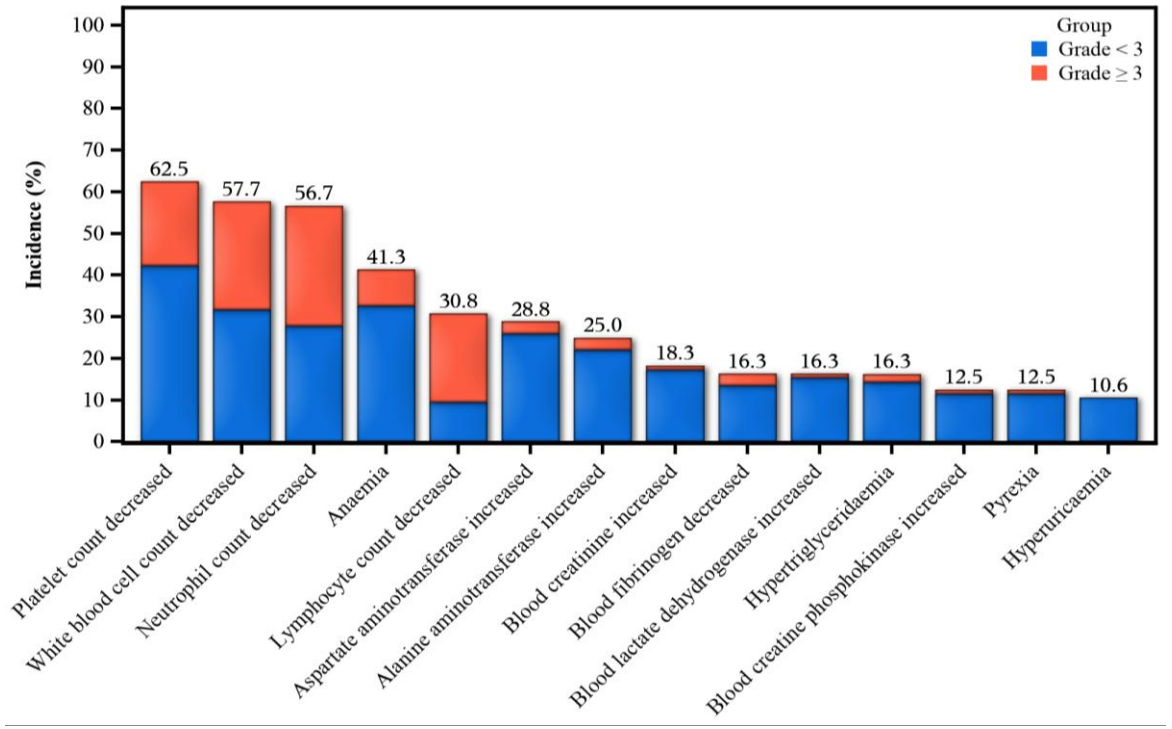


The following subjects were **not** included in the efficacy analysis set: 4 confirmed as non-PTCL by central pathology review, 9 not providing sufficient tumor tissue for central pathology confirmation, and 3 no baseline measurable lesions by IRC assessment.
Abbreviations: CR, complete response; IRC, independent review committee; ORR, objective response rate; PR, partial response; PTCL, peripheral T cell lymphoma.

Summary of Safety

THE UNIVERSITY OF TEXAS MD Anderson Cancer Center
Making Cancer History®

TRAE, n (%)	n = 104
Any TRAE	96 (92.3)
Any TRAE with Grade ≥ 3	62 (59.6)
Any TRSAE	25 (24.0)
Any TRAE leading to dose interruption	40 (38.5)
Any TRAE leading to dose reduction	8 (7.7)
Any TRAE leading to drug discontinuation	9 (8.7)
Any TRAE with fatal outcome	1 (1.0)



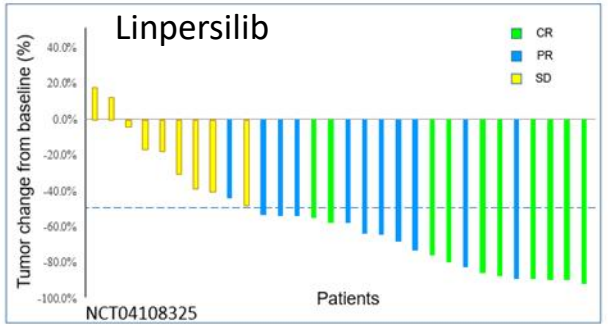
The most common (incidence > 10%) Grade 3+ TRAEs included platelet count decreased, white blood cell count decreased, neutrophil count decreased and lymphocyte count decreased.

Abbreviations: TRAE, treatment-related adverse event; TRSAE, treatment-related serious adverse event
Note: Adverse events were coded using MedDRA version 25.1. Adverse event grades were evaluated based on NCI-CTCAE Version 5.0.
TRAEs with incidence ≥ 10% were presented in the figure.

PI3K dependent pathway inhibition- Clinical studies in TCL

This project is aimed at identifying mechanisms of response and resistance to PI3K inhibitors in TCL and at developing hypothesis-driven therapeutic combination with Bcl2 inhibition to enhance their responses.

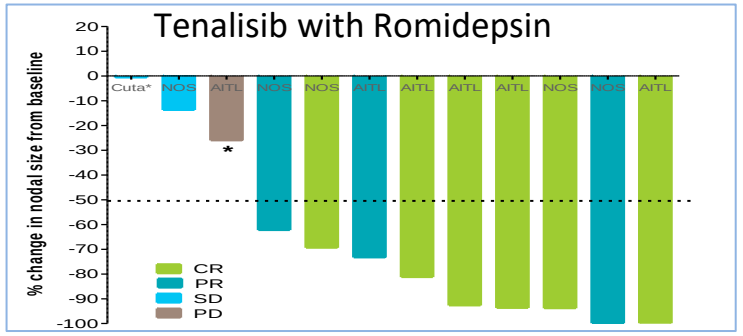
- PI3K/AKT/mTOR pathway hyperactivated in many T-cell lymphomas.
- GATA3+ TCL (45%), a poor-risk subset show significant enrichment of PI3K-associated pathway gene expression.
- Two PI3K inhibitors-Linpersilib (δ) & Tenalisib (δ and γ) have shown encouraging activity in r/r TCL as a single agent and in combinations.



N=38 patients enrolled, 30 evaluable

70% ORR
- **36.7% CR** (11 patients)
- **33.3% PR** (10 patients)
- 30% SD (9 patients)
- 0% PD (0 patients)

100% Disease control rate

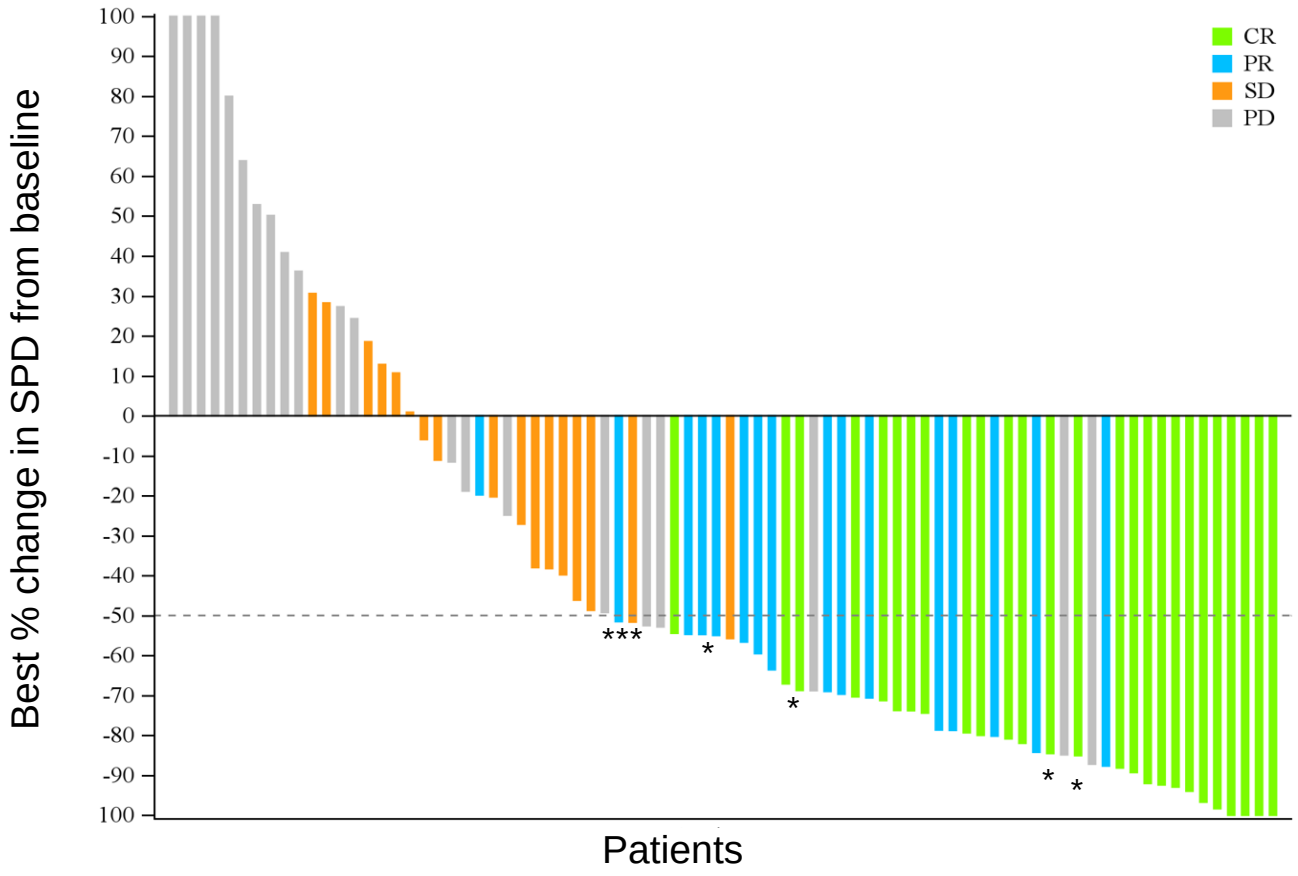


N=12 patients enrolled,
75% ORR
- **50% CR-** (6 patients)
- **25% PR-** (3 patients)
- 16.6% SD- (2 patients)
- 91.7% DCR- (11 patients)

PI3K DRUG	Dose	% in Urine	% in Feces
Linperlisib	80 mg, po	58	34
Idelalisib	25 mg, po	14	78
Duvelisib	150 mg, po	14	79
Copanlisib	12 mg, iv	22	64
Umbralisib	800 mg, po	3	81

- **There are three clinical studies completed with Linpersilib in r/r-PTCL.**

Linperlisib Efficacy



Response	n(%)
ORR, n(%)	42(48)
95% CI	(37, 59)
CR	**26(30)**
PR	16(18)
SD	18(21)
PD	21(24)
NE	7(8)
DCR, n(%)	60(68)
95% CI	(57, 78)

- FAS, n=88 patients
  - ✓ The study met the primary endpoint
  - ✓ CR 30%, PR 18%
- A disease control rate of 69% observed

* Five PD patients had new lesions appearing, even though target lesions met the response criteria

Best response AITL: ORR-65% and CR-48%

Song Y. ASH. 2023.

Phase II US & Europe: Efficacy Summary in Linperlisib

THE UNIVERSITY OF TEXAS MD Anderson Cancer Center
Making Cancer History®

	YY-20394-012 PTCL Phase 2 US & EU FAS N=35[b]	YY-20394-012 CTCL Phase 2 US & EU FAS N=10
	PTCL	CTCL
ORR	45.7 % (INV), N=16	40 % (INV), N=4
	Lugano 2014	Olsen 2011
CR	31.4 %	0 %
PR	14.3 %	40 %
SD	5.7%	40 %
DCR	51.4%	70 %
DOR Rate, % (95% CI)		
3 Month	78.6(47.2,92.5)	33.3(0.9,77.4)
6 Month	47.1(16.6,73.0)	33.3(0.9,77.4)
9 Month	47.1(16.6,73.0)	33.3(0.9,77.4)
PFS Rate, % (95% CI)		
3 Month	53.7(35.2,69.0)	85.7(33.4,97.9)
6 Month	40.4(23.5,56.8)	14.3(0.7,46.5)
9 Month	26.2(11.2,44.0)	14.3(0.7,46.5)

- Opened in August 2022
  - First trial to evaluate linperlisib-treated patients in the U.S. and E.U.
  - Stage 1, interim analysis for safety,
  - Stage 2, study completion N=36 pts
- r/r T-cell lymphomas having ≥1 prior therapy
  - All PTCL subtypes enrolling, PTCL-NOS, AITL, ALCL, NKT, EATL, MEITL and CD30+ brentuximab-progressing or intolerant.
  - There is a Central Lab confirmation of diagnosis in this study
  - CTCL patients are enrolling
- Dose schedules for 28-day cycles
  - 80 mg QD (RP2D) to progression
  - 80 mg QD for 4 cycles or until response, followed by 40 mg QD
- Primary endpoint is Overall Response Rate
- Principal Investigators: Dr. Swami Iyer (Study Chair), Dr.Pierluigi Zinzani, Dr.Ranjit Nair, Dr.Neha Mehta-Shah

[a] ≥6 months follow-up; INV: Investigator response assessment; IRC, Independent Review Committee
[b] 2 unevaluable patients included: One patient had initial CR on PTCL but was diagnosed with newly developed DLBCL by biopsy after Cycle 3.
[c] 12 month DOR rate (67.75%, 95%CI: 49.07%, 80.82%)
[d] 36 month OS rate (55.4%)

Iyer S. ASH. 2024, NCT05274997.

Safety

THE UNIVERSITY OF TEXAS MD Anderson Cancer Center
Making Cancer History®

Any Grade TRAEs, Preferred Term	(≥10%) n (%)
Neutropenia	58 (59)
Leukopenia	46 (47)
Thrombocytopenia	31 (32)
Anemia	24 (24)
Elevated ALT	23 (23)
Elevated AST	20 (20)
Pneumonia	20 (20)
Lymphocytopenia	17 (17)
Hypertriglyceridemia	15 (15)
Fever	15 (15)
Diarrhea	14 (14)
Elevated lipase	13 (13)
Hyperuricemia	13 (13)
Rash	13 (13)
Hypercholesterolemia	12 (12)
Hyponatremia	11 (11)
Elevated lactate dehydrogenase	10 (10)
Elevated creatinine	10 (10)

SAS = 98 patients

≥Grade 3 TRAE, Preferred Term	(≥5%) n (%)
Neutropenia	31 (32)
Pneumonia	14 (14)
Leukopenia	10 (10)
Anemia	6 (6)
Thrombocytopenia	5 (5)
Upper respiratory tract infection	5 (5)
Lymphocytopenia	5 (5)

- TRAEs were observed in 94 pts (95.9%)
- The most frequent ≥Grade 3 TRAE were **neutropenia, pneumonia and leukopenia;**
- ***Immune-related ≥Grade 3 TRAEs as elevated ALT,AST, diarrhea, colitis, rash were observed at <5%;***
- The most frequent drug-related SAE was pneumonia (11%);
- Twenty-two pts (22.4%) had dose reductions, and 9 pts (9.2%) discontinued from the study due to AEs.

Song Y. ASH. 2023.

Safety

THE UNIVERSITY OF TEXAS MD Anderson Cancer Center
Making Cancer History®

TEAE , All Grades	n (%)
All Grades TEAE occurring at ≥10%	43(95.6)
Rash maculo-papular	10(22.2)
Diarrhoea	10(22.2)
Pneumonia	7(15.6)
Anaemia	7(15.6)
Fatigue	7(15.6)
Pyrexia	7(15.6)
Neutropenia	6(13.3)
Cough	6(13.3)
Oedema peripheral	5(11.1)
Rash	5(11.1)
Cytomegalovirus infection	5(11.1)
Thrombocytopenia	5(11.1)
TEAE ≥Grade3	**n (%)**
Any TEAE ≥Grade3 and occurring at ≥10%	24 (53.3)
Neutropenia	6 (13.3)
Pneumonia	5 (11.1)

TRAE, All Grades	n (%)
All Grades TRAE occurring at ≥5%	25(55.6)
Neutropenia	5(11.1)
Thrombocytopenia	4(8.9)
Anaemia	3(6.7)
Cytomegalovirus infection	3(6.7)
Rash	3(6.7)
Diarrhoea	4(8.9)
Hypertriglyceridaemia	3(6.7)
TRAE ≥Grade3	**n (%)**
Any TRAE ≥Grade3 and occurring at ≥3%	13 (28.9)
Neutropenia	5 (11.1)
Pneumonia	2 (4.4)
Rash	2 (4.4)

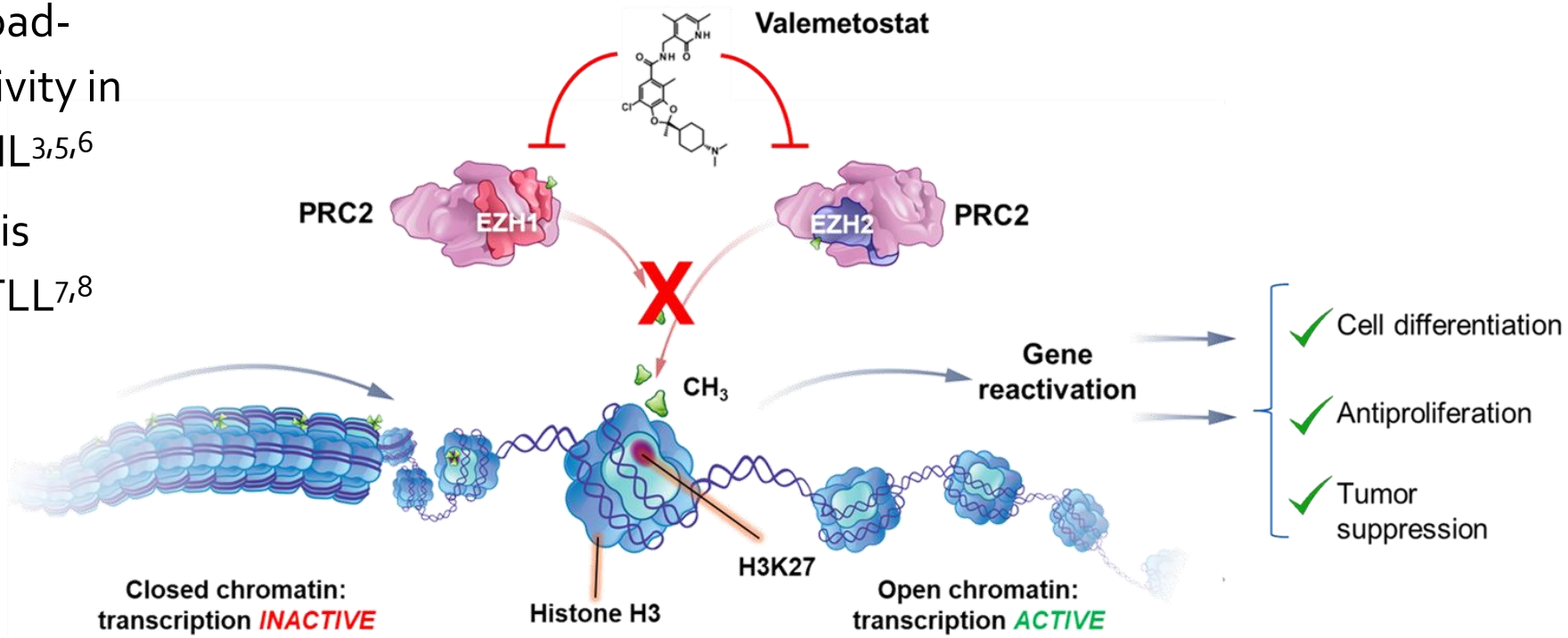
Serious adverse events occurred in 42.2% of patients, with serious treatment-related adverse events in 8.9%. No treatment-related deaths were observed

- *Few immune-mediated, GI, and liver tox AEs*
- *Low discontinuation rate due to AE (1/45 pt/ 2.2%)*

Iyer S. ASH. 2024, NCT05274997.

Valemetostat

- EZH2 and EZH1 catalyze the trimethylation of histone H3 at lysine 27 (H3K27me3), leading to transcriptional repression[1,2]
- Valemetostat tosylate (valemetostat) is a novel, potent, and selective dual inhibitor of EZH2 and EZH1 that suppresses aberrant H3K27me3, thereby promoting antitumorigenic processes[2-4]
  - Valemetostat shows broad-spectrum antitumor activity in preclinical models of NHL[3,5,6]
- Valemetostat monotherapy is approved in Japan for R/R ATLL[7,8]



Zinzani PL, et al…VALENTINE-PTCL01. Lancet Oncol. 2024

Baseline Demographics and Disease Characteristics

THE UNIVERSITY OF TEXAS MD Anderson Cancer Center
Making Cancer History®

Characteristic	PTCL (N = 133)
Median age, years (range)	69.0 (22–85)
Sex, n (%)	
Male	91 (68.4)
Female	42 (31.6)
ECOG PS score, n (%)	
0	58 (43.6)
1	65 (48.9)
2	9 (6.8)
3	1 (0.8)
Median prior lines of therapy (range)	2.0 (1–12)
1	36 (27.1)
2	36 (27.1)
3	29 (21.8)
≥ 4	32 (24.1)
Prior HCT, n (%)	35 (26.3)
Autologous	32 (24.1)
Allogeneic	5 (3.8)

PTCL subtypes, n (%) (WHO 2016 classification; central review)	PTCL (N = 133)
TFH phenotype	
AITL	42 (31.6)
Nodal PTCL with TFH phenotype	8 (6.0)
FTL	3 (2.3)
PTCL-NOS	41 (30.8)
ALCL	
ALK^{+}	7 (5.3)
ALK^{-}	2 (1.5)
MEITL	1 (0.8)
CD8^{+} PCAECTCL	1 (0.8)
PCGTL	1 (0.8)
Other TCL[a]	13 (9.8)
Non-TCL or undetermined[b]	6 (4.5)
Missing[c]	8 (6.0)

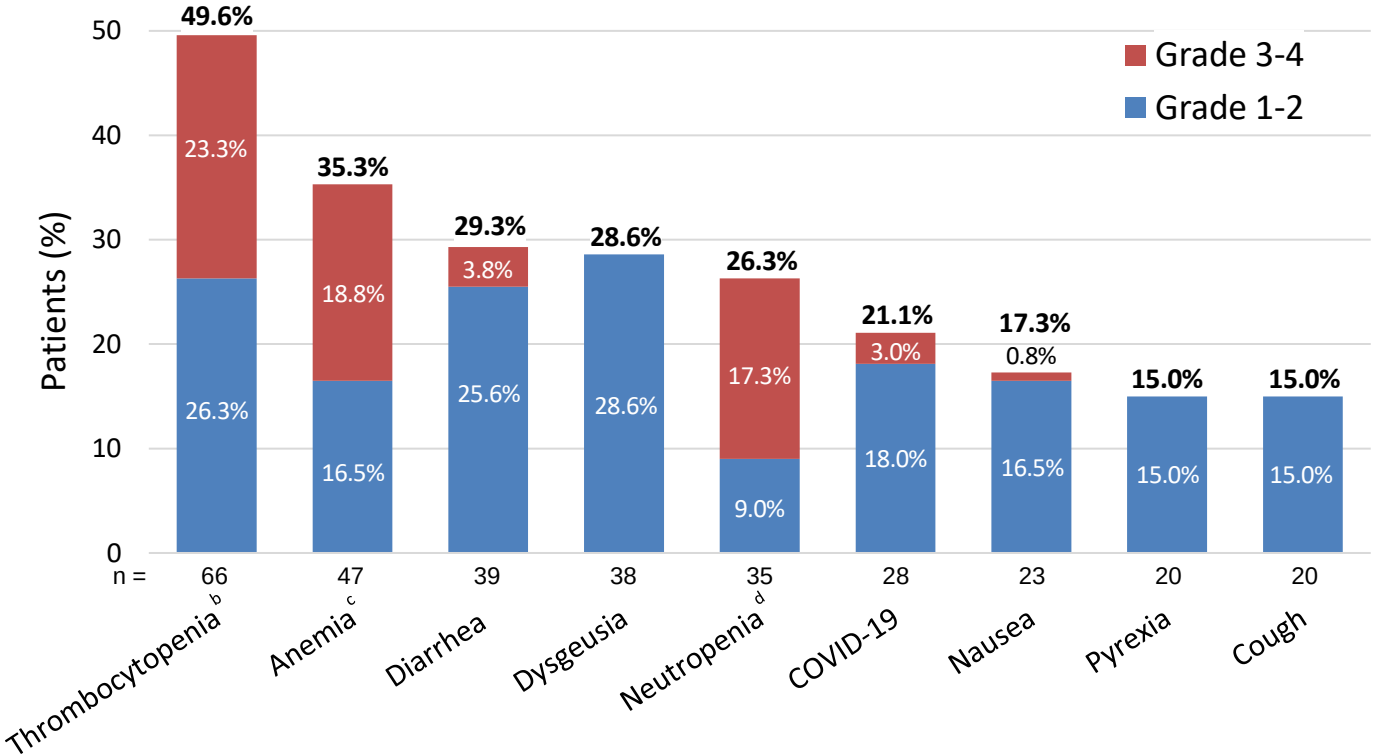
Efficacy analysis set

Zinzani PL, et al…VALENTINE-PTCL01. Lancet Oncol. 2024

Common TEAEs (Occurring in ≥ 15% of Patients) and Dose Modifications

THE UNIVERSITY OF TEXAS MD Anderson Cancer Center
Making Cancer History®

- Cytopenias were common, and were manageable with dose modifications and/or supportive therapies such as transfusions and G-CSF
  - Thrombocytopenia was the most frequent any grade (49.6%) and grade ≥ 3 (23.3%) TEAE
  - The median time to first onset of platelet count < 50×10^9/L was 18 days from the first dose and the median time to recovery was 12 days
- 2 patients developed secondary AML and discontinued treatment



TEAEs leading to dose modifications[a] (N = 133)

Preferred term	Treatment discontinuation %	Dose reduction %	Dose interruption %
Any TEAE	**9.8**	**15.8**	**49.6**
Thrombocyt[b]	2.3	5.3	16.5
Anemia[c]	0	3.8	9.8
COVID-19	0	1.5	8.3
Neutropenia[d]	0	2.3	5.3

Zinzani PL, et al…VALENTINE-PTCL01. Lancet Oncol. 2024

Clinical Response (BICR Assessment)

THE UNIVERSITY OF TEXAS MD Anderson Cancer Center
Making Cancer History®

CT–based assessment

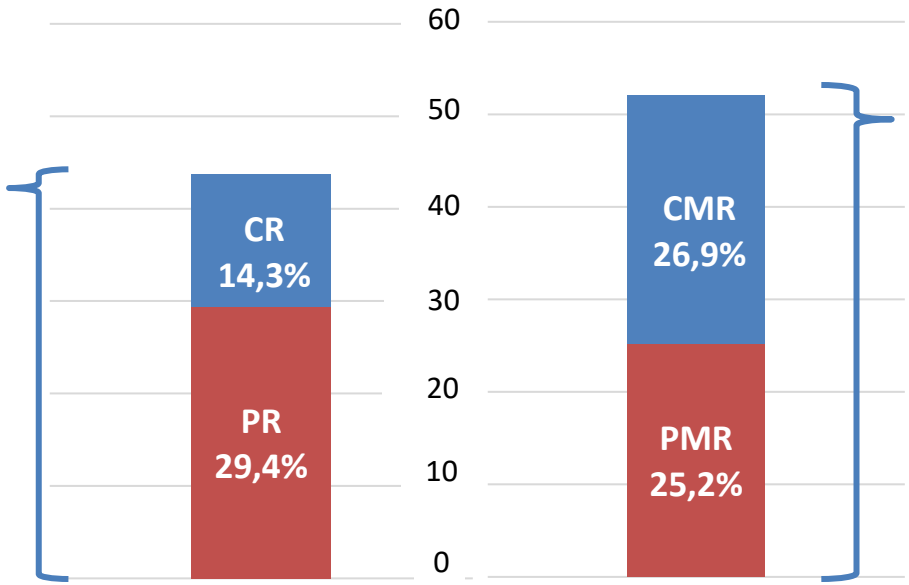
(Primary endpoint)

ORR was **43.7**%
(n = 52; 95% CI, 34.6–53.1)

17 patients **(14.3%)** achieved a **CR**

35 patients **(29.4%)** achieved a **PR**

Efficacy-evaluable population (N = 119)



PET-CT–based assessment

(Exploratory endpoint)

ORR was **52.1%**
(n = 62; 95% CI, 42.8–61.3)

32 patients **(26.9%)** achieved a **CMR**

30 patients **(25.2%)** achieved a **PMR**

- Ten (8.4%) patients treated with valemetostat proceeded to allo-HCT, including 8 patients (6.7%) with a CR[a] and 2 patients with an unknown response
  - The median time from first dose of valemetostat to subsequent allo-HCT was 6.9 months

Zinzani PL, et al…VALENTINE-PTCL01. Lancet Oncol. 2024

SOQUELITINIB: Phase 1 Subject Enrollment and Patient Characteristics

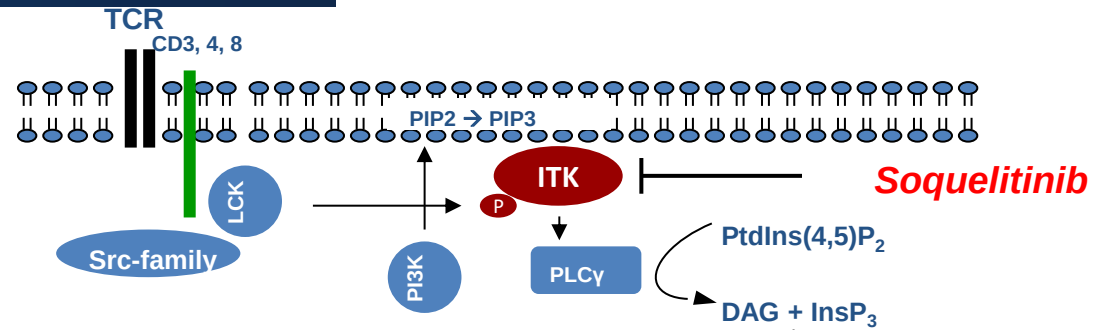
THE UNIVERSITY OF TEXAS MD Anderson Cancer Center
Making Cancer History®

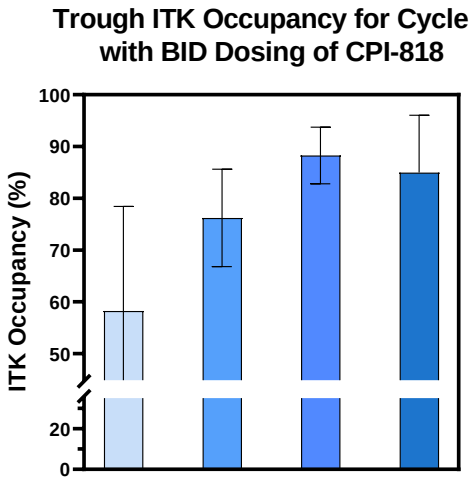
Enrollment in US, AUS, KOR and China (n=60)

31 patients enrolled at 200 mg BID

Patient Characteristics	100 mg (N=4)	200 mg (N=31)	400 mg (N=9)	600 mg (N=16)
Age (yrs.), median (range)	51 (29, 75)	60 (29, 81)	69.0 (41, 80)	63.5 (34, 84)
Gender, male N (%)	3 (75)	14 (45.2)	6 (66.7)	8 (50)
No. of prior therapies, median (range)	3.5 (2, 4)	3 (1,18)	5 (2, 15)	5 (1, 9)
Histologies				
PTCL-NOS	1	13	2	9
AITL	1	4	2	0
ALCL	1	3	0	0
CTCL Sezary	0	2	4	1
CTCL Mycoses	0	5	1	5
Other	1	4	0	1

Data: 18 May 2023

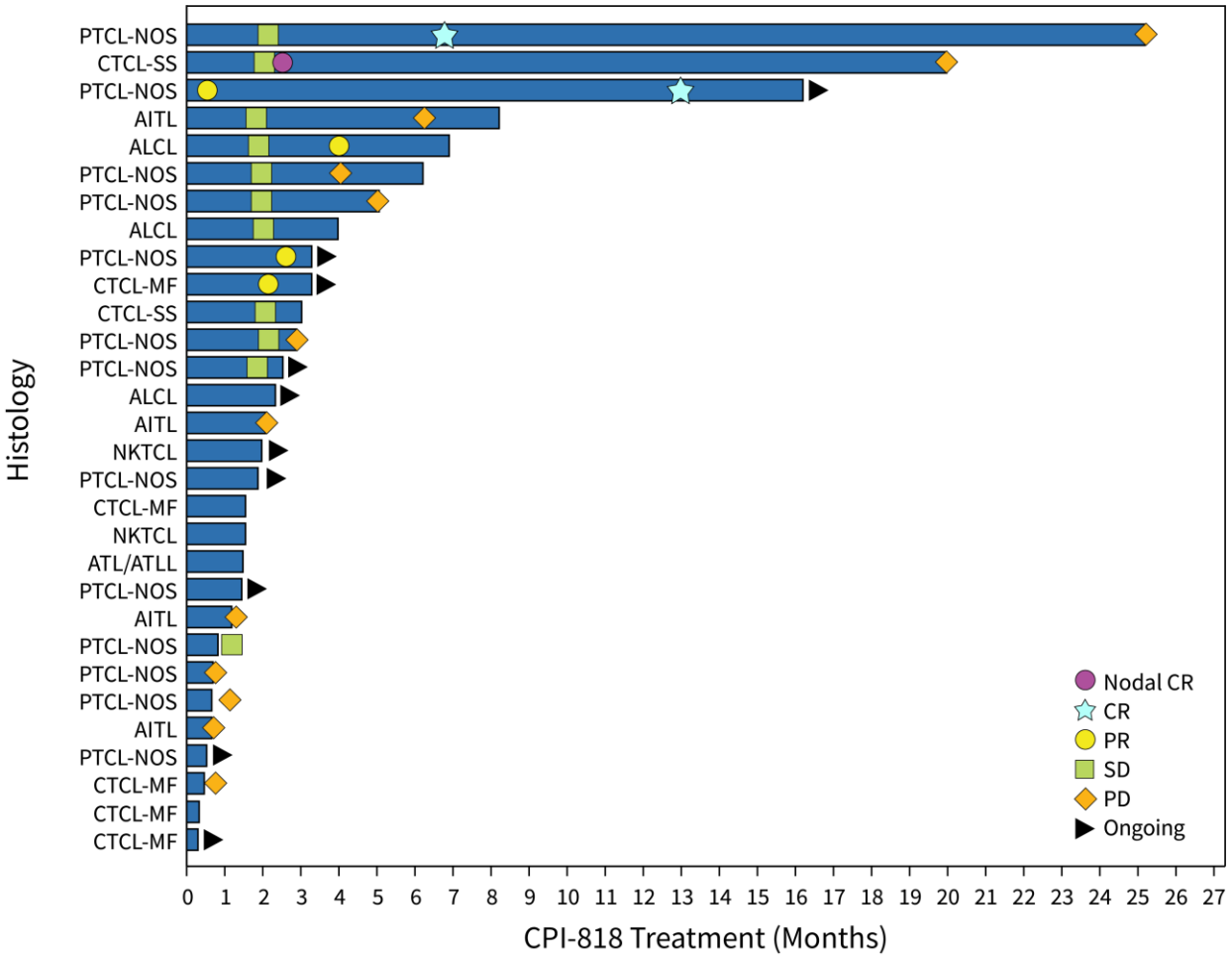


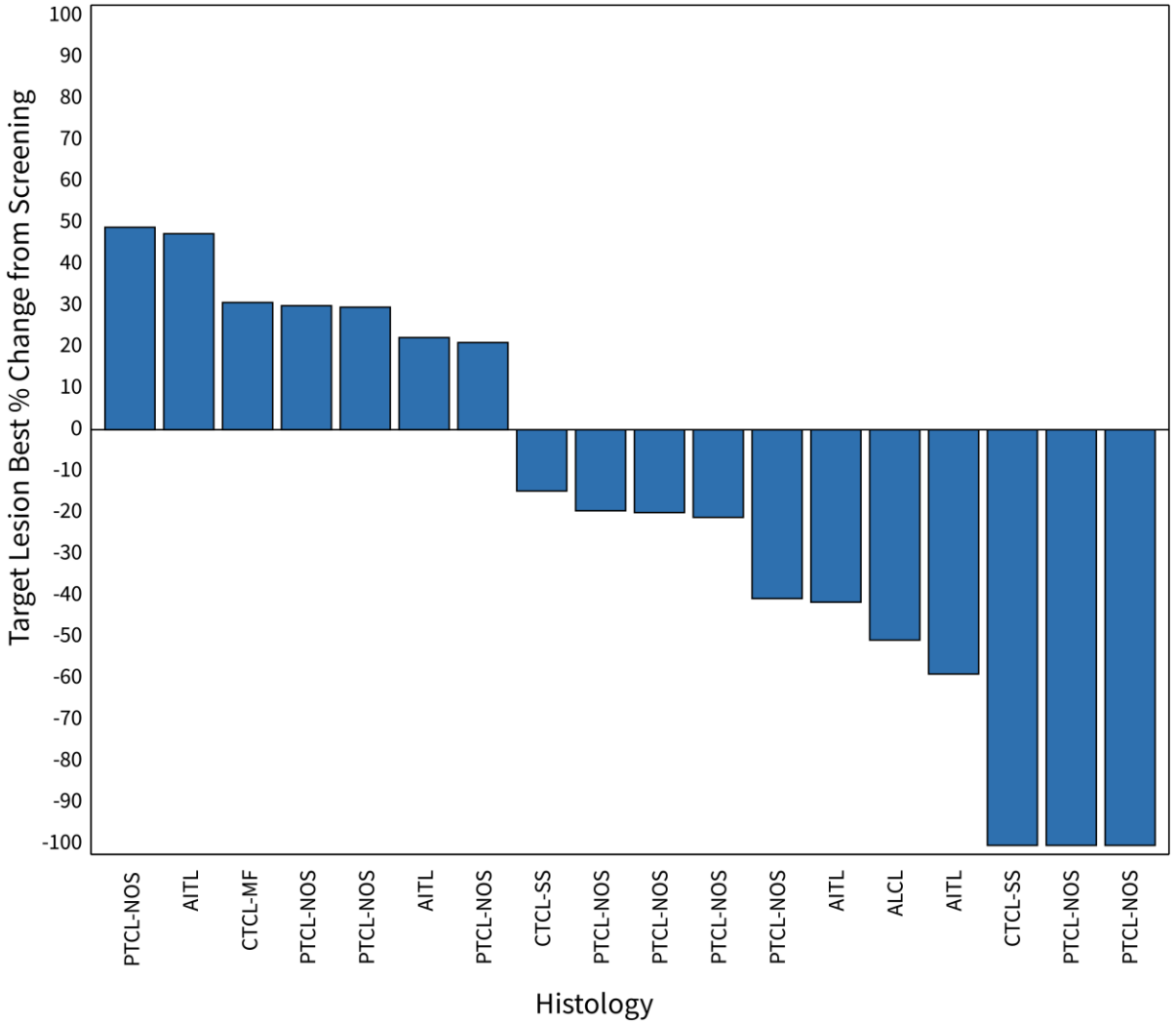


- Good occupancy achieved at 200 mg BID and beyond
- Excellent correlation between PBMC and tissue occupancy in both LN core and skin punch samples
- Conclusion: Occupancy in PBMCs = Occupancy in Lymph nodes = Occupancy in Skin

Clinical Results in Optimum Dose Cohort

THE UNIVERSITY OF TEXAS MD Anderson Cancer Center
Making Cancer History®

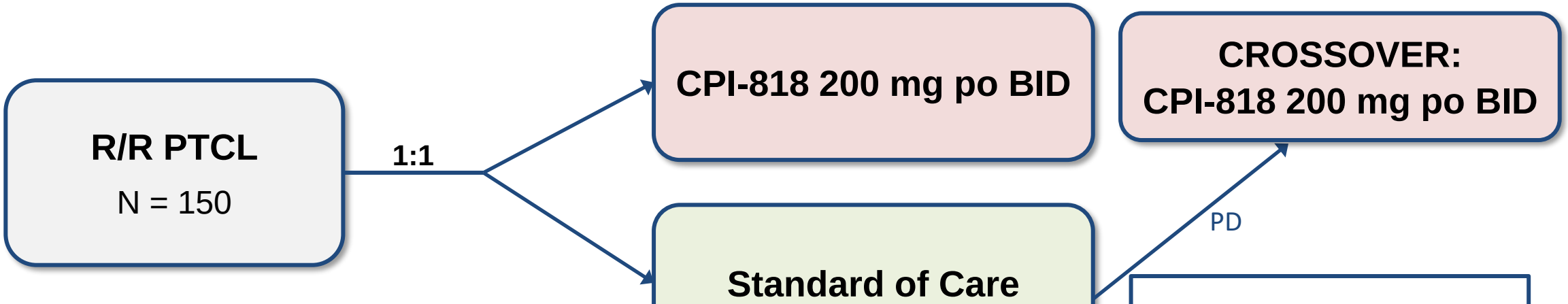




Data: 18 May 2023

Randomized Phase 3 Trial

THE UNIVERSITY OF TEXAS MD Anderson Cancer Center
Making Cancer History®



Eligibility

- >1 and ≤3 prior therapies
- PTCL-NOS, ALCL, AITL, FHTCL-NOS, or FHTCL-Follicular

Endpoints

- Primary: PFS
- Secondary:
  - ORR
  - OS
  - DOR

Emerging themes in T cell Lymphomas

THE UNIVERSITY OF TEXAS MD Anderson Cancer Center
Making Cancer History®

- Epigenetic targeting of Tfh
- Targeting dysregulated pathways: JAK/STAT, PI3K, EZH1/2
- Targeting cytotoxic, gamma-delta and NK subtypes
- Immunotherapy: checkpoint blockade and cellular

Cytotoxic lymphomas are rare and have a high unmet need

THE UNIVERSITY OF TEXAS MD Anderson Cancer Center
Making Cancer History®

Cytotoxic Lymphoma Histologies

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

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

- Cytotoxic lymphomas (CTLs) are a group of rare lymphoma subtypes that is driven by CD94 expressing cytotoxic cells of origin
- CTLs account for ~25-40% of NK/T-cell lymphomas (or 3-6% of NHL)
- No standard of care has been established for patients with CTL and few are represented on randomized studies
- Outcomes in R/R PTCL patients are poor with mOS < 6 months, and worse outcomes in R/R ENKTL patients with an mOS of ~3 months[1]
- Therefore, there is a high unmet need for patients with CTLs and safe and effective therapies are needed

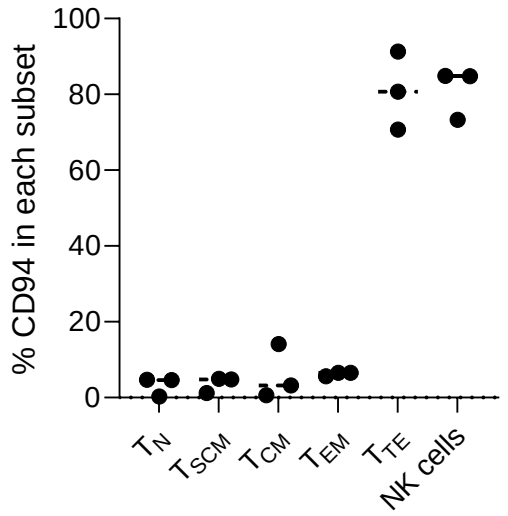
[1]Bellei M et al. *Haematologica* 2018.

DR-01 is Novel Targeted Antibody against CD94

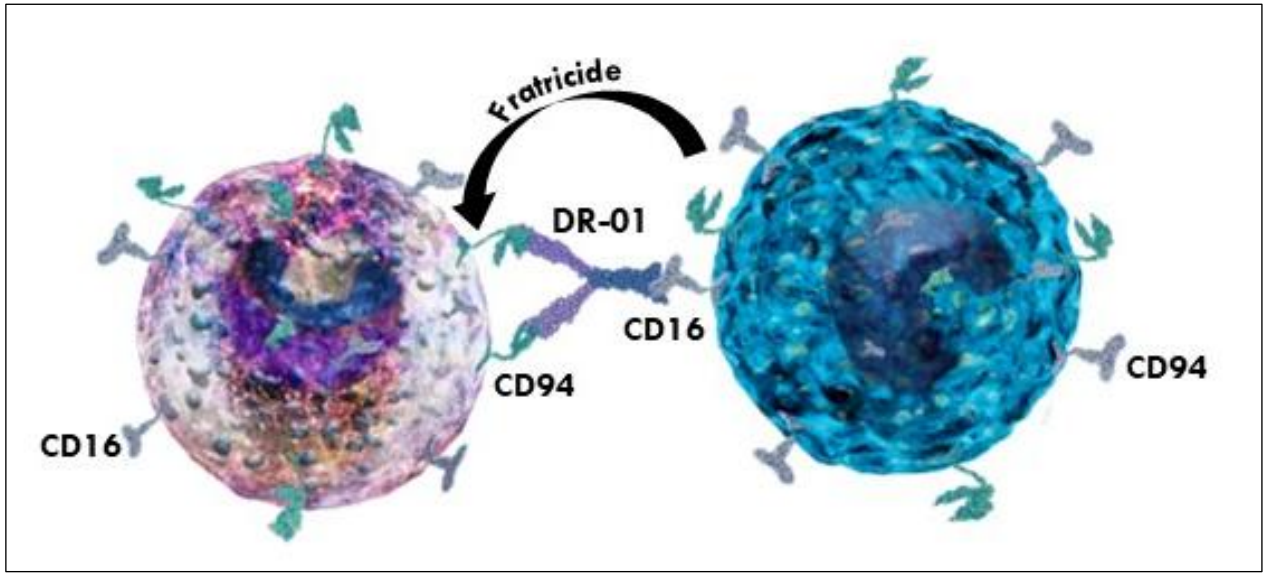
THE UNIVERSITY OF TEXAS MD Anderson Cancer Center
Making Cancer History®

- DR-01 is a non-fucosylated human IgG antibody against CD94 that is selectively expressed on terminally differentiated as well as malignant cytotoxic T cells and NK cells
- Since CD94 is expressed on target and effector cells and engages Fc-gamma receptors, such as CD16a, DR-01 triggers antibody-dependent cellular cytotoxicity (ADCC), by effector cells or fratricide, resulting in rapid target cell depletion

CD94 expression on CD8 T cell subsets in healthy donor PBMCs



N = Naïve
SCM = Stem cell memory
CM = Central memory
EM = Effector memory
TE = Terminal effector
NK = Natural Killer



Target Cell Effector Cell

Zain J, Iyer S et al. Abstract 980: DR-01 in R/R Cytotoxic Lymphomas

Baseline Characteristics for CTL Patients on Dose Escalation (Part A)

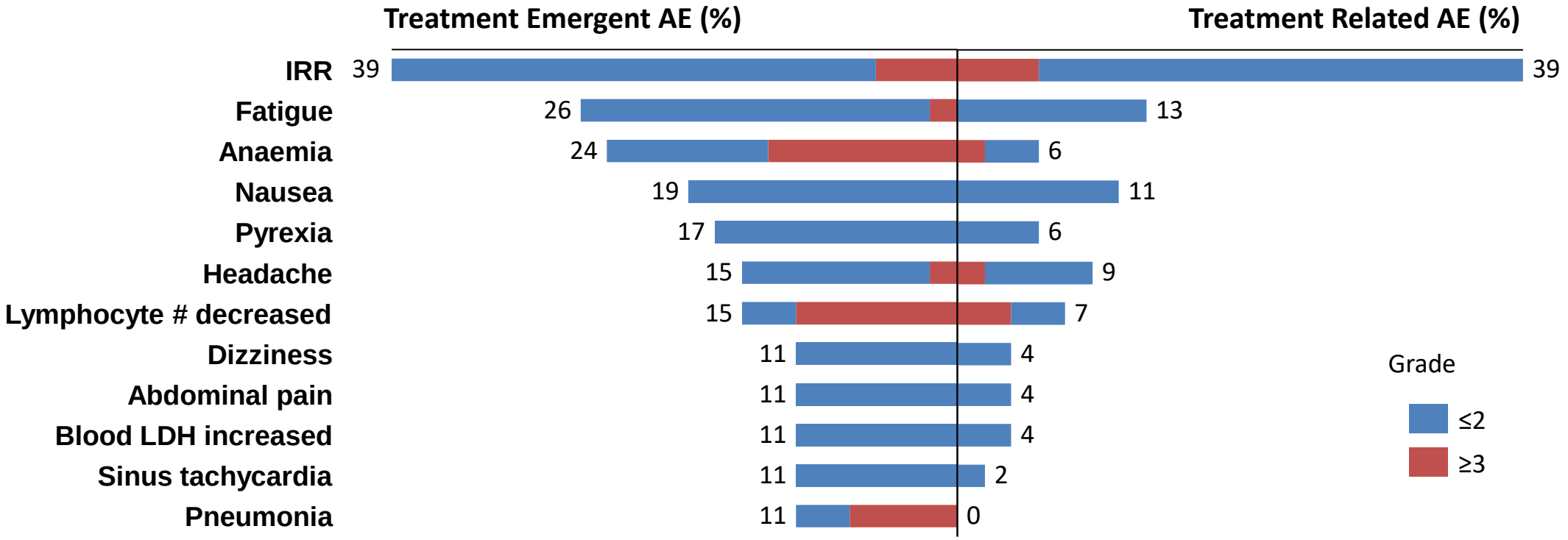
THE UNIVERSITY OF TEXAS MD Anderson Cancer Center
Making Cancer History®

	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 (%)						
PCγδTCL	0	2 (28.6)	0	2 (40)	2 (66.7)	6 (28.6)
ET-CTCL	1 (100)	0	1 (20)	0	0	2 (9.5)
HSTCL	0	0	0	0	1 (33.3)	1 (4.8)
SPTCL	0	1 (14.3)	0	0	0	1 (4.8)
ENKTL	0	1 (14.3)	1 (20)	0	0	2 (9.5)
MEITL	0	0	1 (20)	1 (20)	0	2 (9.5)
PTCL-NOS & Other*	0	3 (42.9)	2 (40)	2 (40)	0	7 (33.3)
Median Prior LoT (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)	1 (20)	2 (40)	2 (66.7)	10 (47.6)
Intolerance	0	0	1 (20)	2 (40)	0	3 (14.3)
Prior autologous or allogeneic HSCT, n(%)	0	1 (14.3)	3 (60)	0	0	4 (19)

*Other includes malignant cells expressing CD8 or CD56 and at least 1 cytotoxic marker (TIA-1, granzyme B, perforin)
HSCT: hematopoietic stem cell transplant; LoT: line of therapy

Most Common Adverse Events in Safety Evaluable Patients (TEAE > 10%)

THE UNIVERSITY OF TEXAS MD Anderson Cancer Center
Making Cancer History®



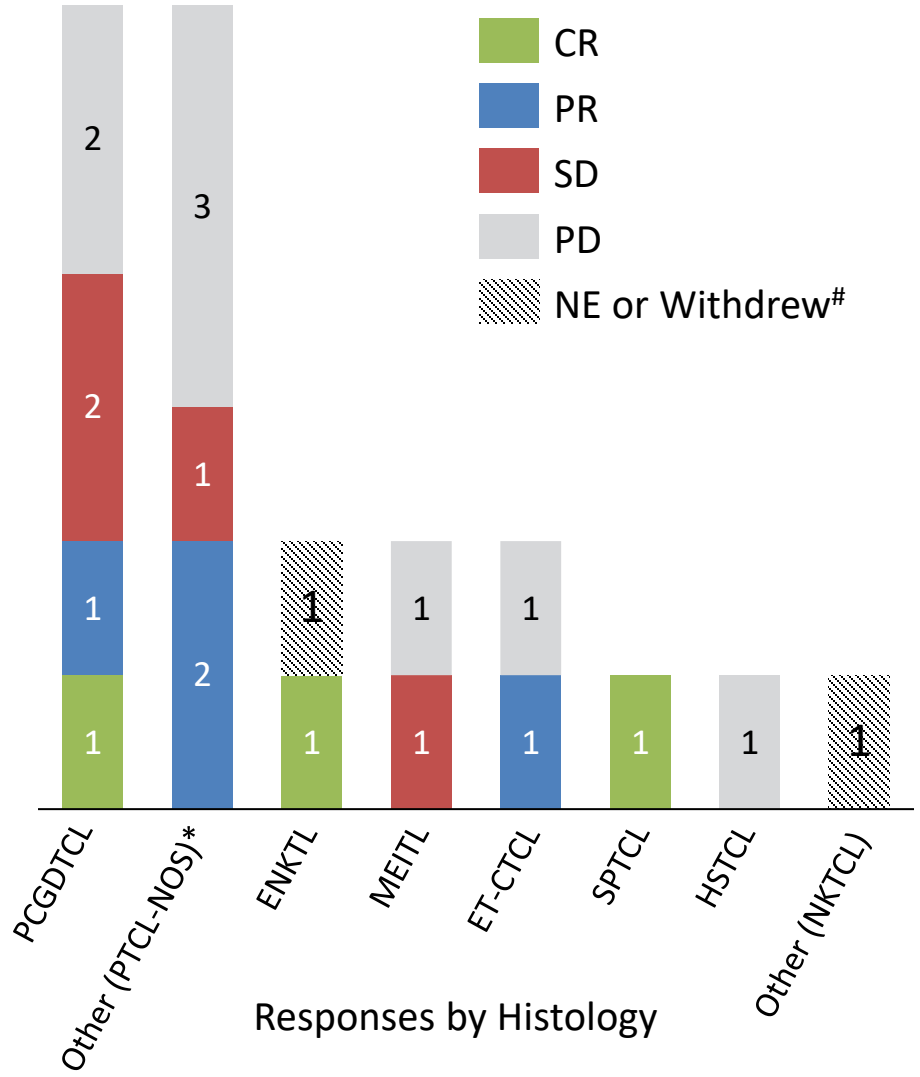
- No DLTs were reported during dose escalation and the MTD was not reached
- Infusion-related reactions (IRR) were the most common TEAE
  - Majority of IRR events were grade 1-2 and all events were manageable with mitigation strategies including standard pre-medications and splitting the initial dose
- Only 2/54 (4%) reported AEs of viral reactivation (< Grade 3). Patients able to continue study treatment

Zain J, Iyer S et al. Abstract 980: DR-01 in R/R Cytotoxic Lymphomas

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

THE UNIVERSITY OF TEXAS MD Anderson Cancer Center
Making Cancer History®

	Dose Level (mg/kg)					
	0.3 (N=1)	1 (N=6)	3 (N=4)	6 (N=5)	10 (N=3)	Total (N=19)#
ORR, n (%)	0	4 (67)	1 (25)	2 (40)	9	7 (37)
CR	0	3 (50)	0	0	0	3 (16)
PR	0	1 (17)	1 (25)	2 (40)	0	4 (21)
SD	0	0	1 (25)	2 (40)	1 (33)	4 (21)
PD	1 (100)	2 (33)	2 (50)	1 (20)	2 (67)	8 (42)



One unrelated AE withdrawal and one PI withdrawal without assessment
*Includes cutaneous subtypes

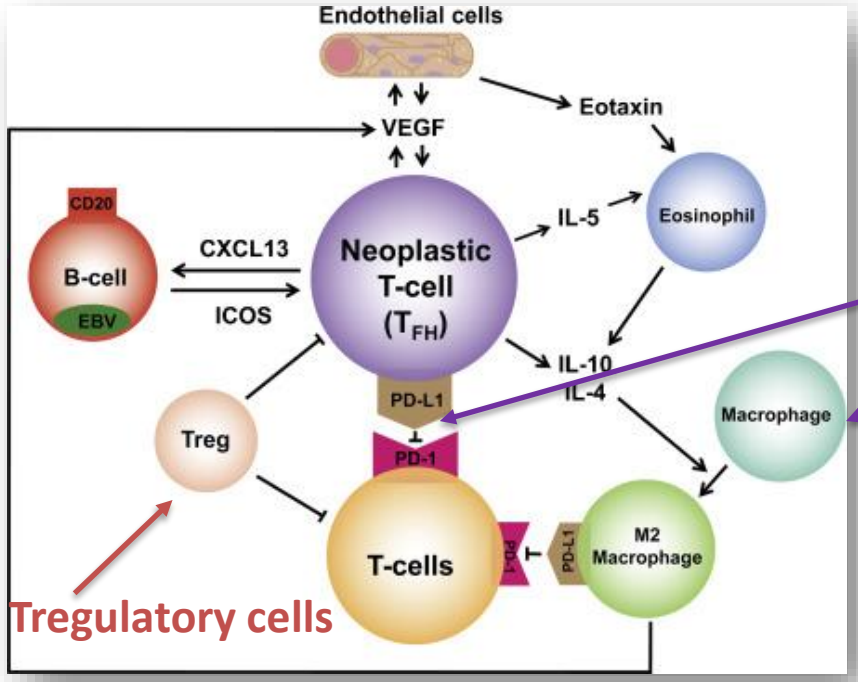
Emerging themes in T cell Lymphomas

THE UNIVERSITY OF TEXAS MD Anderson Cancer Center
Making Cancer History®

- Epigenetic targeting of Tfh
- Targeting dysregulated pathways: JAK/STAT, PI3K, EZH1/2
- Targeting cytotoxic, gamma-delta and NK subtypes
- Immunotherapy: checkpoint blockade and cellular

Role of Tumor microenvironment in PTCL- ALCL

THE UNIVERSITY OF TEXAS MD Anderson Cancer Center
Making Cancer History®

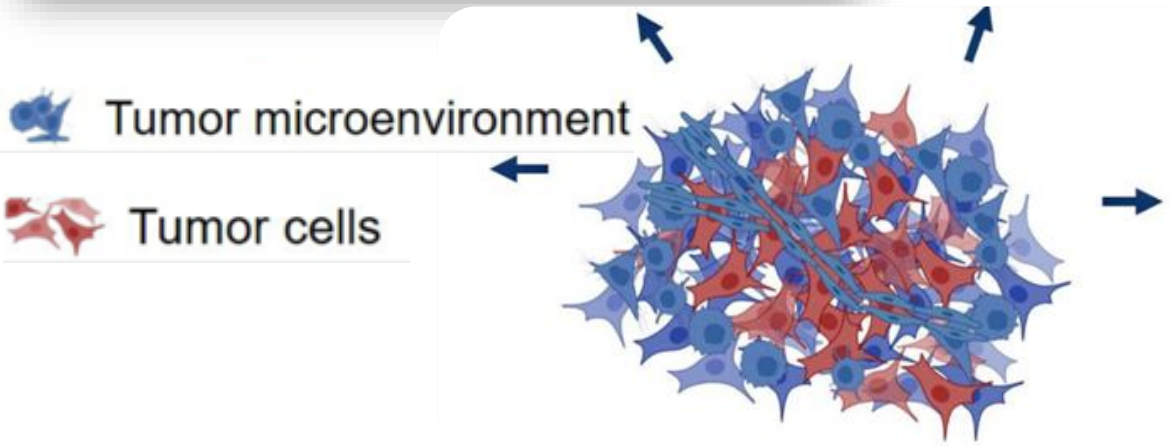


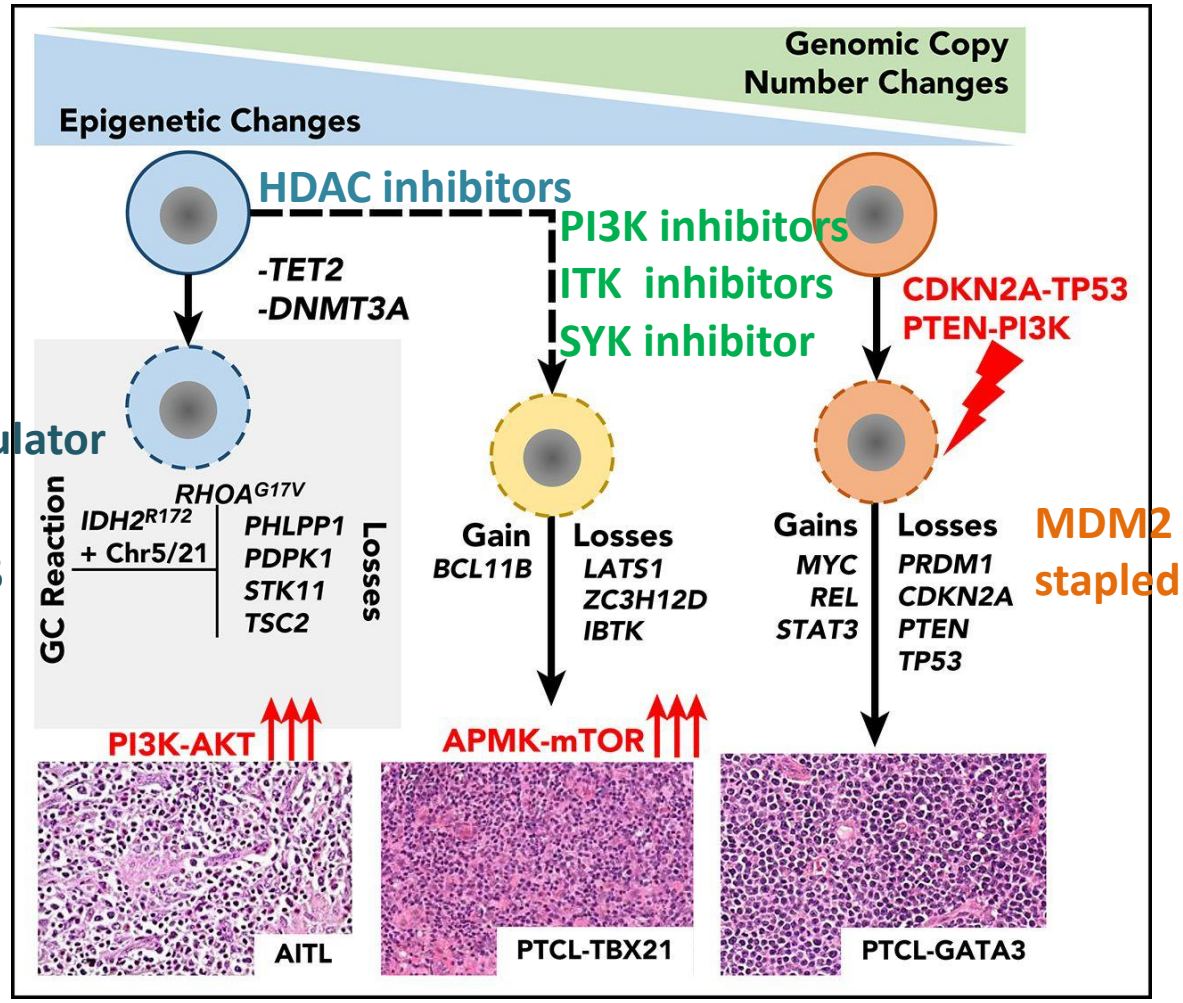
Checkpoint inhibitors: Anti-PD1, antiCD47/SIRα

Immune modulator

IDH2

OXPHOS





Tse E and Kwong YL, Seminars in Cancer Biology (2015), 34:46, Mhaidly et al. Oncogenesis (2020) 9:73, Crescenzo et al., Cancer Cell, (2015) 27:516.

Pembrolizumab and Romidepsin in r/r PTCL: Study Design

THE UNIVERSITY OF TEXAS MD Anderson Cancer Center
Making Cancer History®

Key Eligibility Criteria

- Pathologically confirmed T-cell lymphoma
- Disease status as defined as relapsed after or refractory to at least one systemic therapy.
- No prior PD1 inhibitors or allogeneic Stem cell transplantation.
- No discontinuation due to prior HDAC inhibitors
- ECOG PS ≤ 2

Lead in Phase I

Cohort
Pembrolizumab 200mg IV D1 and Romidepsin (14 mg/m^2 IV on Days 1 and 8, of every 21 day cycle)

R/R CTCL (n=3-6)

Phase I: Escalation Phase

Cohort
Pembrolizumab 200mg IV D1 and Romidepsin (14 mg/m^2 IV on Days 1 and 8, of every 21 day cycle)

R/R PTCL (n=12)

Phase II: Expansion Phase

- Response assessed at C4D1, C7D1 and every 3 months and as clinically indicated.
- Assessments per Lugano classification (Cheson 2014)
- PDL1 by IHC, COO for PTCL

Primary end points: Safety, tolerability and ORR
Secondary end points: CRR, PFS, OS and DoR

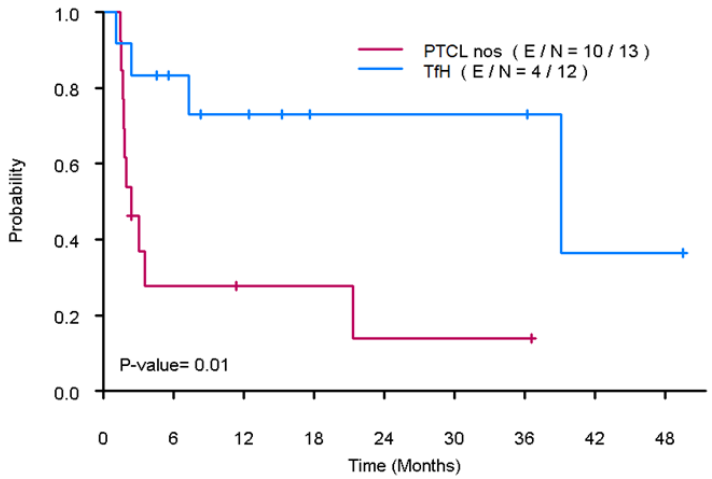
AEs monitored and graded according to the NCI Common Terminology Criteria for Adverse Events version 4.0 guidelines

Investigator-initiated trial of pembrolizumab + romidepsin (HDACi) in r/r PTCL pts

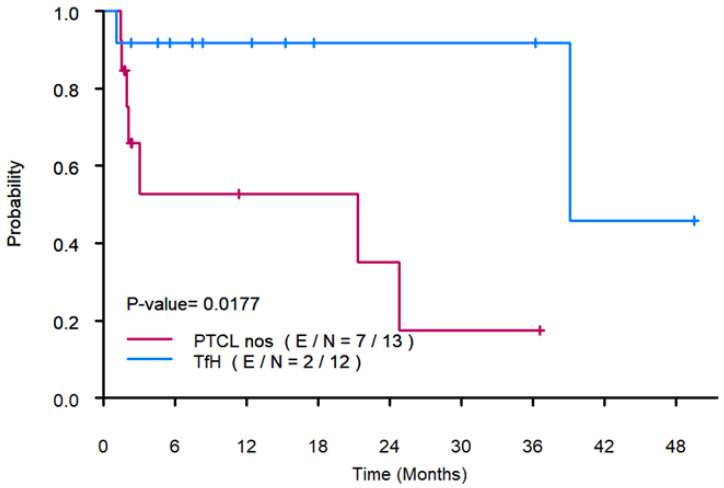
THE UNIVERSITY OF TEXAS MD Anderson Cancer Center
Making Cancer History®

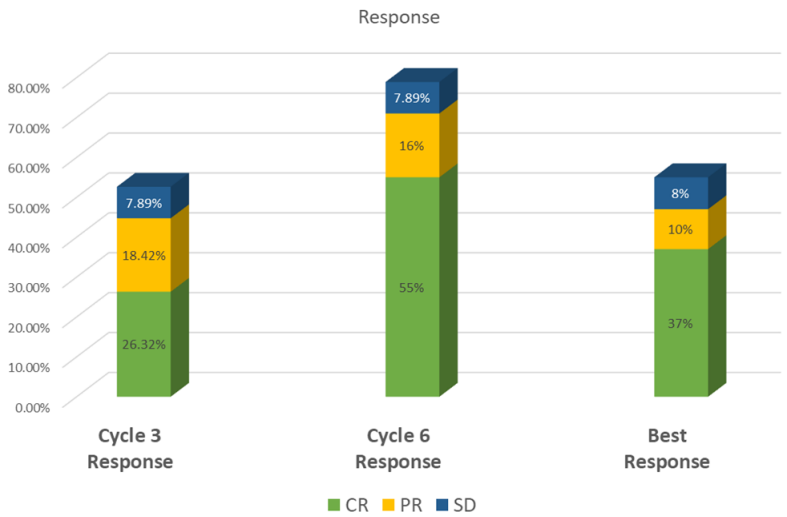
Results	TCL (n=38)
Disease status, n (%)	Relapse: 7 (18.4) Refractory: **31 (81.6)**
PD-L1 by IHC (IQR 0-30, max 95) <7.5 ≥7.5	n=32 16 (50) 16 (50)
Histologic classification, n (%) Nodal TfH PTCL ALCL ALK+ ALK- BIA Cutaneous Extranodal	 29 (76.3) 12 13 1 2 1 4 (10.5) 5 (13.2)
Best Response by ITT: ORR: 47.3%, CR: 37%	

PFS by diagnosis



OS by diagnosis





- FY23 proposed correlative studies to identify predictors of response and resistance
- WES, RNAseq, and in situ CODEX multiplex profiling
- Computational Pathology: machine learning and deep learning computational pathology tools

Agbedia et al. ASH 2022, Oral Presentation

Methods

1

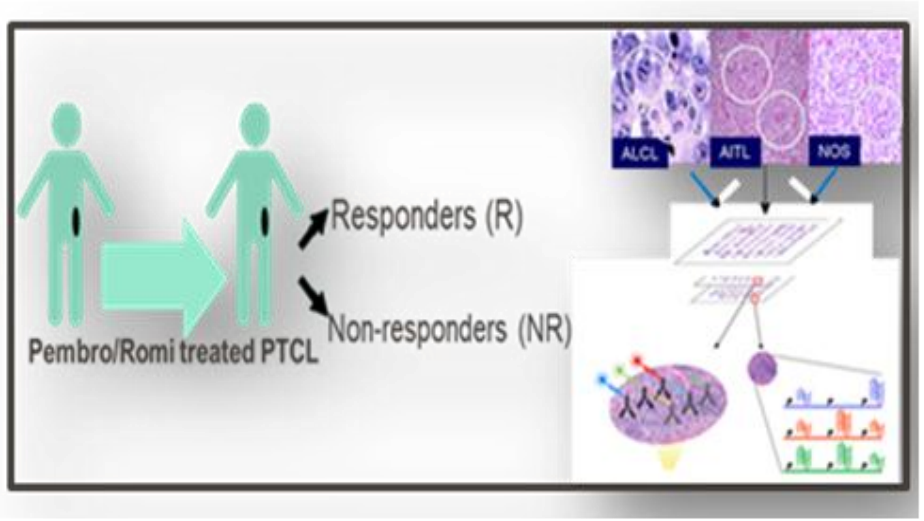
Perform WES and RNAseq of tumor samples at baseline from PTCL patients treated with pembro+romi

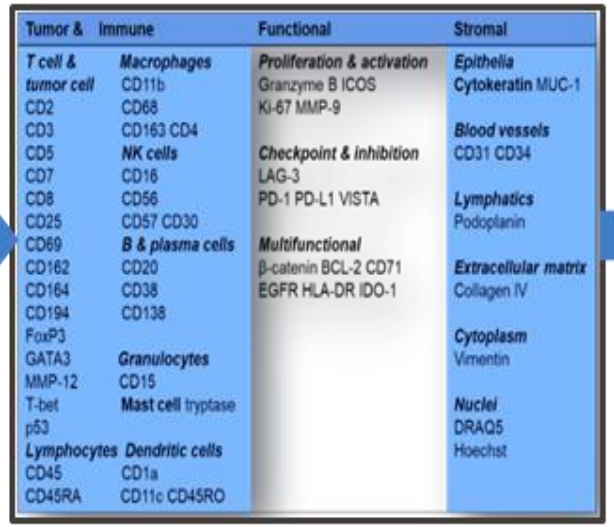
2

Design, develop, and optimize a 33-marker CODEX antibody panel to profile tumor samples at baseline from PTCL patients treated with pembro+romi and identify biomarkers associated with clinical outcome

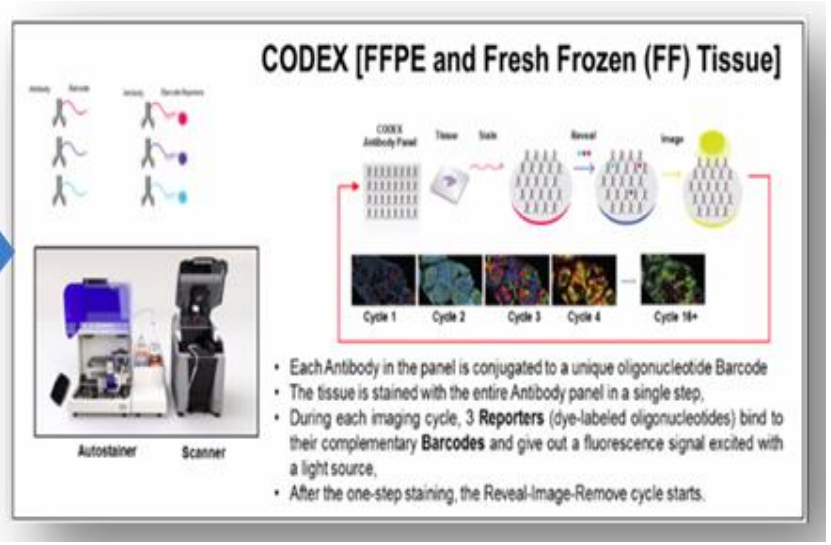
3

To delineate and validate the spatial attributes that define the TME components of lymphoma (L), tumor associated immune cell (TIC) and tumor associated macrophages (TAMs) in TCL using spatial point and computational pathology





Tumor & Immune		Functional	Stromal
T cell & tumor cell	*Macrophages*	*Proliferation & activation*	*Epithelia*
CD2	CD11b	Granzyme B ICOS	Cytokeratin MUC-1
CD3	CD68	Ki-67 MMP-9	
CD5	CD163 CD4		*Blood vessels*
CD7	*NK cells*	*Checkpoint & inhibition*	CD31 CD34
CD8	CD16	LAG-3	
CD25	CD56	PD-1 PD-L1 VISTA	*Lymphatics*
CD69	CD57 CD30		Podoplanin
CD162	*B & plasma cells*	*Multifunctional*	
CD164	CD20	β-catenin BCL-2 CD71	*Extracellular matrix*
CD194	CD38	EGFR HLA-DR IDO-1	Collagen IV
FoxP3	CD138		
GATA3			*Cytoplasm*
MMP-12	*Granulocytes*		Vimentin
T-bet	CD15		
p53	*Mast cell* tryptase		*Nuclei*
Lymphocytes	*Dendritic cells*		DRAQ5
CD45	CD1a		Hoechst
CD45RA	CD11c CD45RO		



Nair….Iyer. ASH 2024, Oral Presentation

Lymphoma Panel: 33 Markers

N	Human Markers (Immuno-Oncology)	Clone	N	Human Markers (Immuno-Oncology)	Clone	N	Human Markers (Immuno-Oncology)	Clone
1	BCL-2	AKYP0120	12	CD56	EP2567Y	23	GATA-3	EPR16651
2	CD3e	EP449E	13	CD57	HNK-1 or Leu-7	24	GZMA	EPR20161
3	CD4	EPR6855	14	CD58	Polyclonal	25	GZMB	D6E9W
4	CD8	C8/144B	15	CD68	KP1	26	ICOS	SP98
5	CD11b	EP1345Y	16	CD123	9F5	27	Ki-67	B56
6	CD14	EPR3653	17	CD163	AKYP0114	28	MCHII	LGII-612.14
7	CD19	D4V4B	18	CD172a		29	PD-1	AKYP0070
8	CD20	L26	19	CXCR3	1C6/CXCR3	30	PD-L1	AKYP0103
9	CD21	EP3093	20	CXCR5	EPR23463-30	31	RORgT	Polyclonal
10	CD30	BLR055F	21	EOMES	EPR21950-241	32	TIA-1	EPR22999-80
11	CD47	SP279	22	Foxp3	AKYP0102	33	TIM-3	BLR033F

Nair….Iyer. ASH 2024, Oral Presentation

Phenotypes

T cells					
1	CD3e	Total T cells'	32	CD3e_CD8_MCHII_	MCHII_CTL
2	CD3e_CD4_	Helper T cells' (Th)	33	CD3e_CD8_PD-1_	CTL antigen-experienced'
3	CD3e_CD8_	Cytotoxic T cells' (CTL)	34	CD3e_CD8_PD-L1_	PD-L1_CTL
4	CD3e_BCL2_	BCL2_T cells'	35	CD3e_CD8_CD47_	CD47_CTL
5	CD3e-CD57_	NKT cells	36	CD3e_CD8_PD-1_PD-L1_	PD-L1_CTL antigen-experienced'
6	CD3e_Ki-67_	'Proliferating T Cell'	37	CD3e_CD4_RORgT_	Th17
7	CD3e_MCHII_	MCHII T Cell'	38	CD3e_CD8_TIA-1_	'Activated Cytotoxic T cells'
8	CD3e_CD11b	CD11b_T cells	39	CD3e_CD8_TIM-3_	TIM3_CTL
9	CD3e_CD58_	CD58_T cells	40	CD3e_CD8_TIM-3_PD1	TIM3_PD-1_CTL
10	CD3e_CD30_	CD30_Tcells	41	CD3e_CD8_CD11b	CD11b_CTL
11	CD3e_CD47_	CD47_T cells	42	CD3e_CD4_CXCR3_	CXCR3_Th
12	CD3e_CD4_CD8_	Double_positive_T cells'	43	CD3e_CD8_CXCR3_	CXCR3_CTL
13	CD3e_PD1_	T cells antigen-experienced'	44	CD3e_CD4_CXCR5	CXCR5_CD4 T cells
14	CD3e_PD-1_PD-L1_	PDL1_T cells antigen-experienced'	45	CD3e_CD4_PD-1_ICOS_CXCR5	T follicular helper (Tfh)
15	CD3e_CD4_Foxp3_CXCR3	CXCR3_Treg	46	CD3e_CD8_CXCR5	CXCR5_CD8 T cells
16	CD3e_CD4_CXCR5_	CXCR5_Th	'NK_T cells'		
17	CD3e_CD4_EOMES_	EOMES_CD4 Tcells	47	CD3e_CD56	NKT cells'
18	CD3e_CD8_EOMES_	EOMES_CTL	48	CD3e_CD56_CD58	CD58_NKT cells
19	CD3e_CD4_Foxp3_	Regulatory T cells (Treg)	49	CD3e_CD56_CD47	CD47_NKT cells
20	CD3e_CD4_Foxp3_MHCII	MCHII_Regulatory T cells (Treg)	50	CD3e_CD56_CD4_	CD4_NKT cells
21	CD3e_CD4_GATA3_	Th2	51	CD3e_CD56_CD8_	CD8_NKT cells
22	CD3e_CD4_PD-1_	Helper T cells antigen-experienced'	52	CD3e_CD56_GZA	Activated NKT cells'
23	CD3e_CD8_GATA3_	GATA3_CTL	53	CD3e_CD56_GZB	Activated NKT cells'
24	CD3e_CD4_GZMA	CD4_ Cytotoxic T cells'	54	CD3e_CD56_TIA1_	Activated NKT cells'
25	CD3e_CD8_GZMA	Activated Cytotoxic T cells'	55	CD3e_CD56_GATA3	NKT2
26	CD3e_CD4_GZMB	CD4_ Cytotoxic T cells'	56	CD3e_CD56_RORgT	NKT17
27	CD3e_CD8_GZMB	Activated Cytotoxic T cells'	57	CD3e_CD56_Foxp3	NKT-reg
28	CD3e_CD4_PD-1_ICOS_	T follicular helper (Tfh)	58	CD3e_CD56_CXCR3_	CXCR3_NKT cells
29	CD3e_CD4_Ki-67_	Proliferating Th'	59	CD3e_CD56_GZA_GZB	Activated NKT cells'
30	CD3e_CD8_Ki-67_	Proliferating CTL'	60	CD3e_CD56_EOMES	EOMES_NKT cells
31	CD3e_CD4_MCHII_	MCHII _Th	61	CD3e_CD56_Ki67	Proliferating_NKT cells'

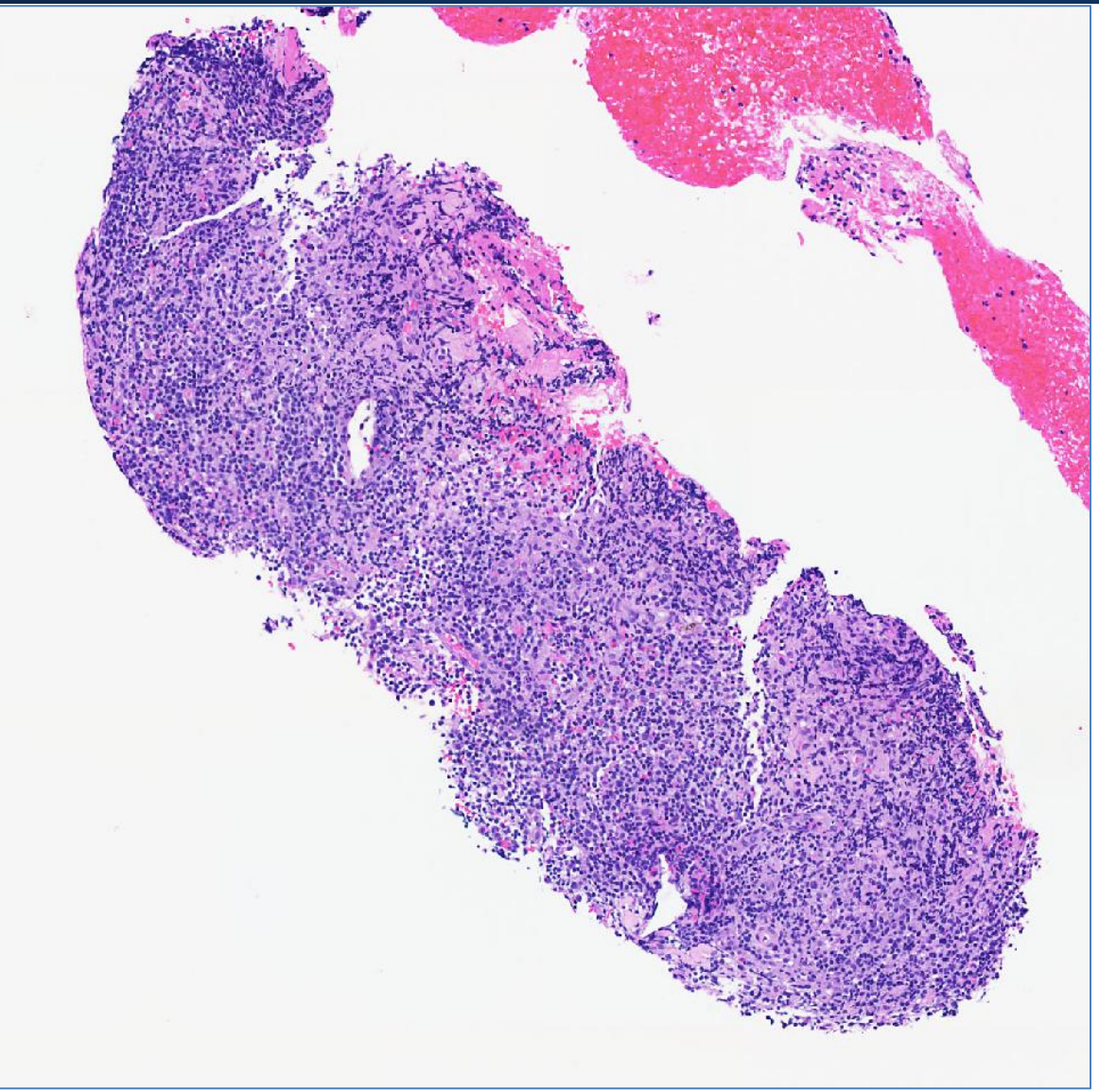
B cells'		
62	CD19	Total B cells'
63	CD20	Total Mature B cells'
64	CD19_CD20_	Total Mature B cells'
65	CD19_CD47_	CD47_B cells
66	CD20_CD47_	CD47_Mature B cells
67	CD19_CD58_	CD58_B cells
68	CD20_CD58_	CD58_Mature B cells
69	CD19_MCHII_	MHCII_ B cells
70	CD19_CD30_	CD30_B cells
71	CD20_MCHII_	MHCII_Mature B cells
72	CD20_CD11b	Total Mature B cells'
73	CD19_Ki67	Proliferating B cells'
74	CD20_Ki67	Proliferating Mature B cells'
75	CD19_CD20_Ki67	Proliferating Mature B cells'
76	CD19_CD30_	CD30_Mature B cells
77	CD20_CD30_	CD30_Mature B cells
78	CD20_CXCR3	CXCR3_B cells
79	CD21	Total Follicular dendritic cells
80	CD19_CD21	Follicular dendritic cells
81	MHCII_CD19_CD21	Follicular dendritic cells
82	CD21_CD11b	CD11b_Follicular dendritic cells
83	MHCII_CD21	Follicular dendritic cells
84	CD21_CD11b_MHCII_	Follicular dendritic cells
Myeloid cells'		
85	CD11b_	Total Myeloid cells
86	CD11b_Ki67	Proliferating Myeloid cells
87	CD11b_CD172	CD172_Myeloid cells
88	CD123_MHCII	Myeloid dendritic cells (mDC)
89	CD123_CD14	CD14_ Dendritic cells (mDC)
90	CD123_MHCII_CXCR3	Plasmocytoid dendritic cells (pDC)
91	CD123_MHCII_CD172a	CD172_DC
92	CD123_MHCII_CXCR3_CD172a	CD172_DC
93	CD123_CD4	Plasmocytoid dendritic cells (pDC)
94	CD123_CD4_CD56	Plasmocytoid dendritic cells (pDC)

Macrophages'		
95	CD68	Macrophages
96	CD68_CD163	M2_Macrophages
97	CD68_PD-L1	PD-L1_Macrophages
98	CD163_PD-L1_	PD-L1_M2_Macrophages
99	CD68_CD11b_	Macrophages
100	CD68_CD14_	Macrophages
101	CD68_MHCII_	MHCII_Macrophages
102	CD68_CD163_PD-L1_	PD-L1_M2_Macrophages
103	CD68_CD14_PD-L1_	PD-L1_Macrophages
104	CD68_CD11b_PD-L1_	PD-L1_Macrophages
105	CD68_CD11b_CD14	Macrophages
106	CD68_CD11b_CD14_PDL1	PD-L1_Macrophages
107	CD172a_CD163	CD172a _M2_Macrophages
108	CD172a_CD163-MHCII-	CD172a _M2_Macrophages
Endotelial cells		
109	CD58	Endotelial cells
110	CD123_	Endotelial cells
111	CD123_CD58	Endotelial cells
NK_cells'		
112	CD56_CD3eNeg	NK cells'
113	CD56_CD3eNeg_CD47	CD47_NK cells
114	CD56_CD3eNeg_CD4_	CD4_NK cells
115	CD56_CD3eNeg_CD8_	CD8_NK cells
116	CD56_CD3eNeg_GZA	Activated NKT cells'
117	CD56_CD3eNeg_GZB	Activated NKT cells'
118	CD56_CD3eNeg_TIA1_	Activated NKT cells'
119	CD56_CD3eNeg_CDXCR3	Immature NK cells (iNK)
120	CD56_CD3eNeg_CD11b	NK cells'
121	CD56_CD3eNeg_CD58	CD58_NK cells
122	CD56_CD3eNeg_EOMES	EOMES_NK cells
123	CD56_CD3eNeg_CDXCR5	CXCR5_NK cells'
124	CD56_CD3eNeg_GZB_CXCR5	CXCR5_Granzyme B_NK cells'
125	CD56_CD3eNeg_CD57	CD57_NK Cells
126	CD56_CD3eNeg_Ki67	'Proliferating_NKT cells'

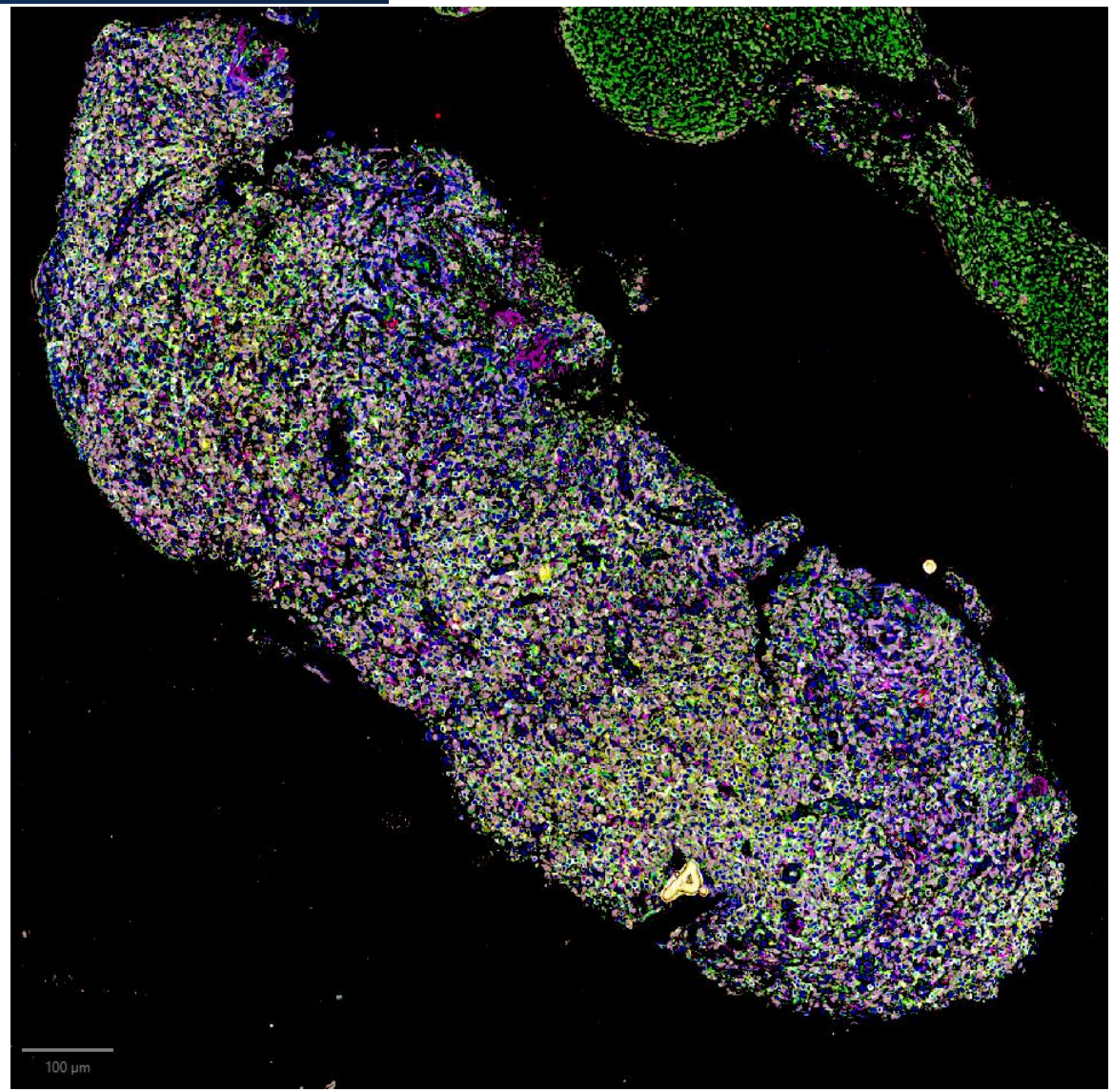
Nair….Iyer. ASH 2024, Oral Presentation

CODEX

THE UNIVERSITY OF TEXAS MD Anderson Cancer Center
Making Cancer History®



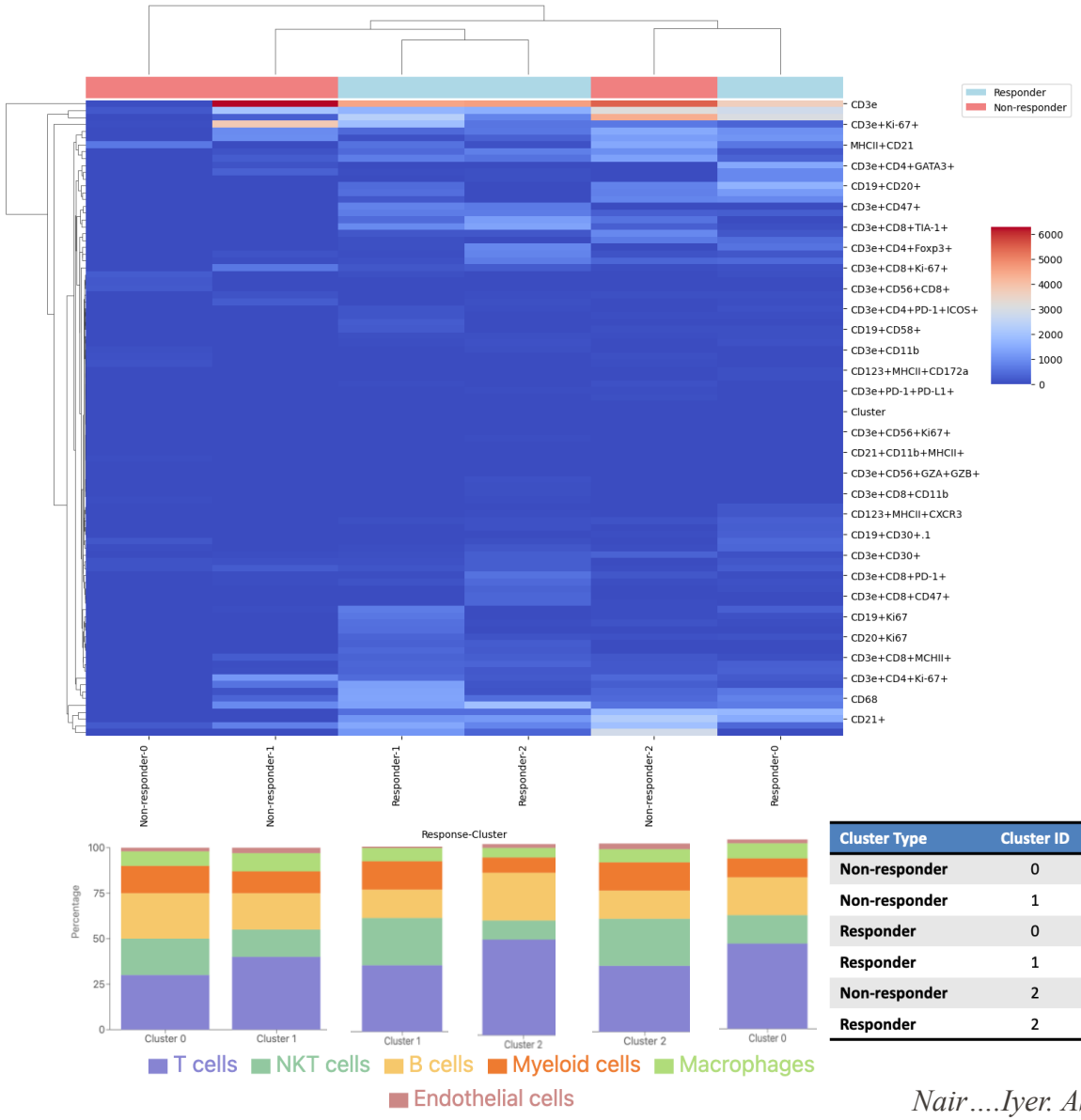
CODEX - Composite



Nair….Iyer. ASH 2024, Oral Presentation

CODEX analysis of the immune landscape in responders versus non-responders.

THE UNIVERSITY OF TEXAS MD Anderson Cancer Center
Making Cancer History®



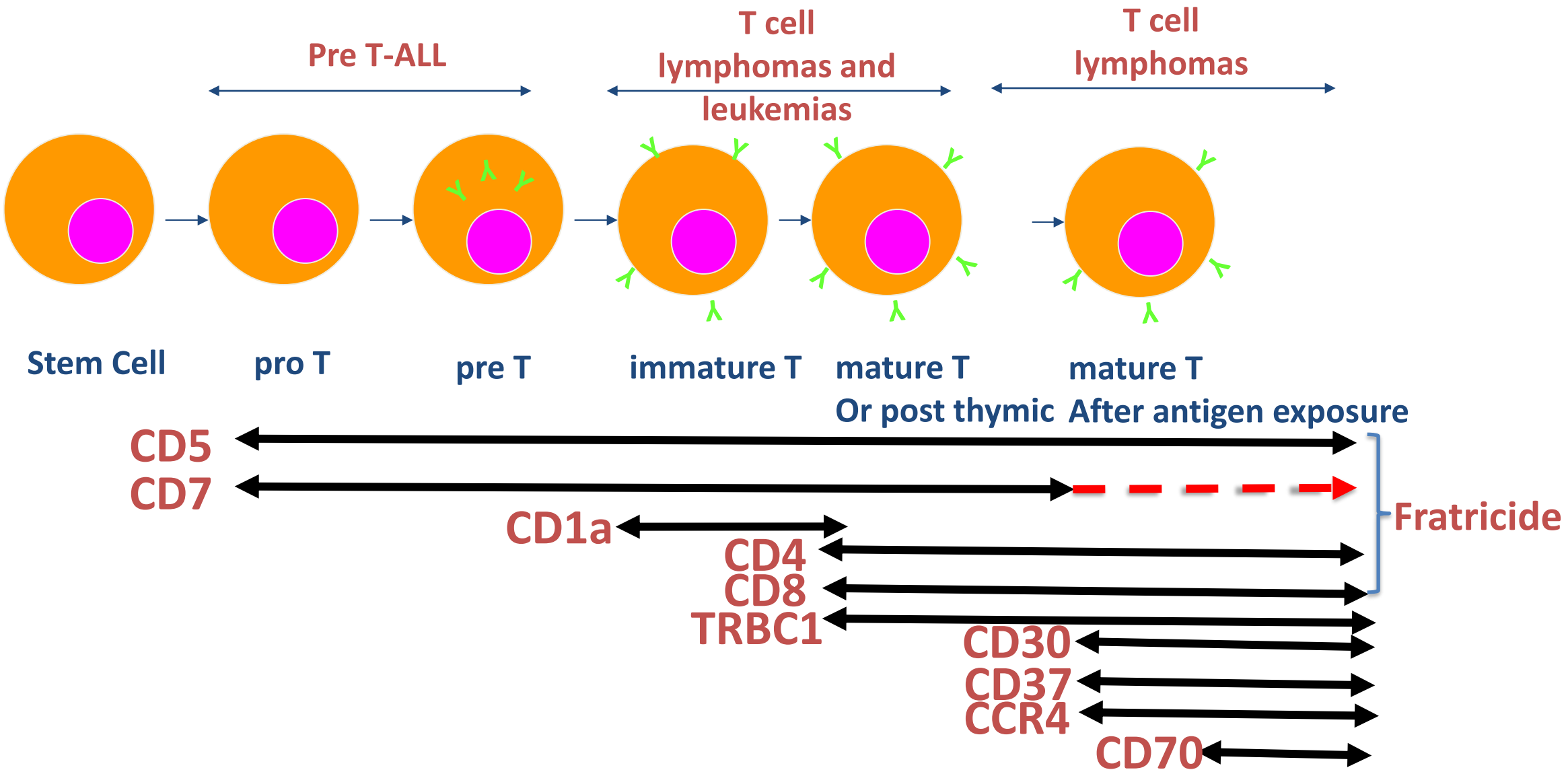
Cluster Type	Cluster ID	Diagnostic Subtypes
Non-responder	0	EATL
Non-responder	1	PTCL1, PTCL2
Responder	0	AITL4, Tfh5
Responder	1	AITL3, AITL6, AITL7
Non-responder	2	AITL2
Responder	2	AITL1

Cell Type	Total Markers	Significant Markers	Trend	Description
T cells	46	15 (32.6%)	↑	Higher in responders
NKT cells	13	6 (46.2%)	↑	Higher in responders
B cells	24	8 (33.3%)	−	No significant difference
Myeloid cells	9	5 (55.6%)	↓	Higher in non-responders
Macrophages	12	8 (66.7%)	↓	Higher in non-responders
Endothelial cells	3	1 (33.3%)	−	No significant difference

Nair….Iyer. ASH 2024, Oral Presentation

Choosing the right targets: expression of CD markers on T lineage and mature T αβ cells

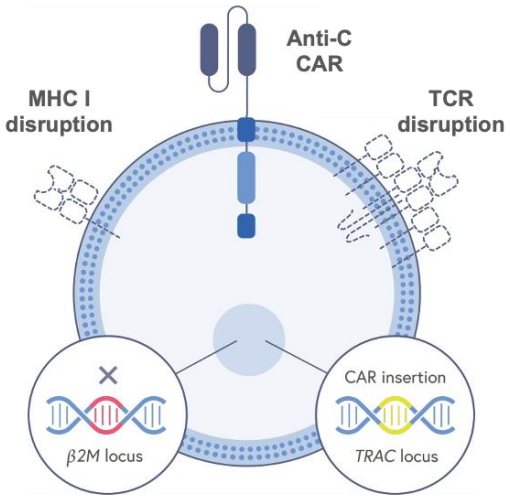
THE UNIVERSITY OF TEXAS MD Anderson Cancer Center
Making Cancer History®



Gene Editing approaches for CAR-T

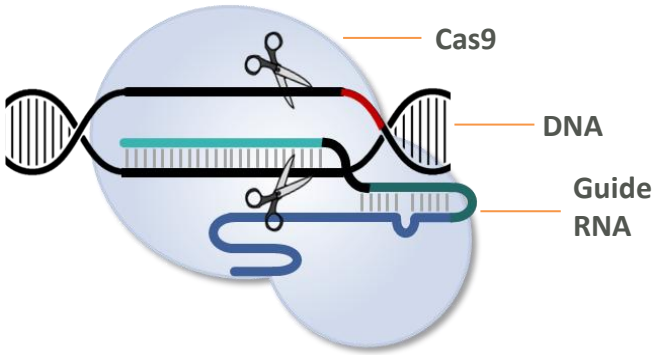
THE UNIVERSITY OF TEXAS MD Anderson Cancer Center
Making Cancer History®

Initial Allogeneic CAR-T Candidate – CTX110



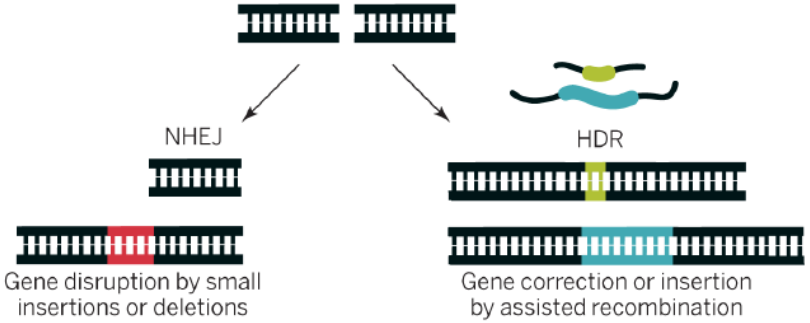
Multiplex editing in one step

CRISPR/Cas9 Allows for Precise Genome Editing



- The **CRISPR/Cas9 complex** is composed of a **single guide RNA** (sgRNA) and the **Cas9 endonuclease**
- The sgRNA binds to a **specific sequence** of DNA
- **Cas9 then creates a double strand DNA** (DSB) break at that precise sequence

DNA Double Strand Breaks Can Be Repaired Via Two Paths



Rapid repair of DNA disrupts genes

High fidelity, insertion-based DSB repair

NHEJ: non-homologous end joining
HDR: homology directed recombination

Iyer S, et al. Lancet Oncology November 2024

Baseline characteristics

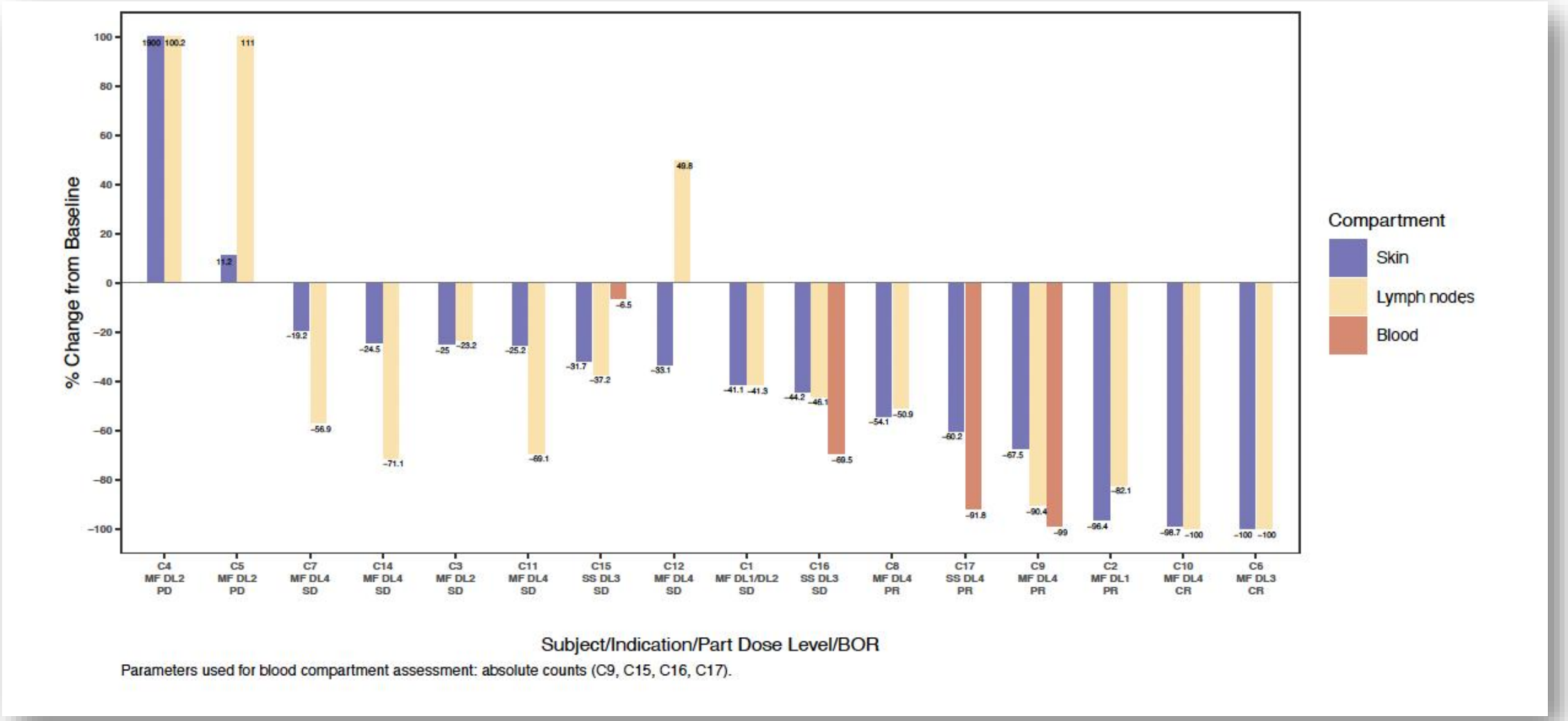
THE UNIVERSITY OF TEXAS MD Anderson Cancer Center
Making Cancer History®

Baseline characteristics					
	Dose level 1 (n=4)	Dose level 2 (n=4)	Dose level 3 (n=5)	Dose level 4 (n=26)	All (n=39)
Age (years)					
Median (IQR)	58.0 (48.0-64.0)	66.0 (52.0-69.0)	67.0 (65.0-72.0)	60.5 (47.0-68.0)	63.0 (47.0-68.0)
Sex					
Male	3 (75.0)	2 (50.0)	2 (40.0)	11 (42.3)	18 (46.2)
Female	1 (25.0)	2 (50.0)	3 (60.0)	15 (57.7)	21 (53.8)
Race					
White	3 (75.0)	2 (50.0)	4 (80.0)	15 (57.7)	24 (61.5)
Black or African American	0	1 (25.0)	1 (20.0)	6 (23.1)	8 (20.5)
Asian	0	0	0	3 (11.5)	3 (7.7)
Other	0	0	0	1 (3.8)	1 (2.6)
Multiple	1 (25.0)	0	0	1 (3.8)	2 (5.1)
Not reported	0	1 (25.0)	0	0	1 (2.6)
Type of Lymphoma					
PTCL	2 (50.0)	1 (25.0)	2 (40.0)	17 (65.4)	22 (56.4)
PTCL-NOS	1 (25.0)	0	0	7 (26.9)	8 (20.5)
ALCL	0	0	0	1 (3.8)	1 (2.6)
ATLL	1 (25.0)	1 (25.0)	1 (20.0)	6 (23.1)	9 (23.1)
AITL	0	0	1 (20.0)	3 (11.5)	4 (10.3)
SS or MF	2 (50.0)	3 (75.0)	3 (60.0)	9 (34.6)	17 (43.6)
Large cell transformation	1 (50.0)	3 (100)	2 (66.7)	5 (55.6)	11 (64.7)
Type of Prior Anticancer Therapies					
Systemic Therapy	4 (100)	4 (100)	5 (100)	26 (100)	39 (100)
Stem Cell Transplant	1 (25.0)	0	1 (20.0)	6 (23.1)	8 (20.5)
Number of prior lines of systemic therapy					
Median (IQR)	3 (2, 5)	6 (5, 7)	5 (3, 6)	4 (2, 5)	4 (2, 6)

Iyer S, et al. Lancet Oncology November 2024

MF/SS: Response across compartments

THE UNIVERSITY OF TEXAS MD Anderson Cancer Center
Making Cancer History®



Parameters used for blood compartment assessment: absolute counts (C9, C15, C16, C17).

Iyer S, et al. Lancet Oncology November 2024

MF/SS: Global Responses

THE UNIVERSITY OF TEXAS MD Anderson Cancer Center
Making Cancer History®

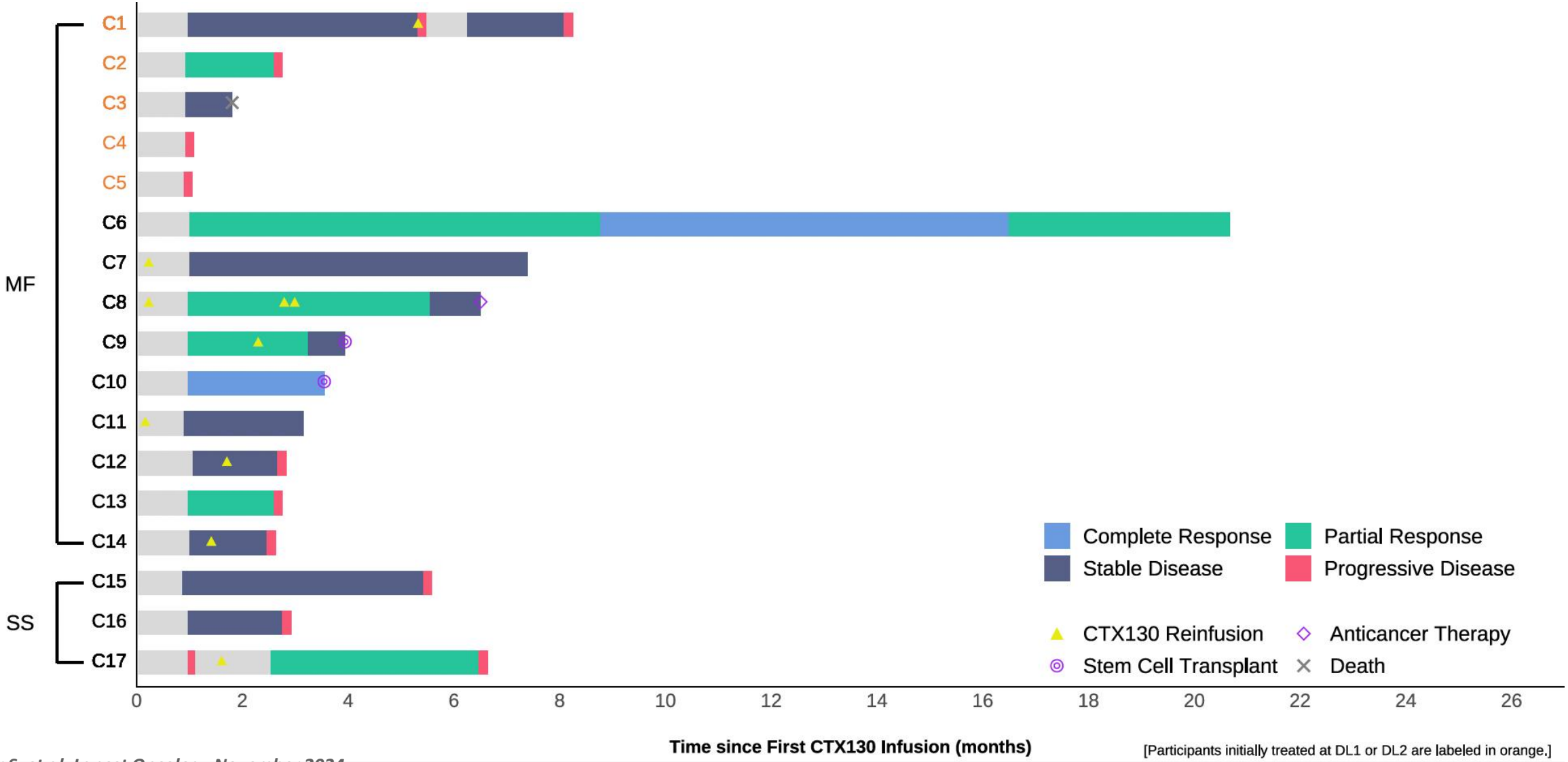
Global Score	Definition	Skin	Nodes/Blood/viscera
CR	Complete disappearance of all clinical evidence of disease	CR	All categories have CR/NI
PR	Regression of measurable disease	CR	All categories do not have a CR/NI and no category has a PD
PR	No category has a PD, if any category involved at baseline, at least one has a CR or PR	PR	No category has a PD and if any category involved at baseline, at least one has a CR or PR
SD	Failure to attain CR, PR, or PD representative of all disease	SD	CR/NI, PR, SD in any category and no category has a PD
PD	Progressive disease	PD	PD in any category
Relapse	Recurrence of disease in prior CR	Relapse	Relapse in any category

Patient	Response in Skin	Response in Nodes	Response in Blood	Response in Viscera	Global Response Score
C1	SD	SD	NE	NE	**SD**
C2	CR	PR	NE	NE	**PR**
C3	SD	SD	NE	NE	**SD**
C4	PD	PD	NE	PD	PD
C5	PD	PD	NE	NE	PD
C6	CR	CR	NE	NE	**CR**
C7	SD	CR	NE	NE	**SD**
C8	PR	PR	NE	NE	**PR**
C9	PR	CR	PR	NE	**PR**
C10	CR	CR	NE	NE	**CR**
C11	SD	PR	NE	NE	**SD**
C12	SD	SD	NE	NE	**SD**
C13	PR	NE	NE	NE	**PR**
C14	SD	SD	NE	NE	**SD**
C15	SD	SD	SD	NE	**SD**
C16	SD	PR	PR	NE	**SD**
C17	PR	NE	PR	NE	**PR**

Olsen E, et al. JCO May 2011
Iyer S, et al. Lancet Oncology November 2024

MF/SS: Response trends

THE UNIVERSITY OF TEXAS MD Anderson Cancer Center
Making Cancer History®



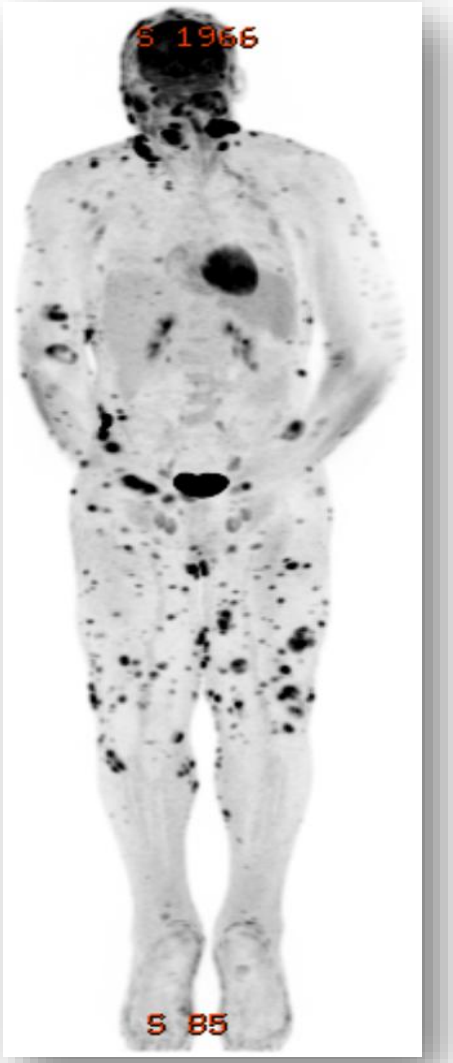
[Participants initially treated at DL1 or DL2 are labeled in orange.]

Iyer S, et al. Lancet Oncology November 2024

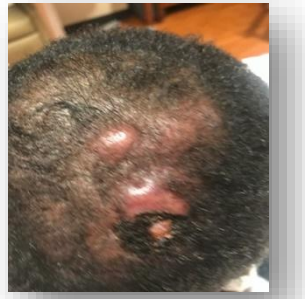
CTX-130 Allo-CD70 CAR-T-MF with LCT

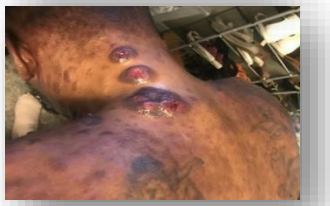
THE UNIVERSITY OF TEXAS MD Anderson Cancer Center
Making Cancer History®

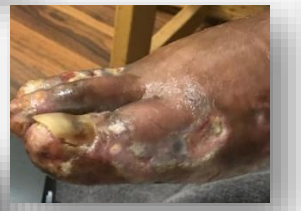
Before CTX-130 Jan 4

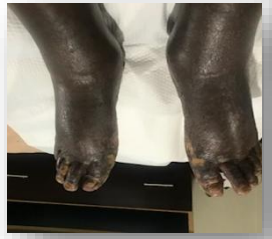


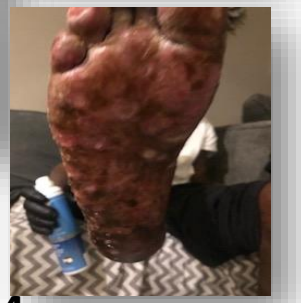
Before CTX-130 Jan 23, 2022





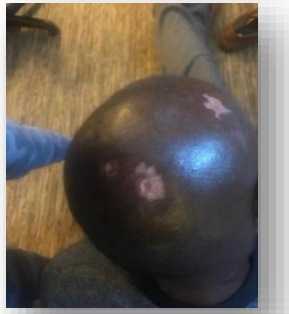


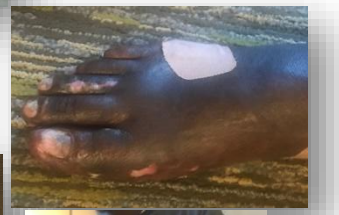


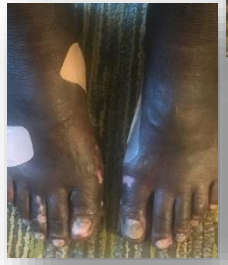


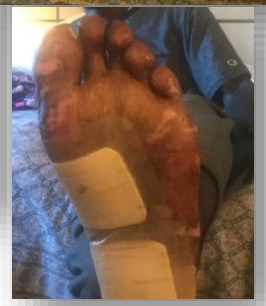
mSWAT 1/13- 84.74

Day 18 CTX-130 Feb 11, 2022

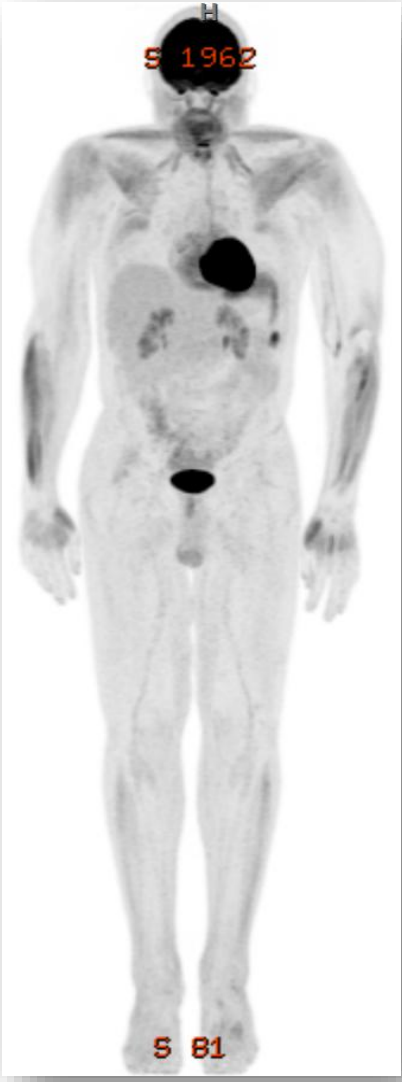








Day 28 CTX-130 Feb 21, 2022



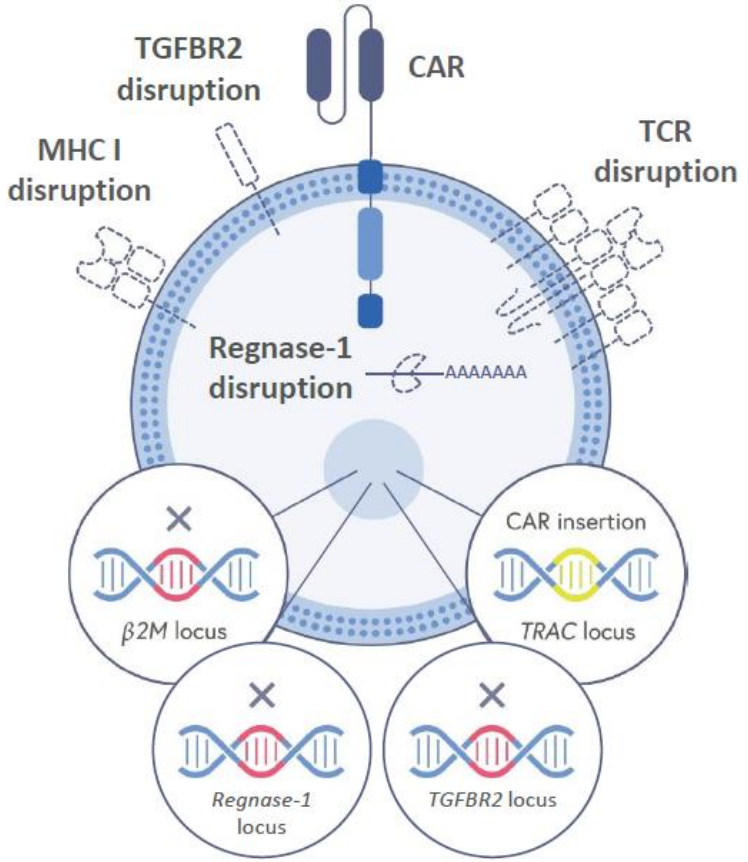
mSWAT 2/21- 0

CTX131 Incorporates Novel Potency Edits

THE UNIVERSITY OF TEXAS MD Anderson Cancer Center
Making Cancer History®

Next-generation CRISPR gene-edited allogeneic CAR T chassis:

- **MHC I KO:** Improve persistence in the allogeneic setting and avoid need for more toxic lymphodepletion
- **TGFBR2 KO:** Reduce tumor microenvironment inhibition of multiple CAR T cell functions

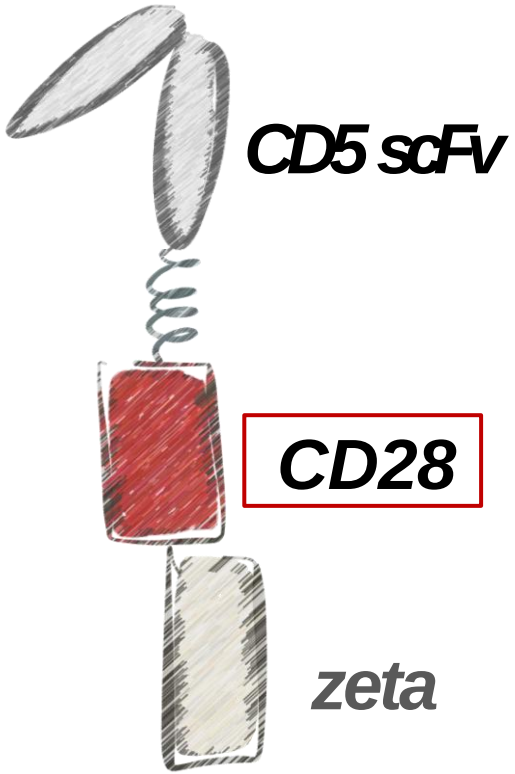


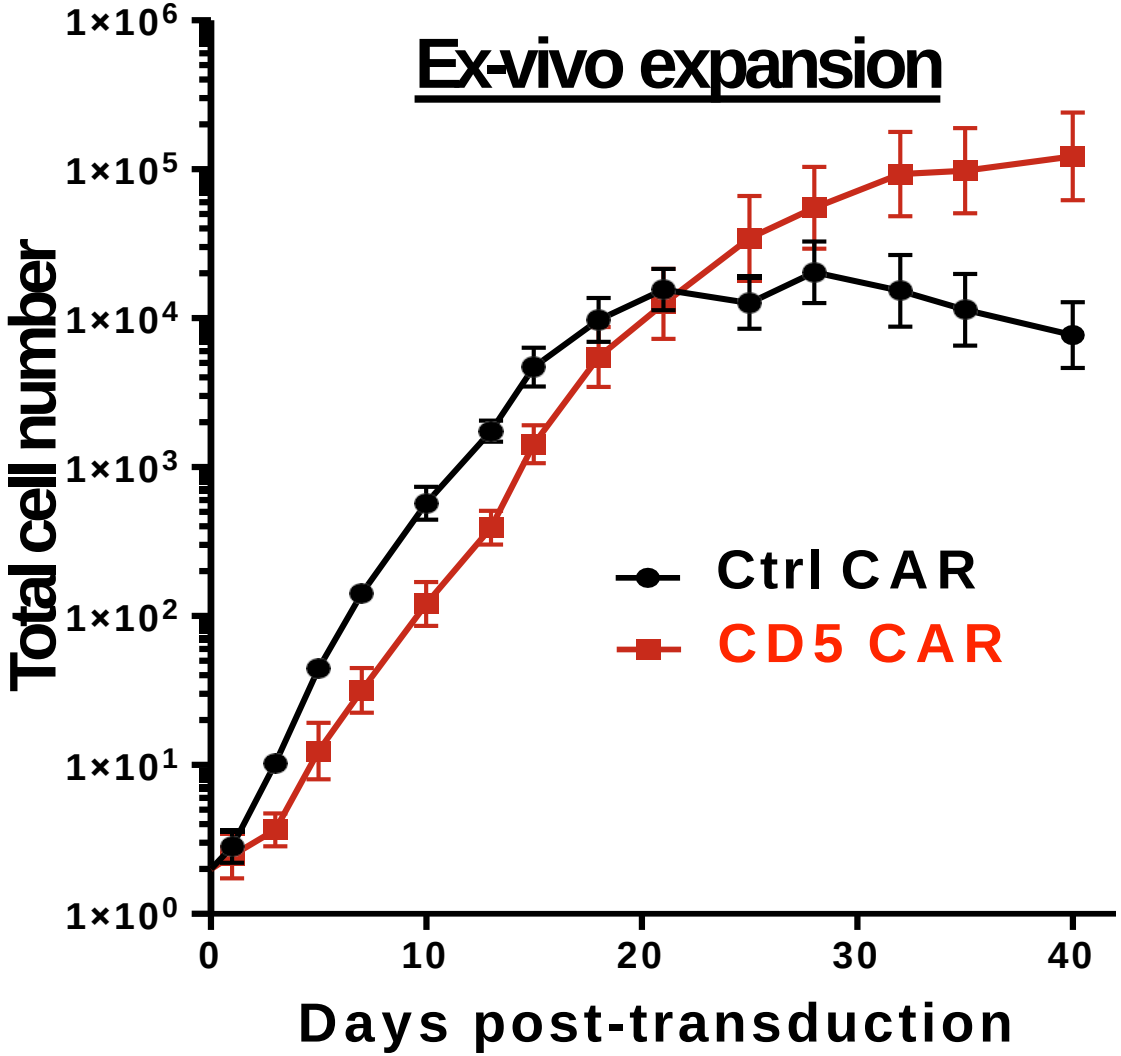
- **TCR KO:** Prevent GvHD
- **Regnase-1 KO:** Increase functional persistence, cytokine secretion and sensitivity, and effector function
- **CAR KI:** Site-specific insertion into TRAC locus without using lentivirus

CTX131 incorporates a CD70-targeted CAR and knock-out of CD70

Anti-CD5 CAR-T without fratricide and with persistence

THE UNIVERSITY OF TEXAS MD Anderson Cancer Center
Making Cancer History®



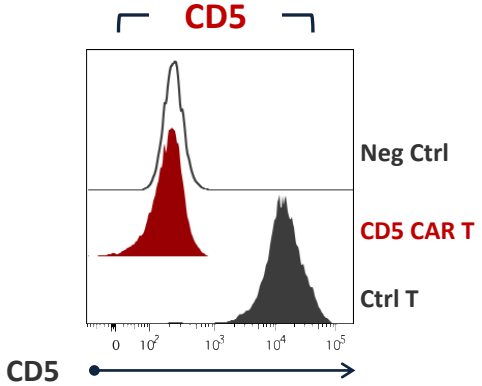


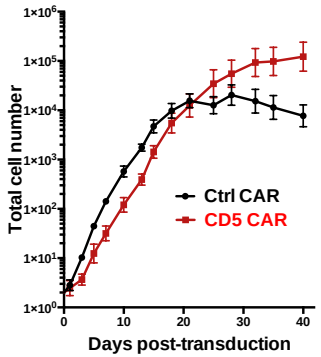
Mamonkin, Rouce et al. Blood. 2015;126(8):983-92; Cancer Immunol Res. 2018;6(1):47-58

CD5 protein is internalized and degraded in CAR T-cells, enabling expansion

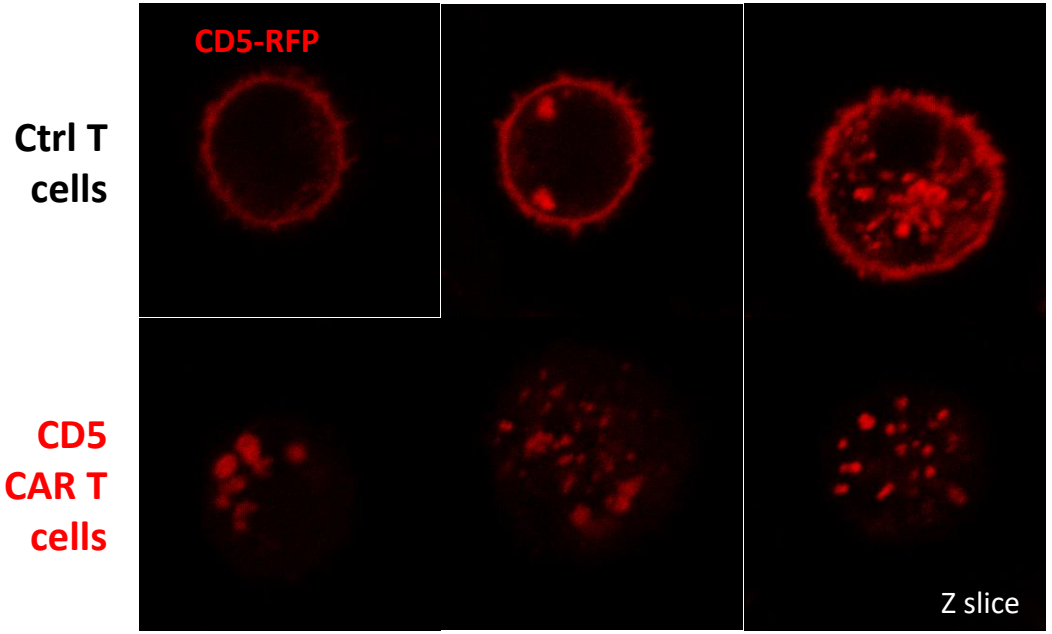
THE UNIVERSITY OF TEXAS MD Anderson Cancer Center
Making Cancer History®

CAR T-cell CD5 expression and expansion

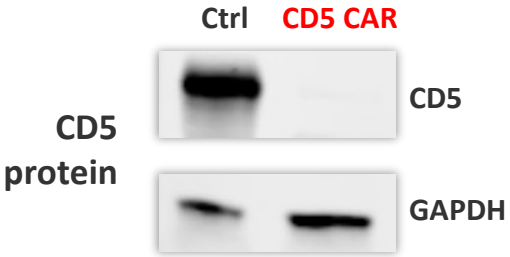


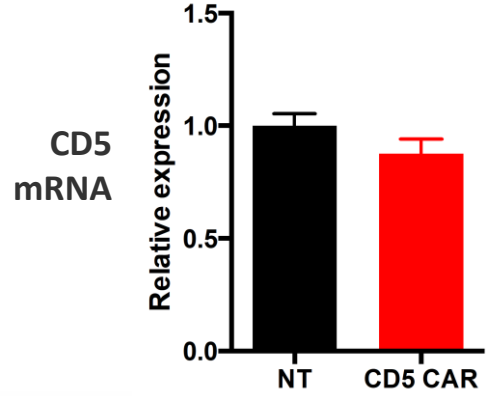


Rapid internalization of CD5 after CD5 CAR transduction



Continuous degradation of the CD5 protein



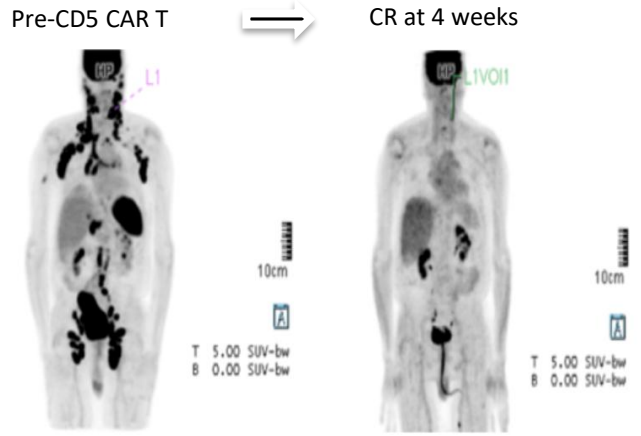


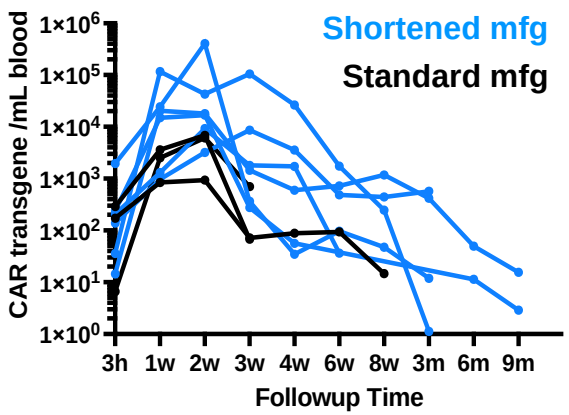
Ma et al., Cell Rep Med 2024

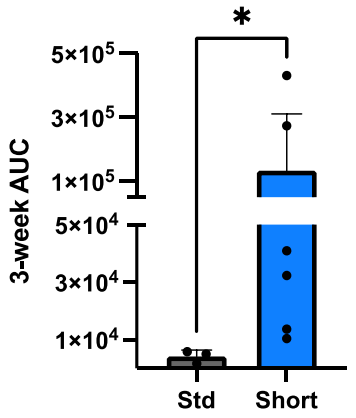
CD5 CAR-T demonstrated significant responses in T-cell Lymphoma Responses associated with shortened manufacturing (no TKI)

THE UNIVERSITY OF TEXAS MD Anderson Cancer Center
Making Cancer History®

Age/ Sex	Disease Type	Dose Level	CRS	ICANS	Best Clinical Response	Mfg Process
Original manufacturing (44% ORR)						
63 F	Sezary	DL1	-	-	PD	Standard
70 M	AITL	DL1	-	-	CR	Short
63 F	AITL	DL2	1	-		Short
67 F	PTCL	DL2	-	-	PD	Short
71 M	PTCL	DL2	2	2		Short
48 M	PTCL	DL2	1	-	PD	Standard
29 F	CTCL	DL3	-	-	PD	Standard
63 M	PTCL	DL3	-	-	**SD**	Short
49 F	ATLL	DL3	1	-		Short







CR = Complete Response **PR = Partial Response** **SD = Stable Disease** PD = Progressive Disease

Hill, L. C., et al. (2023). *Blood.* https://doi.org/10.1182/blood.2023022204

Emerging themes in T cell Lymphomas

THE UNIVERSITY OF TEXAS MD Anderson Cancer Center
Making Cancer History®

- Pan SIRP inhibitor for LA-HLH

sHLH: A Rare, Severe Hyperinflammatory Condition With No Approved Therapies

THE UNIVERSITY OF TEXAS MD Anderson Cancer Center
Making Cancer History®

HLH:

- hyperactivation of CD8+ T lymphocytes and macrophages;
- proliferation, ectopic migration, and infiltration into various organs;
- hypercytokinemia with elevated levels of various cytokines, resulting in progressive organ dysfunction

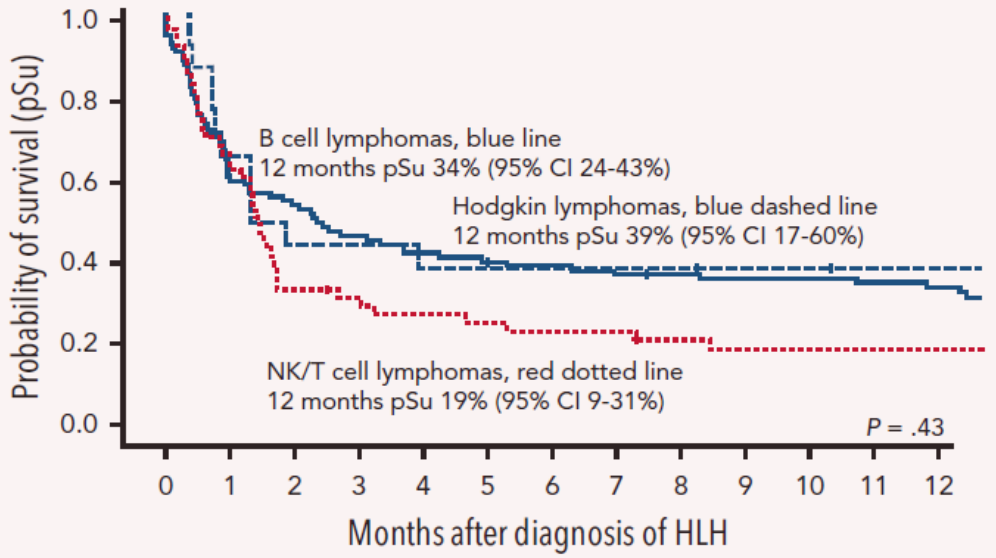
Triggered by malignancy, infection, autoimmune disease, or immunotherapy/CAR-T

Characterized by a failure to terminate activated $CD8^+$ T cells → uncontrolled proliferation and activation of immune cells → massive cytokine storm

Malignancy associated HLH (mHLH) has the worst prognosis

- **~50%** mortality at 2 months[1]
- **~20-30%** inpatient mortality[2]

Overall survival in Lymphoma-associated mHLH patients from the time of diagnosis[2]



[1]Löfstedt A, Jädersten M, Meeths M, Henter J-I. Malignancy-associated hemophagocytic lymphohistiocytosis in Sweden: incidence, clinical characteristics, and survival. Blood 2024;143(3):233–42
[2]Abdelhay A, Mahmoud AA, Al Ali O, Hashem A, Orakzai A, Jamshed S. Epidemiology, characteristics, and outcomes of adult haemophagocytic lymphohistiocytosis in the USA, 2006–19: a national, retrospective cohort study. eClinicalMedicine 2023;62:102143.

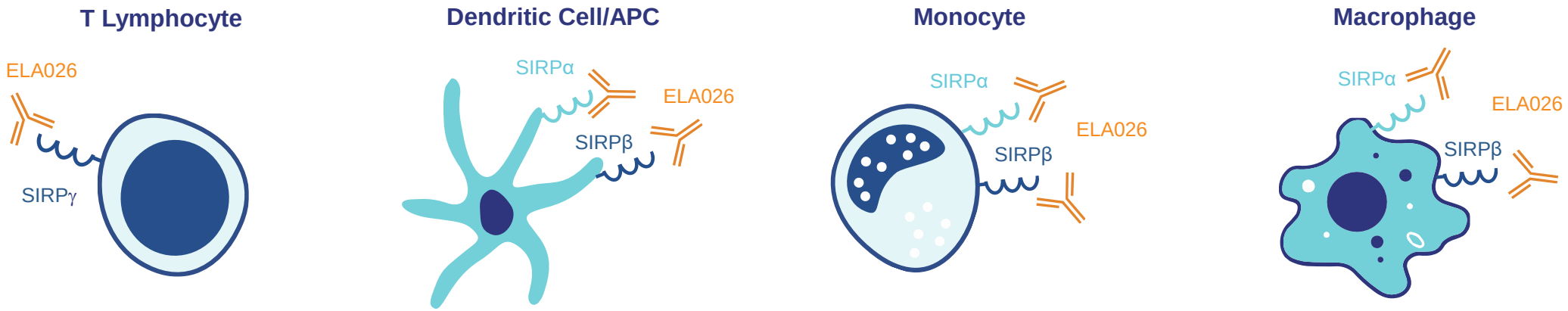
Maiti A….Iyer S, ASH 2024

ELA026 Is a First-In-Class, Clinical Stage mAb Targeting SIRPa/b/g

THE UNIVERSITY OF TEXAS MD Anderson Cancer Center
Making Cancer History®

Hypothesis: Targeted depletion of multiple pathogenic immune cells may rapidly control the cytokine storm in sHLH

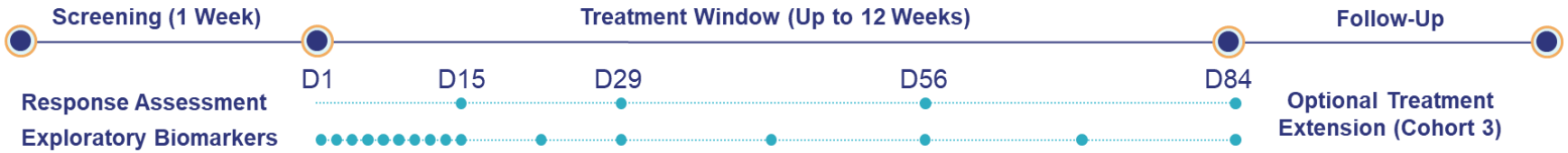
- ELA026 is a fully human IgG1 monoclonal antibody targeting SIRPα/β on myeloid cells and SIRPγ on T lymphocytes
- Mediates ADCC and ADCP *in vitro*, with potent depletion of myeloid cells and T lymphocytes demonstrated in non-human primates



Maiti A.…Iyer S, ASH 2024

Phase 1b: Evaluate Safety and Efficacy of ELA026 in Secondary HLH

THE UNIVERSITY OF TEXAS MD Anderson Cancer Center
Making Cancer History®



Key Eligibility

- Diagnosis of sHLH by HLH-2004 (any trigger)
- Exclude primary HLH
- No anti-HLH-directed therapies, except dexamethasone
- Within 100 days of allogenic stem cell transplant

	Cohort 1	Cohort 2	Cohort 3
Population	TN or R/R N = 6	TN or R/R N = 6	Frontline settings (TN or <1 week of HLH-directed therapy) N = 10
Dosing	Daily Dose Escalation 0.1 to 3.0 mg/kg	Fixed Dose 1.0 mg/kg weekly	Fixed Dose 0.5 mg/kg twice weekly
Objectives	**Safety, Efficacy, and RP3D**		

ClinicalTrials.gov ID: NCT05416307; **EudraCT Number**: 2021-001387-20; sHLH: secondary hemophagocytic lymphohistiocytosis. RP3D: recommended phase 3 dose. R/R: Relapse/Refractory. TN: Treatment-Naïve

Maiti A….Iyer S, ASH 2024

Baseline Characteristics of mHLH Patients Treated in Frontline Settings

THE UNIVERSITY OF TEXAS MD Anderson Cancer Center
Making Cancer History®

N	12
Age, median (range)	47 (21, 78)
Female, N (%)	4 (33)
Days from mHLH diagnosis to first dose of ELA026, median (range)	4 (0, 14)
Malignancy Trigger, N (%)	
T cell lymphoma	7 (58)
B cell lymphoma	2 (17)
Hodgkin lymphoma	1 (8)
Leukemia	2 (17)
Malignancy Status, N (%)	
Relapse/refractory	5 (42)
Newly diagnosed	7 (58)
Diagnostic and Prognostic Indicators at Baseline or Screening	
Ferritin, ng/mL, median (range)	3999 (1383, 74164)
sCD25[1], pg/mL, median (range)	9239 (2356, 142612)
OHI index (+/+)[1,2], N (%)	5 of 12 (42)
LDH, U/L, median (range)	385 (198, 16840)
Platelets, G/L, median (range)	33 (2, 105)
CRP, mg/L, median (range)	9 (3, 87)

Maiti A….Iyer S, ASH 2024

Most Frequent Adverse Events, All Dosed Patients, N=22

THE UNIVERSITY OF TEXAS MD Anderson Cancer Center
Making Cancer History®

Adverse event	All events				Related events			
	n (%)	Grade			n (%)	Grade		
		1/2	3/4	5		1/2	3/4	5
Hypotension	9 (41)	7	2	0	2 (9)	2	0	0
Pyrexia	9 (41)	6	3	0	2 (9)	2	0	0
Hyperkalaemia	8 (36)	8	0	0	0	0	0	0
Sepsis	8 (36)	0	6	2	0	0	0	0
Dyspnoea	7 (32)	6	1	0	1 (5)	1	0	0
Epistaxis	6 (27)	4	2	0	0	0	0	0
Hypoalbuminaemia	6 (27)	6	0	0	0	0	0	0
Peripheral swelling	6 (27)	6	0	0	0	0	0	0
Thrombocytopenia	6 (27)	0	6	0	2 (9)	0	2	0
Abdominal pain	5 (23)	4	1	0	0	0	0	0
Chills	5 (23)	5	0	0	2 (9)	2	0	0
Febrile neutropenia	5 (23)	0	5	0	0	0	0	0
Hyperphosphataemia	5 (23)	5	0	0	0	0	0	0
Hyponatraemia	5 (23)	4	1	0	0	0	0	0
Hypophosphataemia	5 (23)	5	0	0	0	0	0	0
Neutropenia	5 (23)	0	5	0	2 (9)	0	2	0
Pneumonia	5 (23)	0	5	0	0	0	0	0

Adverse event	All events				Related events			
	n (%)	Grade			n (%)	Grade		
		1/2	3/4	5		1/2	3/4	5
Alanine aminotransferase increased	4 (18)	3	1	0	0	0	0	0
Arthralgia	4 (18)	2	2	0	0	0	0	0
Blood alkaline phosphatase increased	4 (18)	2	2	0	0	0	0	0
Blood bilirubin increased	4 (18)	2	2	0	0	0	0	0
Constipation	4 (18)	4	0	0	0	0	0	0
Cough	4 (18)	4	0	0	0	0	0	0
Diarrhoea	4 (18)	3	1	0	1 (5)	1	0	0
Hyperglycemia	4 (18)	3	1	0	0	0	0	0
Hyperhidrosis	4 (18)	4	0	0	0	0	0	0
Hypomagnesaemia	4 (18)	4	0	0	0	0	0	0
Infusion related reaction	4 (18)	1	3	0	2 (9)	0	2	0
Multiple organ dysfunction syndrome	4 (18)	0	2	2	0	0	0	0
Pain in extremity	4 (18)	1	3	0	0	0	0	0
Stomatitis	4 (18)	3	1	0	0	0	0	0
Tachypnoea	4 (18)	4	0	0	0	0	0	0

Maiti A….Iyer S, ASH 2024

High Response Rate by Week 4 in mHLH Treated in Frontline Settings

THE UNIVERSITY OF TEXAS MD Anderson Cancer Center
Making Cancer History®

Response Criteria	Patient 2	Patient 3	Patient 5	Patient 8	Patient 13	Patient 15	Patient 16	Patient 17	Patient 19	Patient 20	Patient 21	Patient 22
1. Afebrile?	●	●	●	●	●	●	●	●	●	●	o	●
2. Normal spleen?	o			o	o	●	●	o	●	o	●	o
3. ANC and platelet criteria met?	●	o	o	o	o	o	o	o	o	o	●	o
4. Ferritin criterion met?	**O**	**O**	o	o	●	o	●	o		●	●	o
5. D-dimer and/or fibrinogen criteria met?	●	●	●	●	●	●	●	●	●	●	●	●
6. Normal neuro exam and CSF?	●	●	●	●	●	●	●	●	●	●	●	●
7. No sustained worsening of sCD25?	●	●	●	●	o	●	●	●	●	●	●	●
Overall response	**PR**	**PR**	**PR**	**PR**	**PR**	**PR**	**mCR**	**PR**	**PR**	**mCR**	**PR**	**PR**

● Criterion met o At least 50% improvement **O** Criterion not met **[blank]** Missing data or not interpretable

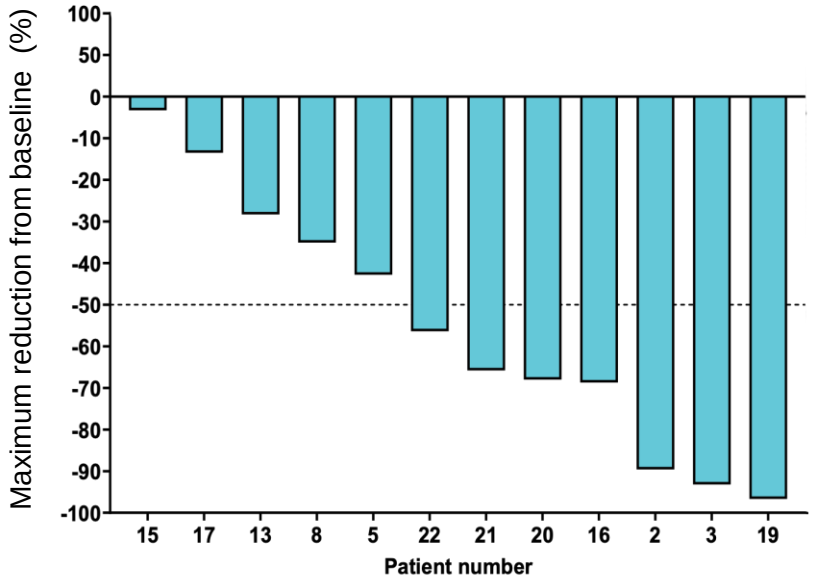
Modified HLH-2004 response criteria adapted from (Locatelli 2020): Complete response (CR): Criteria 1-7 met; Modified CR (mCR): Criteria 1, 4, 5, 6, 7 met; Partial response (PR): Any 3 criteria met; HLH improvement (HI): ≥50% change or improvement from baseline in ≥3 criteria; Overall response is HI or better, without progression of any other clinical or laboratory data. No response (NR): Not meeting CR, mCR, PR or HI; ANC: absolute neutrophil count; CSF: cerebral spinal fluid; sCD25: soluble CD25.

Maiti A….Iyer S, ASH 2024

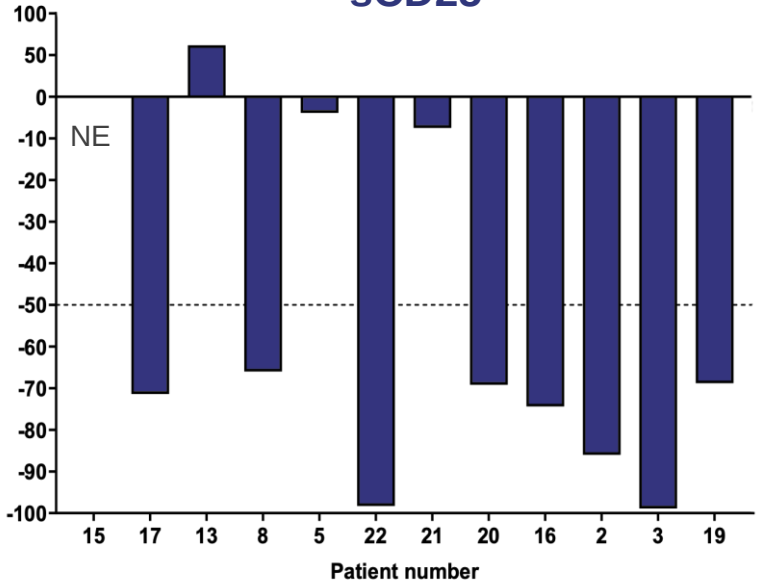
Maximum Biomarker Reduction by Week 4 in mHLH Treated in Frontline Settings

THE UNIVERSITY OF TEXAS MD Anderson Cancer Center
Making Cancer History®

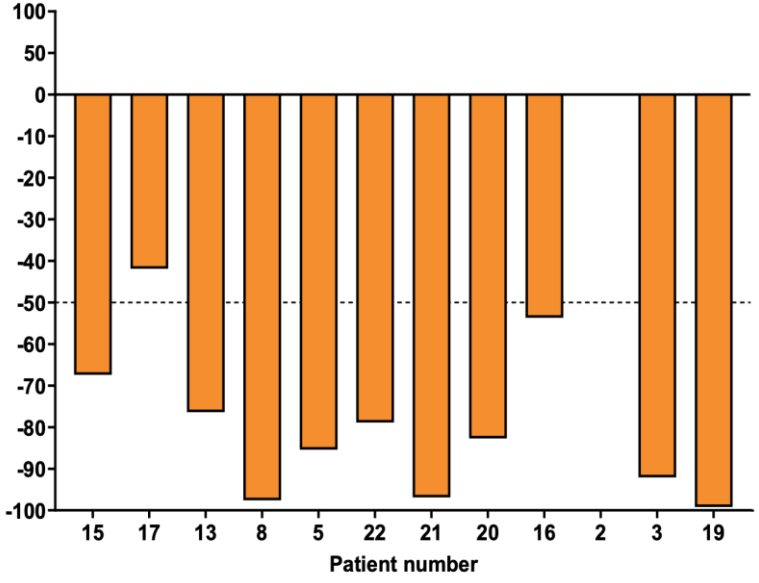
Ferritin



sCD25



CRP



Median change:

-58% | **-67%** | **-83%**

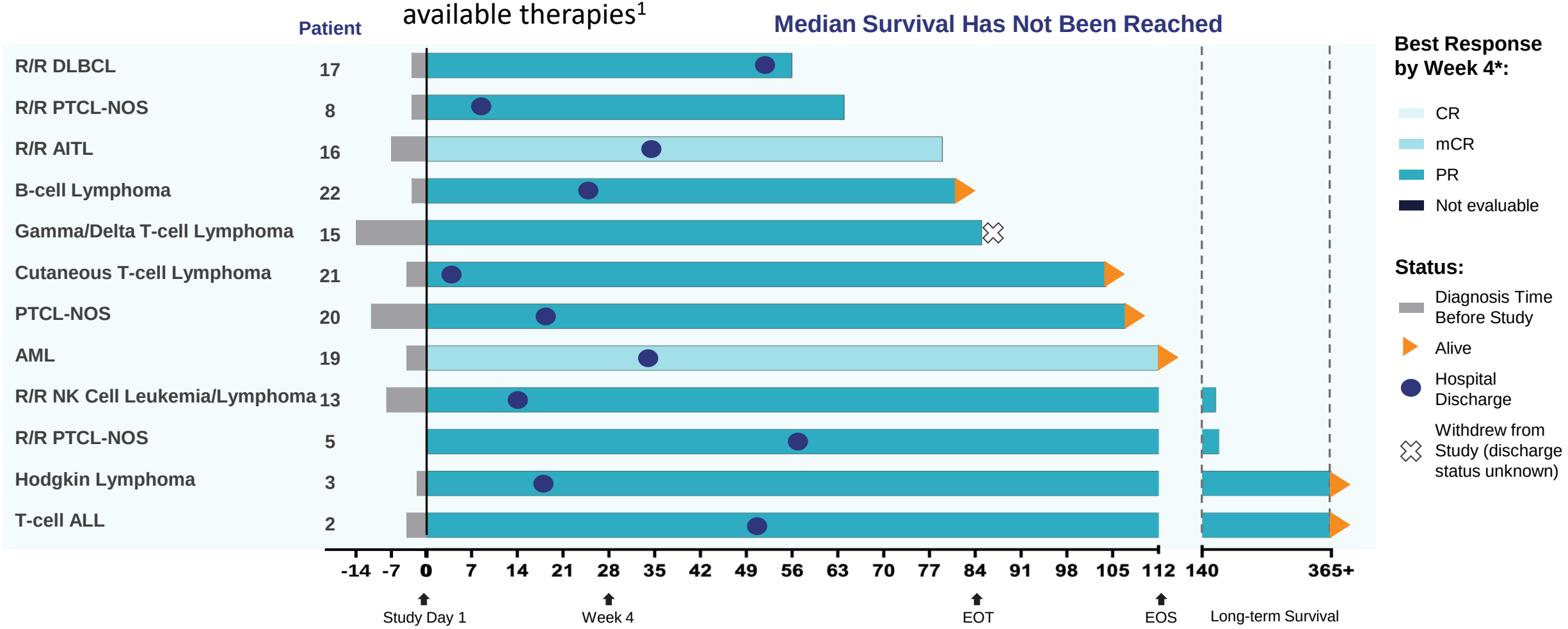
All patients experienced one or more biomarker reductions of >50%

Maiti A….Iyer S, ASH 2024

Improved Survival in mHLH Treated with ELA026 in Frontline Settings:

THE UNIVERSITY OF TEXAS MD Anderson Cancer Center
Making Cancer History®

At 2 months, 92% survival with ELA026 vs. ~50% survival with available therapies[1]



*Using modified HLH-2004 response criteria adapted from (Locatelli 2020)
DLBCL: diffuse large B-cell lymphoma; AITL: angioimmunoblastic T-cell lymphoma; PTCL-NOS: peripheral T-cell lymphoma, not otherwise specified; NK: natural killer; ALL: acute lymphoblastic leukemia; AML: acute myeloid leukemia; CR: complete response; mCR: modified complete response; PR: partial response; HI: HLH improvement; OS: overall survival; EOT: end of treatment; EOS: end of study.

[1]Löfstedt A, Jädersten M, Meeths M, Henter J-I. Malignancy-associated hemophagocytic lymphohistiocytosis in Sweden: incidence, clinical characteristics, and survival. Blood 2024;143(3):233–42

Maiti A….Iyer S, ASH 2024

Emerging themes in T cell Lymphomas

THE UNIVERSITY OF TEXAS MD Anderson Cancer Center
Making Cancer History®

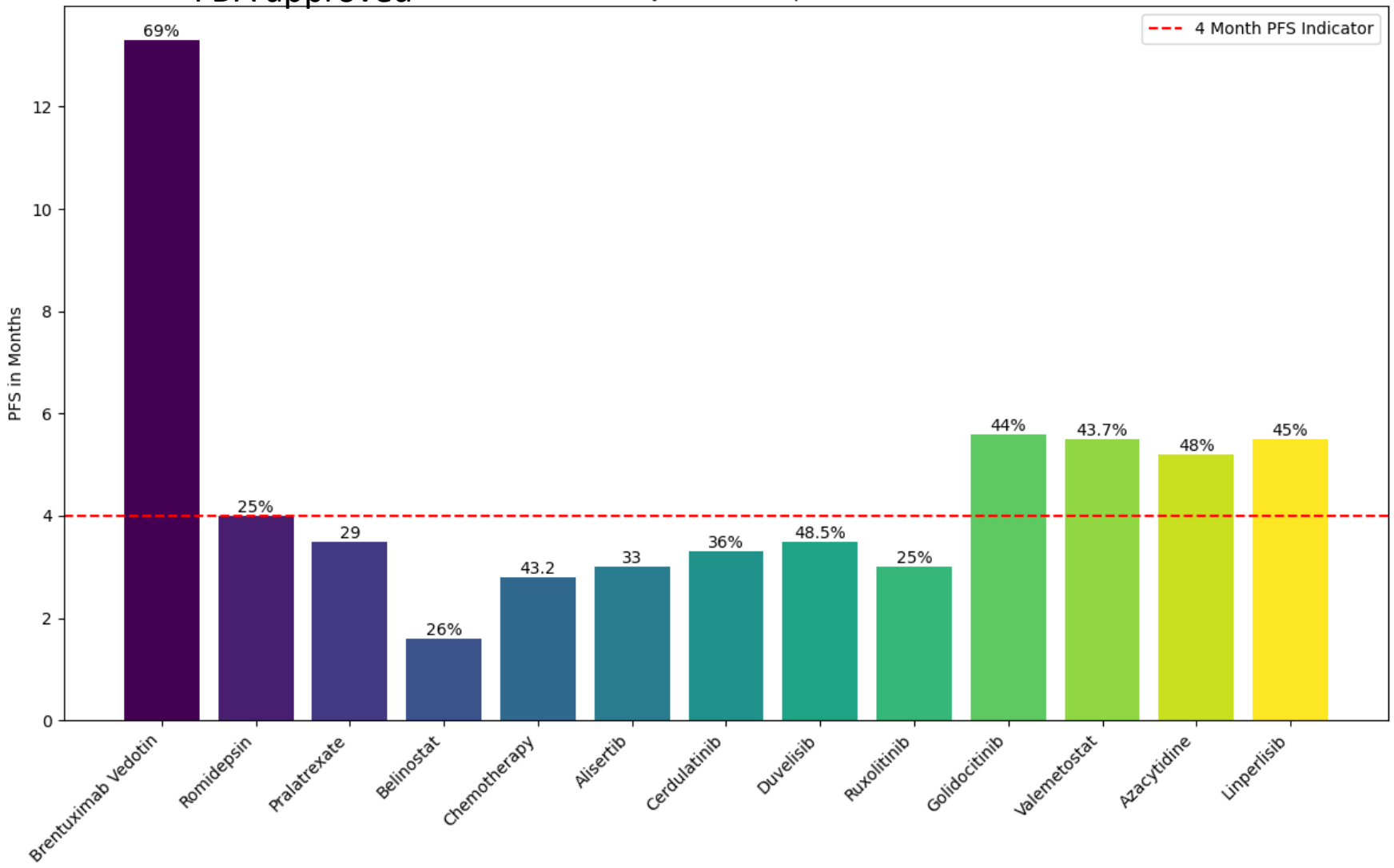
- Epigenetic targeting of Tfh
- Targeting dysregulated pathways: JAK/STAT, PI3K, EZH1/2, ITK
- Targeting cytotoxic, gamma-delta and NK subtypes
- Immunotherapy: checkpoint blockade and cellular
- Pan SIRP inhibitor for LA-HLH

Conclusions: New agents in r/r PTCL

THE UNIVERSITY OF TEXAS MD Anderson Cancer Center
Making Cancer History®

FDA approved

Pivotal studies



Iyer S- unpublished-Modified from pivotal studies

Conclusions: Treatment Landscape

THE UNIVERSITY OF TEXAS MD Anderson Cancer Center
Making Cancer History®

FDA-Approved Agents

•**Brentuximab vedotin** (CD30+ disease): Superior efficacy (13+ months PFS, 69% RR)

•**Other approved agents** with modest efficacy:

- Romidepsin (4 months PFS, 25% RR)- off market
- Pralatrexate (3.5 months PFS, 29% RR)
- Belinostat (1.6 months PFS, 26% RR)

Phase III Study Agents: Promising Alternatives

•All exceed 4-month PFS threshold with improved response rates:

- **Duvelisib:** 3.4 months, 48.5% RR
- **Valemetostat**: 5.4 months PFS, 43.7% RR
- **Linperlisib**: 5.5 months PFS, 45% RR
- **Azacytidine**: 5.2 months PFS, 48% RR
- **Golidocitinib**: 5.6 months PFS, 44% RR
- Soquelitinib: 5.5 months PFS, 40% RR

Cellular Therapy: Allo-CAR-T anti CD70-52% RR and Auto-CAR-T CD5

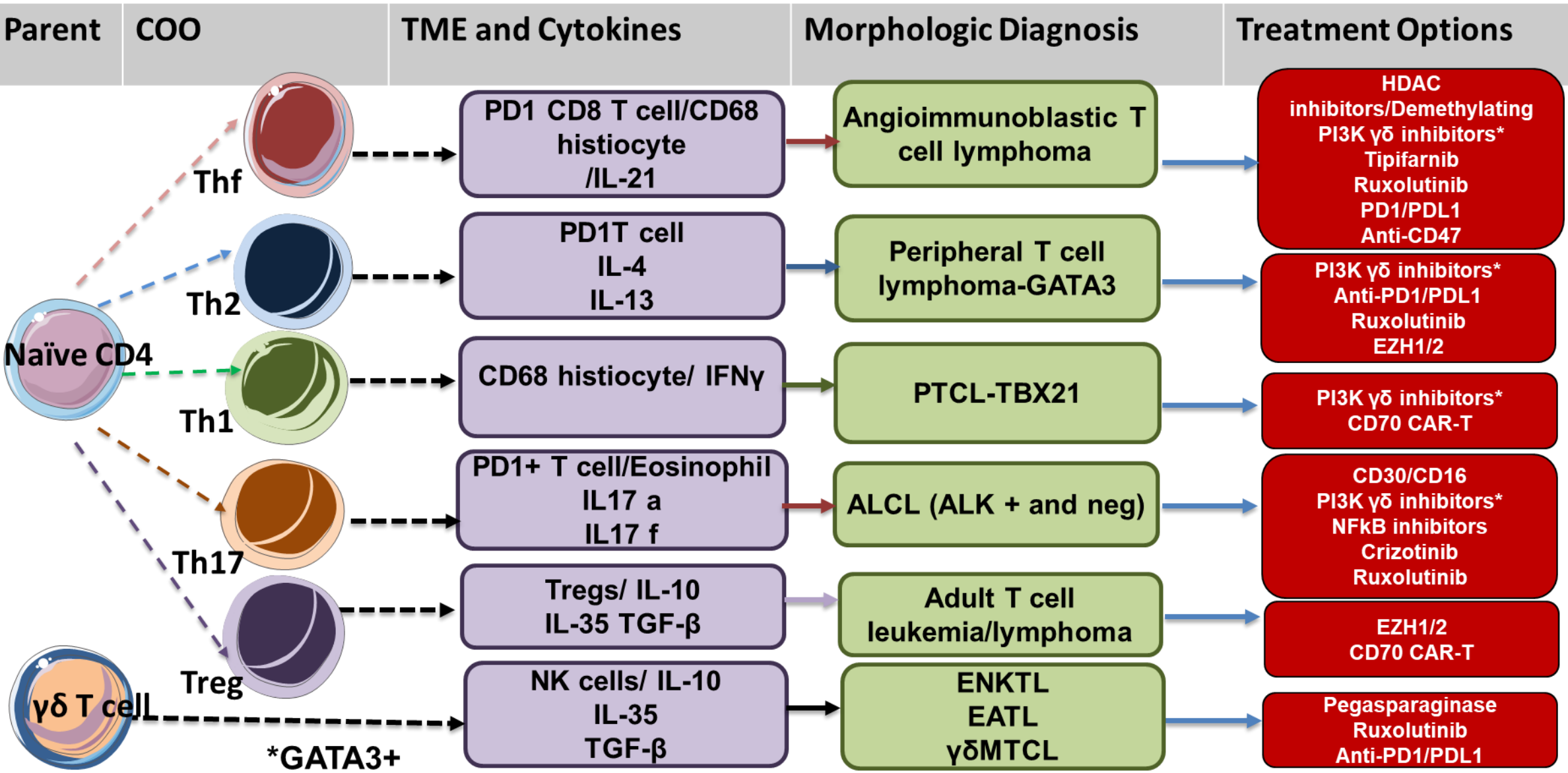
Combinations: Romidepsin+Duvelisib, Romidepsin+ Aza

•**Off-protocol**: Ruxolitinib (3 months, 25% RR)

•**Conventional:** chemotherapy (2.8 months, 43.2% RR)

New agents demonstrate 30-40% longer PFS and ~70% higher response rates compared to most approved agents (except Brentuximab)

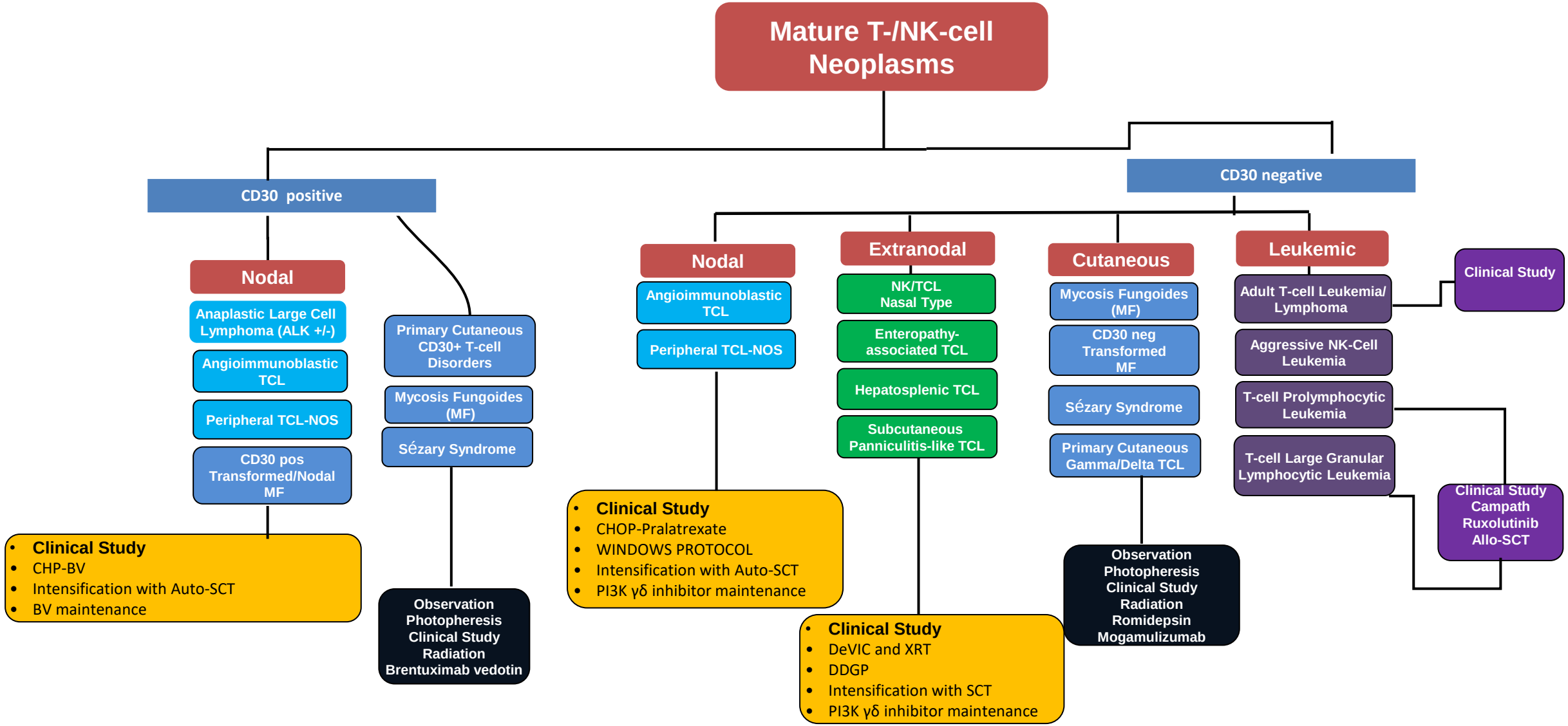
Therapeutic Matching based on Cell of origin (COO) and Tumor microenvironment (TME)



Modified from Marchi, E. and O'Connor, O.A. 2020 CA A Cancer J Clin, 70: 47-70. Vega F, EXABS-TCL-052.2020

Mature T cell Lymphoma Care Pathways

THE UNIVERSITY OF TEXAS MD Anderson Cancer Center
Making Cancer History®



THE UNIVERSITY OF TEXAS
MD Anderson Cancer Center
Making Cancer History®

MOON SHOTS

Proposed-
T/NK-Cell Malignancy Moon Shots

Sattva Neelapu, M.D.
Department of Lymphoma and Myeloma

Swaminathan P. Iyer, M.D.
Department of Lymphoma and Myeloma

Tapan Kadia, M.D.
Department of Leukemia

ADOPTIVE CELL THERAPY
APOLLO
B-CELL LYMPHOMA
BREAST CANCER
CANCER GENOMICS LABORATORY
CANCER PREVENTION AND CONTROL
CLL
COLORECTAL CANCER
ECLIPSE
GLIOBLASTOMA
HIGH-RISK MULTIPLE MYELOMA
HPV-RELATED CANCERS
IMMUNOTHERAPY
INSTITUTE FOR APPLIED CANCER SCIENCE
LUNG CANCER
MDS AND AML
MELANOMA
ORBIT
OVARIAN CANCER
PANCREATIC CANCER
PROSTATE CANCER
PROTEOMICS
TRACTION
TRANSLATIONAL RESEARCH ACCELERATOR & TRACTION

T Cell Lymphoma Group

THE UNIVERSITY OF TEXAS MD Anderson Cancer Center
Making Cancer History®

Lymphoma:

- Dr.Christopher Flowers
- Dr.Sattva Neelapu
- Dr.Loretta Nastoupil
- Dr.Jason Westin
- Dr.Felipe Samaniego
- Dr.Nathan Fowler
- Dr.Luis Malpica
- Dr.Ranjit Nair
- Dr.Luis Fayad
- Dr.Dai Chihara
- Dr.Madeleine Duvic
- Dr.Auris Huen
- Dr.Bouthina Dabaja
- Dr.Jillian Gunther
- Dr.Chitra Hosing
- Dr.Yago Nieto
- Dr.Samer Srour
- Dr.Meghan Heberton
- Dr.Jeff Medeiros
- Dr.Francisco Vega
- Dr.Roberto Miranda
- Dr.Carlos Torres-Cabala
- Dr.Mark Clemens
- Dr.Kelly Hunt
- Dr.Jessie Xu
- Dr.Susan Wu
- Dr.Luis Fayad
- Dr. Chelsea Pinnix
- Dr.Chi Ok
- Dr.MJ You
- Dr.John Stewart
- Dr.Keyur Patel

- Dr.Cara Haymaker
- Dr.Ayse Koksoy
- Dr.Rengenath
- Dr.Daniela Duenas
- Dr.Jingjing Liu
- Dr. John Zhang

Rare Lymphoma:

- Dr.Michael Wang
- Dr.Sairah Ahmed
- Dr.Hun Ju Lee
- Dr.Preetesh Jain

Collaborators:

- Dr.Michael Green
- Dr. Deepa Sampath
- Dr.Eric Davis
- Dr.Simrit Parmar

Collaborators:

- Radiology
- LOD
- Section Rare Lymphoma
- Dept. Lymphoma/Myeloma
- Div. Medicine


THE UNIVERSITY OF TEXAS
MD Anderson Cancer Center
Making Cancer History®
TCLG
RAD-ONC
SCT
HEM-LYM
HEM
PATH
DERM
DERM