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T Cell Lymphoma What's New
Luis E Fayad M.D.
Professor of Lymphoma/Myeloma

Classification of Peripheral T-cell Lymphoma (PTCL)

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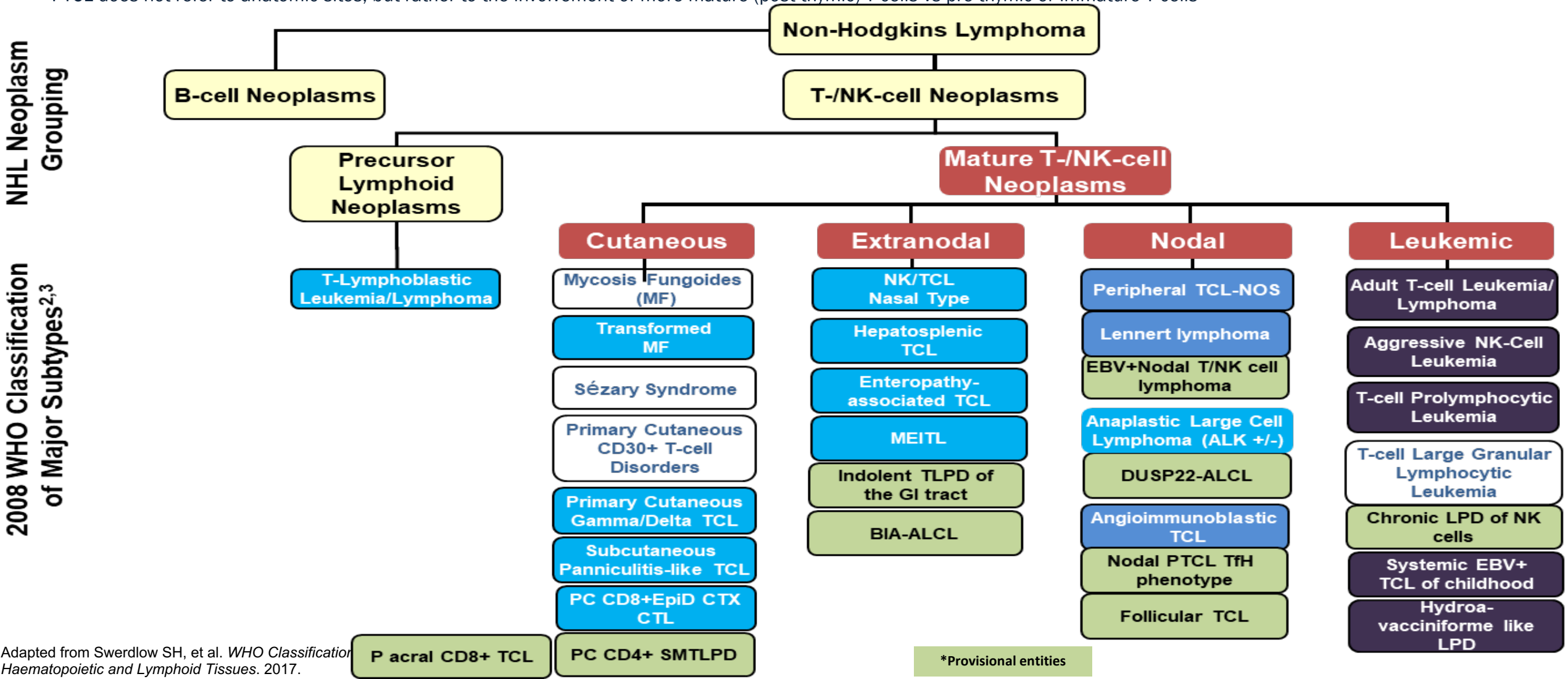
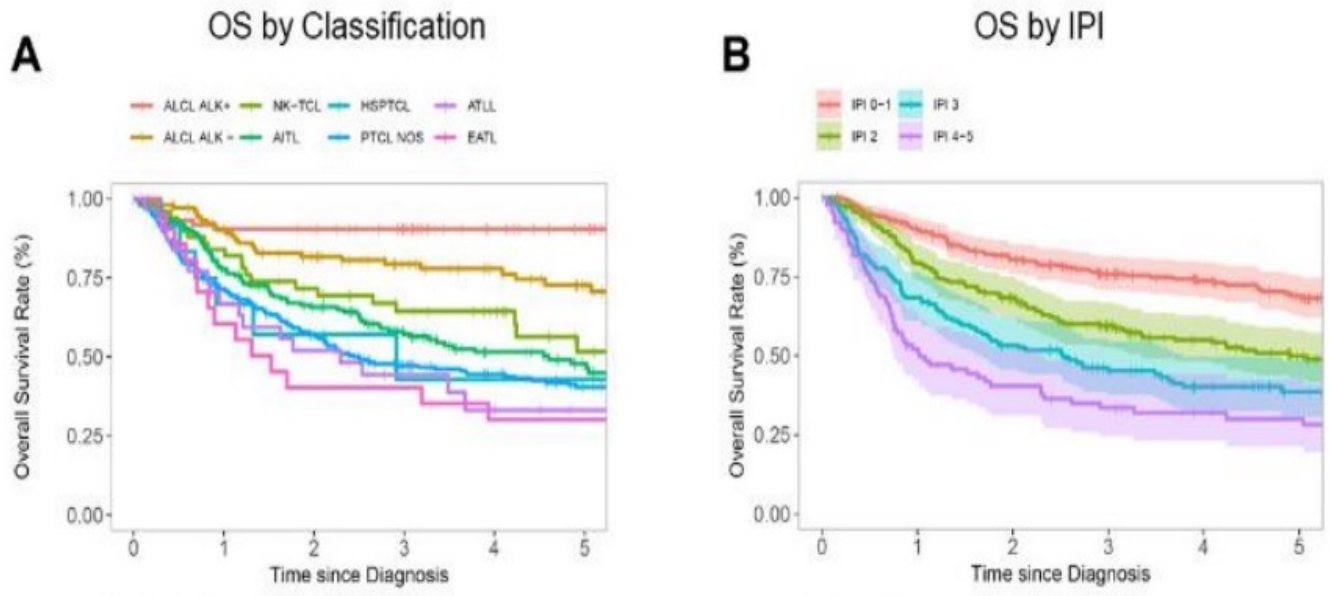
PTCL is a heterogeneous group of aggressive mature T-/NK-cell lymphomas

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 of Tumours of Haematopoietic and Lymphoid Tissues*. 2017.

PATTERNS OF CARE AND CLINICAL OUTCOMES IN PTCL



Lymphoma epidemiology of outcomes and molecular epidemiology resource (leo-mer) prospective cohort study (20 years)

Ruan et al: ASH 2022

the MIRACLE of SCIENCE with SOUL City of Hope

UPDATED CLASSIFICATION OF NODAL PTCL

THE MAIN QUESTIONS IN TREATING T- CELL LYMPHOMAS

- **Upfront therapy- how to choose the best regimen for my patient**
- Should ASCT be offered in CR1-
- **Relapsed disease – how to optimize treatment options**
- Role of allogeneic stem cell transplant
- **Special populations- elderly, frail,**
- Rare subtypes

National Comprehensive Cancer Network®

NCCN Guidelines Version 1.2023
Peripheral T-Cell Lymphomas

NCCN Guidelines Index
Table of Contents
Discussion

SUGGESTED TREATMENT REGIMENS[a]

	FIRST-LINE THERAPY[b]
ALCL[c]	Preferred regimen • Brentuximab vedotin + CHP (cyclophosphamide, doxorubicin, and prednisone)[d] (category 1) Other recommended regimens • CHOP (cyclophosphamide, doxorubicin, vincristine, and prednisone) • CHOEP[e] (cyclophosphamide, doxorubicin, vincristine, etoposide, and prednisone) • Dose-adjusted EPOCH (etoposide, prednisone, vincristine, cyclophosphamide, and doxorubicin)
Other histologies (PTCL-NOS; AITL; EATL; MEITL; nodal PTCL, TFH; and FTCL)[f]	Preferred regimens (alphabetical order) • Brentuximab vedotin + CHP for CD30+ histologies[d,g] • CHOEP[e] • CHOP • Dose-adjusted EPOCH Other recommended regimens (alphabetical order) • CHOP followed by IVE (ifosfamide, etoposide, and epirubicin) alternating with intermediate-dose methotrexate (Newcastle Regimen; studied only in patients with EATL)[h] • HyperCVAD (cyclophosphamide, vincristine, doxorubicin, and dexamethasone) alternating with high-dose methotrexate and cytarabine (category 3)

FIRST-LINE CONSOLIDATION
• Consider consolidation with autologous HCT

Selected Attempts To Improve Upon CHOP for PTCL

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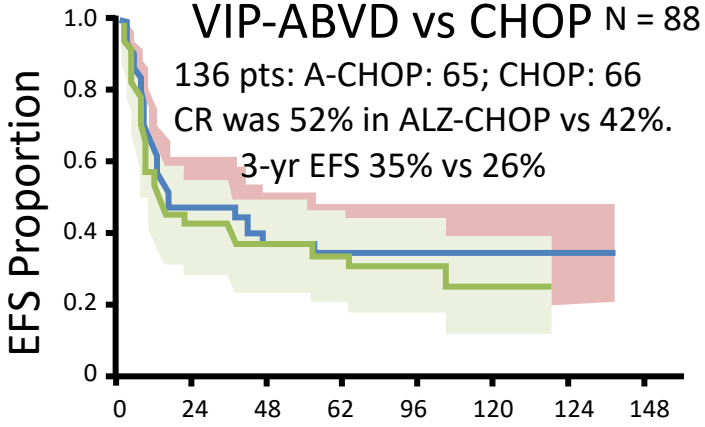
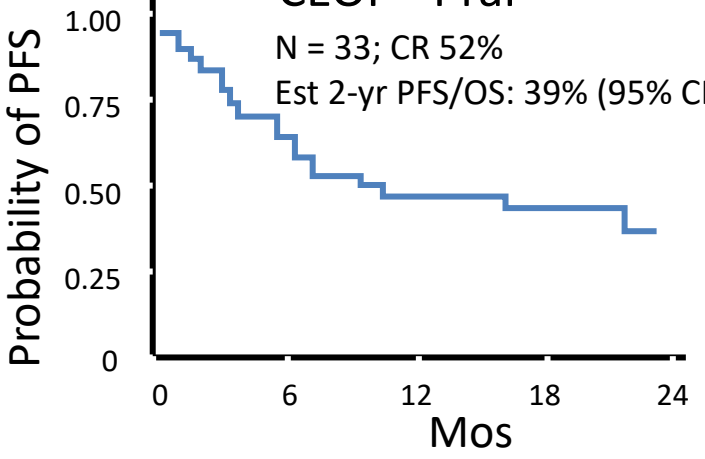
VIP-ABVD vs CHOP N = 88

136 pts: A-CHOP: 65; CHOP: 66
CR was 52% in ALZ-CHOP vs 42%.
3-yr EFS 35% vs 26%

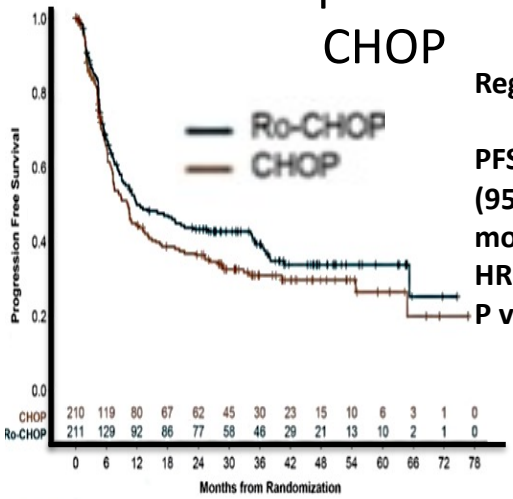


CEOP –Pral

N = 33; CR 52%
Est 2-yr PFS/OS: 39% (95% CI 21-57)

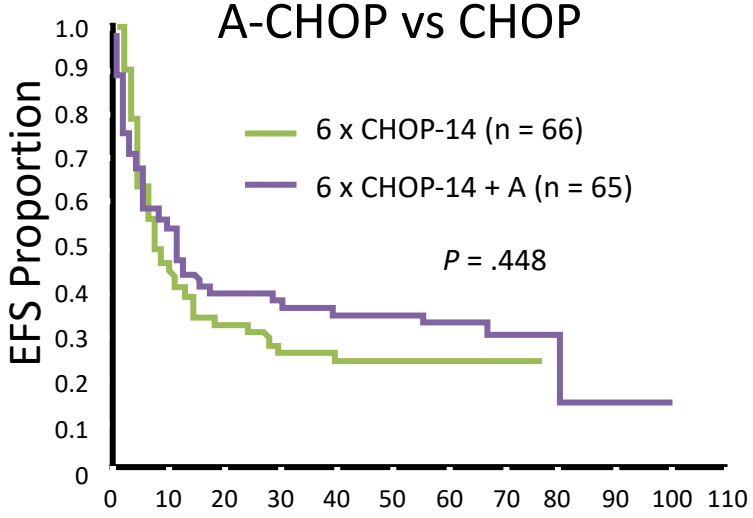


Romidepsin-CHOP vs. CHOP



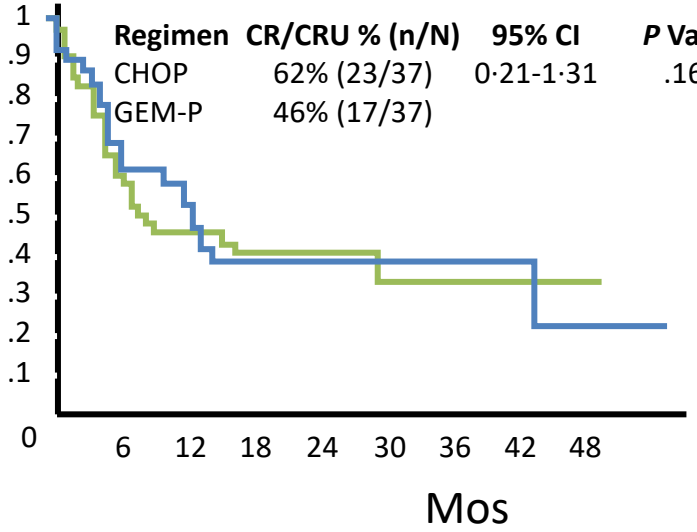
Regimen	Ro-CHOP (n=211)	CHOP (n=230)
PFS median (95% CI), mo	12.0 (9-25.8)	10.2 (7.4-13.2)
HR (95% CI)	0.81 (0.63-1.04)	
P value	0.096	

A-CHOP vs CHOP



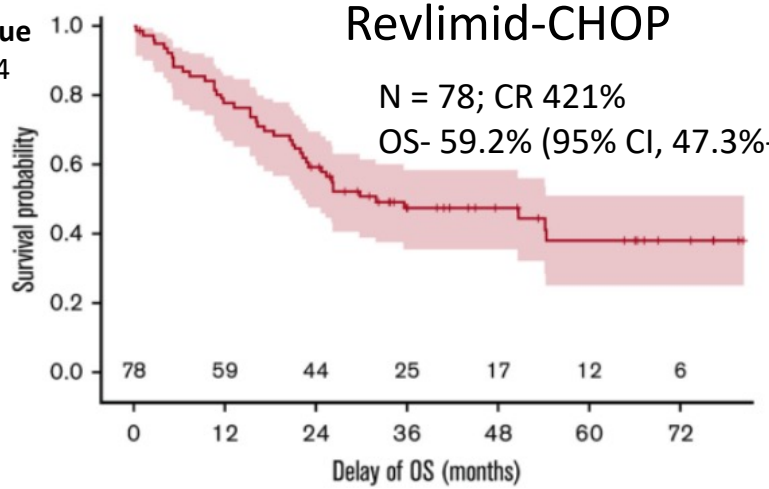
CHOP vs GEM-P

Regimen	CR/CRU % (n/N)	95% CI	*P* Value
CHOP	62% (23/37)	0·21-1·31	.164
GEM-P	46% (17/37)		



Revlimid-CHOP

N = 78; CR 421%
OS- 59.2% (95% CI, 47.3%-69.3%)



Simon. Br J Haem. 2010. d'Amore. ASH 2018. Advani. Br J Haem. 2016;172:636. Gleeson. Lancet Haem. 2018;5:E190; Bachy et al. Lancet Haem. 2021, Lemmonier et al. Blood Adv, 2021

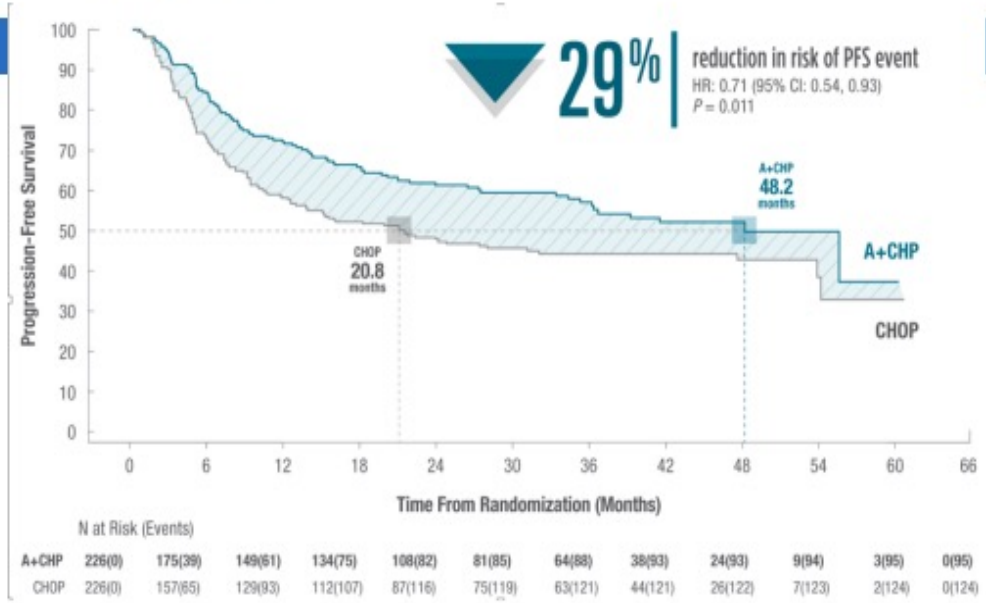
BRENTUXIMAB + CHP FOR CD30 + PTCL

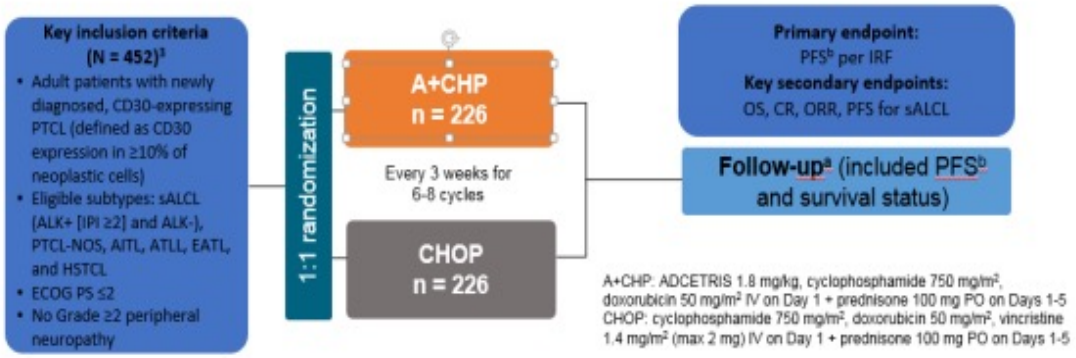
Echelon -2 Frontline treatment with A+CHP vs CHOP for newly diagnosed, CD30-expressing PTCLs demonstrated a 29% reduction in risk of PFS event (HR: 0.71; 95% CI: 0.54-0.93; *P* = 0.011)

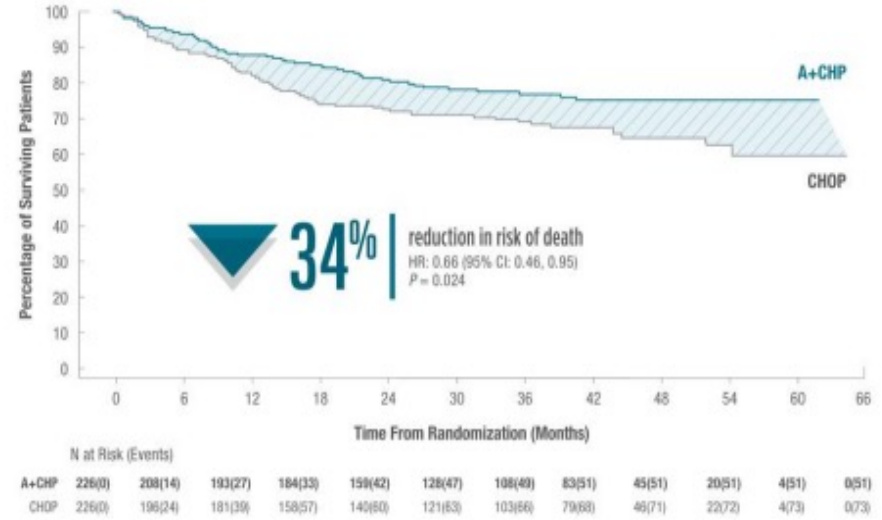
A+CHP more than doubled median PFS vs CHOP (48.2 vs 20.8 months, respectively)

34% reduction in risk of death with A+CHP (HR: 0.66; 95% CI: 0.46-0.95; *P* = 0.024)[1]. Median OS was not reached in either arm

A+CHP has a comparable safety to CHOP







Horwitz et al : Lancet 2019

SUB ANALYSIS ECHELON2 - FOOD FOR THOUGHT

Analysis by Subtypes: Estimated 5-year PFS and OS rates in prespecified subgroups

Subgroup	Estimated 5-year PFS rate A+CHP	Estimated 5-year PFS rate CHOP	HR (95% CI)	P-value	Estimated 5-year OS rate A+CHP	Estimated 5-year OS rate CHOP	HR (95% CI)	P-value
PTCL subtype								
PTCL-NOS, % (n)	26.5 (29)	25.7 (43)	0.79 (0.43, 1.43)	0.4	46.2 (29)	35.9 (43)	0.75 (0.37, 1.48)	0.4003
AITL, % (n)	26.6 (30)	48.1 (24)	1.41 (0.64, 3.11)	0.3958	67.8 (30)	62.5 (24)	1.01 (0.40, 2.55)	0.9855
sALCL								
Overall, % (n)	60.6 (162)	48.4 (154)	0.55 (0.39, 0.79)	0.0009	75.8 (162)	68.7 (154)	0.66 (0.43, 1.01)	0.0529
ALK+ % (n)	87 (49)	67 (49)	0.40 (0.17, 0.98)	0.0372	91.5 (26)	79.6 (27)	0.48 (0.16, 1.40)	0.1688
ALK– % (n)	49 (113)	39 (105)	0.58 (0.40, 0.86)	0.0054	68.7 (50)	63.3 (41)	0.71 (0.44, 1.12)	0.1373
sALCL, IPI Score								
0–1, % (n)	59.5 (41)	47.6 (32)	0.42 (0.18, 0.94)	0.0301	87.0 (41)	86.2 (32)	0.73 (0.20, 2.73)	0.6411
2–3, % (n)	68.5 (95)	50.9 (100)	0.57 (0.35, 0.90)	0.0158	80.6 (95)	68.7 (100)	0.57 (0.32, 1.01)	0.0496
4–5, % (n)	27.2 (26)	36.4 (22)	0.73 (0.35, 1.50)	0.3839	38.0 (26)	43.2 (22)	0.89 (0.42, 1.89)	0.7606

Presentation last saved: Just now

ITT, intent-to-treat; IPI, International Prognostic Index

ACLE of SC

Horwitz et al: ASH 2021

Frontline CHOEP → ASCT in PTCL

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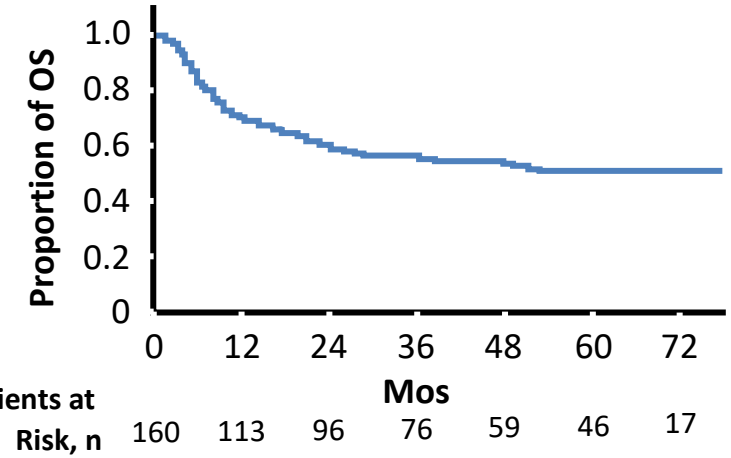
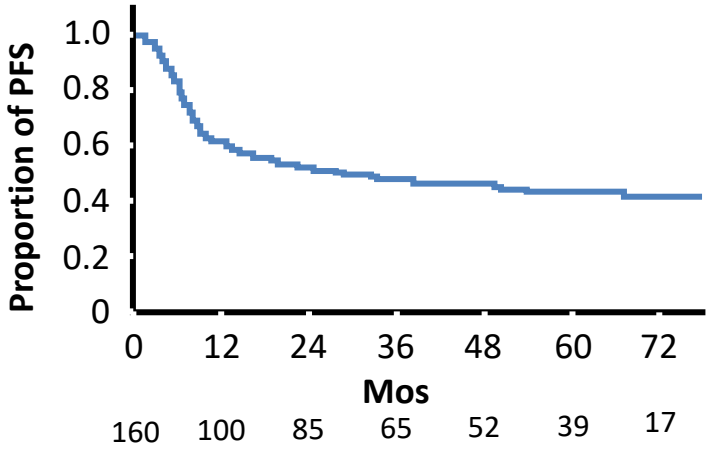
- Phase II NLG-T-01 Trial (aka The Nordic Trial)
- N = 160 patients with untreated systemic PTCL
- Treatment: CHO(E)P-14* Q2W x 6 cycles
  - ORR: 82% with CR 51%
  - BEAM or BEAC plus ASCT (n = 115; 72%)

*Etoposide omitted for patients older than 60 yrs of age.

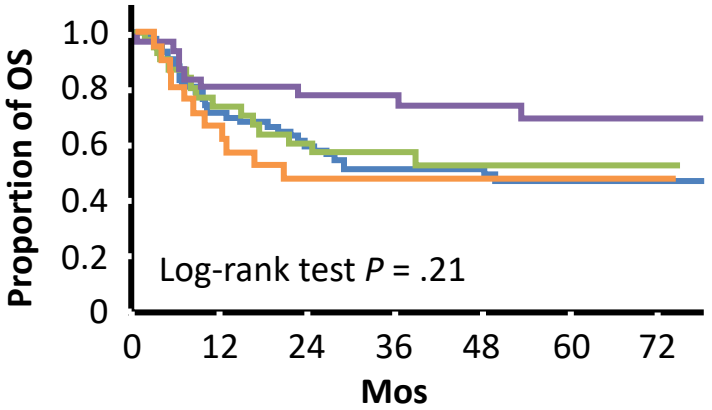
5-Yr OS, All Patients: 51%



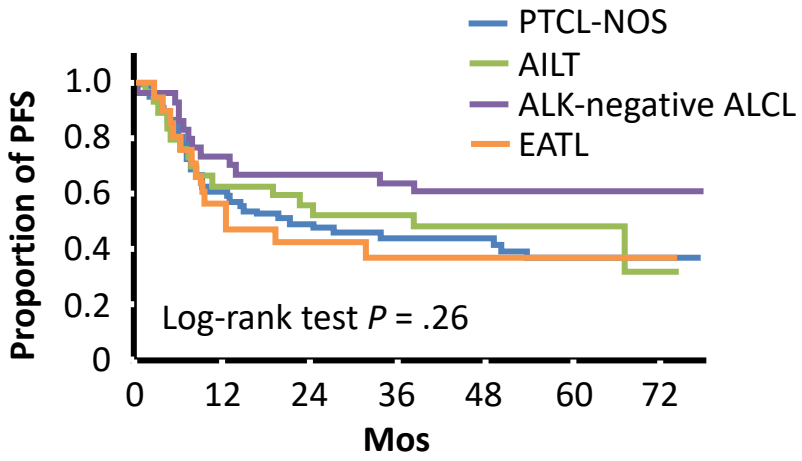
5-Yr PFS, All Patients: 44%



5-Yr OS by PTCL Subtype

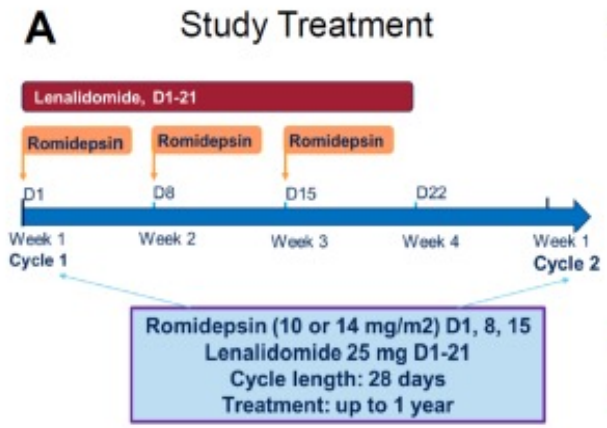


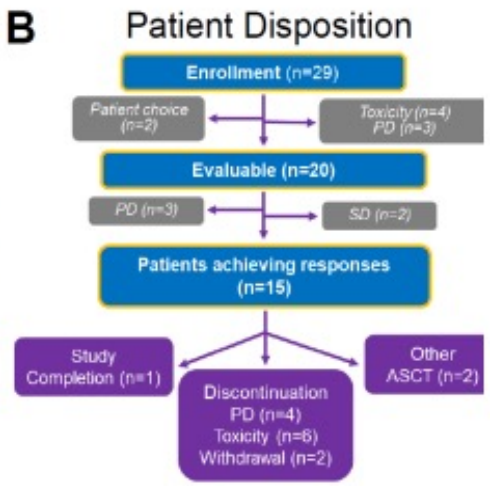
5-Yr PFS by PTCL Subtype

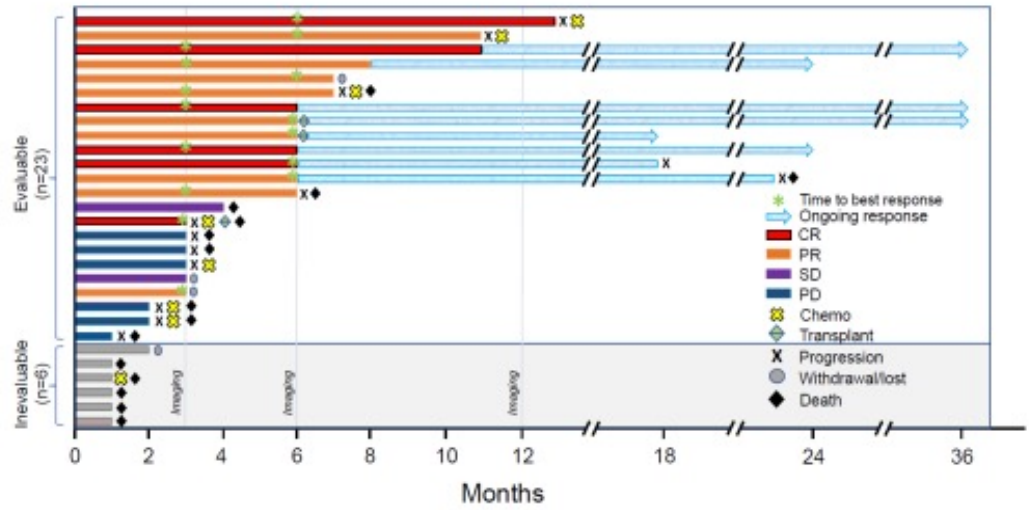


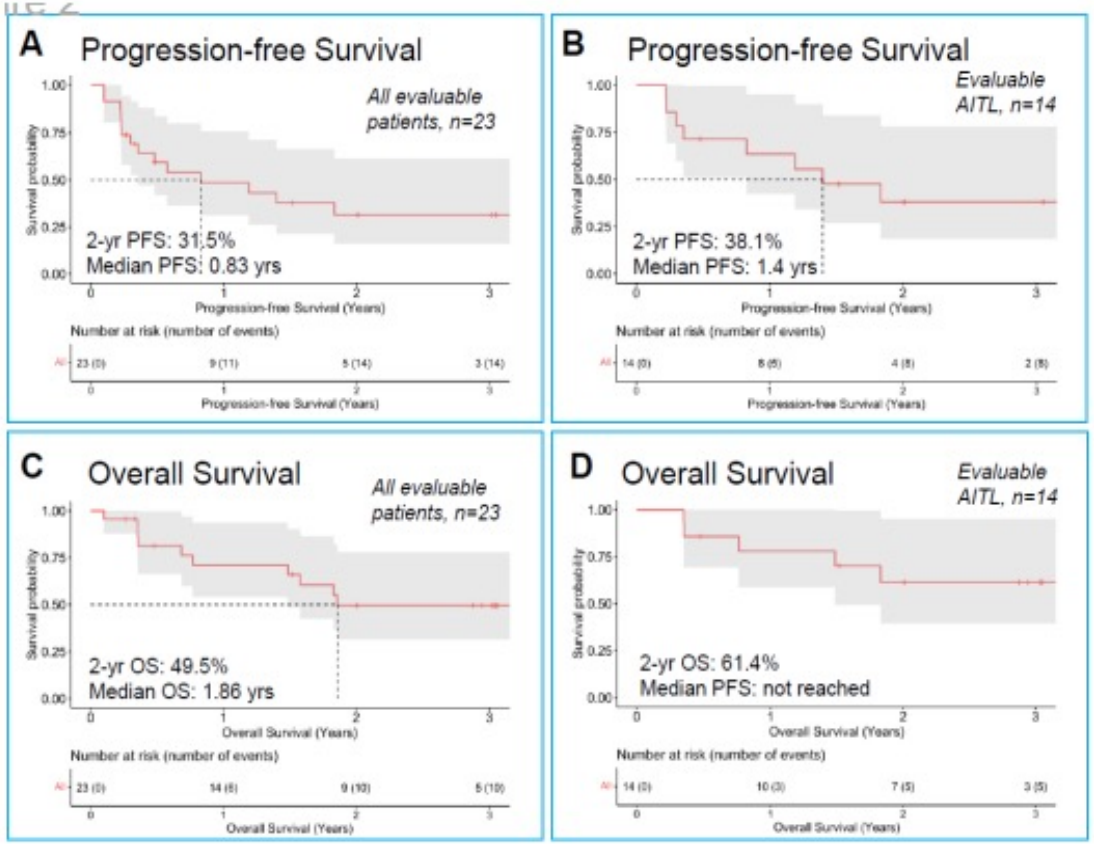
d'Amore. J Clin Oncol. 2012;30:3093.

CHEMOFREE COMBINATIONS FOR UPFRONT THERAPY





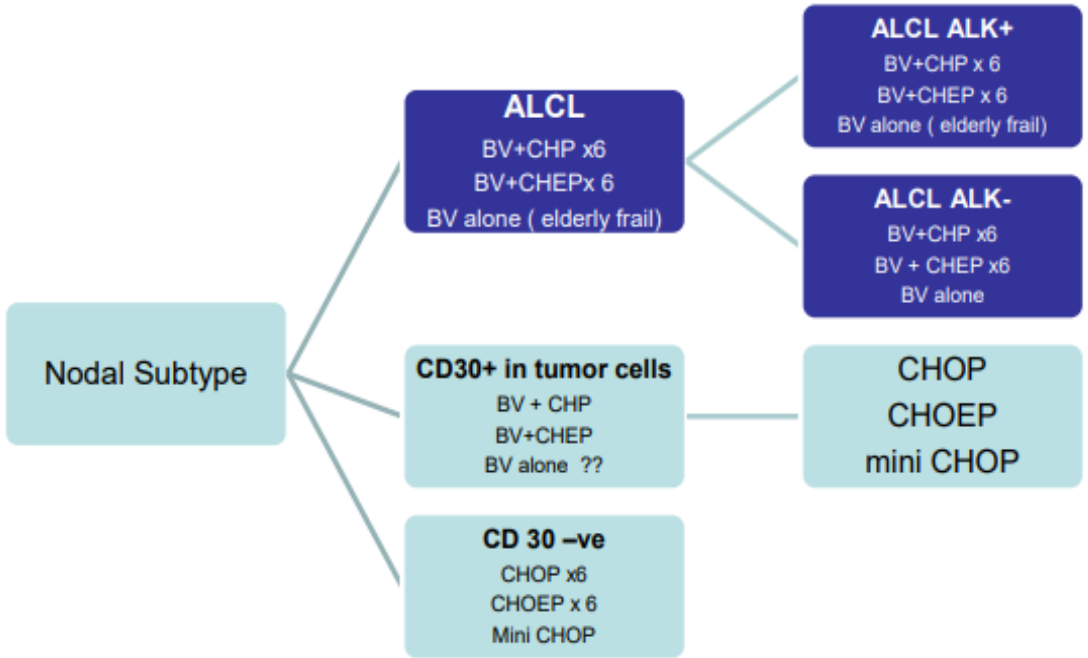




Favorable safety signal
Favorable efficacy esp in TFH subtype

Ruan et al: Blood advances 2023

UPFRONT THERAPY – WHAT WE KNOW SO FAR



Always consider a clinical trial if available

Horwitz et al; 2019,Hererra et al 2021, Lunning et al 2019 ASH 2022 abstract 2922, 2909

- CHOP - remains the backbone of upfront therapy (CR 31-67%) - Etoposide- role in upfront regimen continues to be debated.
- **BV+CHP - CD30+ lymphomas and ALCL (randomized trial**
- CHEP+BV – ORR 94%, Possible EPCH+BV?
- CHOP+ Romidepsin (Ro-CHOP) – Initial results ORR 78% including 66% CR. Randomized phase 3 is negative Romidepsin +CHOEP – did not meet primary end point
- CHOP+ Pralatrexate - ORR 89%, CR 67%
- CHOP+ Belinostat – ORR 86%, CR 67%, PR 19%
- CHOEP+ Revlimid – ORR 88% and CR 38%. Len maintenance arm- toxic
- 5- aza + CHOP- 2 yr PFS 68.4%, 76.1% for PTCL-TFH
- phase III study of Chidamide +azacytidine +CHOP vs CHOP- no significant improvement in ORR or PFS

RELAPSED DISEASE

Treatment Goals

Induce remission – need agents with high ORR and CR

Consider allogeneic stem cell transplant in eligible patients

Second line agents should be considered a bridge to transplant at least in 2023 in eligible patients

In transplant ineligible patients, goal is palliation

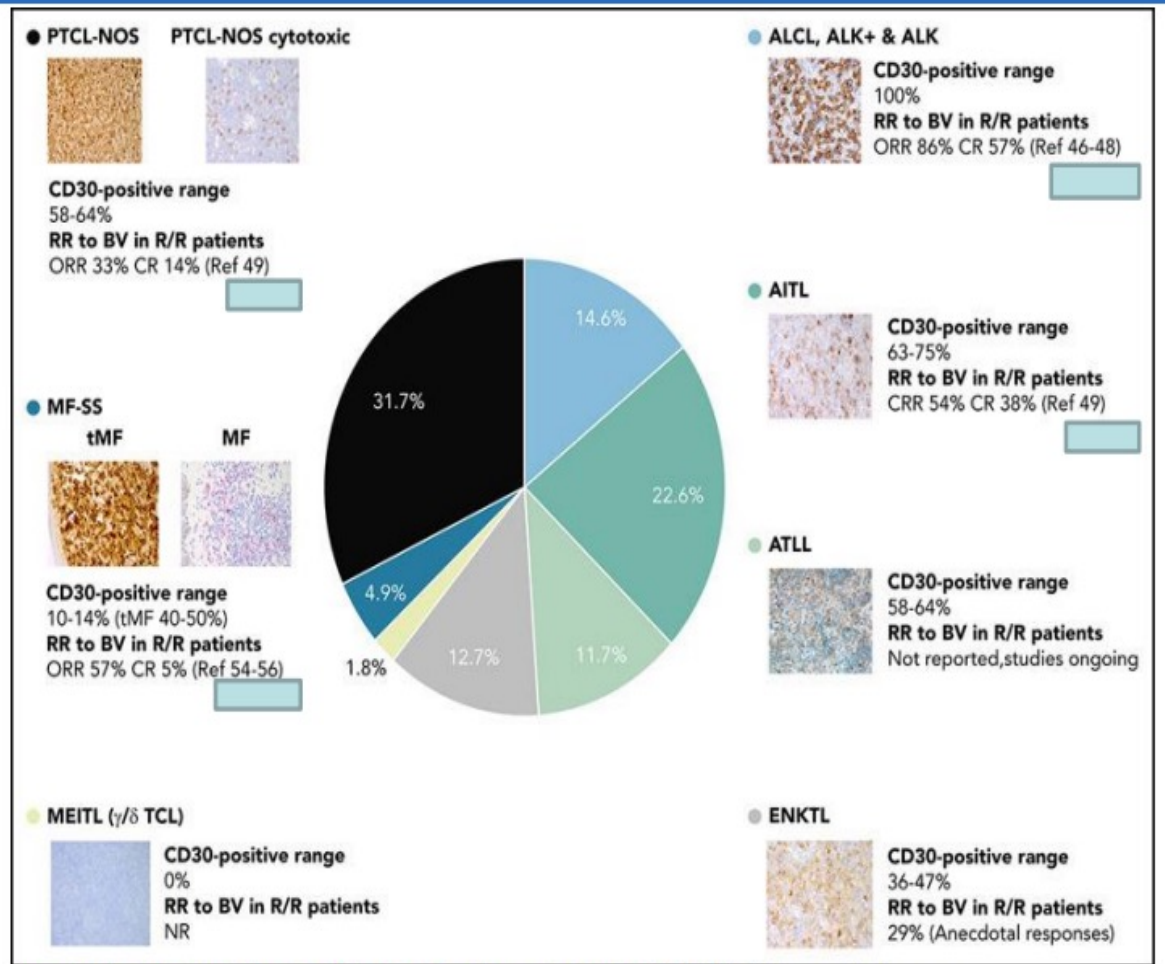
Challenges

Rare and heterogeneous diseases

Lack of adequate tumor models to study the disease

Limited interest from pharmaceuticals

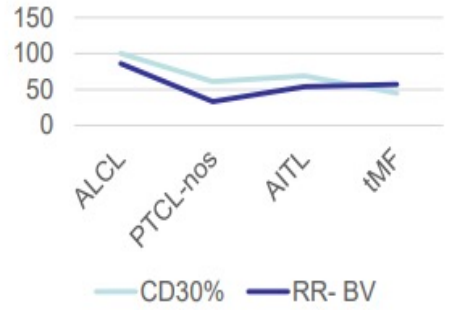
CD30 EXPRESSION AND RESPONSE TO BV IN PTCL



Immunohistochemistry on FFE with monoclonal antibody BerH2

Lack of consensus on positive cutoffs (>1%, >10%, >20-25%

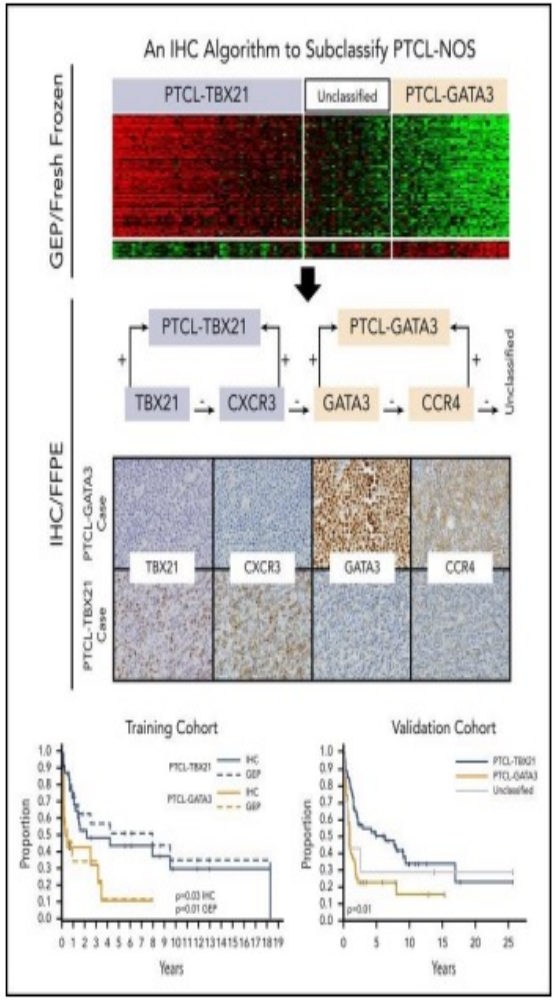
Clinical significance of cutoffs is unclear- ongoing study ---

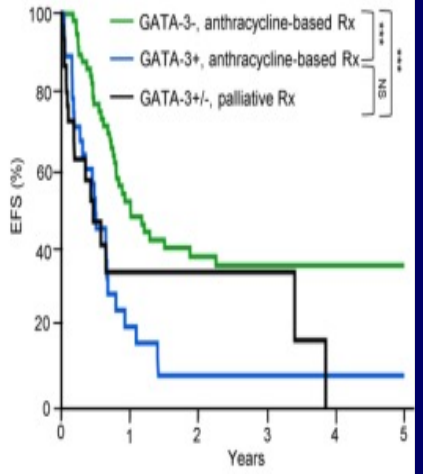


Barta et al, Blood (134) 26, 2339-2345

RELAPSED PTCL- NOS

Single Agent	CR/PR	DOR
Pralatrexate (2009)	32%	10.1 months
Romidepsin (2009)	29%/ 14%	28 months
Belinostat (2014)	23%	13.6 months
Brentuximab Vedotin	33%/14%	
Duvelisib	48.1%	5.5 months
Ruxolitinib	18%	
Valemetostat	55%	





GATA3 subtype has a worse prognosis

Weiss et al: Frontiers Oncology 2023

Amador et al : Blood 2019

HOW TO MAKE SENSE OF ALL THIS DATA FOR RELAPSED REFRACTORY PTCL

- Clinical trial – novel agents in study – CDK9 inhibitors , EZH2 inhibitors
- Send for mutation analysis if possible
- For TFH subtypes – prefer
  - Epigenetic therapies – Romidepsin alone or in combination– (5 aza, lenalidomide)
  - Duvelisib
- ALCL- alk+
  - Alk inhibitors
  - BV- can try again if not previously refractory
  - Pralatrexate
- ALCL- alk –ve
  - BV- can try again if not previously refractory, BV + bendamustine
  - Pralatrexate
- PTCL-nos
  - Duvelsib
  - Epigeneitic therapy
  - Pralatrexate

Allogeneic stem cell transplant in eligible patients

If transplant ineligible, consider maintenance strategies

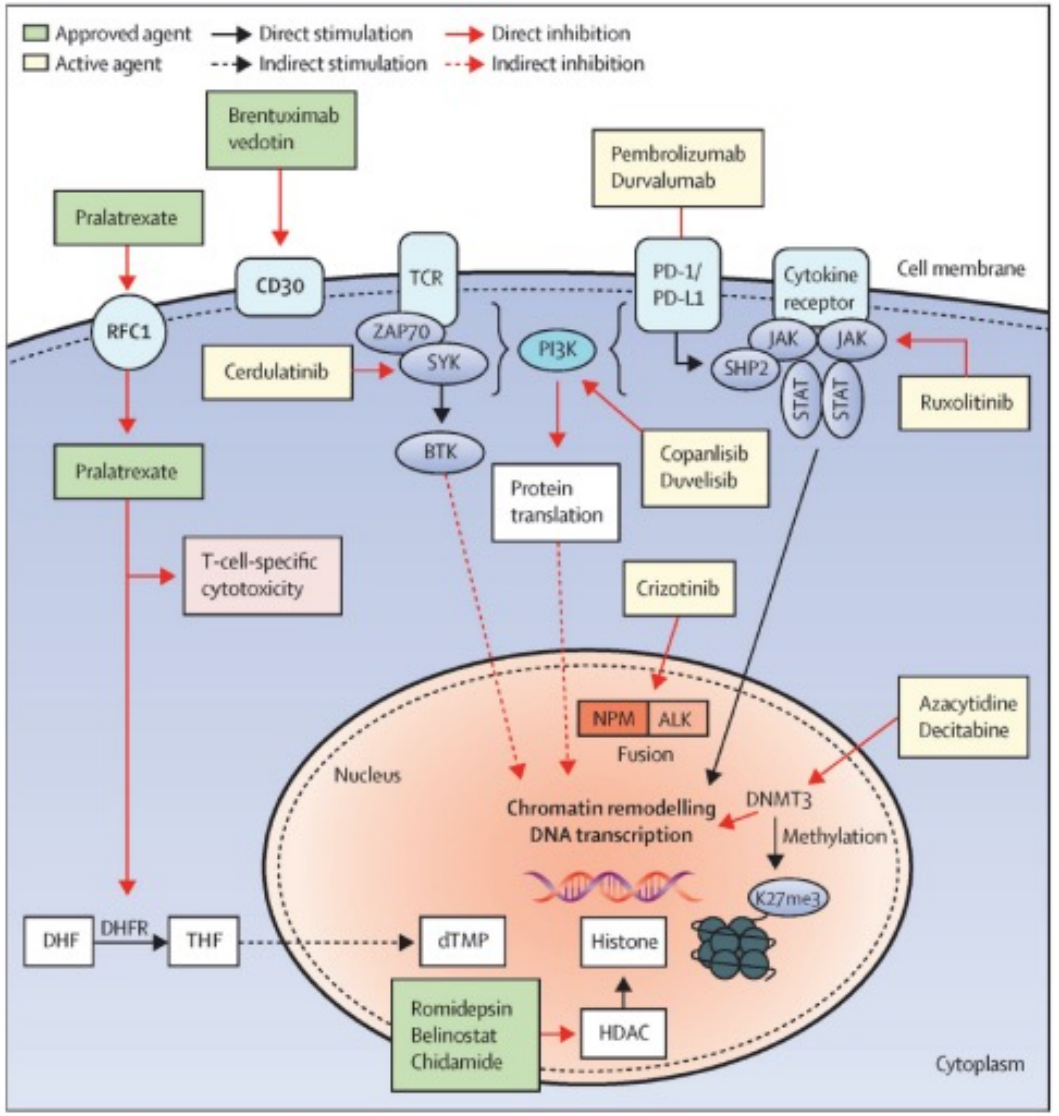
Potentially targetable intracellular signals in PTCL

Pi3K
Copanlisib
Duvelisib
Tenalisib
Linperlisib

JAK: Ruxolitinib
Golidocitinib

ALK inhibitors:
Crizotinib
Alectinib

EZH1/EZH2 inhibitors:
Valemetostat



SYK/(JAK)
Cerdulatinib

BCL2:
Venetoclax

Hypomethylators
Azacytidine
Decitabine

HDAC:
Romidepsin
Belinostat
Chidamide

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PI3K inhibitors in PTCL

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PI3K Inhibitor	# pts	ORR	CR	Reference
Duvelisib	35	50%	19%*	Horwitz et al.
Tenalisib	35	45.7%	26%	Huen et al.
Linperlisib	48	48%	30%	Song et. al

*CR=34% in PRIMO study (n=101)

PI3K Inhibitor	Neutropenia	Diarrhea /Colitis	Elevated Liver Enzymes	Infections (e.g., Pneumonitis)	Rash	Hyperglycemia	Hypertension	Other Side Effects
Duvelisib	↑↑	↑↑	↑↑	↑↑	↑			
Parsaclisib	↑	↑	↑↑		↑↑			Dermatological reactions (↑)
Tenalisib	↑↑		↑		↑			Thrombocytopenia (↑↑)
Linperlisib	↑			↑				
Copanlisib	↑↑		↑	↑		↑↑	↑↑	Hepatotoxicity (↑)

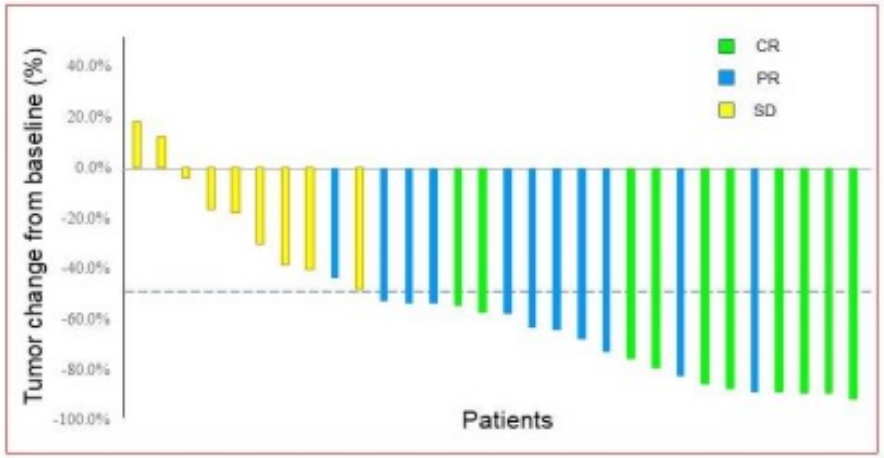
Horwitz S.M., et al. Blood. 2018; Huen A, et al. Cancers (Basel). 2020;Song Y, et al. ASH 2023

Phase Ib trial of linperlisib in relapsed/refractory PTCL

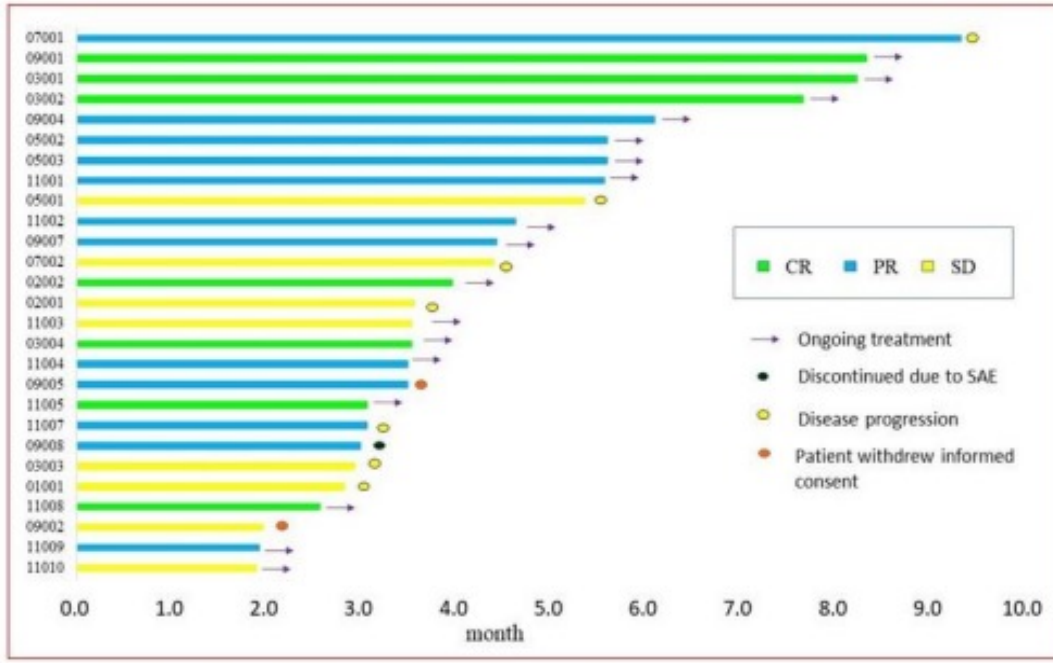
38 PTCL patients enrolled
Stage III 42.1%
Stage IV 52.6%

Histology:
PTCL-NOS (n=13)
AITL (n=11)
ALCL (n=3)
NKTCL (n=2)
MEITL (n=1).

70% ORR
33% CR
37% PR
30% SD
100% DCR



r/r PTCL patients on the study



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Jin J. *J Clin Oncol (ASCO annual meeting abstracts)*, 2021; 39: 753

Golidocitinib in Treating Refractory or Relapsed Peripheral T- Cell Lymphoma: Primary Analysis of the Multinational Pivotal Study Results (JACKPOT8)

Demographics & Characteristics	n = 112
Median age, y (range)	58 (20 - 79)
Female/Male, n (%)	39 (34.8)/73 (65.2)
ECOG PS, n (%)	
0/≥1	51 (45.5)/61 (54.5)
Median prior lines of systemic therapies (range)	2 (1 - 3)
Prior systemic therapies, n (%)	
Chemotherapy	110 (98.2)
Mitoxantrone	3 (2.7)
HDAC inhibitor	51 (45.5)
CD30 targeted therapy	18 (16.1)
Prior HSCT, n (%)	2 (1.8)
Bone marrow involvement at baseline, n (%)	22 (19.6)
LDH elevation at baseline, n (%)	56 (50.0)

Demographics & Characteristics	n = 112
Histology subtypes by central review, n (%)	
PTCL, NOS	51 (45.5)
AITL	16 (14.3)
ALCL	11 (9.8)
NKTCL	4 (3.6)
Others*	9 (8.0)
Central confirmed non-PTCL	4 (3.6)
Unable to confirm	9 (8.0)
Sample under testing	8 (7.1)

Data cut-off date: February 16, 2023

- A total of 112 subjects with r/r PTCL were enrolled from sites in Australia, China, South Korea, and the US.
- All subjects received at least one dose of golidocitinib at 150 mg QD.

Kim WS. *Hematol Oncol (17 ICML meeting abstracts)*, 2023; 41(S2): 79-80

Tumor Response

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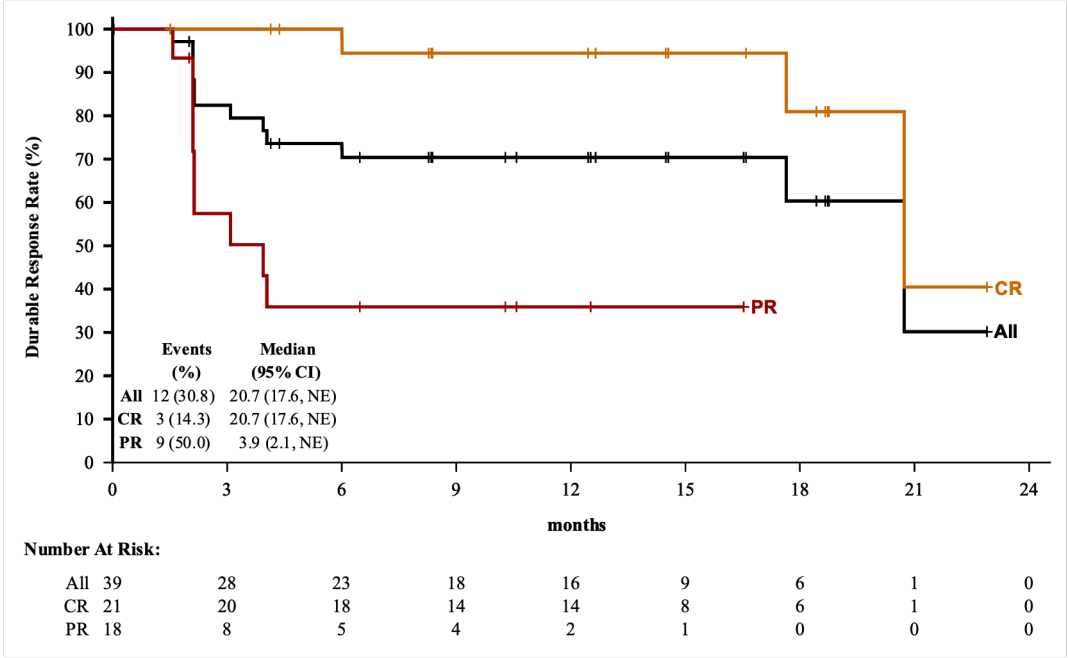
Tumor Response	n = 88	
	By IRC	By Investigator
ORR, n (%)	39 (44.3)	35 (39.8)
Overall response, n (%)		
Complete response	21 (23.9)	10 (11.4)
Partial response	18 (20.5)	25 (28.4)
Stable disease	17 (19.3)	15 (17.0)
Progressive disease	20 (22.7)	26 (29.5)
Not evaluable	12 (13.6)	12 (13.6)

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.

Phase 1 multicenter study of valemetostat in relapsed/refractory NHL

Patients with R/R NHL

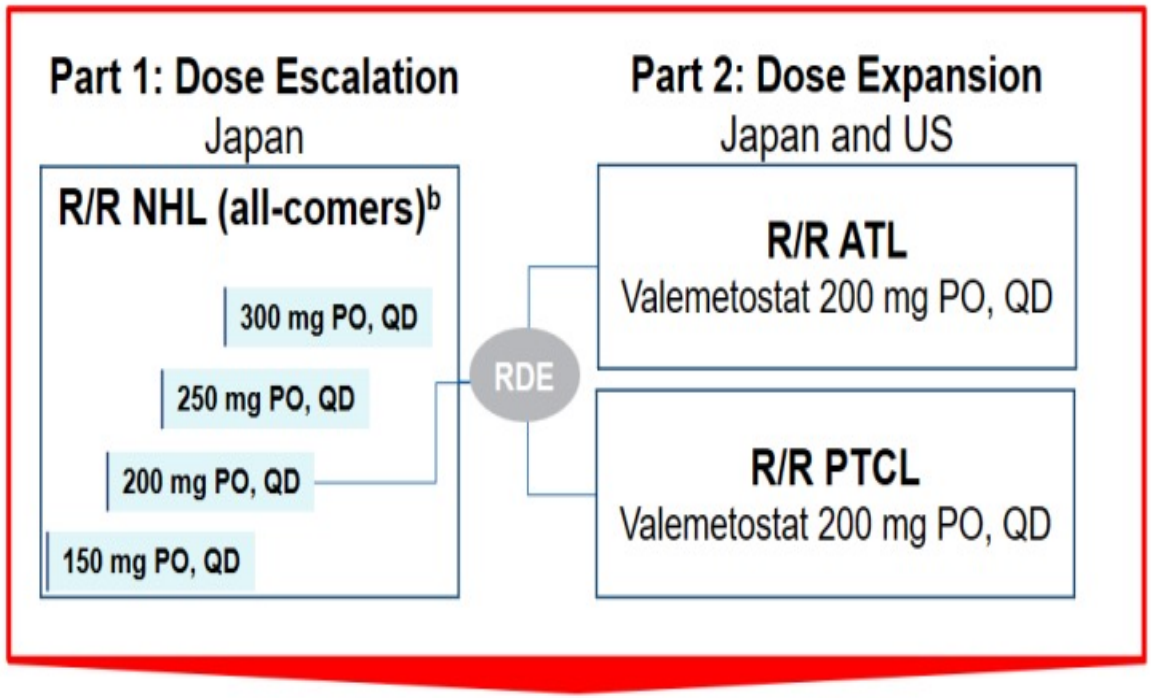
- Age ≥20 (Japan) or ≥18 (US) years
- ECOG PS 0 or 1
- Patients with ATL: positive test result for HTLV-1

Primary endpoints

- Safety (including DLTs, TEAEs)
- Recommended phase 2 dose
- Pharmacokinetics

Secondary endpoints

- Safety
- Antitumor effect



- Safety analysis: all NHL (N=77)
- Safety and efficacy analyses: T-cell NHL (n=58)
  - PTCL (n=44)
  - ATL (n=14)

Kusumoto S. *EHA virtual meeting*. 2021; S218

Clinical Response (BICR Assessment)

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CT–based assessment

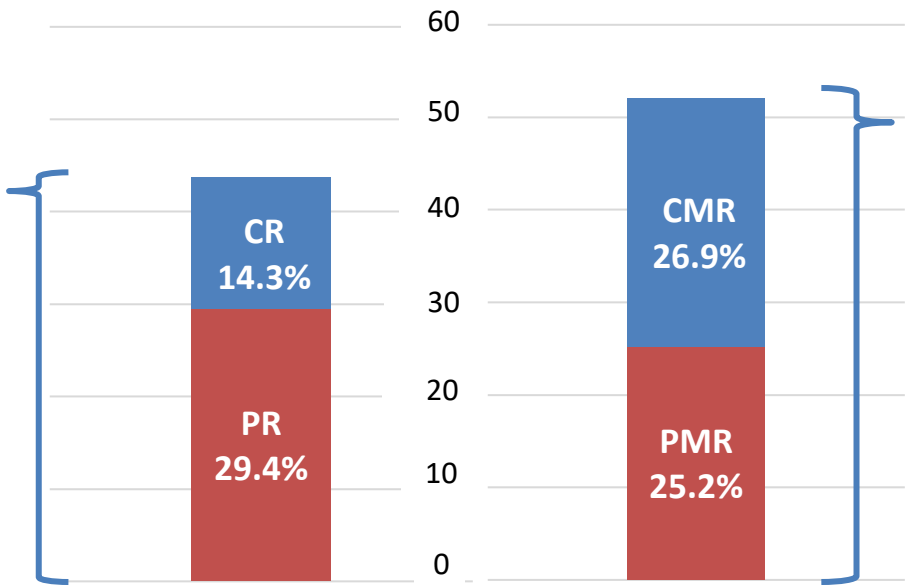
(Primary endpoint)

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

Horwitz SM, et al. ASH 2023 #302

Progression-Free Survival and Overall Survival

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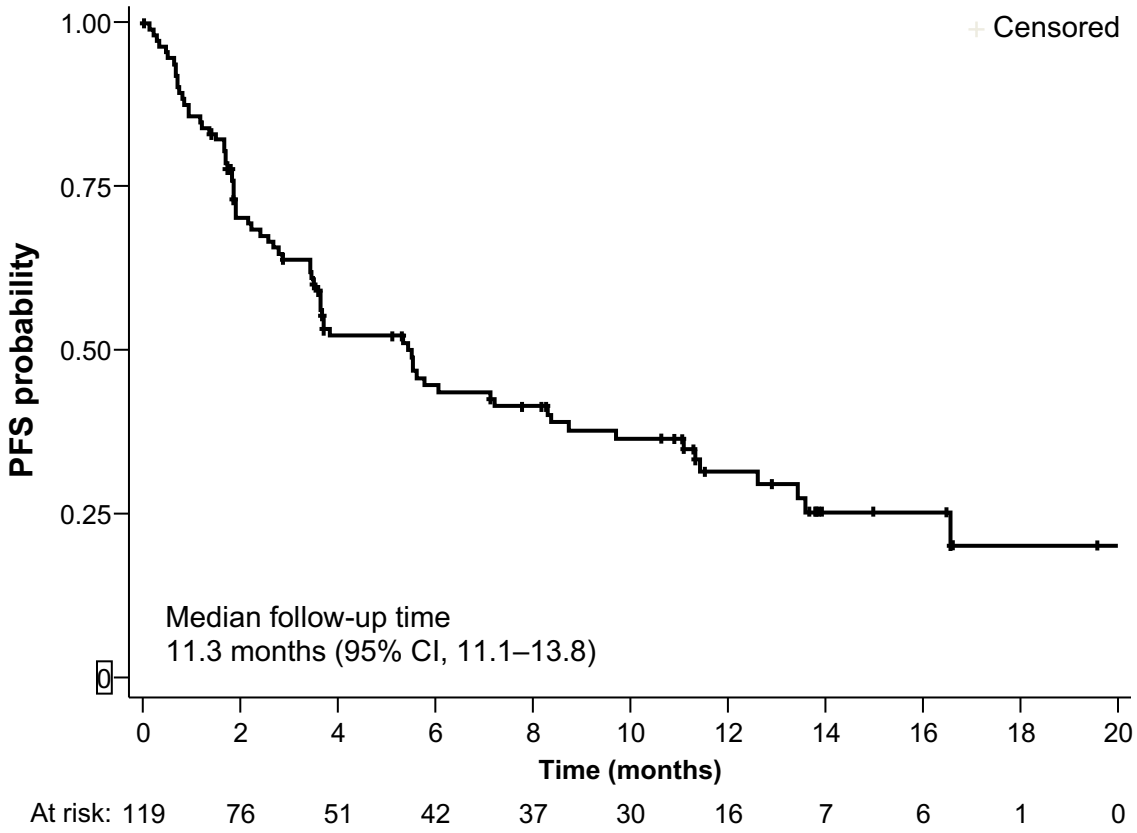
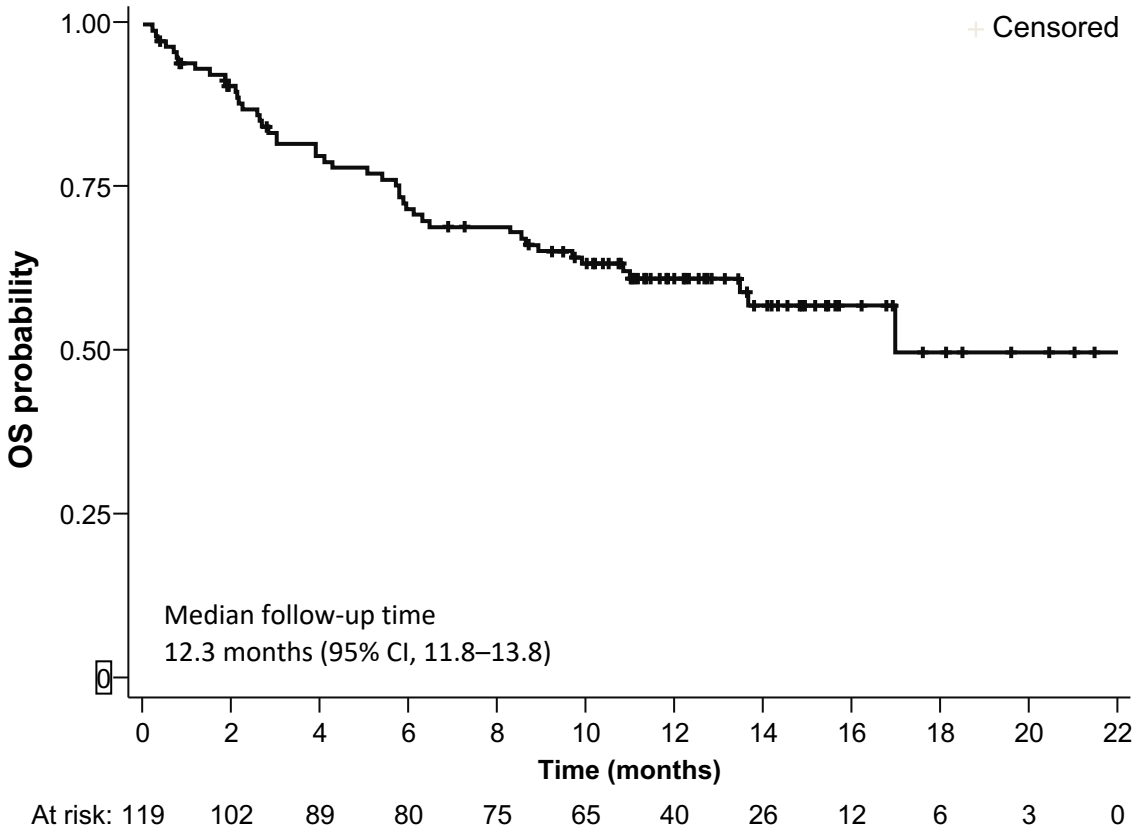
PFS[a]

Median 5.5 months (95% CI, 3.5–8.3)
(N = 119)



OS

Median 17 months (95% CI, 13.5 months to NE)
(N = 119)

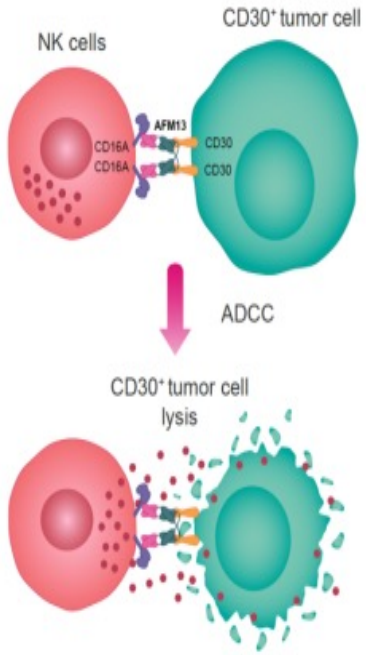


Data cutoff: May 5, 2023.
[a] PFS evaluated by BICR CT-based assessment.

Horwitz SM, et al. ASH 2023 #302

AFM13 in patients with CD30-positive relapsed or refractory (R/R) peripheral T cell lymphoma (PTCL): Results from the Phase 2 REDIRECT study

AFM13 mechanism of action



AFM13 is a tetravalent, bispecific CD30/CD16A, designed to redirect and enhance NK cell-mediated ADCC towards CD30⁺ PTCL tumor cells

AFM13 monotherapy in patients with CD30⁺ R/R HL and R/R lymphomas with cutaneous presentation

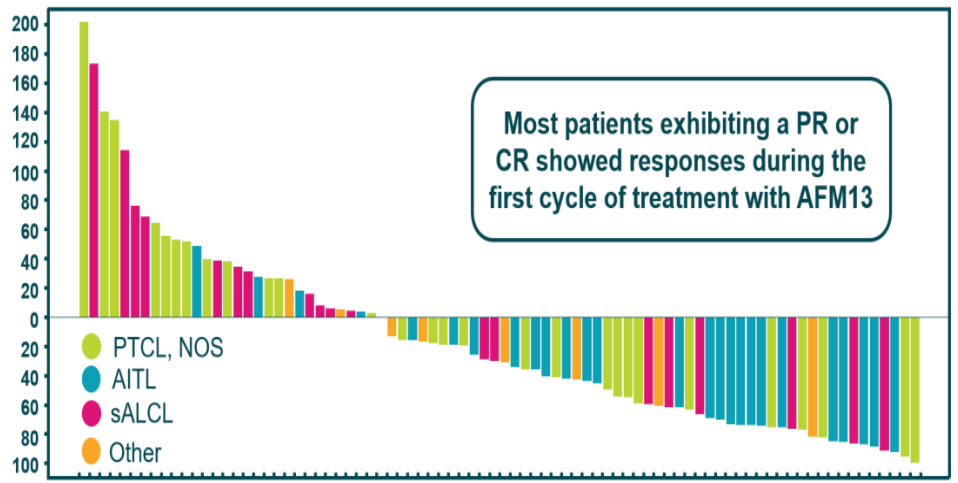
- **AFM13 exhibited targeted lysis of CD30⁺ tumor cells**, with **ORRs of 11.5%–42.0%**
- **A well-managed safety profile was observed**; the most common TEAEs were IRRs, and **no cases of CRS**
- Early correlative science data showed **enhanced activation of NK cells** immediately after AFM13 infusion and **greater NK cell activation and tumor infiltration of NK cells in the presence of AFM13**

Based on these trials, the RP2D of 200 mg AFM13 was established

Kim WS. *Hematol Oncol (17 ICML meeting abstracts)*, 2023; 41(S2): 195-196

AFM13

AFM13 in patients with CD30-positive relapsed or refractory (R/R) peripheral T cell lymphoma (PTCL): Results from the Phase 2 REDIRECT study



ORR 32.4%; CRR 10.2%

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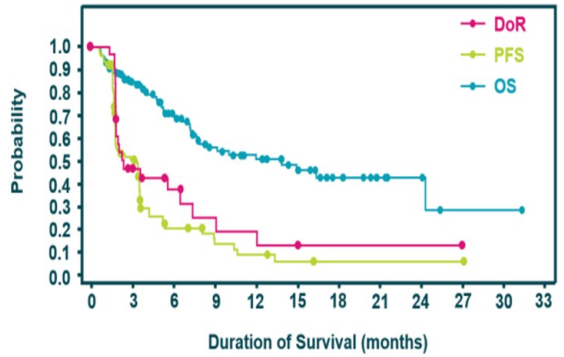
Kim WS. *Hematol Oncol (17 ICML meeting abstracts)*, 2023; 41(S2): 195-196

AFM13 in patients with CD30-positive relapsed or refractory (R/R) peripheral T cell lymphoma (PTCL): Results from the Phase 2 REDIRECT study

Kaplan-Meier Plot of DoR, PFS, OS



Number of Patients at Risk:

DoR	35	12	7	4	2	1	1	1	1	0	0	0
PFS	108	37	11	8	4	2	1	1	1	1	0	0
OS	108	79	55	36	25	19	10	6	4	1	1	0

DoR, N=35	
Patients censored, N	13
Median DoR, months (95% CI)	2.3 (1.9, 6.5)

PFS, N=108	
Patients censored, N	46
Median PFS, months (95% CI)	3.5 (1.9, 3.6)

OS, N=108	
Patients censored, N	62
Median OS, months (95% CI)	13.8 (5.0, NE)

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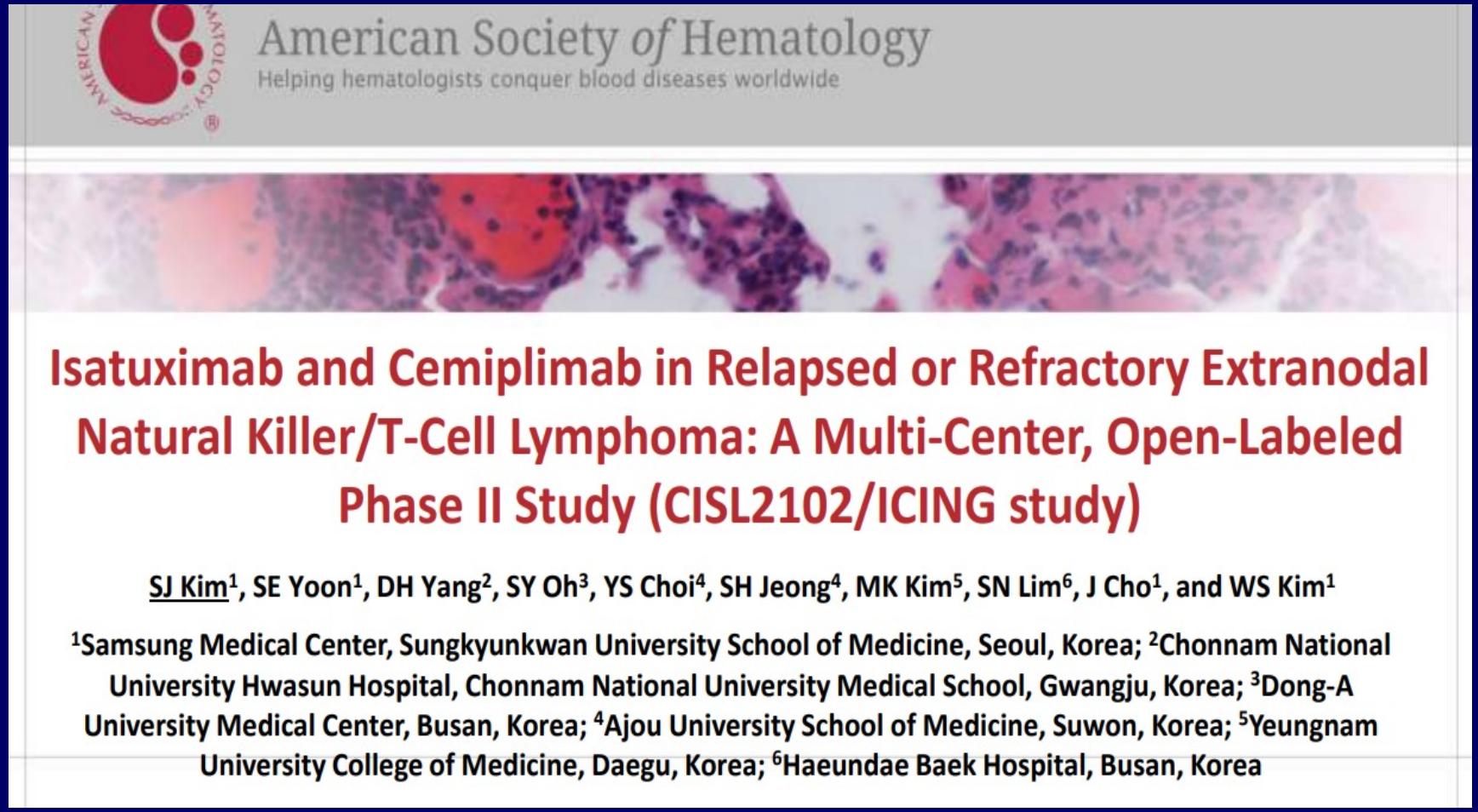
Kim WS. *Hematol Oncol (17 ICML meeting abstracts)*, 2023; 41(S2): 195-196

Isatuximab and Cemiplimab for Rel/Ref NK/T-Cell NHL: ICING Study

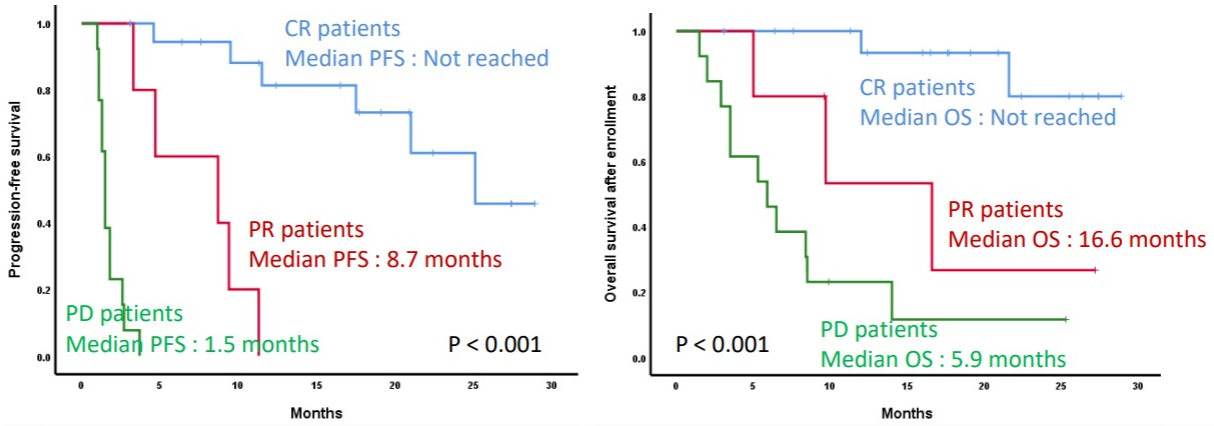


Kim et al. ASH 2023, Abst 301.

Isatuximab and Cemiplimab for Rel/Ref NK/T-Cell

Survival

- Median follow-up : 19.1 months (95% CI: 14.5 – 23.7)
  - 37 patients median PFS : 9.5 months (95% CI: 0.8 -18.2); median OS : Not reached



Other upcoming

- More bi-specific
- Allo CAR and CAR T
- CD47 blockers
- Pembrolizumab+ others
- Romidepsin + Others (Tenalisib, Pembrolizumab, lenalidomide, Azacitidine, etc) (attention to FHT phenotype), other HDAC inhibitors
- Better understanding of biology TBX21, GATA 3, DUSP22, TP63, and other mutations

T Cell Lymphoma Group

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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

Rare Lymphoma:

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

Collaborators:

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

Collaborators:

- Statisticians

Preclinical

- Dr.Michael Green
- Dr. Deepa Sampath
- Dr.Eric Davis
- Dr.Simrit Parmar
- Dr.Kumar Pappa
- Dr.Pavan Bachireddy

BACK UP SLIDES

Gene Editing approaches for CAR-T

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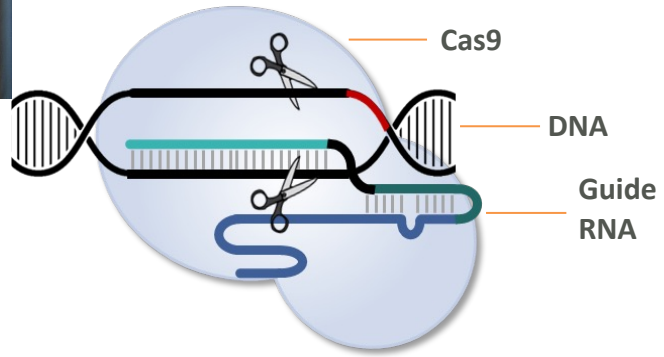
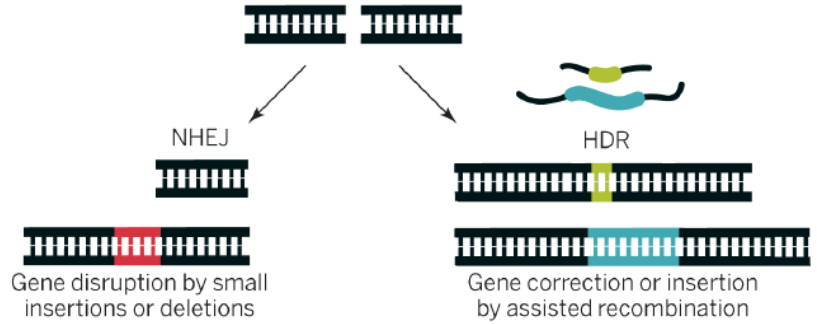
CRISPR/Cas9 Allows for Precise Genome Editing



- 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

"THE COBALT-LYM STUDY OF CTX130: A PHASE 1 DOSE ESCALATION STUDY OF CD70-TARGETED ALLOGENEIC CRISPR-CAS9–ENGINEERED CAR T CELLS IN PATIENTS WITH RELAPSED/REFRACTORY (R/R) T-CELL MALIGNANCIES

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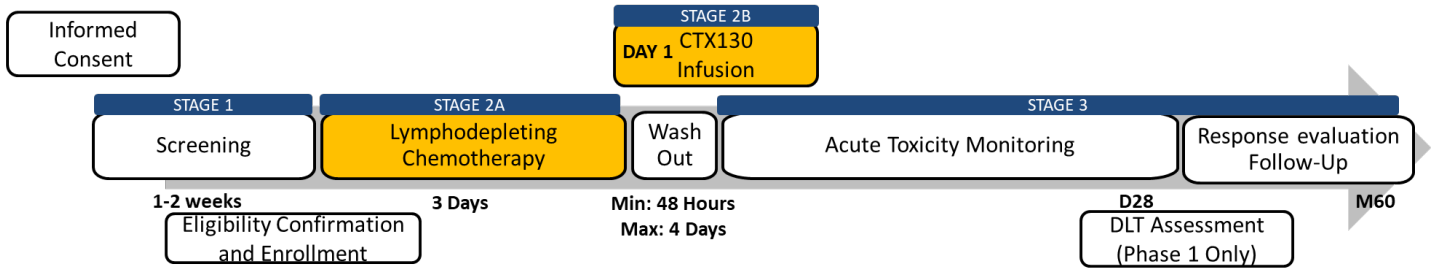

Patient characteristics, *All Dose Levels n = 18*

Age, median years (range)	65 (39 – 78)
ECOG PS at screening, n (%)	
0	8 (44)
1	10 (56)
Prior lines of therapy, median n (range)	4 (1 – 8)
TCL subtype, n (%)	
PTCL	8 (44)
AITL	3 (17)
ALCL	1 (6)
ATLL	3 (17)
PTCL - NOS	1 (6)
CTCL (MF, SS, tMF)	10 (56)
Skin involvement, n (%)	12 (67)
Blood involvement, n (%)	6 (33)
Bone marrow involvement, n (%)	4 (22)
CD70 expression level, median % (range)	90 (20 – 100)
Second CTX130 infusion received, n (%)	5 (28)

Best overall response, n (%)

Cell dose (CAR+ T cells)	DL1 $3x10^7$ N=4	DL2 $1x10^8$ N=4	DL3 $3x10^8$ N=5	DL4 $9x10^8$ N=5	DL≥3 N=10
Overall Response Rate (ORR)	2 (50)	0	3 (60)	4 (80)	**7 (70)**
CR	1 (25)	0	2 (40)*	1 (20)	**3 (30)**
PR	1 (25)	0	1 (20)	3 (60)	**4 (40)**
Disease Control Rate (DCR = CR + PR + SD)	3 (75)	1 (25)	5 (100)	4 (80)	**9 (90)**

Iyer S, et al. European Hematology Association Annual Meeting. 11 June 2022

CTX-130 Allo-CD70 CAR-T-Pt 1 (MF with LCT)

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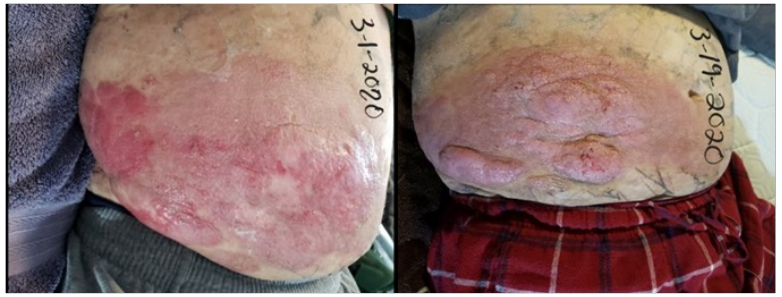
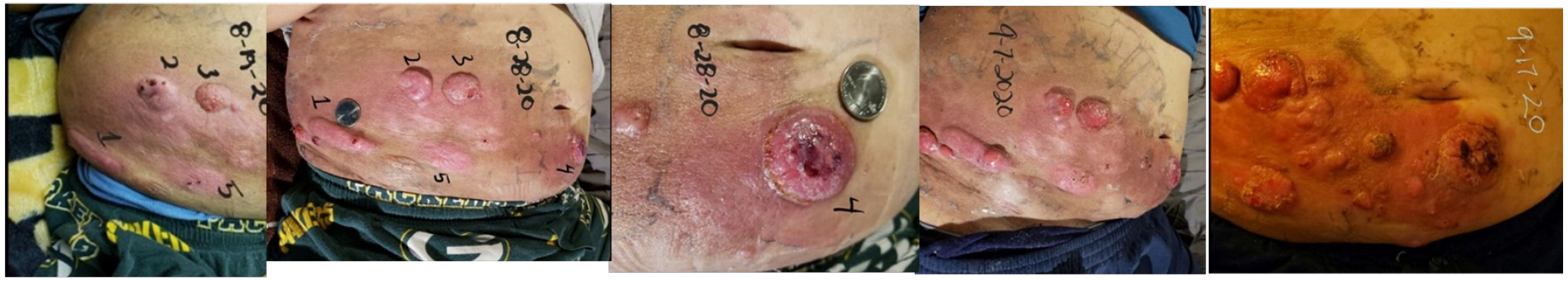
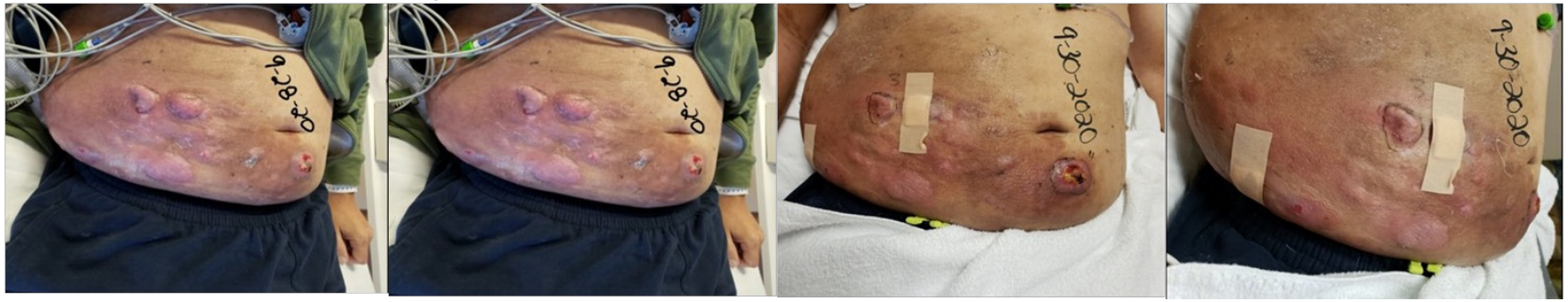
PR to BV in March 2020



Relapse in Aug 2020



Post anti-CD70 infusion Day 0-9/23



CTX-130 Allo-CD70 CAR-T-Pt 1

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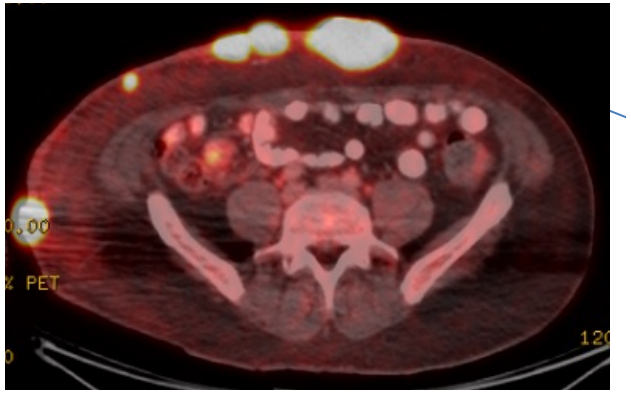
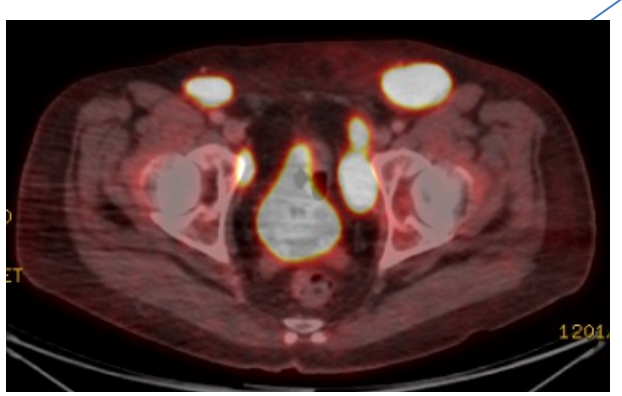
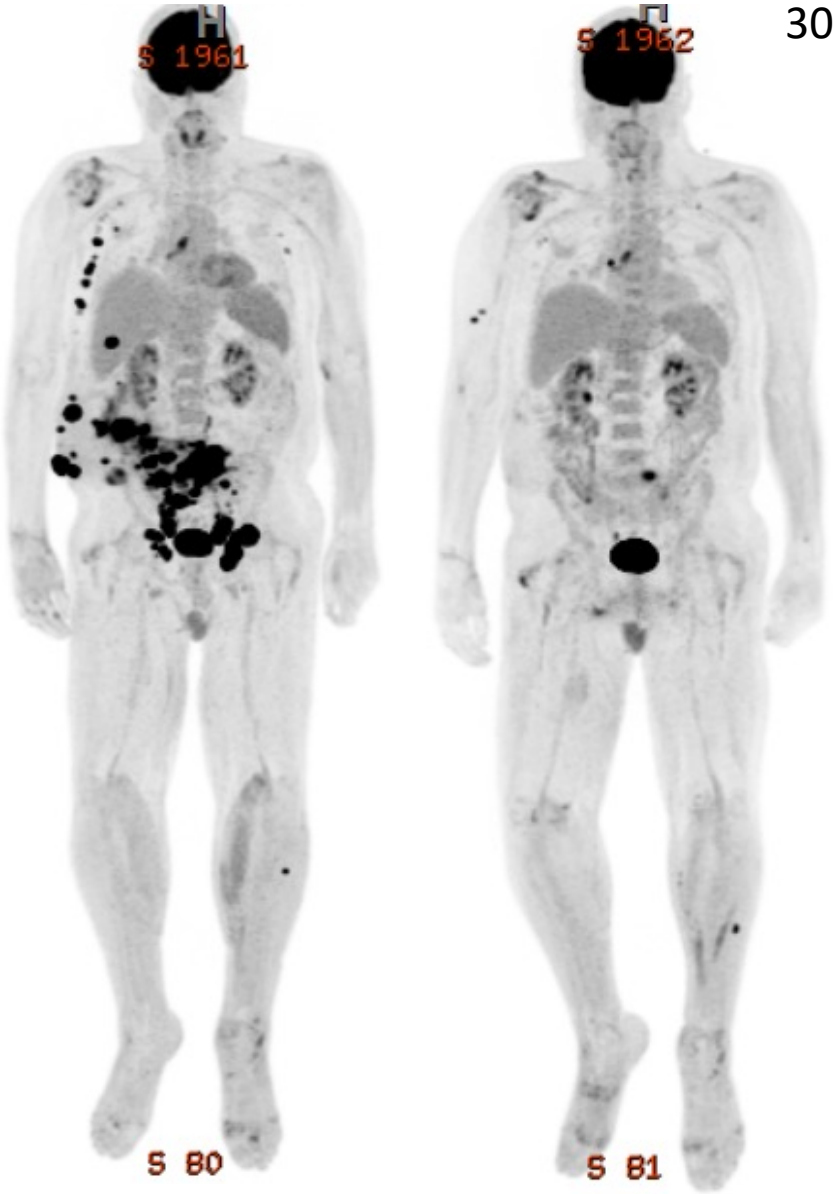
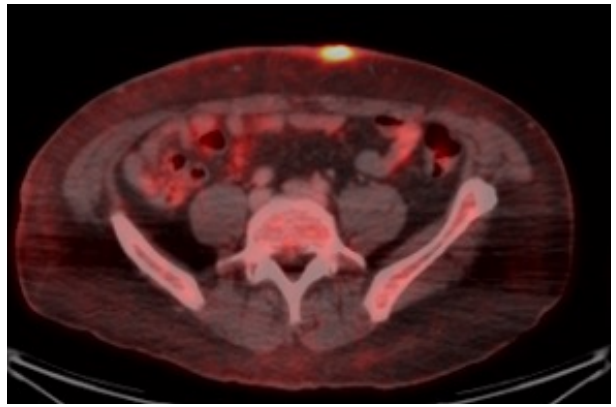
Pre-anti-CD70 infusion- 9/14/20

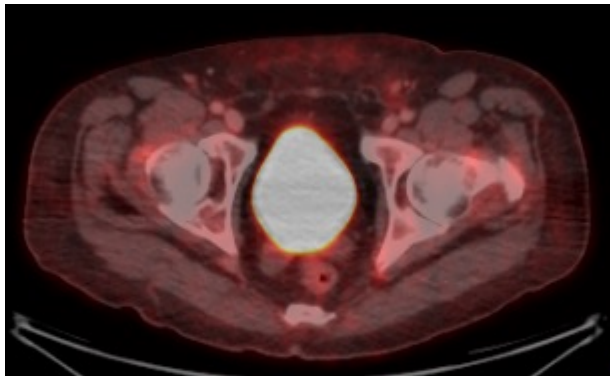
30 day Post-anti-CD70 infusion 10/20/20











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

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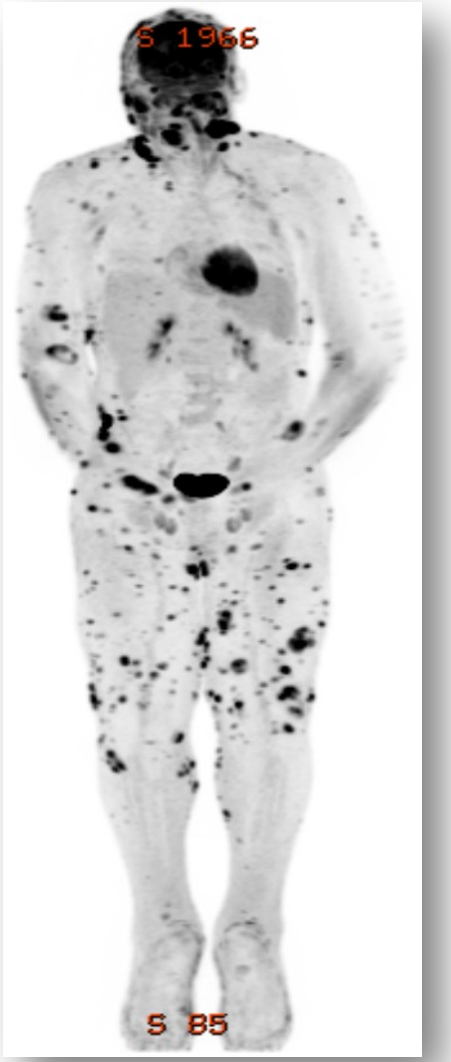
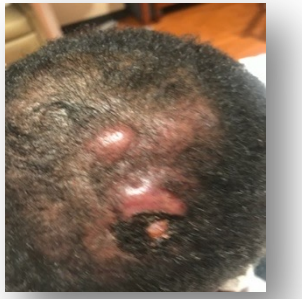
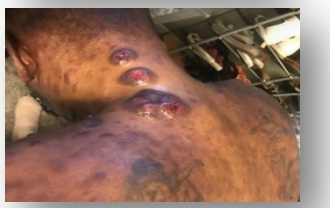
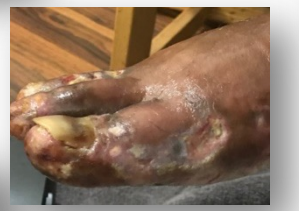
Before CTX-130 Jan 4

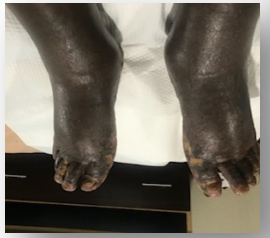


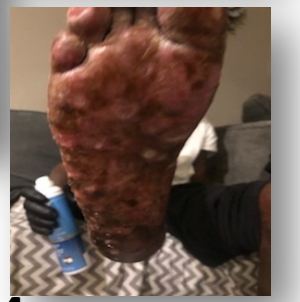
Before CTX-130 Jan 23, 2022





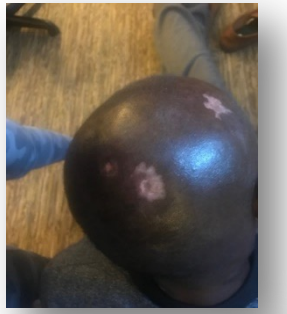


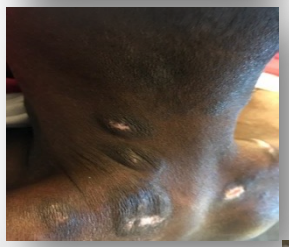


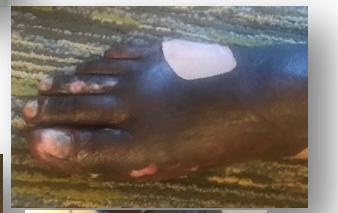


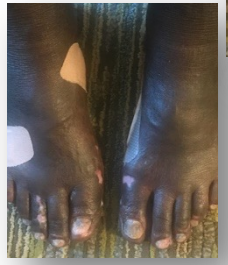
mSWAT 1/13- 84.74

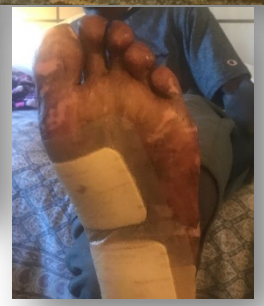
Day 18 CTX-130 Feb 11, 2022



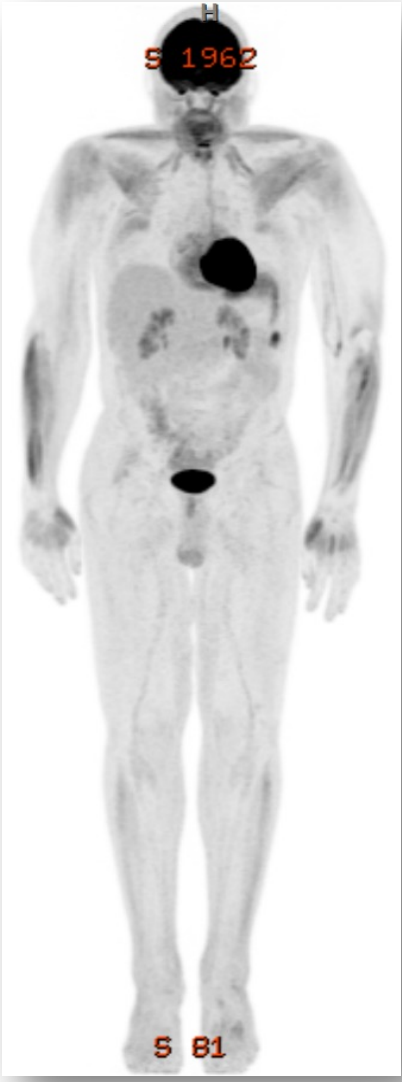








Day 28 CTX-130 Feb 21, 2022



mSWAT 2/21- 0

Landscape of somatic mutations in PTCL

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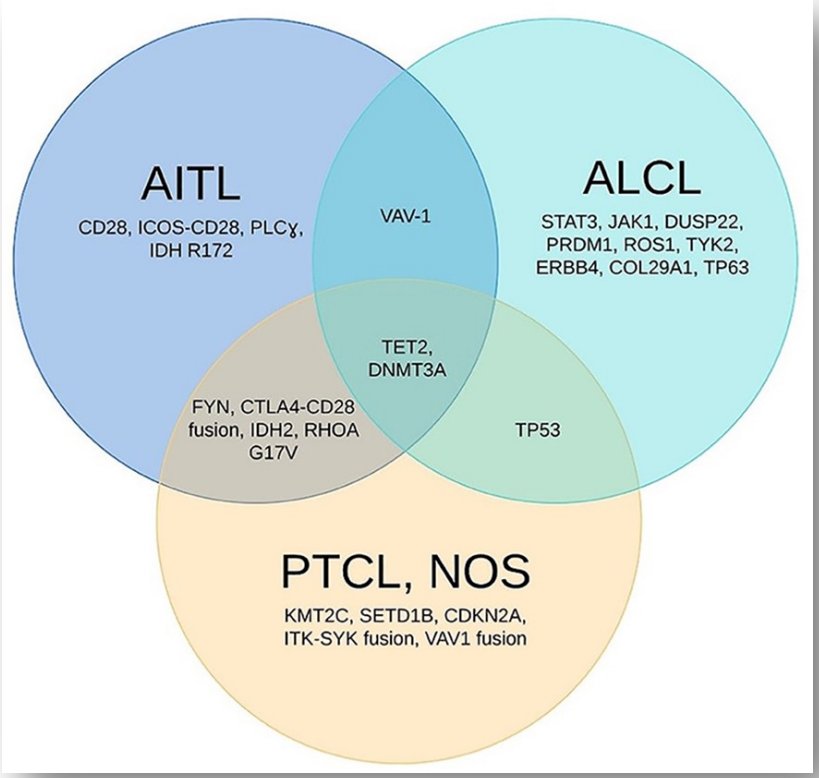

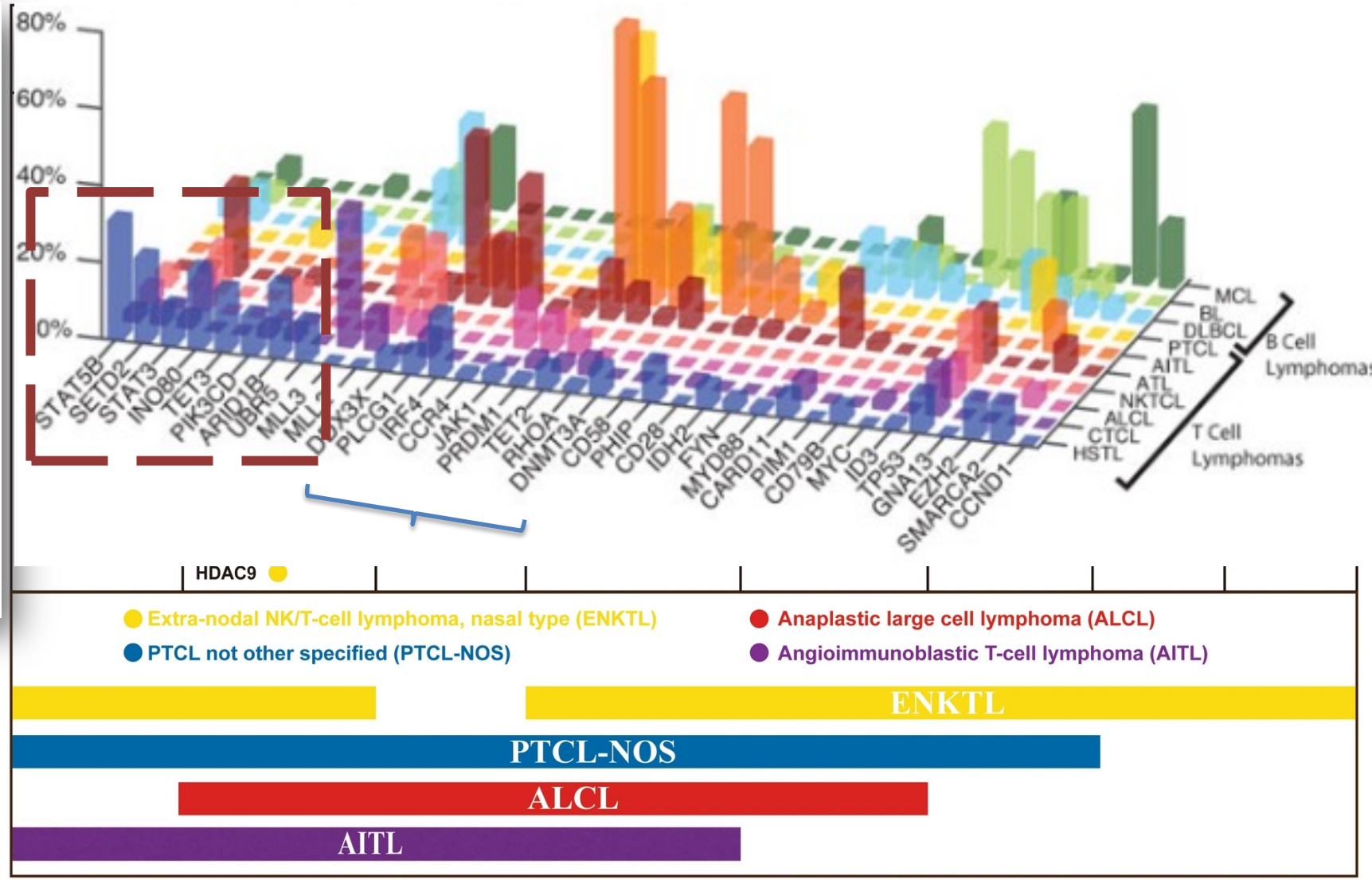

MD Anderson Genomic roadmap in TCL

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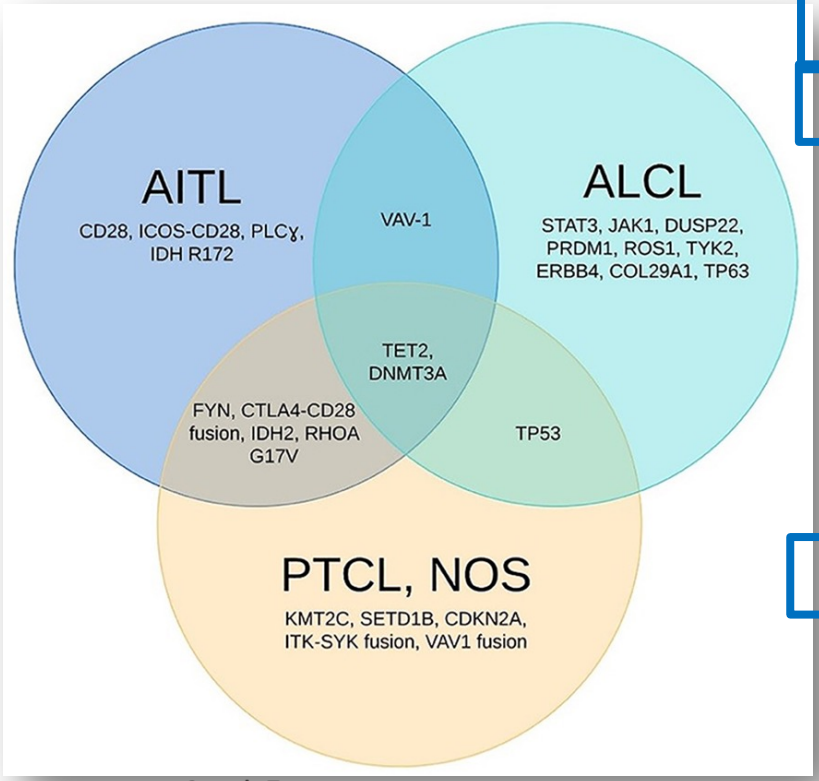
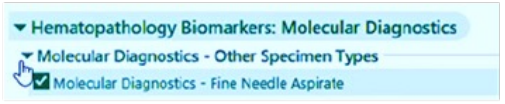


Sample Types

- Minimum 10% lymphoma cells required
- Fresh: Prospective Collection
  - FNA suspensions/rinse (preferred)
  - PB
  - BM
- Fixed: Archival Tissue Retrieval
  - FFPE Biopsy

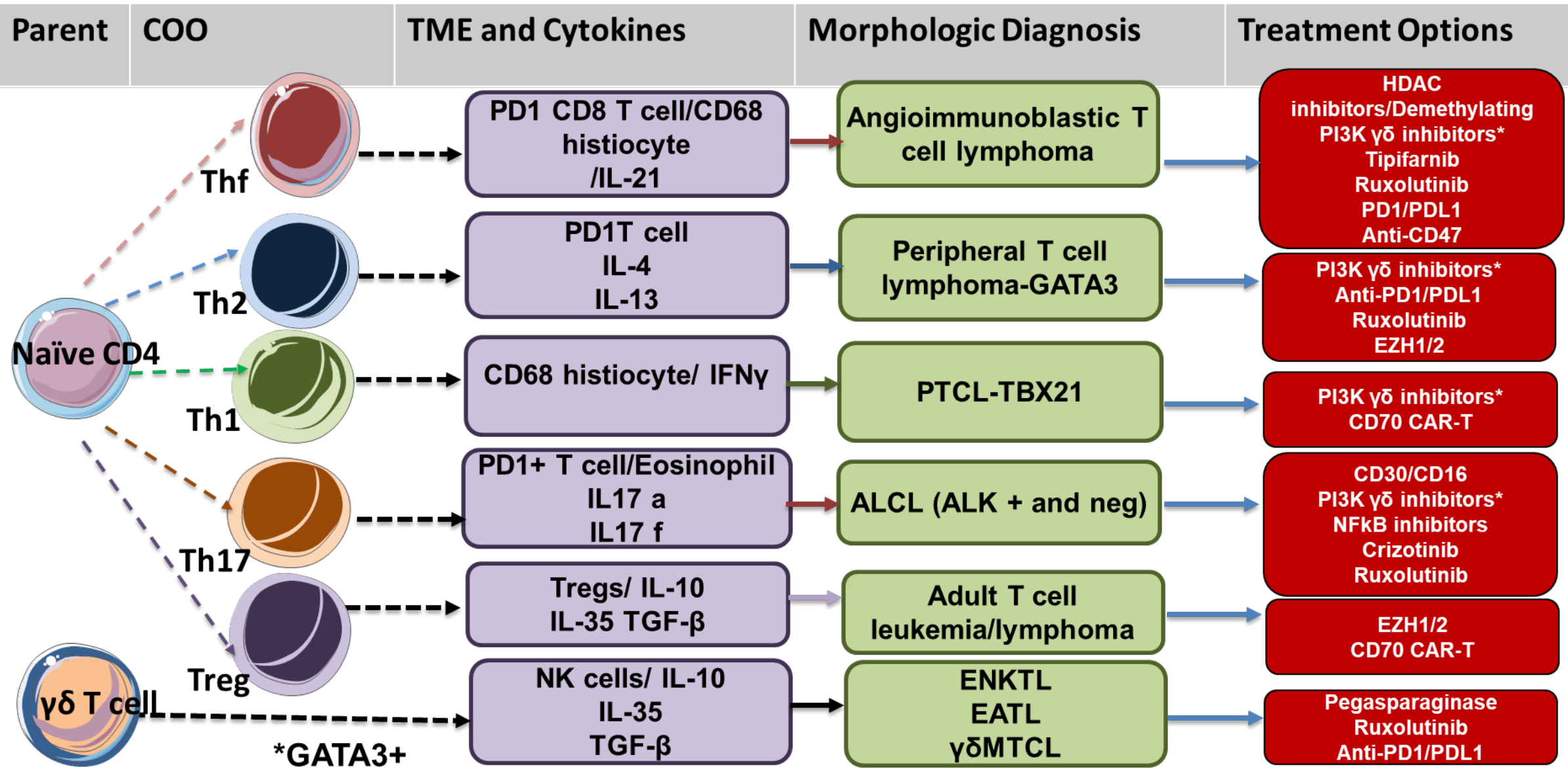
Ordering

IP/AMB – Hematopathology <ST> Orderset/SmartSet
- Specimen Types (ST):
  - PB, BM, Other Specimen Type (FNA, FFPE)



ARID1A	CCND1	DIS3	GNAS	ITPKB	MYC	PLCG1	RRAS	SYK
ASXL1	CCND3	DNMT3A	GPR183	JAK1	MYD88	PLCG2	S1PR1	TBL1XR1
ATM	CCR4	DUSP2	HIST1H1C	JAK2	NF1	PLEKHG5	S1PR2	TCF3
B2M	CCR7	EGR1	HIST1H1E	JAK3	NFKB2	POLE	SAMHD1	TET2
BAZ2A	CD274	EGR2	HIST1H3B	KIT	NFKBIA	POT1	SETD2	TMEM30A
BCL10	CD28	ELF4	HRAS	KLF2	NFKBIE	PRDM1	SF3B1	TNFAIP3
BCL2	CD58	EP300	HUWE1	KLHL6	NOTCH1	PTEN	SGK1	TNFRSF14
BCL6	CD79A	EWSR1	HVCN1	KMT2D	NOTCH2	PTPN1	SMARCA4	TP53
BCL7A	CD79B	EZH2	ID3	KRAS	NPM1	PTPN11	SMO	TRAF2
BCOR	CDKN2A	FAM46C	IDH1	LTB	NRAS	PTPRD	SOCS1	TRAF3
BIRC3	CDKN2B	FAM50A	IDH2	LYN	NSD2	RASSF1	SOX11	TRAF6
BLNK	CHD2	FAS	IFNGR1	MAP2K1	NXF1	RB1	SP140	U2AF1
BRAF	CHEK2	FAT1	IGLL5	MAP3K14	P2RY8	RBMX	SPEN	UBR5
BRCC3	CIITA	FBXW7	IKZF3	MAPK1	PAX5	RFTN1	SRSF2	VAV1
BTG1	CNOT3	FGFR3	IL2RG	MAX	PCBP1	RHOA	STAT3	XPO1
BTG2	CREBBP	FOXO1	IRAK1	MED12	PIK3CA	RIPK1	STAT5B	ZFAT
BTK	CXCR4	FYN	IRF4	MEF2B	PIK3R1	RPS15	STAT6	ZMYM3
CARD11	DDX3X	GNA13	IRF8	MFHAS1	PIM1	RRAGC	STK11	ZRSR2

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