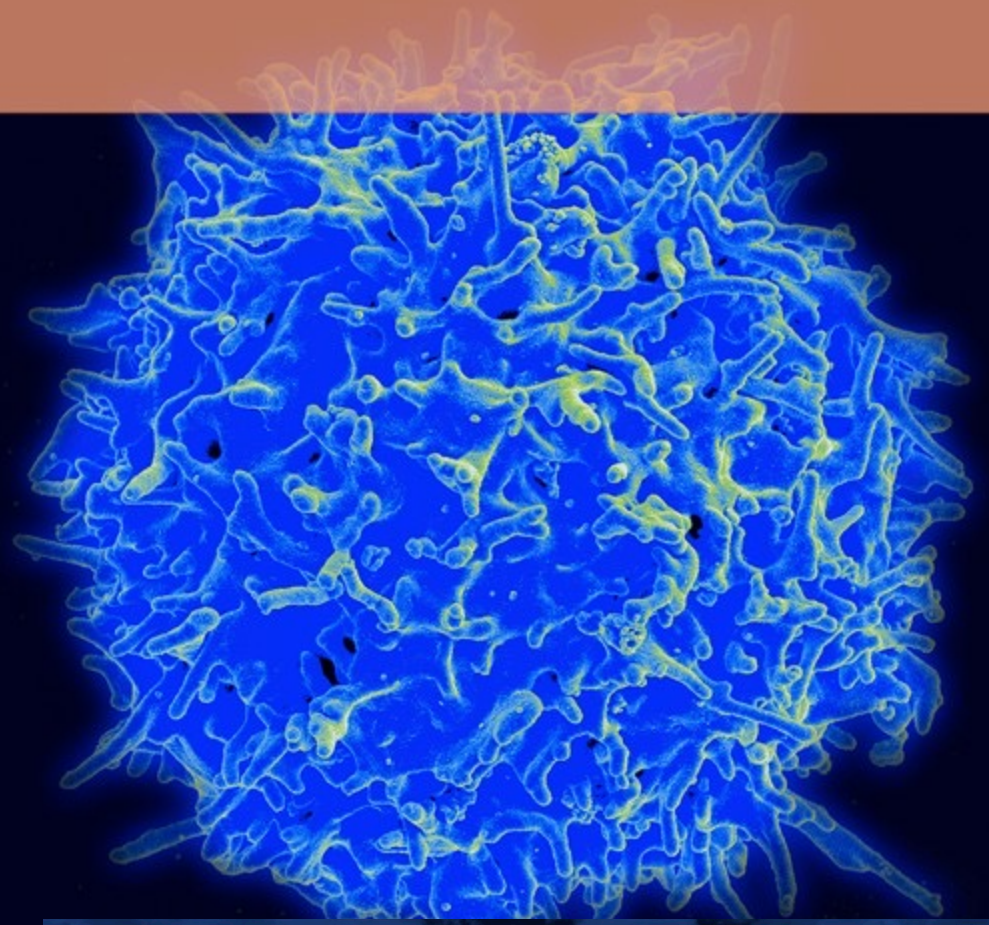
Yale SCHOOL OF MEDICINE

T-cell Lymphomas

Updated Treatment Options



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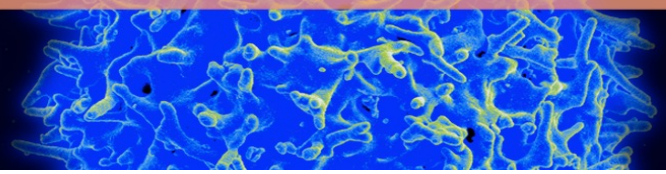
WHO classification of T cell Lymphomas



Legend: Most common Less common Rare

Leukemic

- T-cell PLL
- **T-cell LGL leukemia**
- *Chronic LPDs of NK cells*
- Aggressive NK-cell leukemia
- **ATLL**
- Systemic EBV+ T-cell lymphoma of childhood
- Hydroa vacciniforme-like lymphoproliferative disorder

Nodal

- PTCL-NOS
- AITL (angioimmunoblastic)
- Follicular T-cell lymphoma
- Nodal PTCL with TFH phenotype
- ALCL, ALK-positive
- ALCL, ALK-negative

Cutaneous

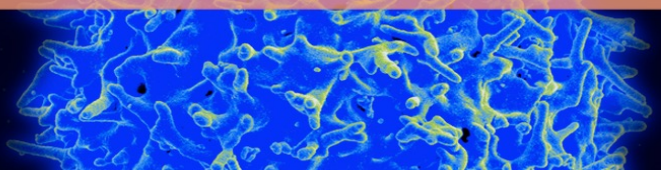
- MF/Sezary Syndrome
- Primary cutaneous CD30+ LPD
- LyP, pcALCL
- Primary cutaneous $\gamma\delta$ TCL
- Primary cutaneous CD8+ aggressive epidermotropic cytotoxic TCL
- Primary cutaneous acral CD8+ TCL
- Primary cutaneous CD4+ small/medium T-cell LPD

Extranodal

- Extranodal NK/TCL, nasal type
- Enteropathy-associated TCL
- Monomorphic epitheliotropic intestinal T-cell lymphoma
- Indolent T-cell proliferative disorder of the GI tract
- Subcut. panniculitis-like TCL
- Hepatosplenic TCL
- Breast implant-associated ALCL

Courtesy of L. de Level Swerdlow. WHO Classification of Tumours, revised 4th edition, Vol. 2 (2017)

Molecular testing in T cell lymphoma- what you need to know

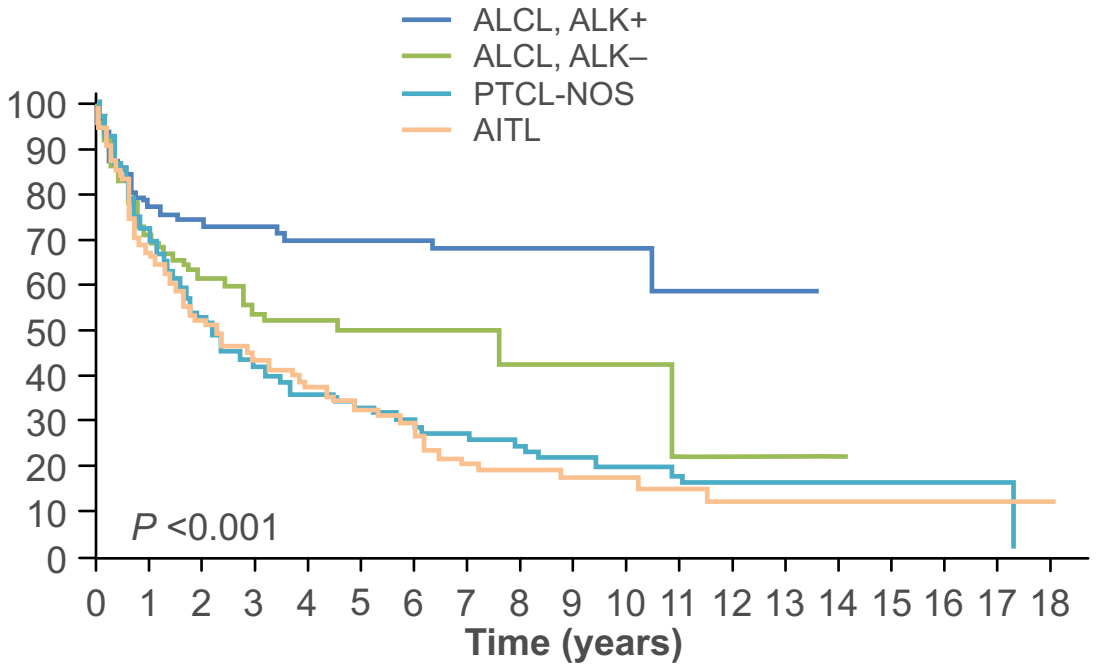


Gene	Characteristics	Disease subtype
ALK	FISH t(2;5)(p23;q35)	ALCL, candidate for ALK inhibitors
Dusp22-IRF4	FISH tumor suppressor gene Rearrangements associate with better outcomes	ALK negative ALCL CTCL subset
TP63	FISH TP63(3q28) and TBL1XR1: TP63 Rearrangements associated with poor outcomes	ALK negative ALCL
TCL-1, TRA	FISH translocations Inversion or translocation chromosome 14 T(14;14)(q11;q32) TCRa or TCRB translocated to activate TCL1A or MTCP1-B1	T PLL
Tet2; IDH1,2; DNMT3; RhoA	Mutational analysis Follicular helper subtype Response to epigenetic modifiers	Distinguishes PTCLnos from AITL or follicular helper subtype PTCL
STAT3, STAT5	Bidirectional sequencing STAT3,5 STAT5 associated with poor outcomes	LGL and NKTCL- 50% have STAT3 mutations Hepatosplenic T cell lymphoma NK leukemia
HAVCR2 (Tim3)	Tumor suppressor gene Mutations lead to loss of function, increase in inflammatory cytokines Associated with HLH	Subcutaneous panniculitis like T cell lymphoma

NCCN Guidelines, 2023

Outcomes for PTCL-then and now

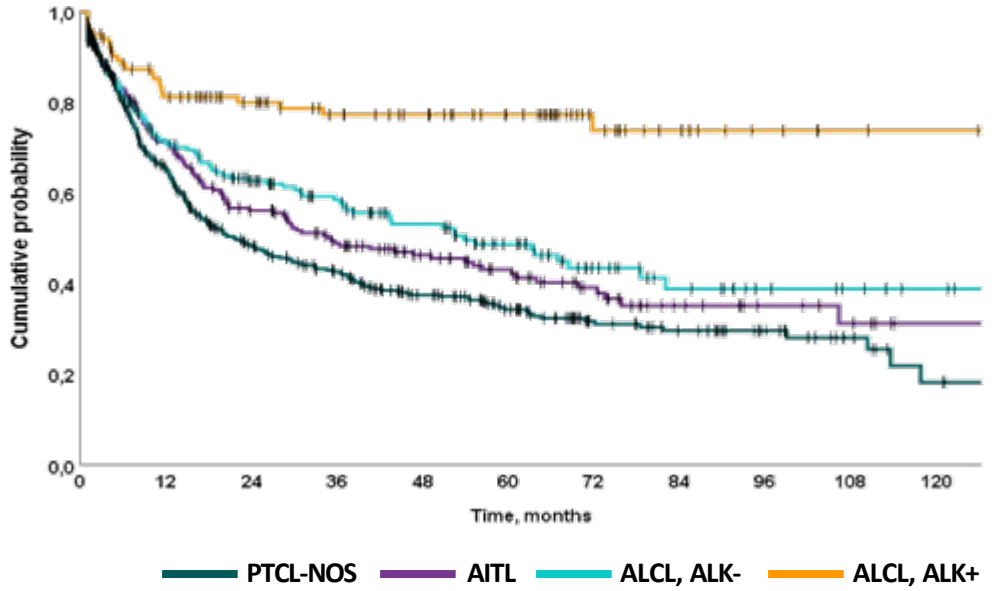
International T cell Lymphoma Project



Diagnosis	5-year OS (%)
PTCL-NOS	32
AITL	32
ALCL, ALK+	70
ALCL, AKL–	49

Vose JM, et al. *J Clin Oncol*. 2008

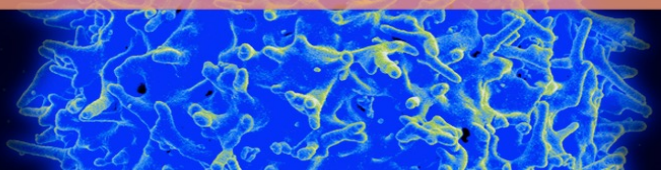
T Cell Project(T1)



Diagnosis	5-yr PFS	5-yr OS
PTCL-NOS	**24%**	**34%**
ALCL ALK -	**43%**	**49%**
ALCL ALK +	63%	77%
AITL	**30%**	**42%**

Bellei et al, Hematologica 2019

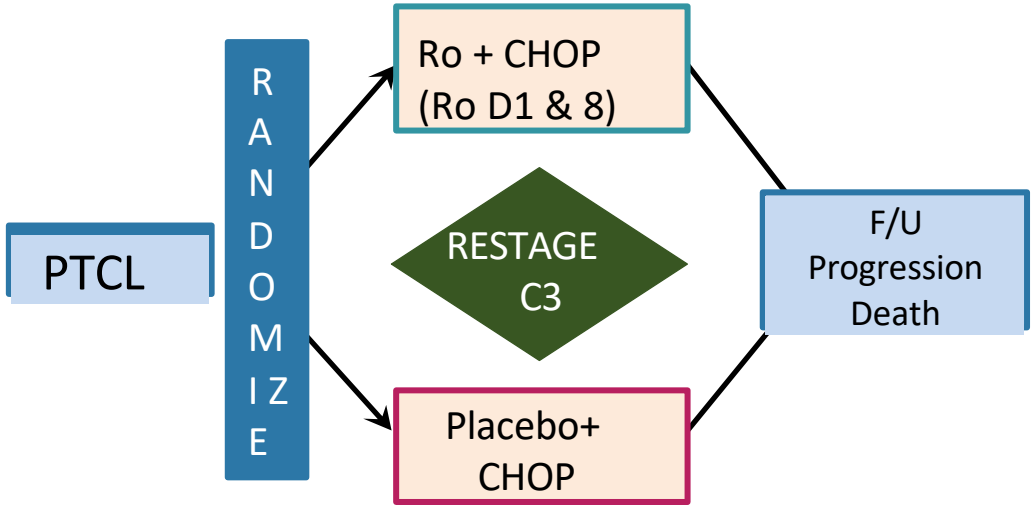
Front line therapy for PTCL: NCCN guidelines

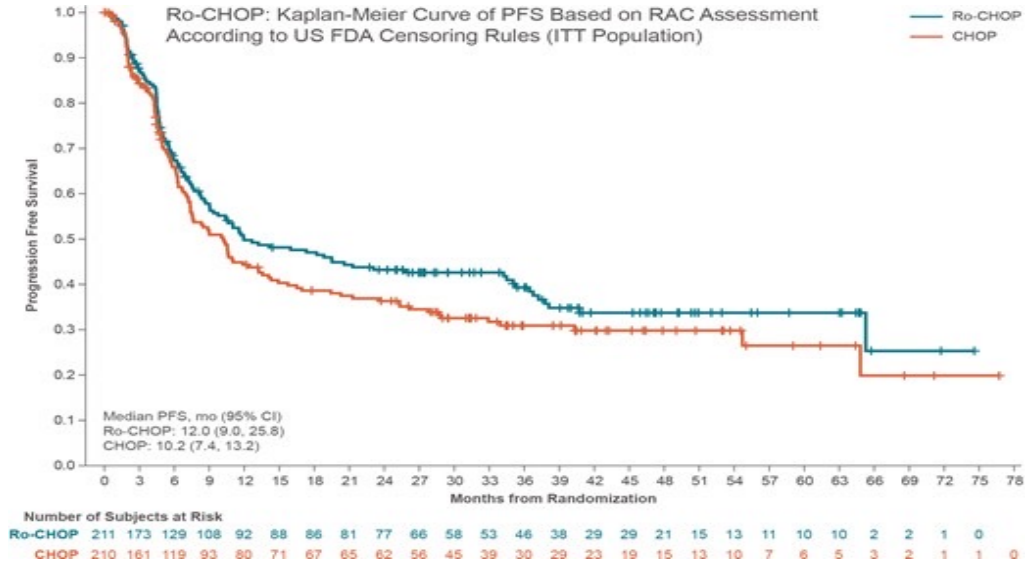


	First-line Therapy*	ALCL†
Preferred regimens	**PTCL-NOS, AITL; EATL; MEITL; Nodal PTCL, TFH; FTCL** ▪ Brentuximab-CHP can be considered for CD30+ histologies ▪ Anthracycline-based combination chemotherapy	▪ CD30-directed ADC in combination with anthracycline-based combination chemotherapy (Category 1)
Other recommended regimens	▪ Newcastle regimen‡ (CHOP followed by IVE/MTX and ASCT for EATL) ▪ Asparaginase regimen for NK/T cell- R-GemOX, SMILE,etc	
First-line consolidation	▪ In patients with ALK-positive ALCL, HDT/ASCR should be considered only for high-risk IPI patients ▪ For other histologies (i.e., PTCL-NOS, ALCL, ALK–, and AITL, including nodal PTCL, TFH, and FTCL), consider HDT with ASCR ▪ Role of alloBMT upfront not defined, consider in aggressive histologies (hepatosplenic , gamma delta)	

*Although anthracycline-based regimens confer a favorable prognosis in ALK+ ALCL, these regimens have not provided the same favorable results for other PTCL histologies; clinical trial is therefore preferred for the management of these other histologies; †ALK– ALCL with a *DUSP22* rearrangement has been variably associated with a prognosis more similar to ALK+ ALCL disease, and treatment according to the ALK+ ALCL algorithm may be considered. ‡Studied only in patients with EATL.

Front line randomized trials in PTCL



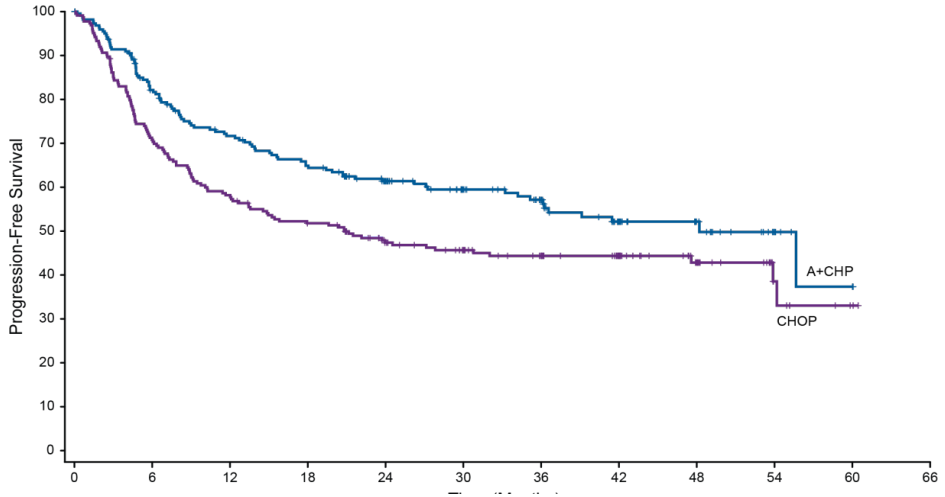


PFS 12.0 mo Ro-CHOP vs 10.2 mo CHOP, hazard ratio 0.81 (95% CI, 0.63-1.04; *P* = 0.096)

Bachy et al, JCO 2022

BV+CHP
Brentuximab Vedotin† + CHP‡
Q3W for 6-8 cycles +
Placebo for Vincristine
(n = 226)

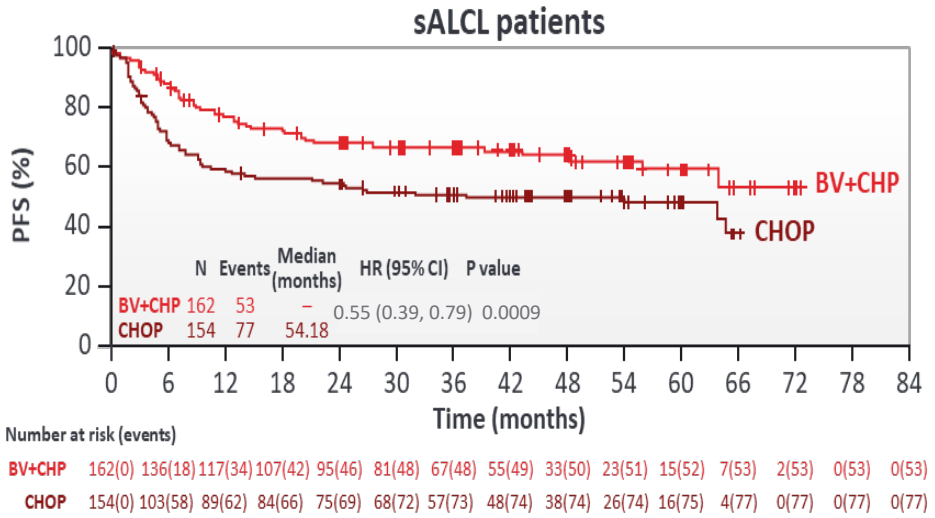
CHOP‡
Q3W for 6-8 cycles +
Placebo for Brentuximab Vedotin (n = 226)

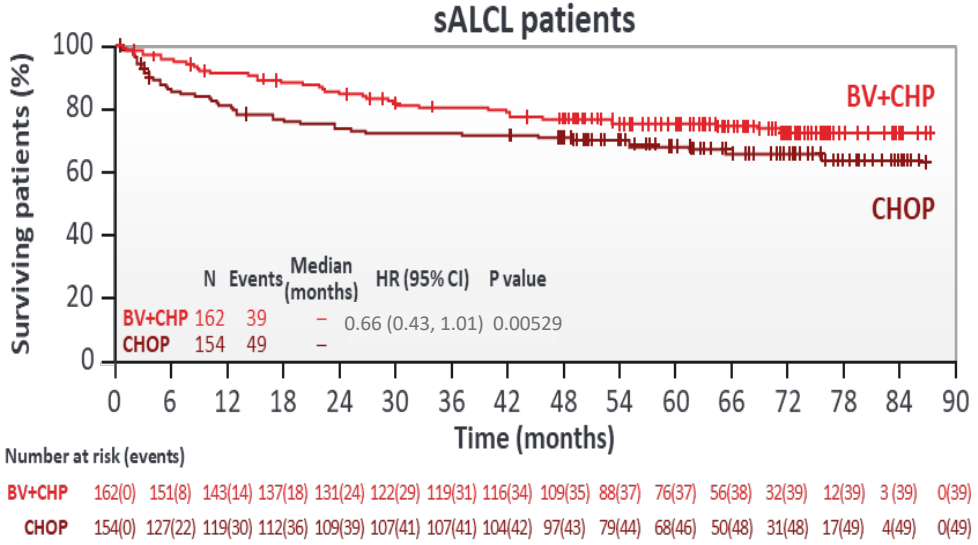


Treatment	Events, n (%)	HR (95% CI)	*P* Value
BV+CHP	95 (42)	0.71 (0.54-0.93)	.011
CHOP	124 (55)		

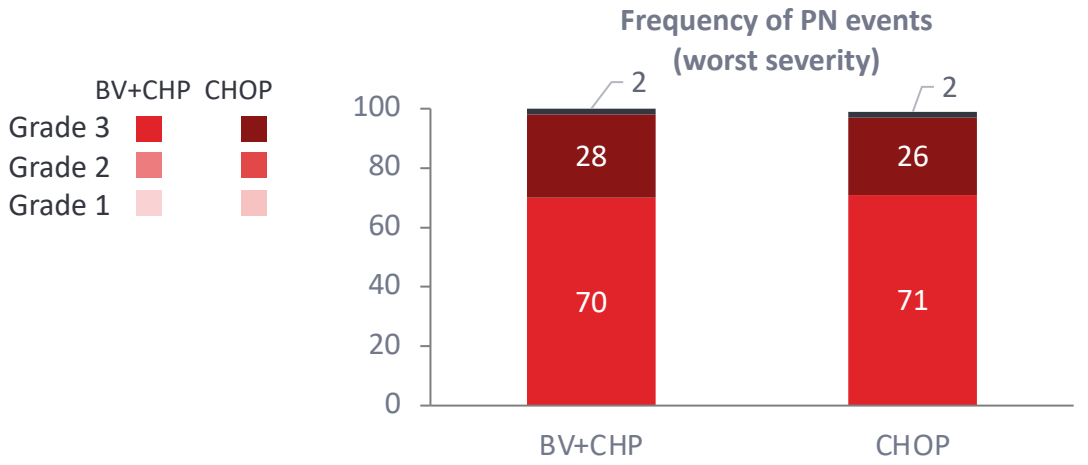
Horwitz et al, Lancet 2019

Echelon-2: outcomes in ALCL- 5 year update





Median follow up
47.6 months



	BV+CHP (n=223)	CHOP (n=226)
Any PN event, n (%)	117 (52)	124 (55)
Resolution of all PN events, n (%)*	71 (85)	82 (85)
Improvement of PN events, n (%)†	13 (15)	15 (15)

- At 5-year follow-up, similar resolution or improvement of PN events was seen for BV+CHP (n (%), 84 [72]) vs CHOP (97 [78]).
  For ongoing PN events, BV+CHP 98% vs CHOP 98% were Grade 1 or 2

Horwitz SM, et al. Ann Oncol 2022;33:288–98.

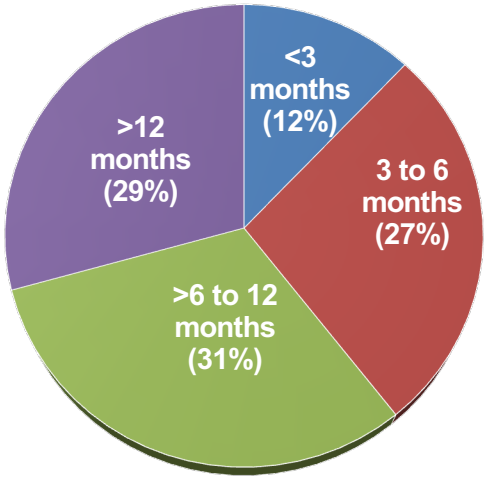
Front line treatment in PTCL in US

Study	CR rate
BV-CHP vs CHOP	64% vs 56%
Romi-CHOP	41% vs 37%
COMPLETE Registry	44%

Complete Registry (N = 499)

Time to relapse from front-line treatment (N = 58)

Observed median time from PTCL diagnosis to R/R PTCL	
First relapse (n = 58)*	12.1 months (8.5-20.5)
Primary refractory† (n = 97)	3.8 months (2.4-6.0)



*Response assessment was undertaken by the treating investigator according to the Revised Response Criteria for Malignant Lymphoma. *PTCL-NOS (29%), AITL (14%), ALCL (14%). †PTCL-NOS (26%), AITL (22%), ALCL (10%).[2]
CR, complete response; PR, partial response; R/R, relapsed/refractory.
Lansigan F, et al. *Acta Haematol*. 2020;143:40-50.

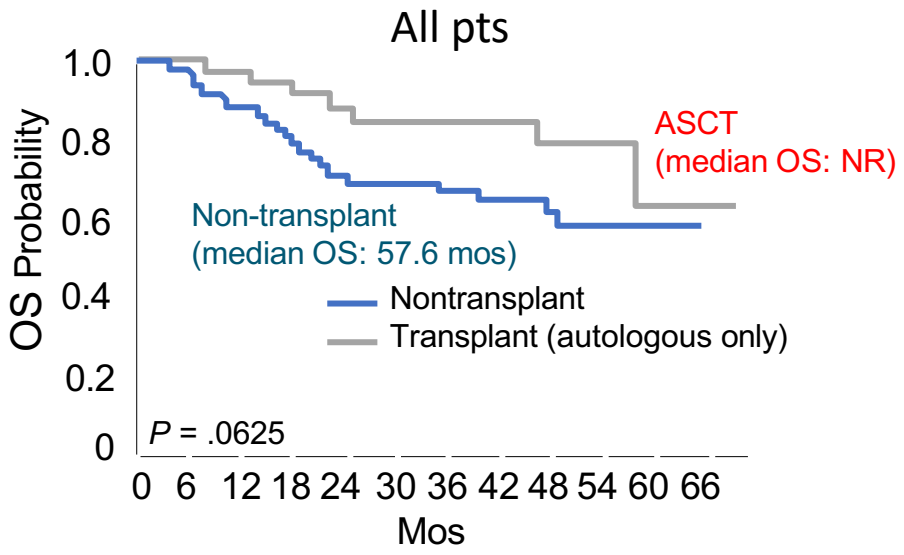
Transplant in first remission: COMPLETE STUDY

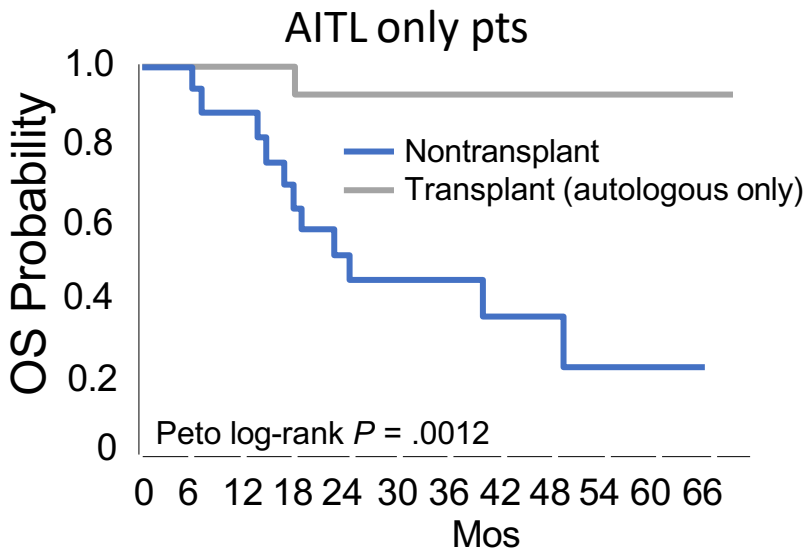
NCCN recommends transplant in first remission for nodal subtypes of PTCL

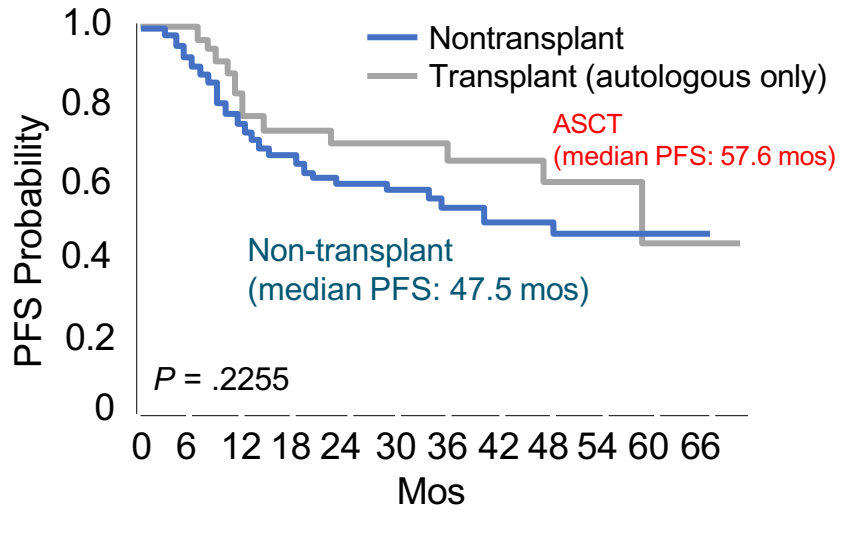
- COMPLETE is a prospective Registry study of patients with PTCL enrolled at diagnosis in the US
- 119 pts with nodal PTCL had CR
- 36 of those underwent ASCT
- ASCT was associated with superior survival for stage III–IV and intermediate-to-high IPI
- ASCT improved OS and PFS with AITL but not other PTCL subtypes
- Multivariate analysis, ASCT was independently associated with improved survival
  (HR: 0.37; 95% CI 0.15, 0.89)

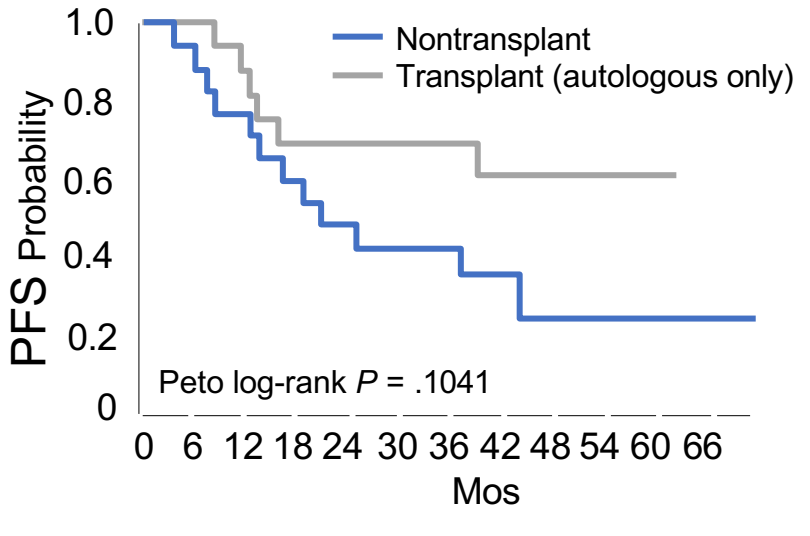
Park. Cancer 2019; 125:1507.

COMPLETE is a prospective registry of 500 patients in the US enrolled at diagnosis



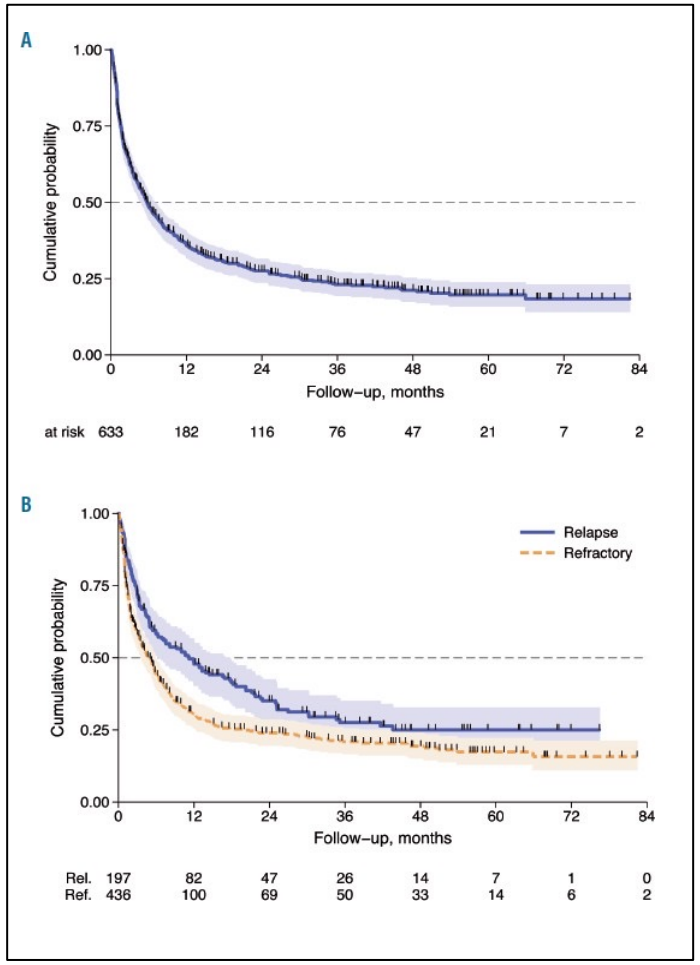






Relapsed/refractory PTCL- available therapies

Outcomes for relapsed/refractory patients from the T Cell Project

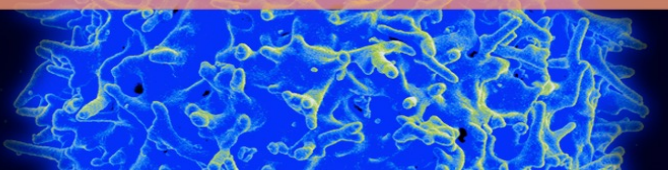


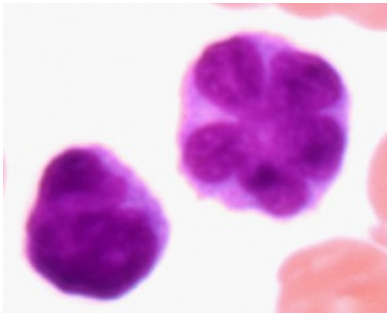
Bellei et al Hematologica 2018, Bachy E, Coiffier B. Blood 2014;

Approved drugs for relapsed/refractory PTCL

Drugs	Class	Indications
Pralatrexate	Antifolate	US FDA: PTCL (2009)
Romidepsin	HDAC inhibitor	US FDA: CTCL (2009) and PTCL (2011)
Brentuximab vedotin	Anti-CD30 ADC	US FDA: ALCL (2011)
Belinostat	HDAC inhibitor	US FDA: PTCL (2014)
Mogamulizumab	Anti-CCR4 mAb	Japan: ATLL (2012), PTCL and CTCL (both 2014)
Chidamide	HDAC inhibitor	China: PTCL (2014)
Forodesine	PNP inhibitor	Japan: PTCL (2017)
E7777 (Ontak)	IL2 Fusion Toxin	Japan: PTCL, CTCL (2021)

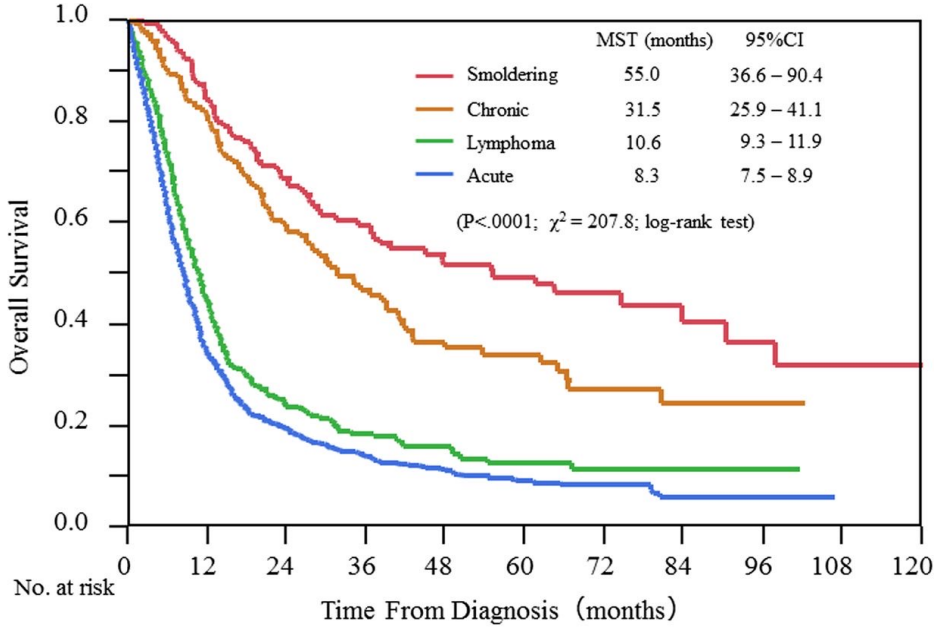
NCCN Update: HTLV-1 associated Lymphoma/Leukemia

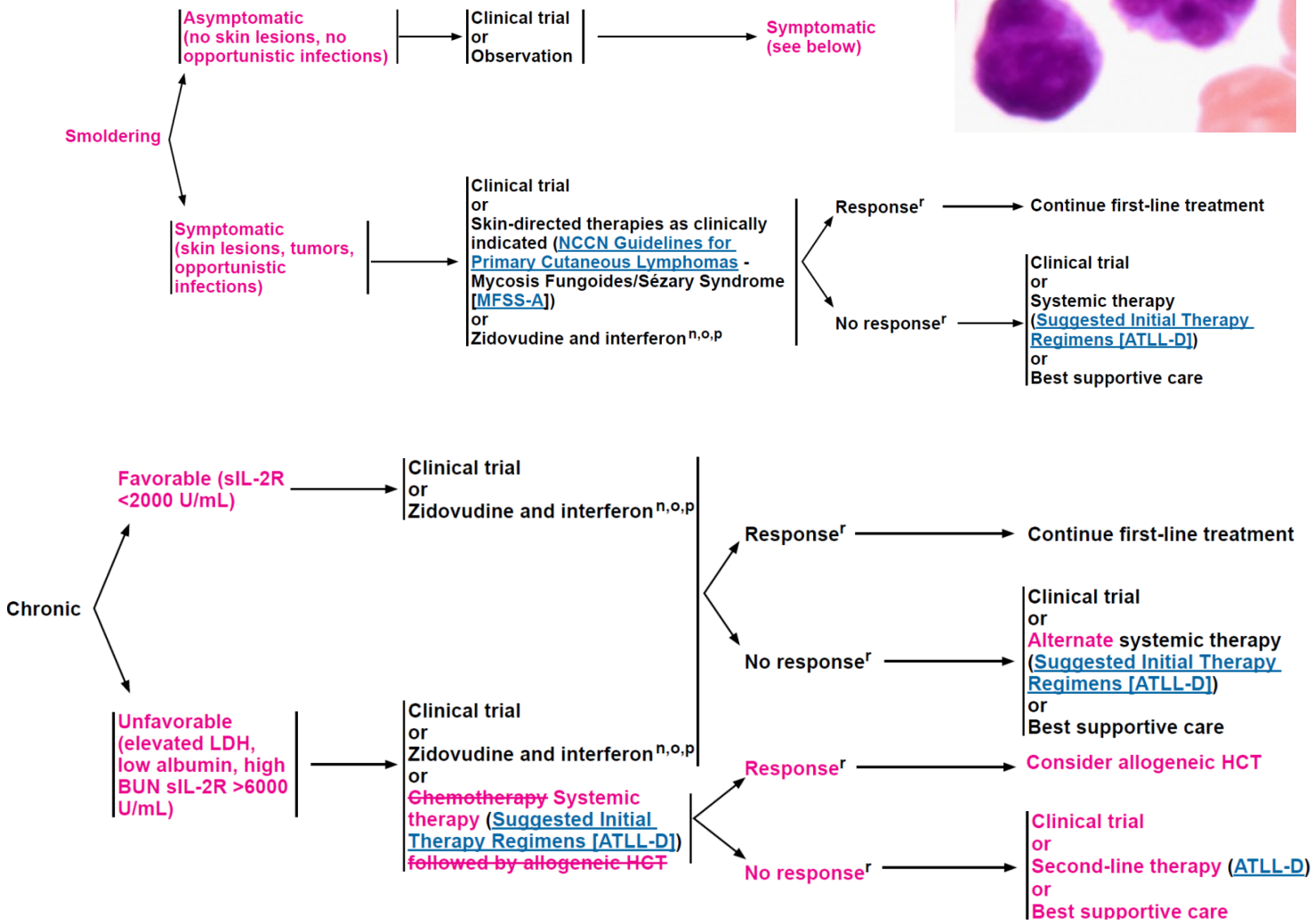




DIAGNOSTIC CRITERIA FOR ATLL

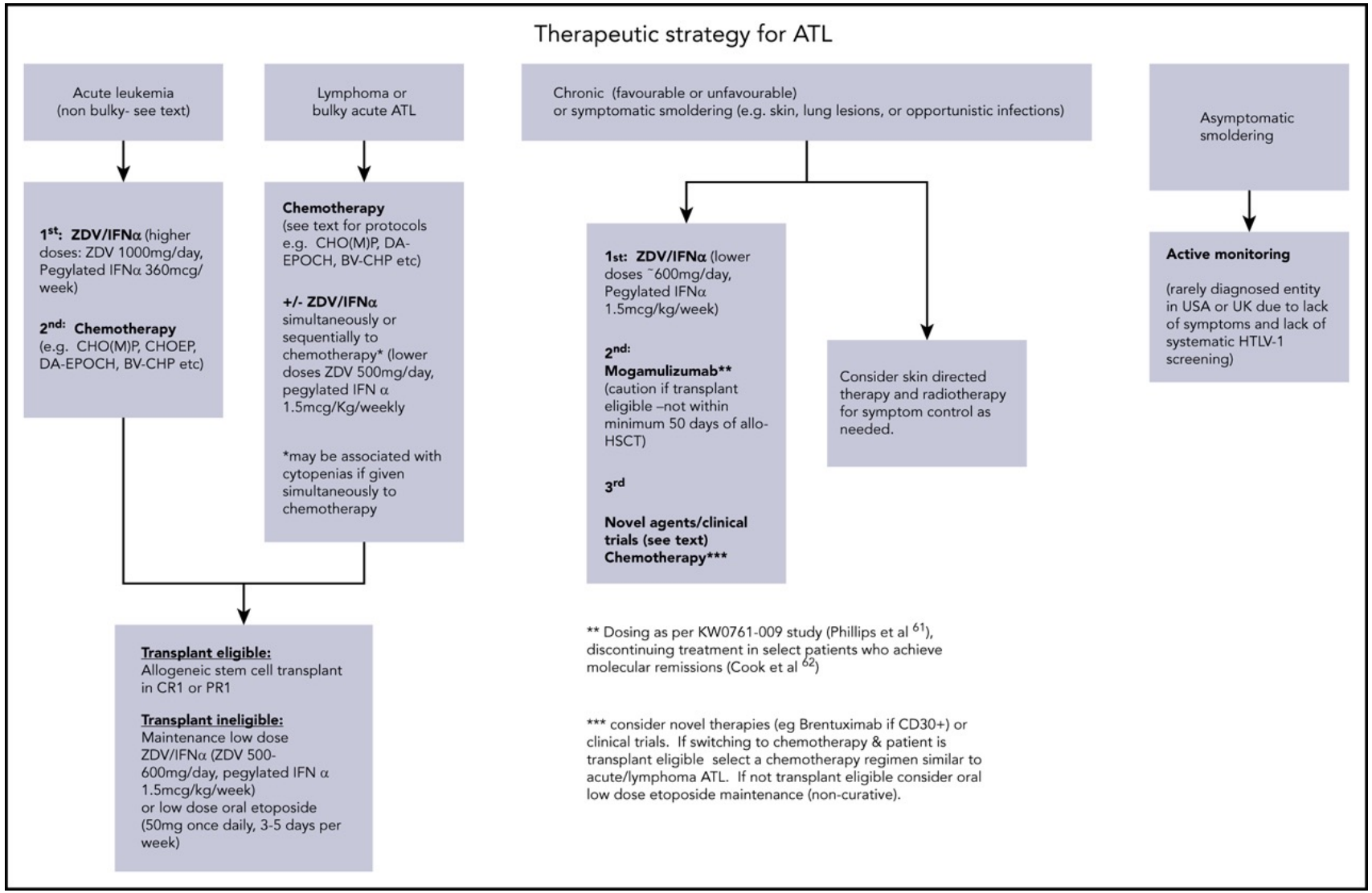
	Smoldering	Chronic	Lymphoma	Acute
Anti-HTLV-1 antibody	+	+	+	+
Lymphocyte (x 10^9 /1/L)	<4	≥4[a]	<4	*
Abnormal T lymphocytes	≥5%	+[b]	≤1%	+[b]
Flower cells of T-cell marker	Occasionally	Occasionally	No	+
LDH	≤1.5N	≤2N	*	*
Corrected Ca (mmol/1/L)	<2.74	<2.74	*	*
Histology-proven lymphadenopathy	No	*	+	*





HTLV-1 associated Lymphoma/Leukemia: treatment

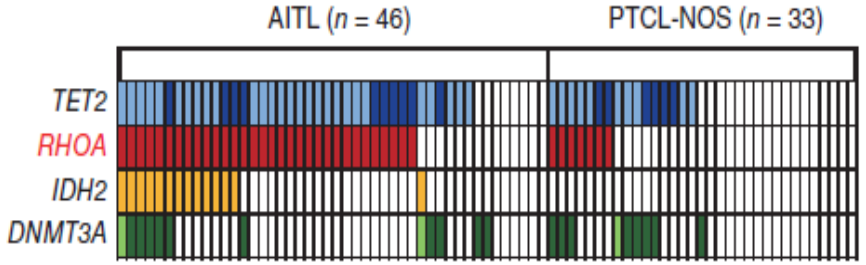
- Brentuximab vedotin -CHP for CD30+ cases
- Dose-adjusted EPOCH, CHOPE, etc
- Zidovudine and interferon (acute, chronic, and symptomatic smoldering subtypes)
- Mogamulizumab (not for transplant eligible)
- Other agents with activity- lenalidomide
- Belinostat/AZT+/- IFN (Ramos, Miami)
- Valemetostat (investigational)



Cook et al, Blood 2021

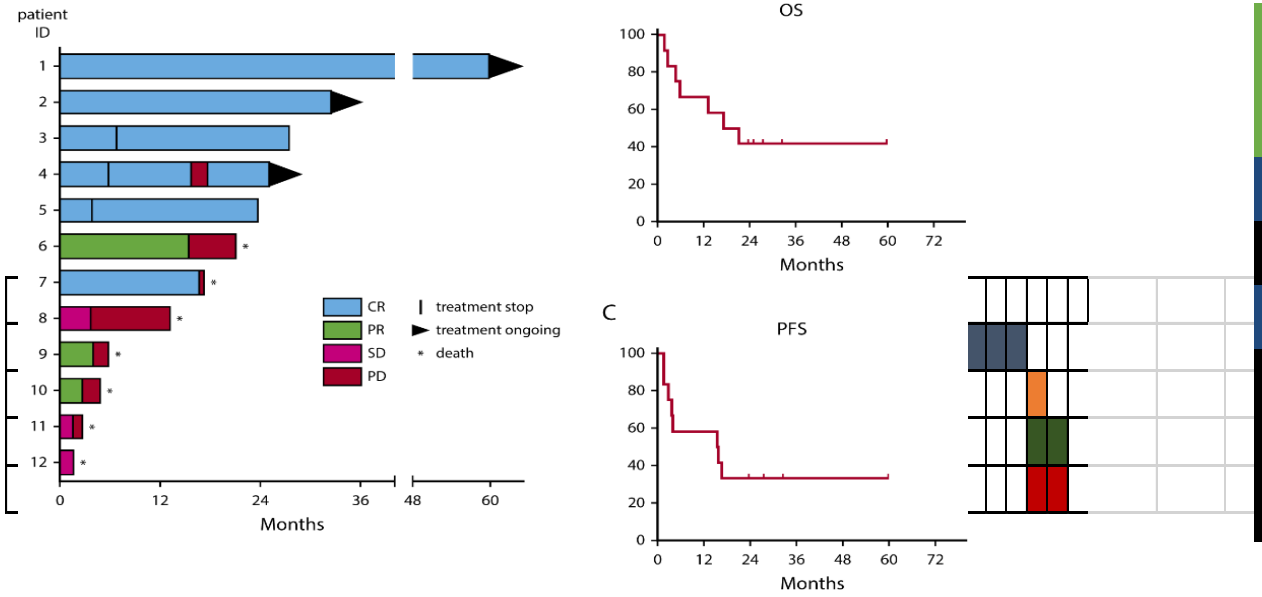
Mutations of DNA methylation genes in PTCL

Recurrent mutations of genes involved in DNA methylation regulation have been described in PTCL and in angioimmunoblastic T cell lymphoma



Phase II study of 5-azacitidine in AITL

- N = 12 patients with stage III/IV AITL
- **5-azacytidine** (median of 5.5 cycles), plus rituximab in 6/12 patients
- ORR 75%: CR 6/12 ; PR 3/12; SD 3/12



Phase I study of oral 5-azacitidine and romidepsin

5-azacitidine: 100 mg/day d1-14, to 300 mg/day, d1-21

Romidepsin 10 mg/m², d8,15,to 14 mg/m²,d8,15,22,21-35 day cycles

Response, n (%)	All Patients (N = 31)	T-cell Lymphoma (n = 11)
ORR	10 (32)	8 (73)
CR	7 (23)	6 (55)
PR	3 (10)	2 (18)
SD	7 (23)	0
PD	11 (35)	2 (18)
Not evaluable	3 (10)	1 (9)

Sakata-Yanagimoto et al. *Nat Gen* 2014; Courtesy of Dr. F. Lemonnier & Pr. Ph. Gaulard

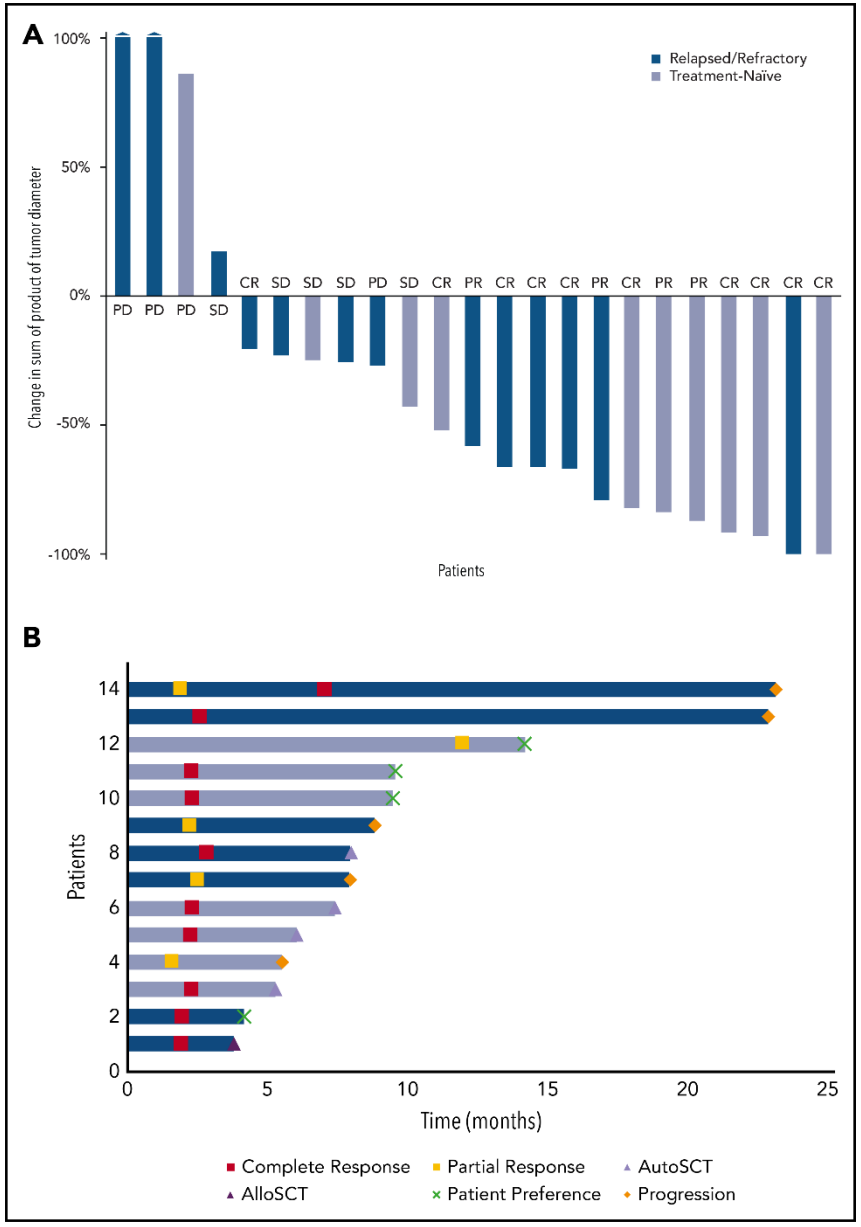
Falchi et al, Blood 2021

Epigenetic therapy: phase II study of romdepsin and 5-azacytidine

- Front line or R/R PTCL pts eligible
- Azacytidine 300 mg days 1 to 14, Romidepsin 14 mg/m^2 on days 8, 15, and 22 every 35 days.
- ORR 61% , CR 48%
- T-follicular helper cell (tTFH) higher ORR
- Gr 3 to 4 AEs were thrombocytopenia (48%), neutropenia (40%), lymphopenia (32%), and anemia (16%)
- Median PFS 8 mo, median OS not reached , median DOS 20.3 months
- Responders had higher average number of mutations in genes involved in DNA methylation and histone deacetylation

	Overall response	**Complete response**	**Partial response**
All pts (23)	61%	43%	17%
Front line (10)	70%	50%	20%
R/R disease (13)	54%	38%	15%
tFH (15)	80%	60%	20%

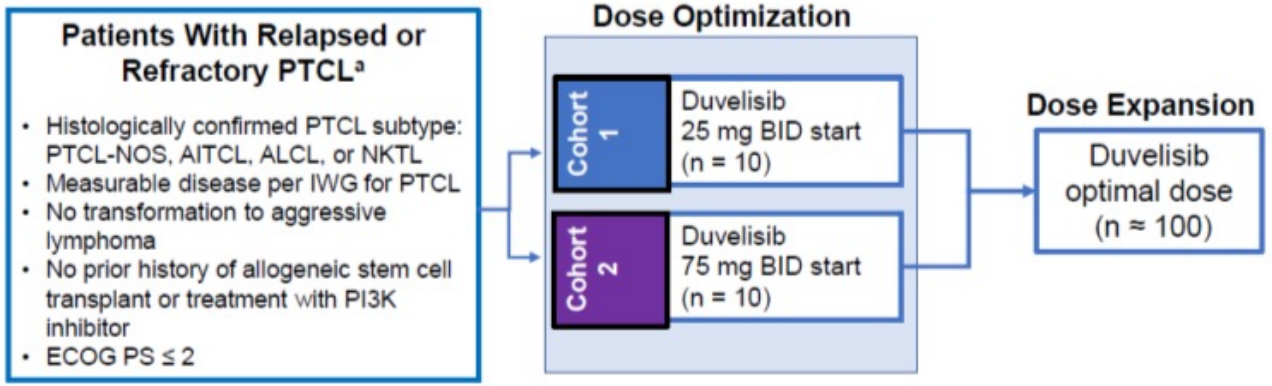
Falchi et al, Blood 2022



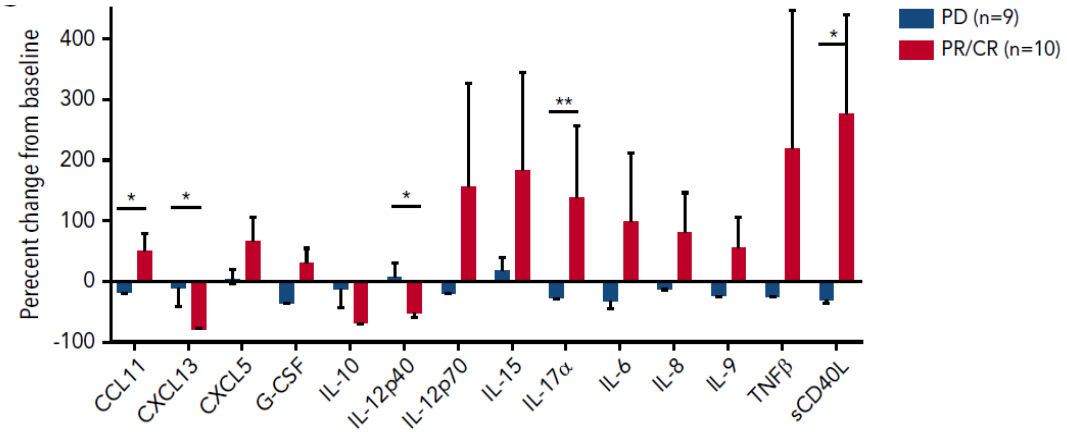
PI3Kinase as a target: Duvelisib Phase II study

- Single agent phase II study in PTCL (PRIMO) n=78
  - 75mg BID x 2 cycles→ 25mg BID unless progression/intolerance
  - ORR 50%, CR 32%
  - Grade ≥3 transaminitis 24%

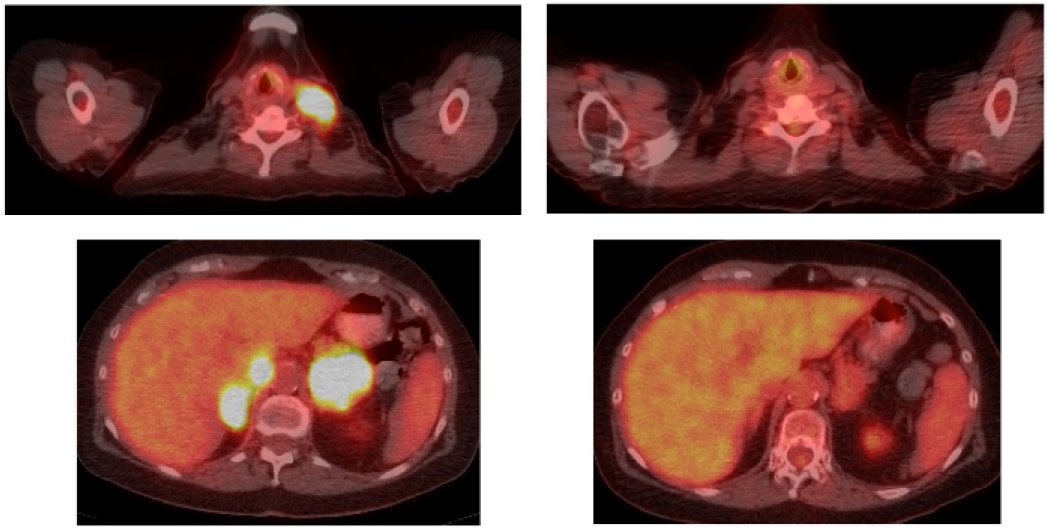
Safety:
Treatment interruptions and/or dose reductions most commonly required for AST/ALT elevation, rash, diarrhea, and pyrexia. Neutropenia in 20%. Grade ≥ 3 infections in 29%.



	Cohort 1	Cohort 2	Overall
ORR (%)	35%	54%	50%
CR (%)	25%	31%	32%



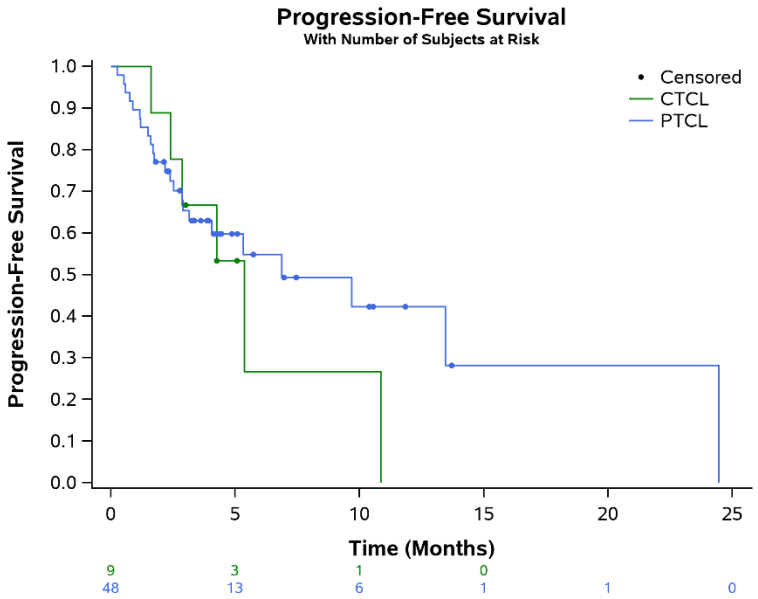
Horwitz et al Blood 2018, Brammer ASH 2021; Cheun et al Cancers 2020



Predose | Post Cycle 1

Duvelisib and romidepsin- a novel combination

	PTCL	CTCL
n	48	9
events	23	6
Censored	25	3
Median PFS (95% CI)	6.8 Mo (4.0 – NR)	5.3 Mo (2.8 – NR)
# of patients → Transplant	14 (29%)	0



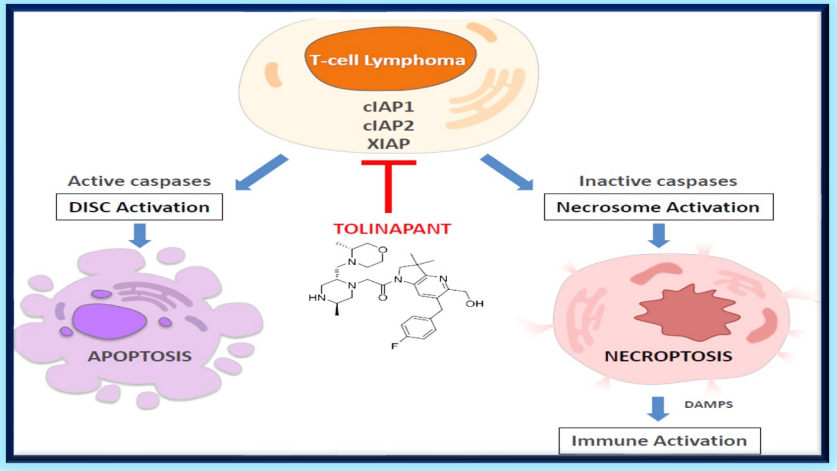
Fewer immune mediated side effects of duvelisib when given with romidepsin

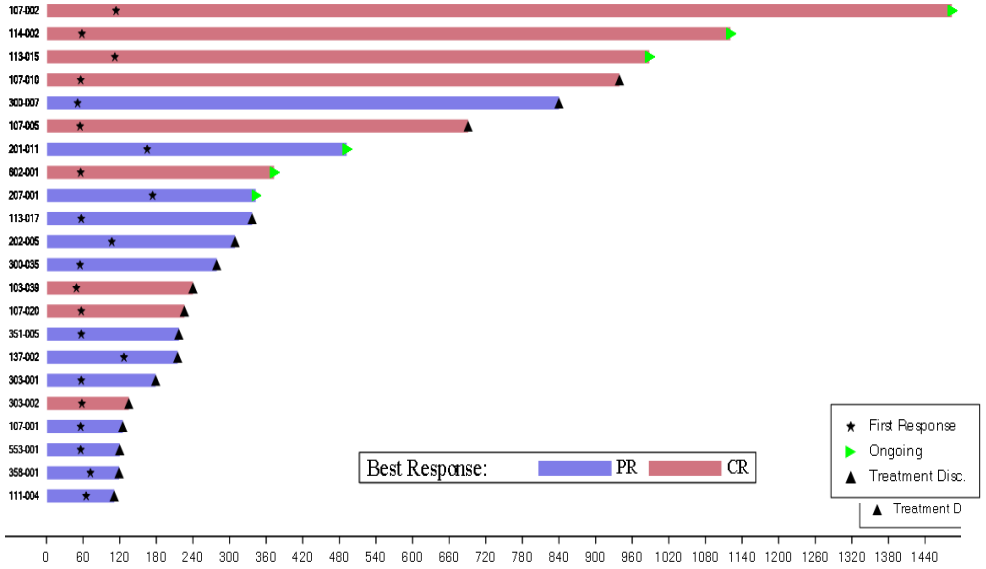
Event	initiated with single agent lead in cycle n=10	initiated with combination at MTD n=49
Transaminase	**4 (40%)**	**4 (8%)**
ALT	3 (30%)	4 (8%)
AST	1 (10%)	2 (4%)
Diarrhea	**3 (30%)**	**6 (12%)**
Neutrophil count decreased	**2 (20%)**	**19 (39%)**
Platelet count decreased	**1 (10%)**	**5 (10%)**
Infections	**0**	**6 (12%)**
Rash	**2 (20%)**	**4 (8%)**

Horwitz et al, Hematologic Oncology 2021

ASTX660 in Relapsed/Refractory PTCL and CTCL

ASTX660 is an XIAP inhibitor





Michot et al, EHA 2022

Phase 2: Open Label Trial , PTCL and CTCL cohorts

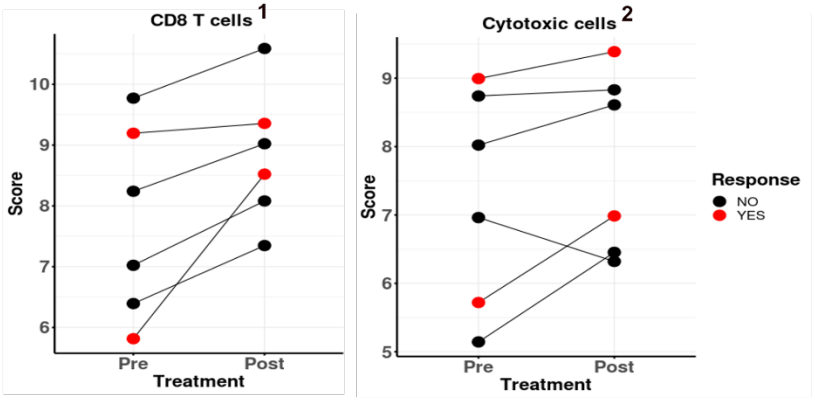
	PTCL(n=99)	CTCL (n=51)
ORR	22% (22 pt)	28% (14 pt)
PFS median	1.8 mo	5.5 mo
DOR median	6.5 mo	8.8 mo

Best overall response PTCL	N = 96
CR	9 (9.4%)
PR	13 (13.5%)
SD	16 (16.7%)
PD	58 (60.4%)

ASTX660 in Relapsed/Refractory PTCL and CTCL

Biopsies

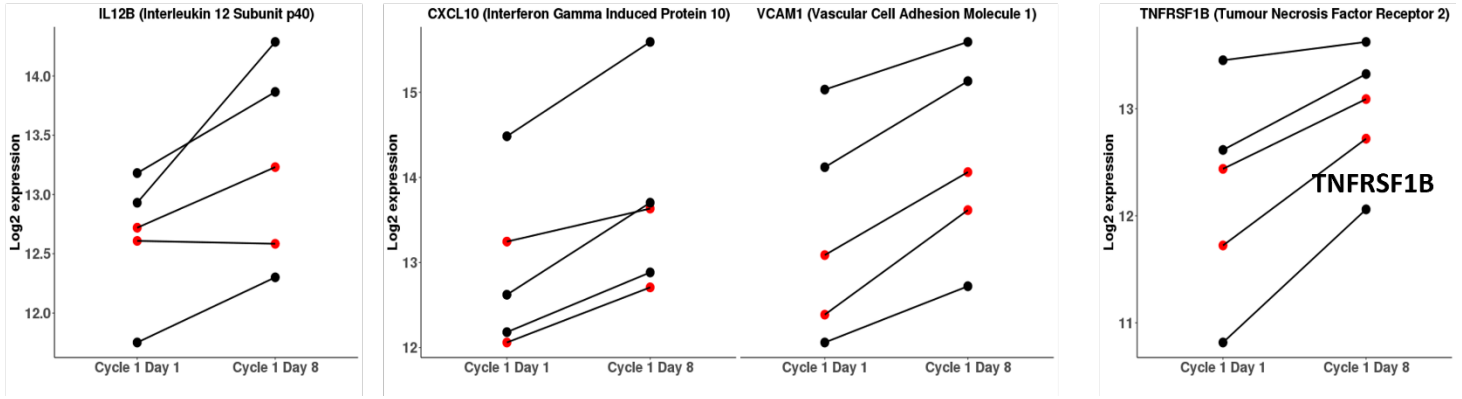
CD8 and cytotoxic cell recruitment



- Consistent with preclinical models, post-treatment PTCL samples show evidence of increased immune cell recruitment and soluble immune mediators

Plasma

T cell differentiation | Mediators of leukocyte recruitment | TNF pathway modulation

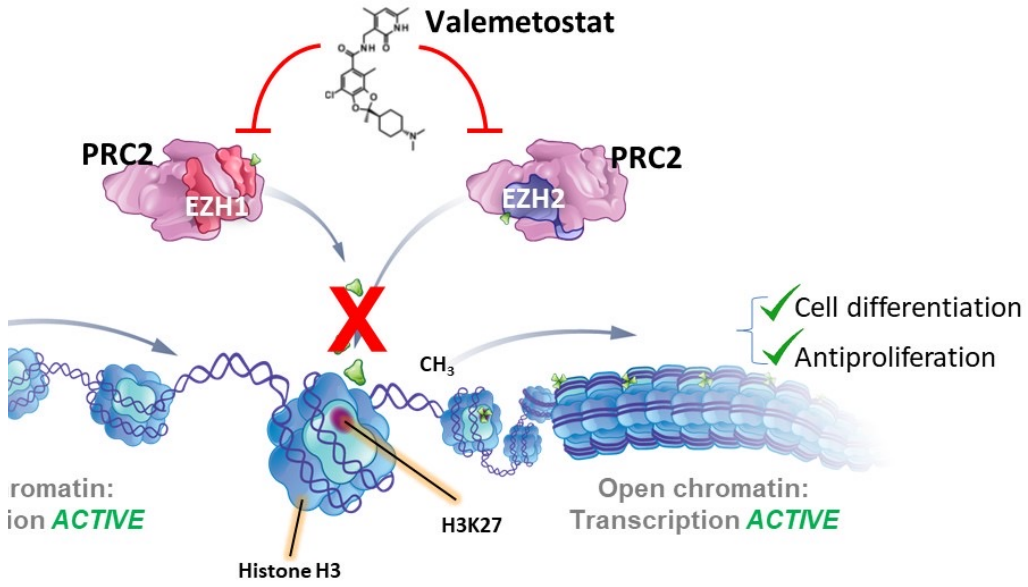


Adverse Event	Phase 2 Total (N=150) N (%)
Total Number of TEAEs	142
Subjects with >1 TEAE	68 (45.3)
Lipase increased	23 (15.3)
Rash (combined terms)	16 (10.7)
Amylase increased	10 (6.7)
Anaemia	7 (4.7)
Thrombocytopenia	7 (4.7)
Neutropenia	6 (4.0)
Febrile neutropenia	3 (2.0)
Pancreatitis	2 (1.3)
Tumor Flare	2 (1.3)
Acute kidney injury	2 (1.3)
Ejection fraction decrease	2 (1.3)
Hypercalcemia	2 (1.3)
Pruritis	2 (1.3)

Ferrari N *et al.*, *Blood Advances, 2021*

Valemetostat Tosylate: inibiitor of EZH1/EZH2

- Prevents trimethylation of H3K27
- Increases expression of genes silenced by H3K27me3, including those associated with the regulation of cell proliferation and differentiation[1-4]
- EZH2 is overexpressed in PTCLs and significantly overexpressed in ATL cells[1,2]



Phase I/II study of valemetostat in PTCL

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

Part 1: Dose Escalation
Japan

R/R NHL (all-comers)[b]

- 300 mg PO, QD
- 250 mg PO, QD
- 200 mg PO, QD
- 150 mg PO, QD

RDE

Part 2: Dose Expansion
Japan and US

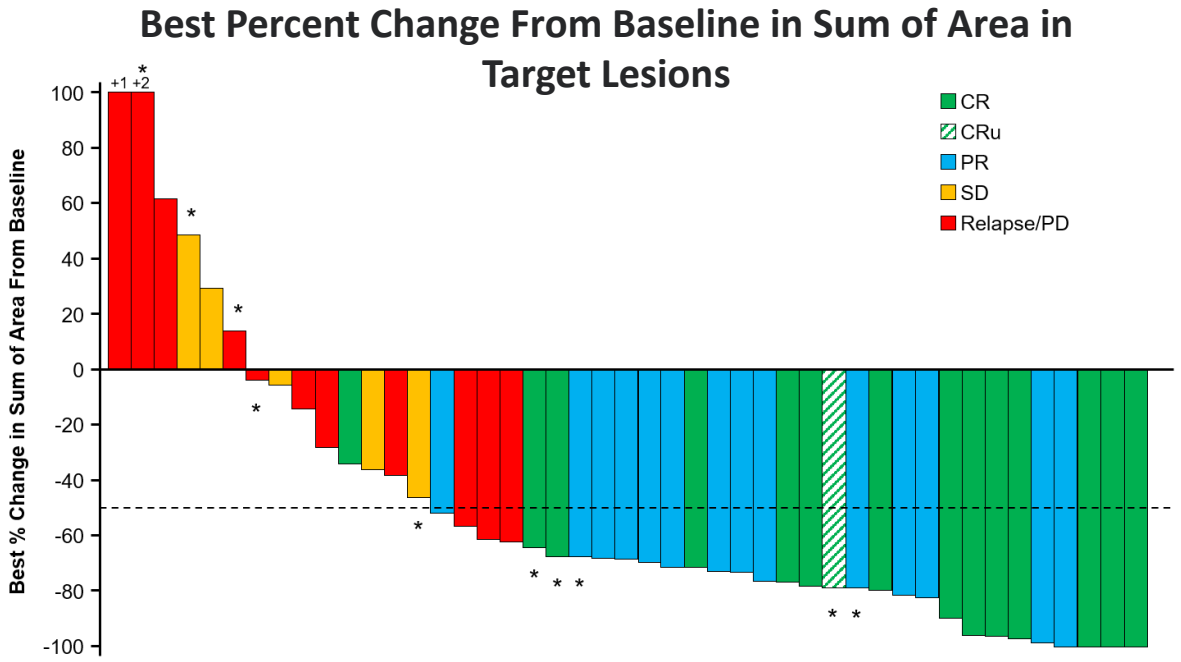
R/R ATL
Valemetostat 200 mg PO, QD

R/R PTCL
Valemetostat 200 mg PO, QD

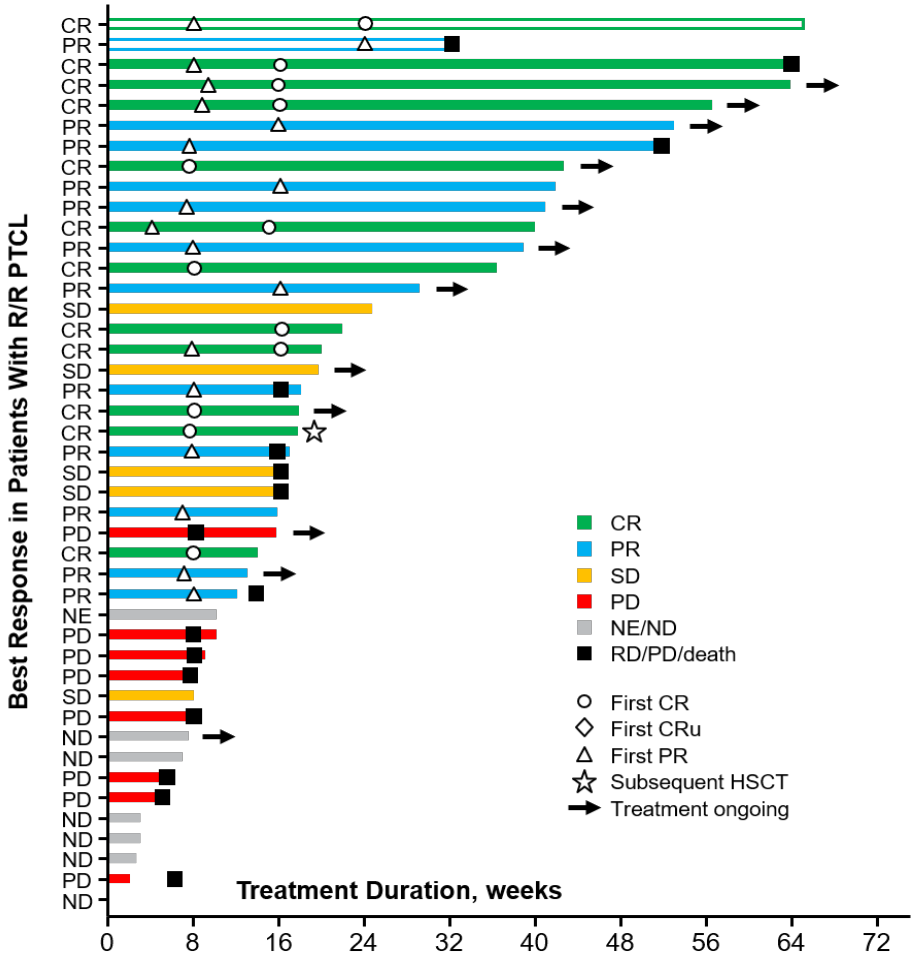
1. Honma D, et al. *Cancer Sci*. 2017;108(10):2069-2078. **2.** Yamagishi M, et al. *Cell Rep*. 2019;29(2017. Abstract 4670. **4.** Nakagawa M, et al. ASH 2017. Abstract 590. **5.** Juan AH, et al. *Cell Rep*. 2016;17(5):1369-1382. **6.** Peirs S. *Immunol Rev.* 2015;263:50-67.

Phase I/II study of Valemetostat: results

	All PTCL (n=44)	AITL (n=17)	PTCL-NOS (n=20)	ALCL (n=2)	ATLL (N=14)
ORR (%)	54.5%	65%	50%	50%	57%
CR (%)	27.3%	47%	20%	50%	28%



Foss et al, Blood 2021



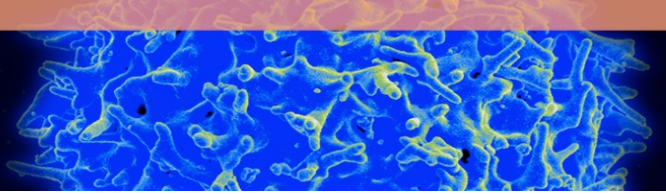
Phase I/II study of valemetostat: adverse events

- Grade ≥3 platelet count decreased and thrombocytopenia[a] occurred in 13 (16.9%) and 2 (2.6%) patients with all histologies, respectively

Most Common TEAEs (occurring in ≥20% of patients with TCL)[b]	All Histologies[c] (N=77)		PTCL (N=44)		ATL (N=14)	
	All grades	Grade ≥3	All grades	Grade ≥3	All grades	Grade ≥3
Platelet count decreased[d]	47 (61.0)	13 (16.9)	21 (47.7)	5 (11.4)	9 (64.3)	3 (21.4)
Dysgeusia	40 (51.9)	0	20 (45.5)	0	8 (57.1)	0
Anemia	31 (40.3)	9 (11.7)	15 (34.1)	6 (13.6)	5 (35.7)	1 (7.1)
Neutrophil count decreased	27 (35.1)	18 (23.4)	13 (29.5)	8 (18.2)	6 (42.9)	5 (35.7)
Alopecia	26 (33.8)	0	12 (27.3)	0	6 (42.9)	0
WBC count decreased	23 (29.9)	12 (15.6)	10 (22.7)	6 (13.6)	4 (28.6)	3 (21.4)
Diarrhea	22 (28.6)	1 (1.3)	13 (29.5)	0	3 (21.4)	0
Lymphocyte count decreased	22 (28.6)	17 (22.1)	7 (15.9)	6 (13.6)	2 (14.3)	2 (14.3)
ALT increased	16 (20.8)	1 (1.3)	7 (15.9)	0	3 (21.4)	1 (7.1)
Nausea	16 (20.8)	0	11 (25.0)	0	3 (21.4)	0

Foss et al, Blood 2021

Phase II (Valentine) study of valemetostat



- 133 patients with relapsed/refractory PTCL enrolled
- Median 2 prior therapies
- 26% had prior stem cell transplant 32 auto, 5 allo)
- 119 efficacy evaluable
- ORR 43%
- Median PFS 5.5 mo
- Median OS 17 mo

- 57% of patients had grade ≥3 AE
- 13 pts had treatment discontinuation for AE

Table 1. Efficacy results per CT-based blinded independent central review assessment by PTCL subtype

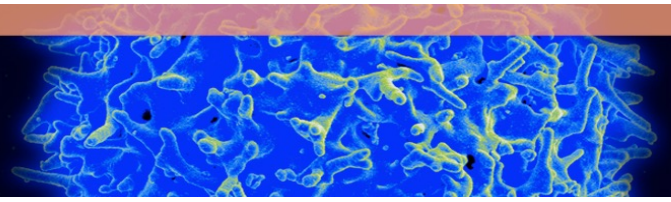
Response	AITL (n = 42)	PTCL, NOS (n = 41)	PTCL TFH (n = 8)	ALCL (*ALK*-positive or *ALK*-negative) (n = 9)	Other[a] (n = 19)	All (N = 119)
ORR (CR or PR), n (%)	23 (54.8)	13 (31.7)	4 (50)	3 (33.3)	9 (47.4)	52 (43.7)
95% CI[b]	38.7–70.2	18.1–48.1	15.7–84.3	7.5–70.1	24.4–71.1	34.6–53.1
CR, n (%)	8 (19.0)	4 (9.8)	1 (12.5)	1 (11.1)	3 (15.8)	17 (14.3)
95% CI[b]	8.6–34.1	2.7–23.1	0.3–52.7	0.3–48.2	3.4–39.6	8.5–21.9
PR, n (%)	15 (35.7)	9 (22.0)	3 (37.5)	2 (22.2)	6 (31.6)	35 (29.4)
95% CI[b]	21.6–52.0	10.6–37.6	8.5–75.5	2.8–60.0	12.6–56.6	21.4–38.5
DOR[c], median (range), months	11.9 (1.6–14.9+)	7.9 (0+–14.9+)	NE (5.1–11.1+)	3.8 (3.7–12.0+)	9.2 (3.7–9.5+)	11.9 (0+–14.9+)
95% CI[d]	10.8–NE	3.7–NE	5.1–NE	3.7–NE	3.7–NE	7.8–NE
DOCR[e], median (range), months	NE (0+–12.0+)	11.2 (2.7+–11.2)	5.1 (5.1–5.1)	NE (8.3+–8.3+)	NE (6.5+–9.5+)	11.2 (0+–12.0+)
95% CI[d]	1.7–NE	4.2–NE	NE–NE	NE–NE	NE–NE	4.2–NE

Table 2. TEAEs in ≥ 10% of patients with R/R PTCL

	R/R PTCL (N = 133)	
	Any grade	Grade ≥ 3
Preferred term	n (%)	
Pts with ≥ 1 TEAE	128 (96.2)	77 (57.9)[a]
Thrombocytopenia[b]	66 (49.6)	31 (23.3)
Anemia[c]	47 (35.3)	25 (18.8)
Diarrhoea	39 (29.3)	5 (3.8)
Dysgeusia	38 (28.6)	0
Neutropenia[d]	35 (26.3)	23 (17.3)
COVID-19	28 (21.1)	4 (3.0)
Nausea	23 (17.3)	1 (0.8)
Cough	20 (15.0)	0
Pyrexia	20 (15.0)	0
Decreased appetite	19 (14.3)	2 (1.5)
Fatigue	19 (14.3)	2 (1.5)
Asthenia	17 (12.8)	4 (3.0)
Oedema peripheral	16 (12.0)	1 (0.8)
Pruritus	16 (12.0)	0
Alopecia	14 (10.5)	0
AST increased	14 (10.5)	1 (0.8)

Horwitz et al, ASH 2023

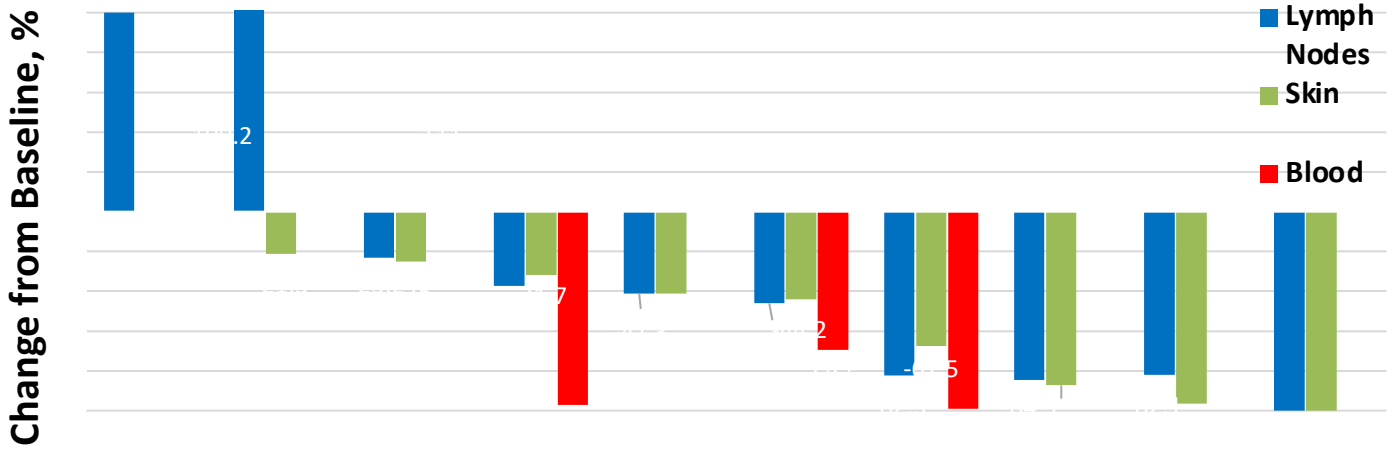
Immunotherapy in PTCL

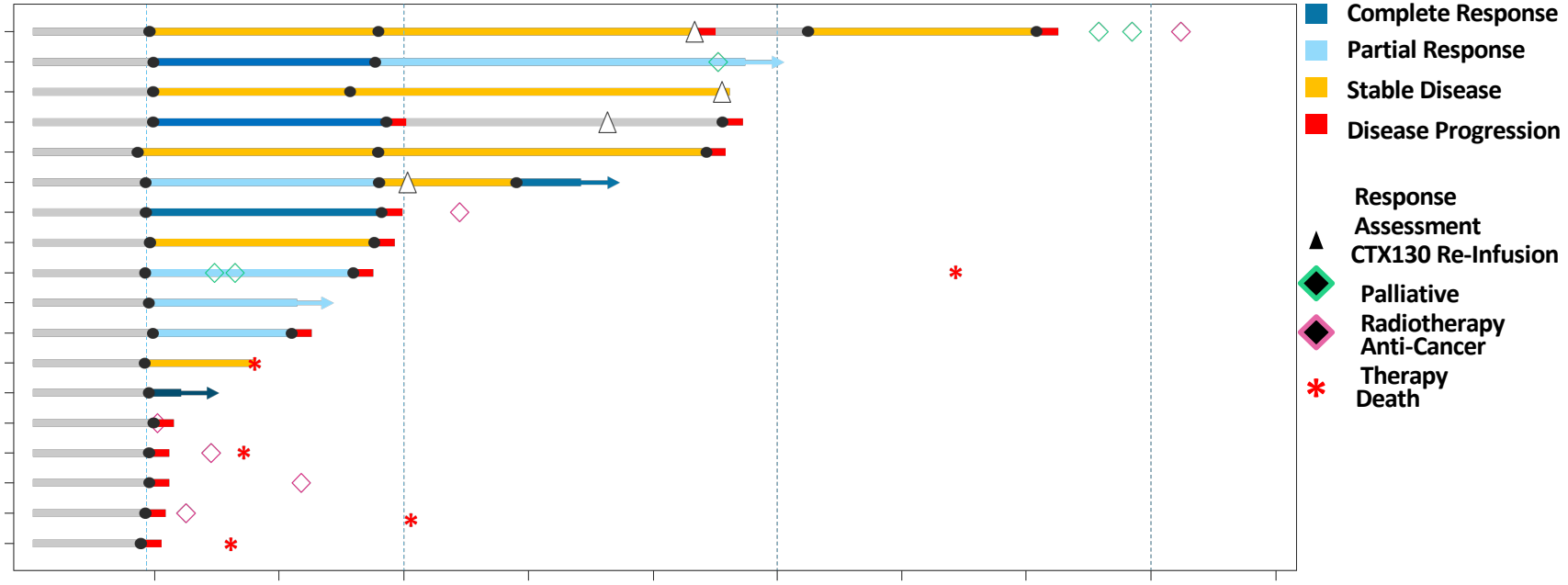


- Allogeneic SCT is potentially curative in relapsed setting
- T-cell Checkpoint inhibitors
  - Subtype specific responses
  - NK, MF/SS
  - Risk of hyper-progression and lack of predictors precludes wider use
- CD47 Strategies
  - Combination Studies ongoing (Magrolimab + Mogamulizumab in CTCL)
- CAR
  - CART-Early studies CD5, 7, 30, 37, 4, CCR4, TCRB1, others
  - ? Need for allo backup
  - Other cell types/sources
  - Allo-T, NK, Myeloid
- Bi-specifics
  - CD30, PD-1

COBALT-LYM Allogeneic CAR T trial

Responses were observed across compartments (lymph nodes, skin, blood) in patients with CTCL





- CAR directed to CD70
- Median CD70+ expression amongst patients with relapsed / refractory T cell lymphoma was 90%
- CTX130 has demonstrated an acceptable safety profile in heavily pretreated patients with relapsed / refractory T cell lymphomas
- We have observed clinically meaningful responses with CTX130, including a 40% CR rate at DL ≥3

COBALT-LYM Allogeneic CAR T trial

Subject Overview

Patient profile

- 47-year-old male with stage IVA2 transformed mycosis fungoides (tMF)
- 5 prior lines of therapy
- Refractory after last treatment with brentuximab vedotin
- CD70+ expression was 100% at baseline

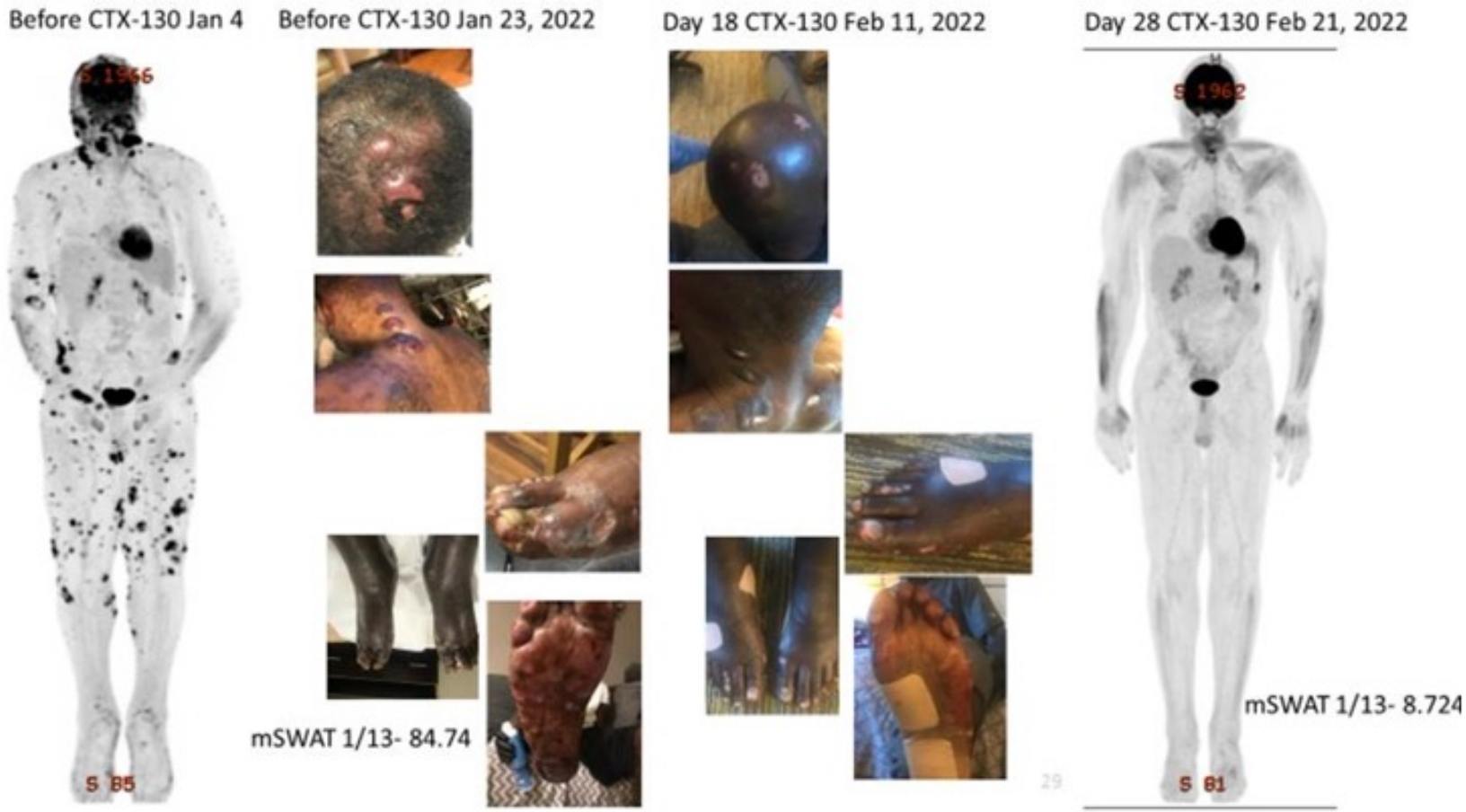
Efficacy

- CR at D28 after a single infusion of 9 x 10^8 CAR+ T cells
- Remains in CR at M3

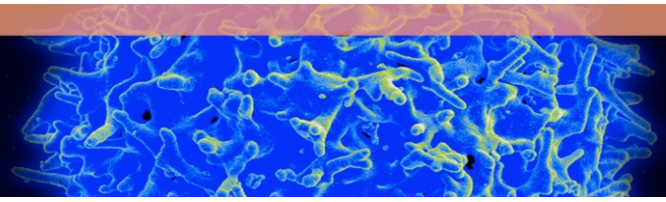
Safety

- Gr 3 anemia (D3) & Gr 3 neutropenia (D4)
- All other AEs were Gr 1

Responses



Therapy of PTCL as we move forward..



- Relapsed PTCL remains heterogeneous group of diseases most with poor prognosis and little overall improvement in outcomes
- Front line therapy remains CHOP/chemo based but novel agents and combinations are being explored
- Allogenic transplant only potentially curative option at relapse or for high-risk subtypes
- New agents and combinations are promising
  - need subtype specific approaches
  - Targeted agents
- Clinical trial enrollment and international cooperation critical