2025 DEBATES AND DIDACTICS in Hematology and Oncology

EMORY WINSHIP CANCER INSTITUTE
National Cancer Institute-Designated Comprehensive Cancer Center
Where Science Becomes Hope

JULY 24 - 27, 2025 • SEA ISLAND, GEORGIA

This activity is jointly provided by Partners for Advancing Clinical Education and Bio Ascend

Update in the Management of Relapsed/Refractory PTCL: Focus on Recent Data and Upcoming Studies

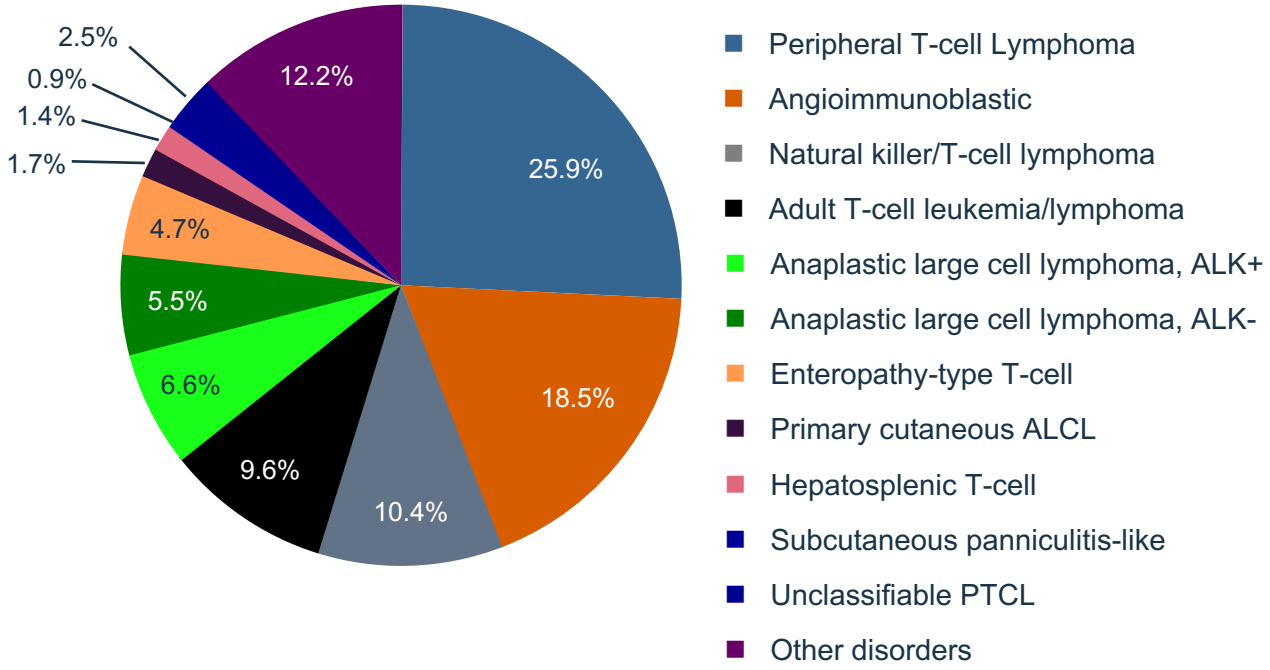
Mary Jo Lechowicz, MD

July 25, 2025

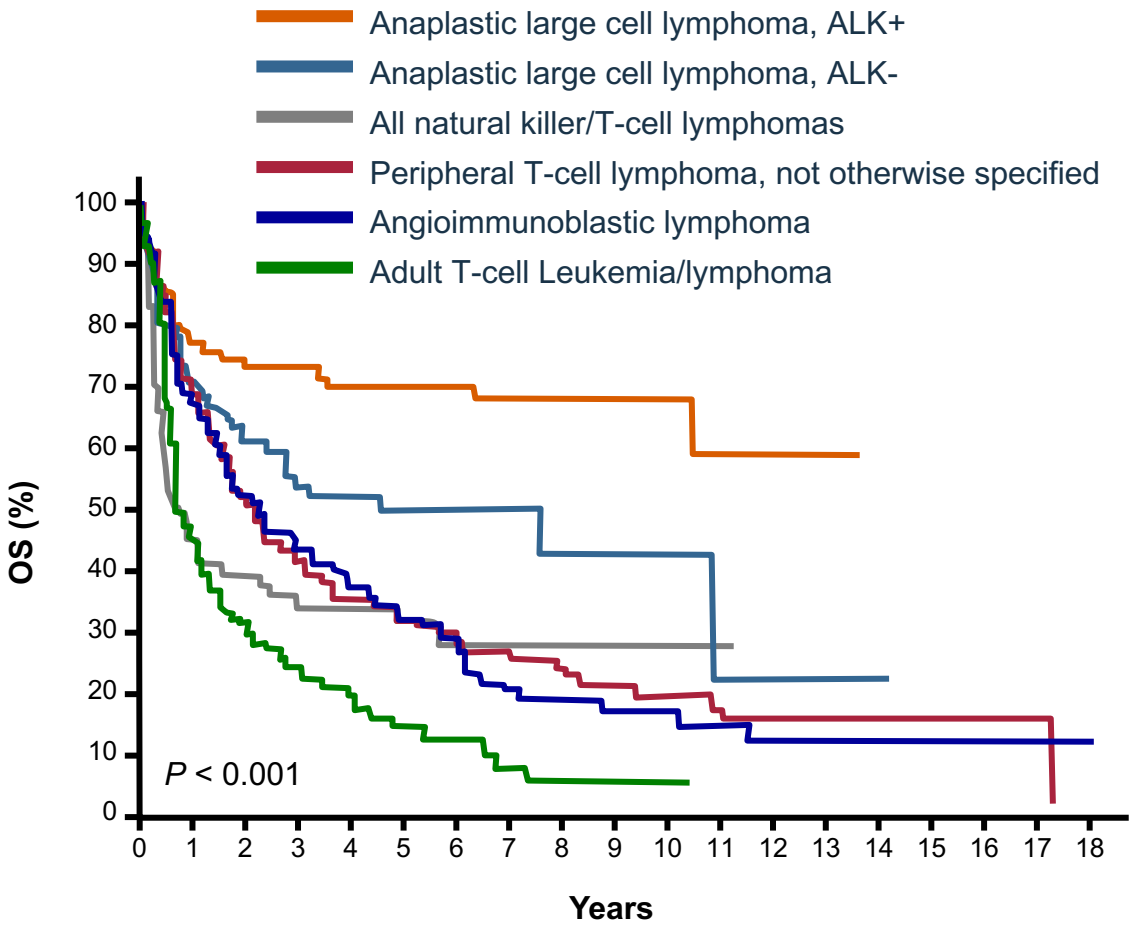
Disclosures

DSMB: Solgenix

T-Cell Lymphomas: Heterogenous Diseases and Heterogenous Outcomes With a Similar Approach

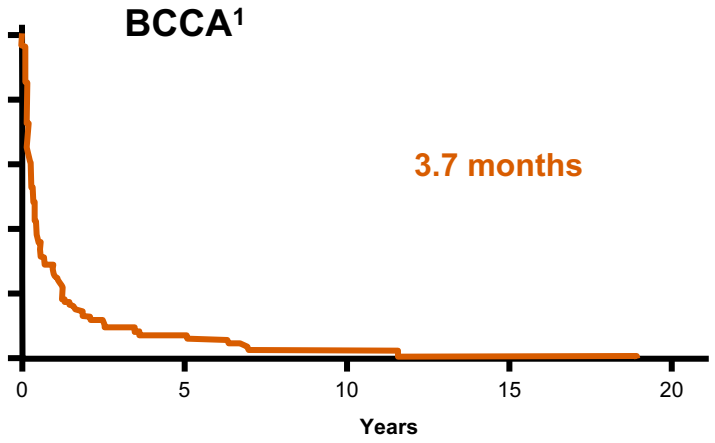


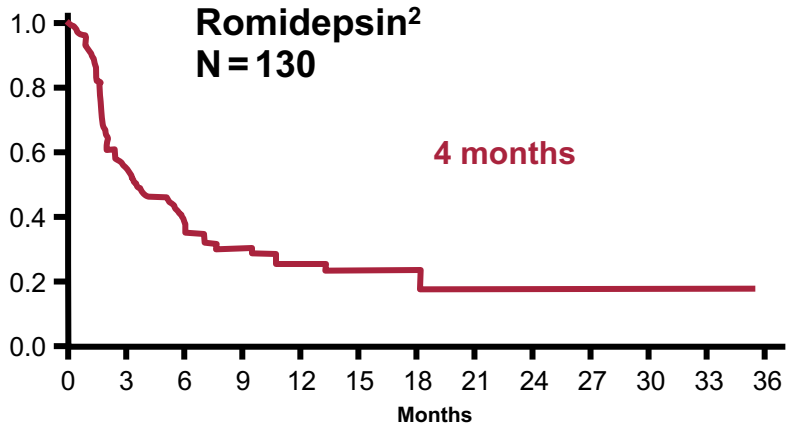
Most patients were treated with anthracycline-based combination chemotherapy

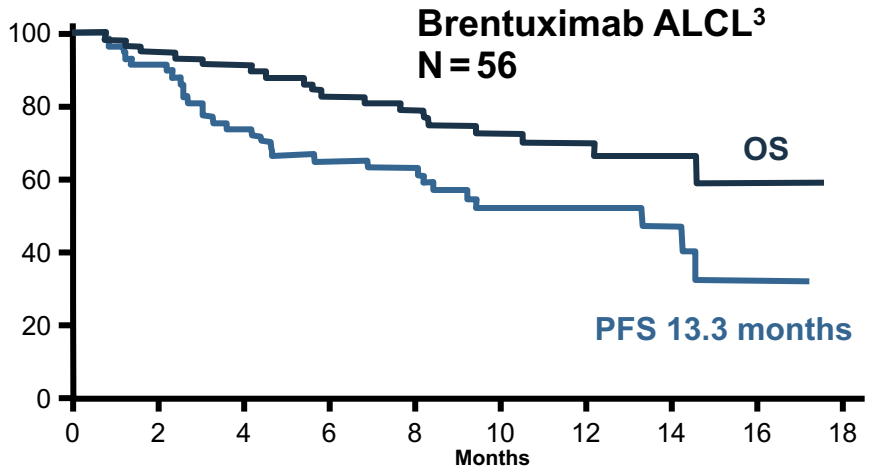


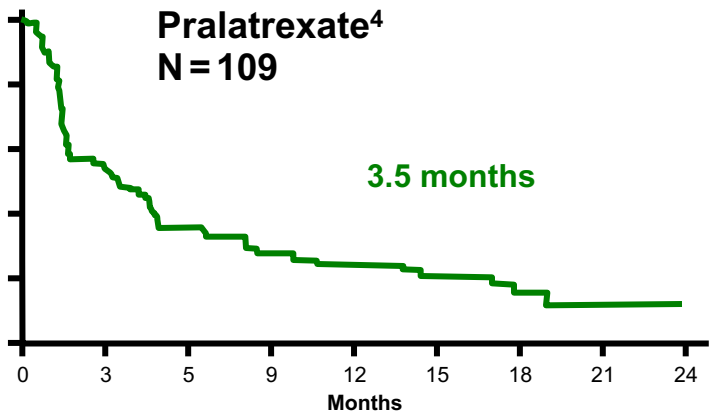
Vose J, et al. *J Clin Oncol*. 2008;26(25):4124-4130.

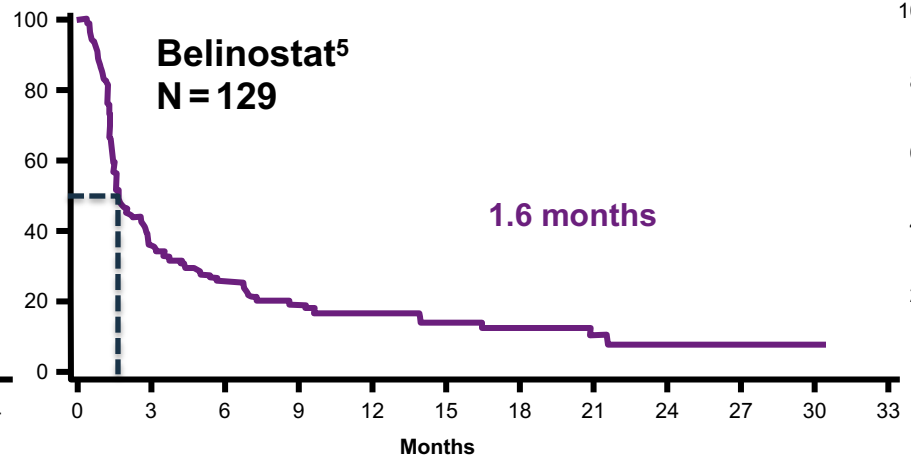
PFS of Relapsed/Refractory PTCL

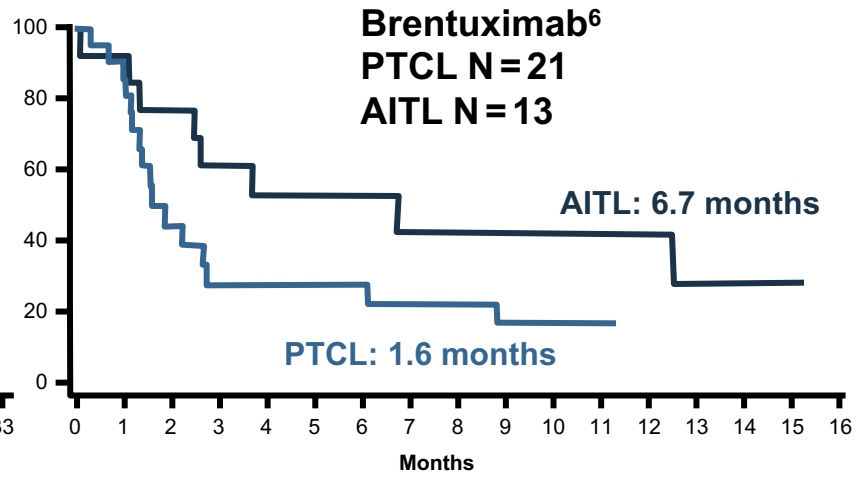












BCCA is without newer approved therapies, but when those therapies are studied as all comers in PTCL, ORR is low (excepting ALCL). Therefore, the **median is driven by non-responders** and true clinical benefit is only for a minority of responders with a durable response.

1. Mak V, et al. *J Clin Oncol*. 2013;31(16):1970-1976. 2. Coiffier B, et al. *J Clin Oncol*. 2012;30:631-636. 3. Pro B, et al. *J Clin Oncol*. 2012;30(18):2190-2196. 4. O'Connor OA, et al. *J Clin Oncol*. 2011;29:1182-1189. 5. O'Connor OA, et al. *J Clin Oncol*. 2015;33(23):2492-2499. 6. Horwitz SM, et al. *Blood*. 2014;123(20):3095-3100.

FDA-Approved and Off-Label Standard Agents in PTCL

Outcomes	Belinostat[1]	Romidepsin[2]	Pralatrexate[3]	Brentuximab vedotin[4]	Lenalidomide[5]	Bendamustine[6]
Setting Approval Date	R/R PTCL July 2014	R/R PTCL* June 2011	R/R PTCL Sept. 2009	R/R ALCL Aug. 2011	R/R Off-label	R/R Off-label
Median prior Tx	2	2	3	2	—	≤3
ORR	26%	25%	29%	86%	22%	50%
CR	11%	15%	11%	59%	11%	28%
PR	15%	11%	18%	27%	11%	22%
Median duration of response	8.4	17 mos	10.1 mos	13.2 mos	—	3.5 mos
Median PFS	1.6	4 mos	3.5 mos	14.6 mos	—	3.6 mos

*2021 withdrawn in US for R/R PTCL indication due to negative phase III study Ro-CHOP vs CHOP

- Crizotinib approved for pediatric patients (>1 year) and young adults with R/R ALK+ ALCL

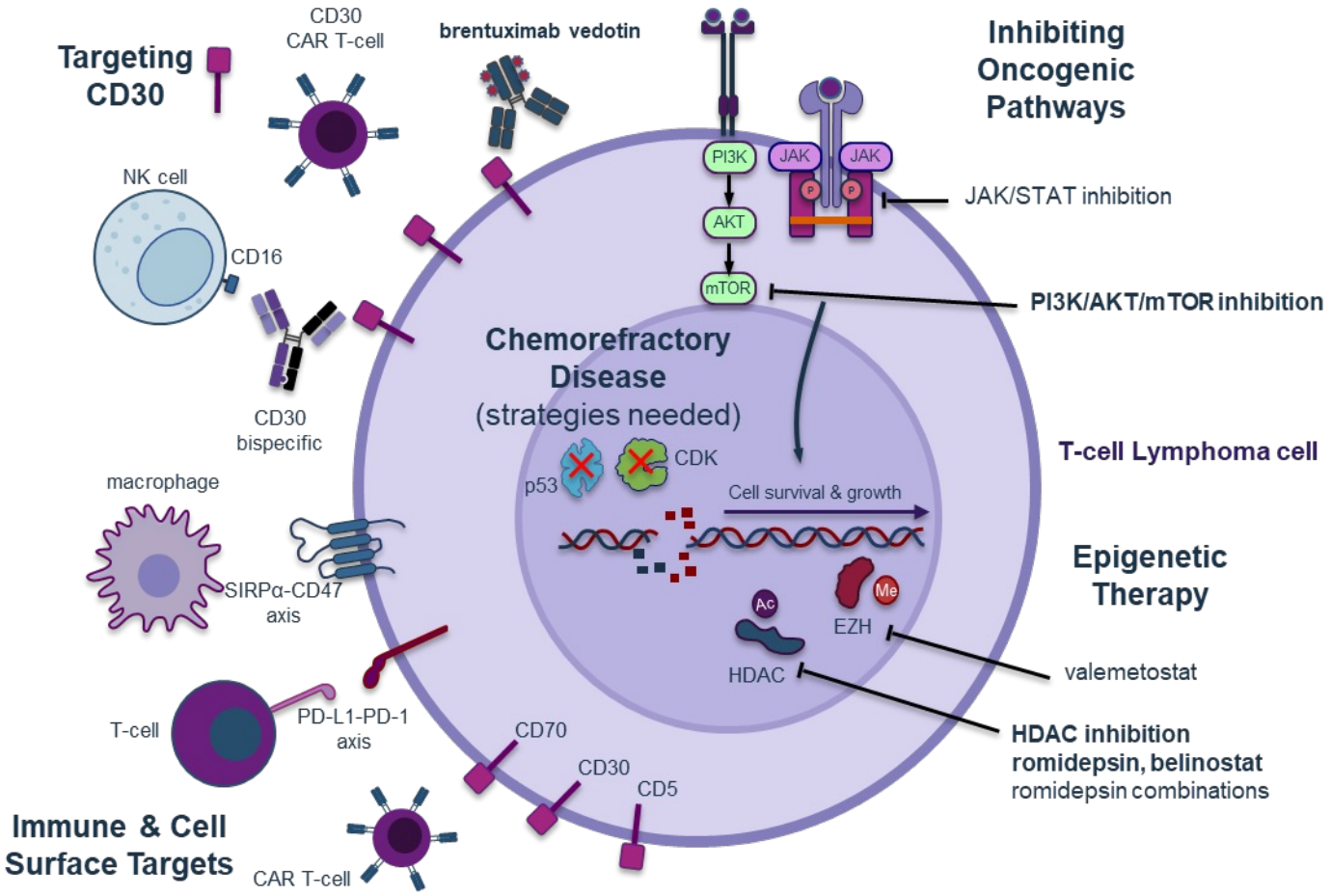
1. O'Connor OA, et al. *J Clin Oncol*. 2015;33(23):2492-2499. 2. Coiffier B, et al. *J Clin Oncol*. 2012;30:631-636. 3. O'Connor OA, et al. *J Clin Oncol*. 2011;29:1182-1189. 4. Horwitz SM, et al. *Blood*. 2014;123(20):3095-3100. 5. Morschhauser F, et al. *Eur J Cancer*. 2013;49(13):2869-2876. 6. Damaj G, et al. *J Clin Oncol*. 2013;31(1):104-110.

PTCL Genetics and Molecular Pathogenesis Help Explain Heterogeneity and Identify Therapeutic Targets

- Increasing understanding of biology of T-cell lymphomas[1]
  - AITL and TFH (T-follicular helper PTCL) develop on a background of epigenetic dysregulation
    - *TET2, DMNT3A, IDH2, CHiP*
- Aberrant T-cell receptor (TCR) signaling is common[2]
  - *RHOA, VAV1, SYK*
- Other signaling pathways are frequently dysregulated[3]
  - PI3K, JAK/STAT
- Alterations in tumor suppressor genes are common[3]
- Subtype-specific or subtype-independent[3,4]
- Aberrant signaling in pathways may converge or be present simultaneously[3]

1. Tigu AB, et al. *Curr Issues Mol Biol*. 2023;45(11):8974-8988. 2. Fujisawa M, et al. *Leukemia*. 2018;32(3):694-702. 3. Luan Y, et al. *Mol Cancer*. 2024;23(1):2. 4. Weiss J, et al. *Front Oncol*. 2023;13:1101441.

Other Targets in T-Cell Lymphoma



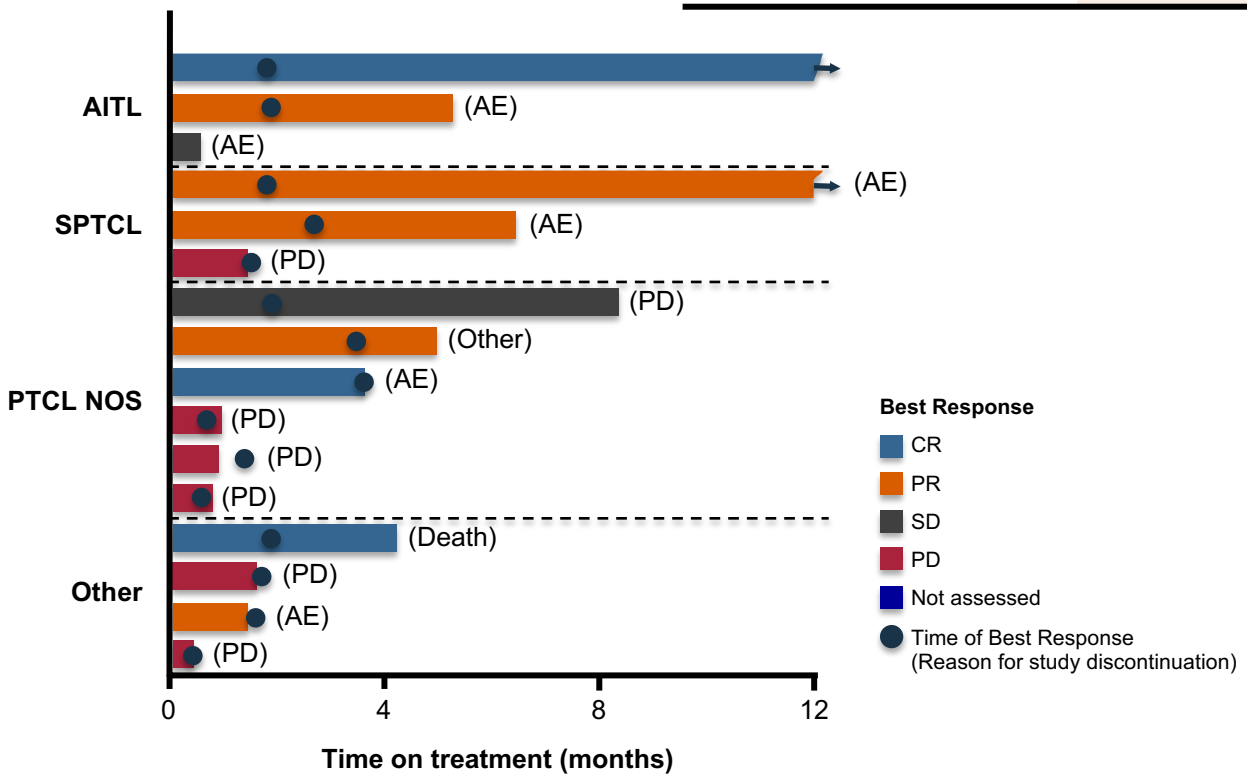
- PI3Kα, PI3Kβ, PI3Kγ, PI3Kδ and PTEN were analyzed in 88 cases of PTCL and NKTCL[1]
- High expression of PI3K isoforms were found in all samples[1]
- High PI3Kα expression was linked to poor survival[1]
- Inhibition of PI3Kα and PI3Kδ isoforms resulted in suppression of tumor cell growth *in vitro* and *in vivo*[1]
- Examples of agents that target PI3K include **duvelisib** and **tenalisib**

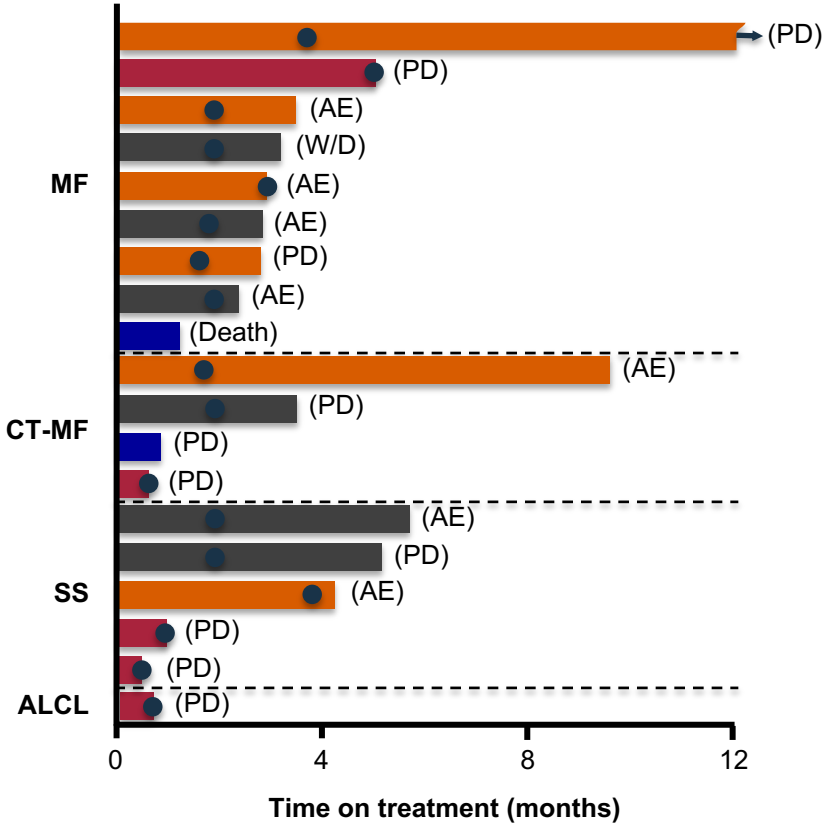
1. Huang D, et al. Br J Haematol. 2020;189(4):731-744

Courtesy of Robert Stuver M.D.

Phase 1 Study of Duvelisib: Results in T-Cell Lymphomas

	PTCL (n = 16)	CTCL (n = 19)
ORR	50%	32%
CR	**3** (19%)	**0**
Median PFS, months	**8.3**	**4.5**





Most patients treated with 75 mg BID

Duvelisib is not FDA approved for PTCL

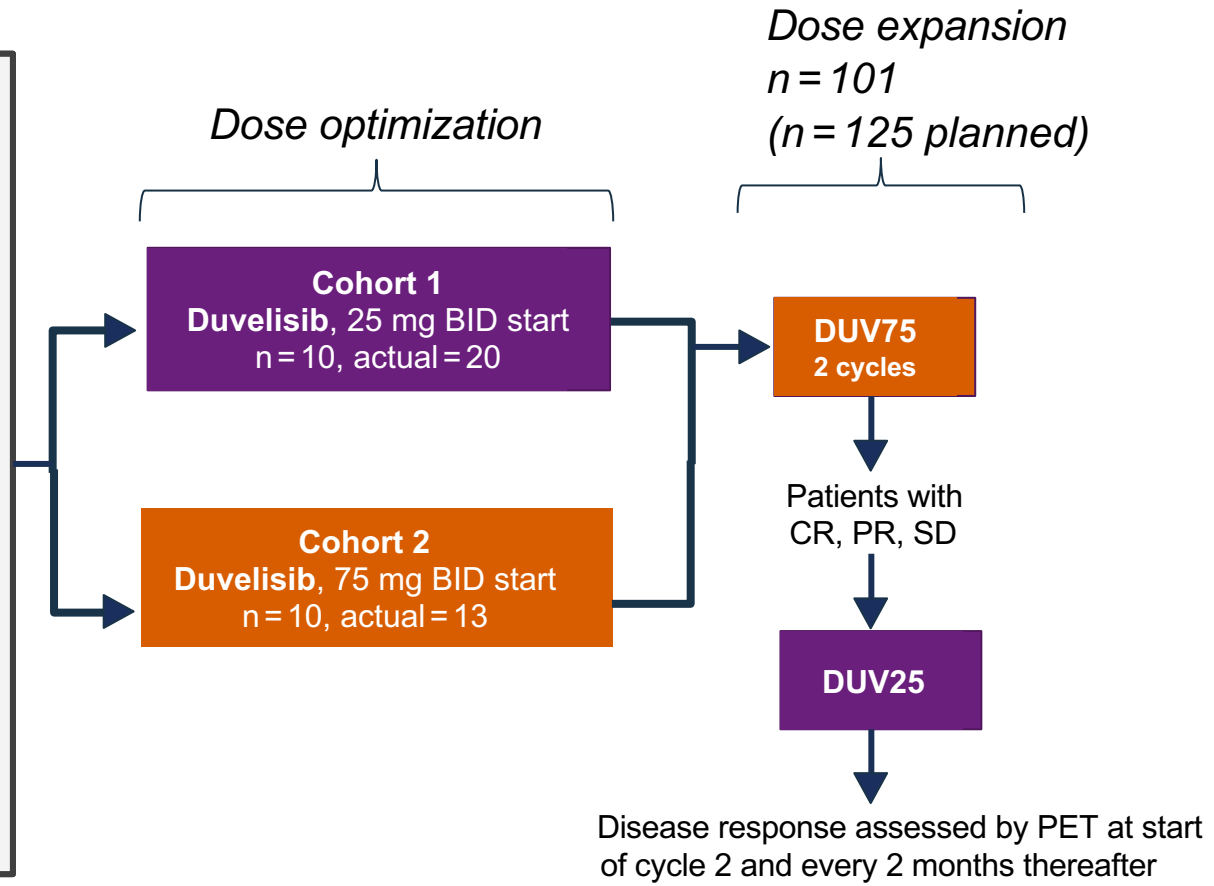
CR, complete response; PR, partial response; CTCL, cutaneous T-cell lymphoma; SD, stable disease; PD, progressive disease

Horwitz, et al. *Blood*. 2018 Feb 22;131(8):888-898

Phase 2 PRIMO Trial: Multicenter, Parallel Cohort, Open-Label Trial of Duvelisib in R/R PTCL

Patient population

- Patients with relapsed or refractory PTCL[a]
- Pathologically-confirmed PTCL subtypes per WHO criteria[b]
- Measurable disease per Lugano for PTCL
- No prior history of allogeneic stem cell transplant or treatment with PI3K inhibitor
- ECOG PS ≤ 2



Primary Endpoint
• IRC-assessed ORR
Key Secondary Endpoints
• Safety • DoR • PFS • DCR (CR + PR+ SD ≥ 8 wks) • OS • PK
Exploratory Endpoints
• PD and Biomarkers

[a] Received ≥ 2 cycles of standard regimen and failed to achieve PR or better after ≥ 2 cycles, or failed to achieve CR after completion of standard therapy, or progressed after initial response.
[b] After the dose optimization phase, the inclusion criteria for subtypes were broadened.

Duvelisib is not FDA approved for PTCL
DCR, disease control rate; PET, positron electron tomography; PD, progressive disease; PK, plasma concentration
ClinicalTrials.gov. **NCT03372057**

Phase 2 PRIMO Trial: Duvelisib Monotherapy

- Median number of prior lines of therapy was 3 (range, 1–9)
  - CHOEP/EPOCH: 36.6%
  - CHOP/R-CHOP: 36.6%
  - Brentuximab vedotin/brentuximab vedotin–containing chemotherapy: 36.6%
  - Salvage chemotherapy after CHOP/R-CHOP or CHOEP/EPOCH: 37.6%
  - Autologous stem cell transplant 21.8%

Outcome	ALL PTCL (n = 101)
ORR	**48.5%** (95% CI, 38.8%–58.3%)
Best overall response, n (%)	
• Complete response, n (%)	**37%**
• Partial response, n (%)	14.9%
Median PFS by IRC (95% CI)	3.6 months (95% CI, 1.9–8.3)
Median DOR by IRC (95% CI)	7.7 months (95% CI, 5.5–9.4)
Median DOR for pts achieving CR (95% CI)	7.4 months (95% CI, 6.4–NC)

DOR, duration of response; IRC, independent review committee; NC, not calculable; PFS, progression-free survival; PTCL, peripheral T-cell lymphoma
Duvelisib is not FDA-approved for PTCL
Mehta-Shah N, et al. *Hemasphere*. 2023;7(Suppl):e3891642.

Phase 2 PRIMO Trial: Duvelisib Monotherapy
Response by Subtype

	PTCL-NOS (n = 52)	AITL (n = 30)	ALCL (n = 15)
ORR by baseline histology, n (%)	25/52 (**48.1**)	20/30 (**66.7**)	2/15 (**13.3**)
Best overall response, n (%)			
Complete response, n (%)	14/52 (26.9)	16/30 (53.3)	2/15 (13.3)
Partial response, n (%)	11 (21.2)	4 (13.3)	NC
Median PFS by IRC, mos (95% CI)	3.4 (1.8, 8.1)	9.1 (6.2, NC)	1.5 (0.7, 1.7)
Median OS, mos (95% CI)	10.9 (5.1, NC)	15.5 (9.5, 18.0)	4.8 (1.7, 15.7)
Median time to response (range)	1.7 (1.7, 0.5)	1.8 (1.9, 0.5)	2.6 (2.6, 1.3)
Median DOR by IRC, mos (95% CI)	5.5 (2.0, 9.2)	8.8 (7.7, NC)	1.9 (1.9, 2.0)
Median DOR for pts achieving CR	7.4 (6.4, NC)	7.9 (3.3, NC)	1.9 (1.9, 2.0)

NC. Not calculable
Duvelisib is not FDA approved for PTCL
Mehta-Shah N, et al. *Hemasphere*. 2023;7(Suppl):e3891642.

Phase 2 PRIMO Trial: Duvelisib Monotherapy
TEAEs

The most common TEAE of special interest was transaminase elevation

Adverse Event	PRIMO-EP (N = 101)	
	Any TEAE*, %	Grade ≥3 TEAE, %
Infections	38	10
Colitis	1	0
Cutaneous reactions	35	9
Diarrhea	31	7
Neutropenia	35	19
Pneumonia	3	2
Pneumonitis	2	1
Transaminase elevation	44	23

*With N=101, all *n* are the same as the percentages shown
TEAE, treatment-emergent adverse event; eg, an AE that emerges or worsens in the period from date of first dose to 30 days after the date of last dose
Duvelisib is not FDA-approved for PTCL
Zinzani PL, et al. *Hemasphere*. 2022;6(Suppl):1058-1059.

- 17 patients had a TEAE resulting in death; 3 of these were treatment-related
- There were no additional TEAE deaths compared with the prior (N = 78) interim analysis except for PD

TEAEs^ resulting in death	n
Pneumonitis*	1
EBV*	1
Sepsis*	1
GI hemorrhage	1
Febrile infection	1
Vascular dementia	1
Completed suicide	1
Progressive disease	10

^TEAE, AE that emerges or worsens in the period from date of first dose to 30 days after the date of the last dose.
*TEAE with a relationship of possible, probable, or definite per investigator are considered related to study treatment

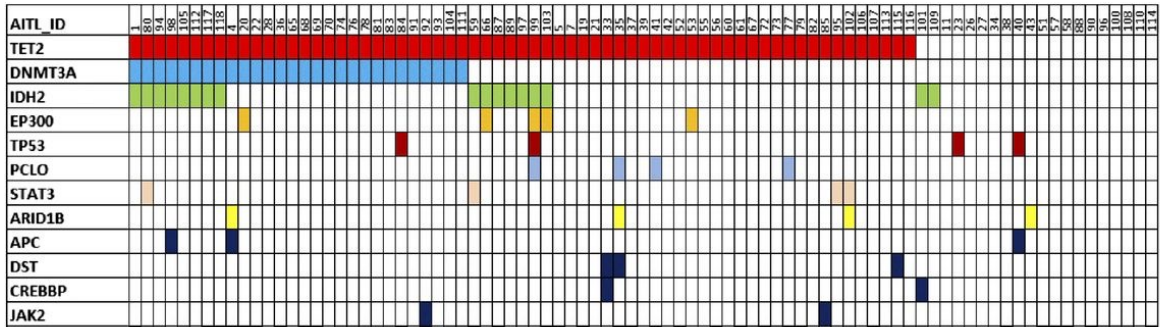
Examples of Other PI3K Inhibitor Monotherapies

	Linperlisib[1]	Tenalisib [2]
Target	PI3Kd	PI3K δ/γ
Trial (Phase)	NCT04108325 (1b)	NCT02567656 (1/1b)
ORR/CR, %	60% / 35%	46.7% / 20% (PTCL subset)
mDoR	15 months (95%CI, 6.9–NE)	6.5 months (95% CI, 2.9–14.9) (PTCL subset)
mPFS	10 months (95%CI, 3.7– NE)	NR
AEs	• TRAEs: 39 of 43 pts (91%) • Most common Grade ≥3 were neutropenia (21%), pneumonia (12%) and hypertriglyceridemia (7%)	• Most frequently reported TEAEs were fatigue (45%), AST increase (36%), ALT increase (35%) and diarrhea (33%) • Most common grade ≥3 TEAEs were transaminase elevations (21%), anemia (8.6%), neutropenia (6.9%) and hyponatremia (6.9%) • Grade 4 related TEAEs included two events of ALT increase and one event of sepsis

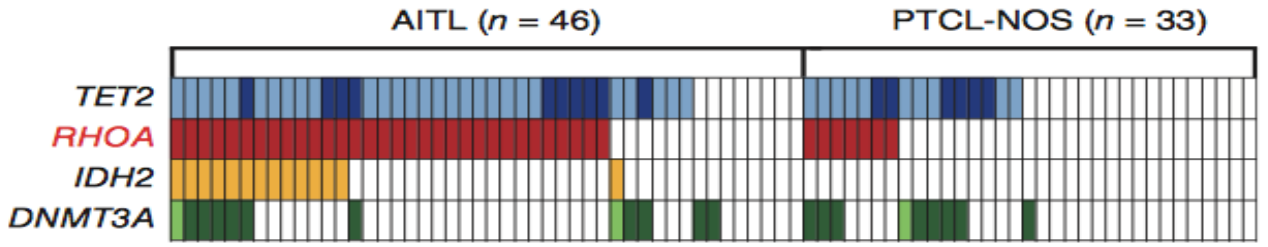
NR, not reported; TRAE, treatment-related adverse event
These agents are not FDA approved
1. Qiu L, et al. *Blood* 2022; 140 (Supplement 1): 9395–9396. 2. Huen A, et al. *Cancers (Basel)*. 2020 Aug 15;12(8):2293.

Genetic Drivers in Subtypes and Subgroups of PTCL

AITL and TFH subtypes of PTCL enriched for mutations in epigenetic modifiers: *TET2, DNMT3A, RHOA, IDH2*



1



2

3

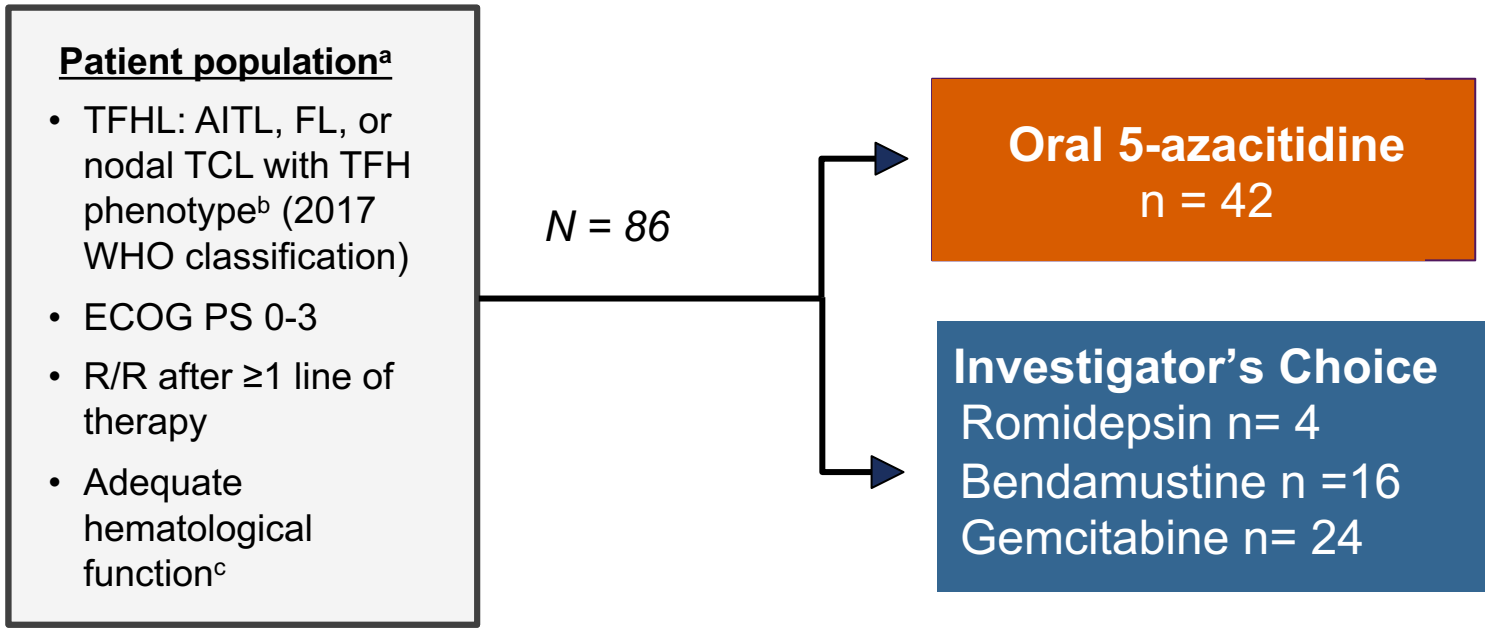
- Epigenetic modifiers are among the most studied and used therapies in T-cell lymphomas
- Examples include:
  - Histone deacetylase (HDAC) inhibitors
  - Inhibitors of DNA methyltransferase
  - EZH inhibitors (*EZH1/EZH2*)

Sundaravel S, et al. Semin Hematol. 2021;58(1):15-26

AITL, angioimmunoblastic T-cell lymphoma; TFH, T follicular helper; PTCL, peripheral T-cell lymphoma

1. Odejide O, et al. *Blood.* 2014;123:1293-1296. 2. Sakata-Yanagimoto M, et al. *Nat Genet.* 2014;46:171-175. 3. Palomero, et al. *Nat Genet.* 2014;46:166-170.

Phase 3 Oracle Study: Oral Azacitidine vs Investigator's Choice



Stratified by:
- Previous lines (1–2 *vs* >2)
- Presence or absence of previous or concomitant MDS or CLL

Primary Endpoint
- PFS by investigator using CT (Cheson 2014)

Key Secondary Endpoints
- OS
- PFS by IRC
- ORR
- CR
- DoR
- TTR
- PFS2
- QoL (EORTC QLQ-C30)
- Safety

[a] To reduce the risk of including patients with alternative diagnoses, pathology reports were systematically validated by one of the principal investigators before inclusion. Patients with CNS involvement, with inadequate renal or hepatic function, previously exposed to hypomethylating agents or investigator's choice of treatment were excluded
[b] Positive with two or more markers among CD10, BCL6, CXCL13, PD1, or ICOS)
[c] Absolute neutrophil count ≥1·5 × 109 cells per L [≥1 × 109 cells per L if bone marrow involvement by lymphoma], platelet count ≥75 × 109 platelets per L [≥50 × 109 platelets per L if bone marrow involvement by lymphoma], and haemoglobin ≥8 g/dL

Azacitidine is not FDA approved for PTCL
Dupuis J, et al ASH 2022. Abstract 959. Dupuis J, et al. *Lancet Haematol*. 2024;11(6):e406-e414.

Phase 3 Oracle Study: Oral Azacitidine vs Investigator's Choice

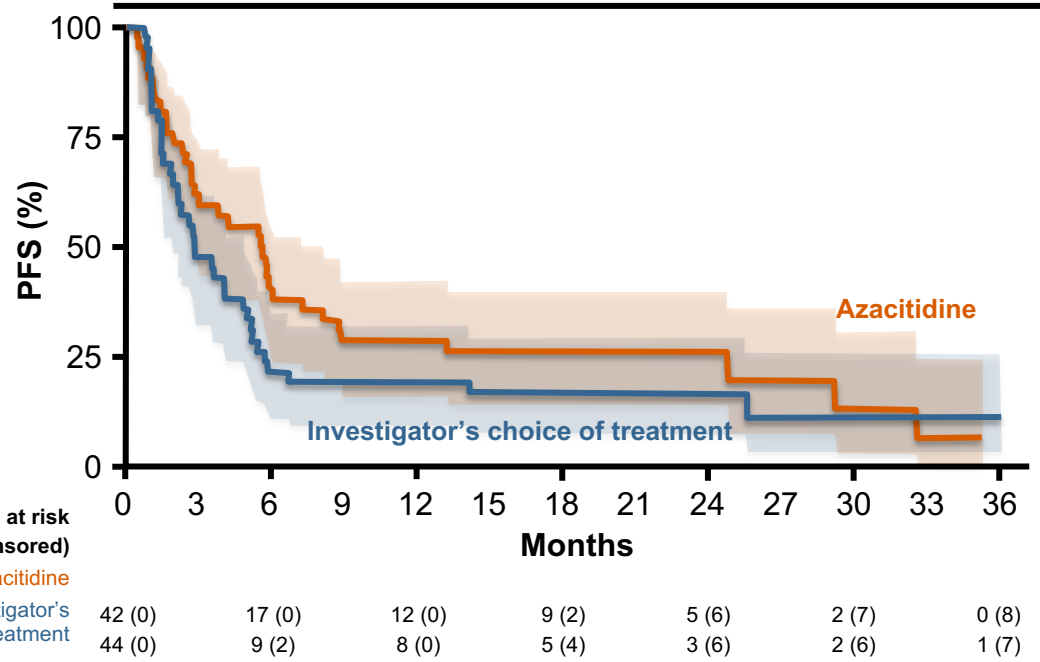
Response	Azacitidine n = 42	Investigator's choice n = 44
3 months (or PTD cycle 1–3)		
ORR, n (%) [CI]	14 (**33**) [19.6–49.5]	19 (**43.2**) [28.3–59.9]
CRR, n (%) [CI]	5 (**11.9**) [4–25.6]	10 (**22.7**) [11.5–37.8]
6 months (or PTD cycle 4–6)		
ORR, n (%) [CI]	13 (**31**) [17.6–47.1]	10 (**22.7**) [11.5–37.8]
CRR, n (%) [CI]	5 (**11.9**) [4–25.6]	7 (**15.9**) [6.6–30.1]

- 32/42 (76%) patients in the azacitidine group vs 42/43 (98%) patients in the ICT group had grade 3–4 AEs
- The most common grade ≥ 3 AEs were hematological (67% vs 93%), infection (19% vs 33%), and gastrointestinal (12% vs 2%) for azacitidine and ICT, respectively
- There were 2 treatment-related deaths in the azacitidine group (one endocarditis and one candidiasis) and 3 in the ICT group (one heart failure, one COVID-19, and one cause unknown)

Azacitidine is not FDA-approved for PTCL
ICT, investigator's choice
Dupuis J, et al. ASH 2022. Abstract 959.

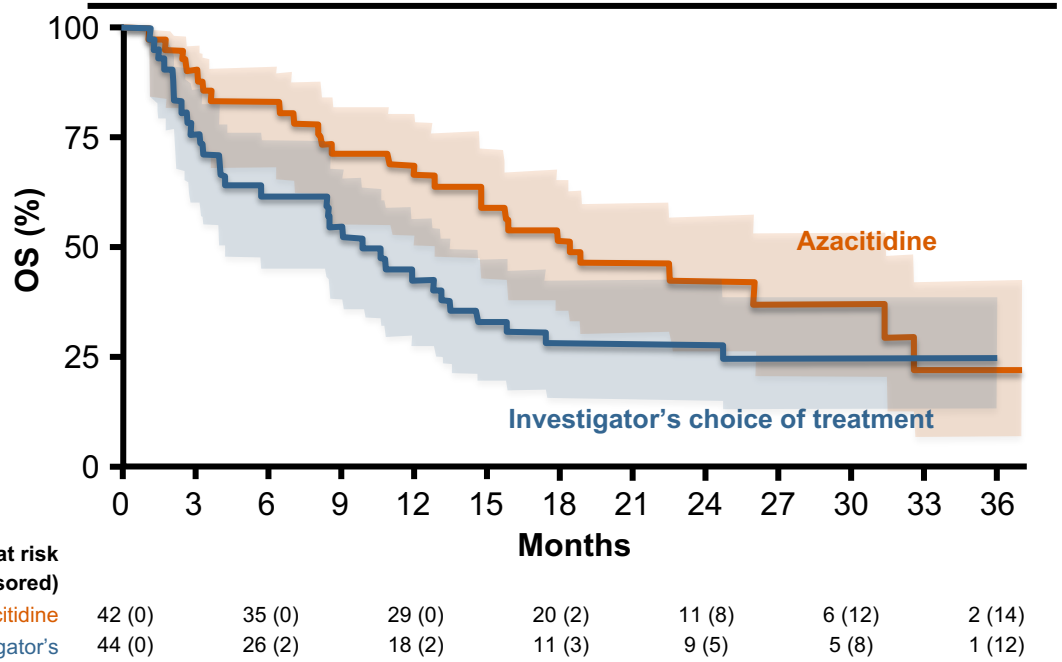
Phase 3 Oracle Study: Oral Azacitidine vs Investigator's Choice

	Azacitidine	Investigator's choice
Median PFS, months (95% CI)	**5.6** (2.7–8.1)	**2.8** (1.9–4.8)
HR (95% CI)	**0.63** (0.38–1.07) 1-sided $P = 0.042$	



No. at risk (no. censored)							
Azacitidine	42 (0)	17 (0)	12 (0)	9 (2)	5 (6)	2 (7)	0 (8)
Investigator's choice of treatment	44 (0)	9 (2)	8 (0)	5 (4)	3 (6)	2 (6)	1 (7)

	Azacitidine	Investigator's choice
Median OS, months (95% CI)	**18.4** (12.9–31.5)	**10.3** (4.2–13.5)
HR (95% CI)	**0.56** (0.32–0.96)	



No. at risk (no. censored)							
Azacitidine	42 (0)	35 (0)	29 (0)	20 (2)	11 (8)	6 (12)	2 (14)
Investigator's choice of treatment	44 (0)	26 (2)	18 (2)	11 (3)	9 (5)	5 (8)	1 (12)

Primary endpoint: PFS based on local assessment

5-Azacitidine is not FDA approved for PTCL

Dupuis J, et al. *Lancet Haematol*. 2024;11(6):e406-e414.

Phase 2 Valentine-PTCL01: Valemetostat in R/R PTCL

Valemetostat tosylate (valemetostat) is a novel and potent dual inhibitor of enhancer of zeste homolog (EZH)2 and EZH1.

Patient population

- ≥ 18 yrs
- Confirmed PTCL diagnosis (WHO 2016 classification)
- ECOG PS ≤ 2
- ≥ 1 prior line of systemic therapy
  - Patients with ALCL received prior brentuximab vedotin treatment

N = 155

- *Non-randomized*
- *Parallel assignment*

Cohort 1: Valemetostat
R/R PTCL (n = 119)
200 mg daily
Continuous 28-day cycles

Cycles continue until disease progression or unacceptable toxicity

Cohort 2: Valemetostat
R/R ATCL (n = 36)
200 mg daily
Continuous 28-day cycles

Primary Endpoint
• ORR (CT-based BICR assessment; ≥ 10 mos follow-up)
Key Secondary Endpoints
• DoR • DoCR • CR rate • PR rate • PFS (CT-based BICR assessment and investigator assessment) • OS • Safety and tolerability

Lugano 2014 response criteria

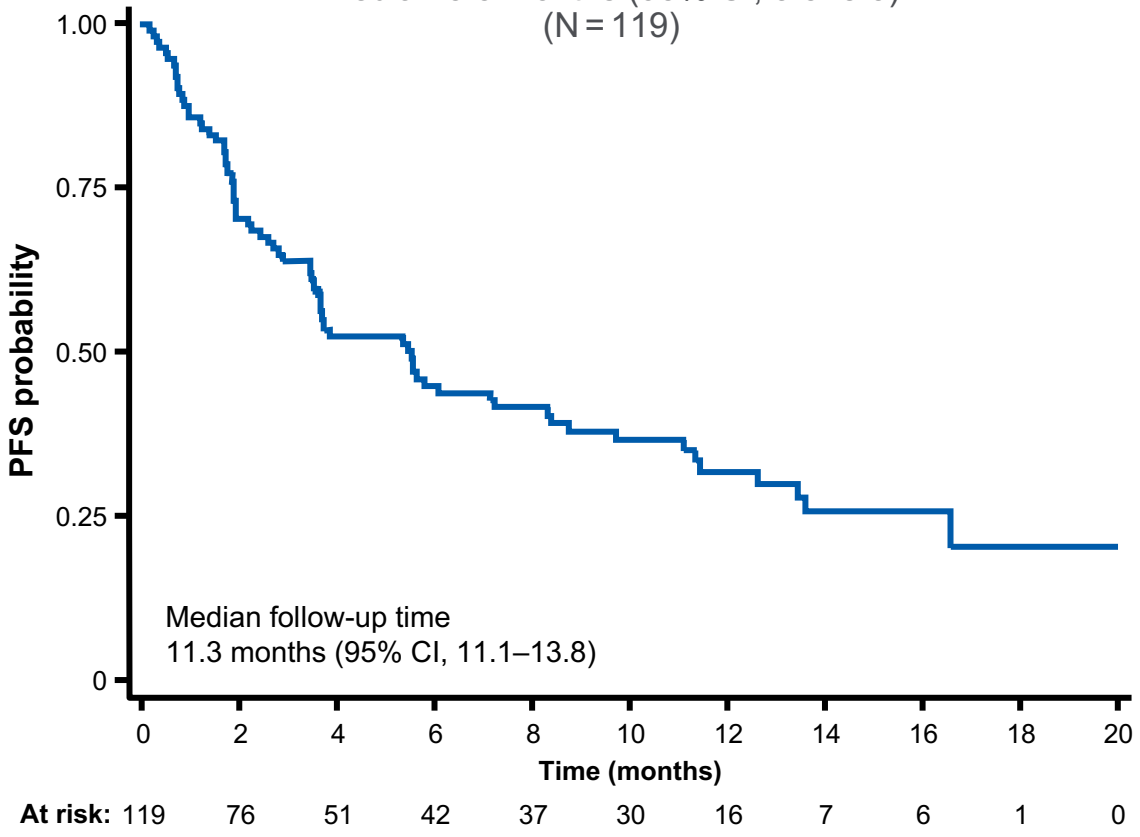
BICR, blinded independent central review; CR, complete response; DoR, duration of response; DoCR, duration of complete response; ECOG PS, Eastern Cooperative Oncology Group performance status; ORR, overall response rate; OS, overall survival; PFS, progression-free survival; PR, partial response

Valemetostat is not FDA approved for PTCL
ClinicalTrials.gov. NCT04703192

VALENTINE-PTCL01: Valemetostat in R/R PTCL

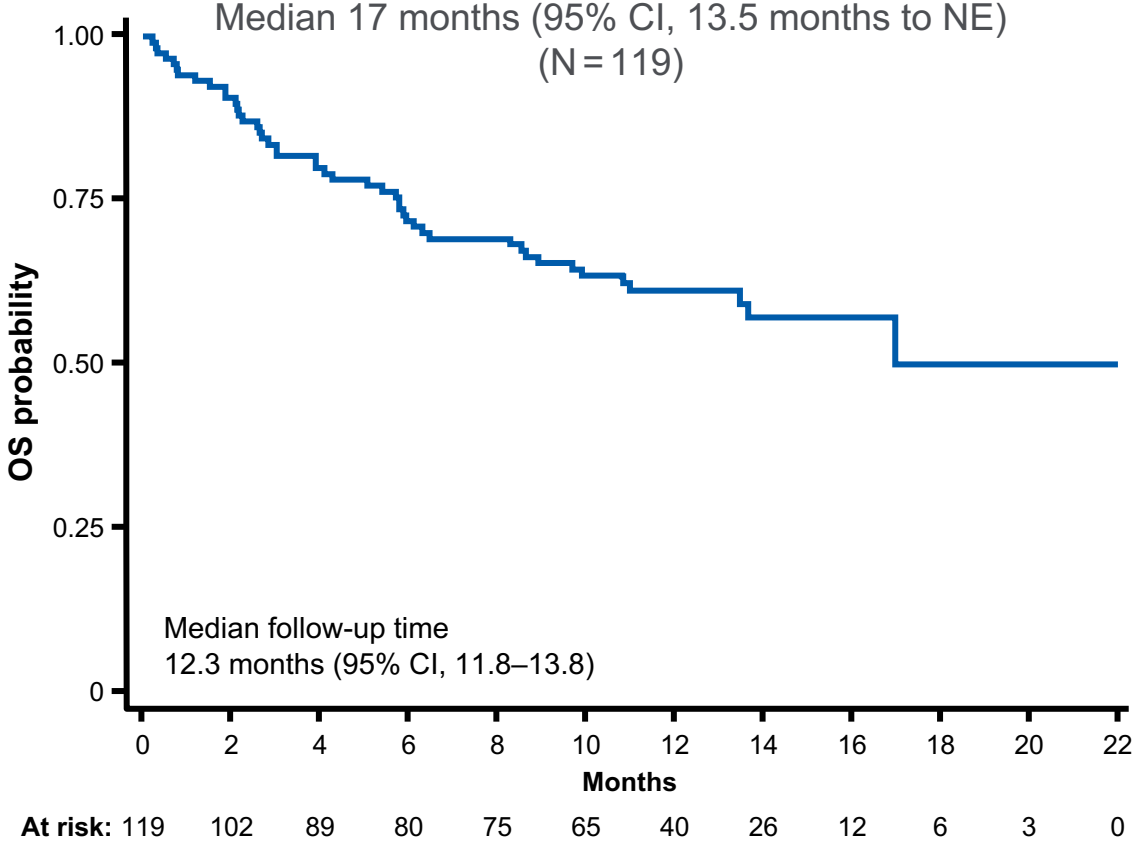
PFS[a]

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)



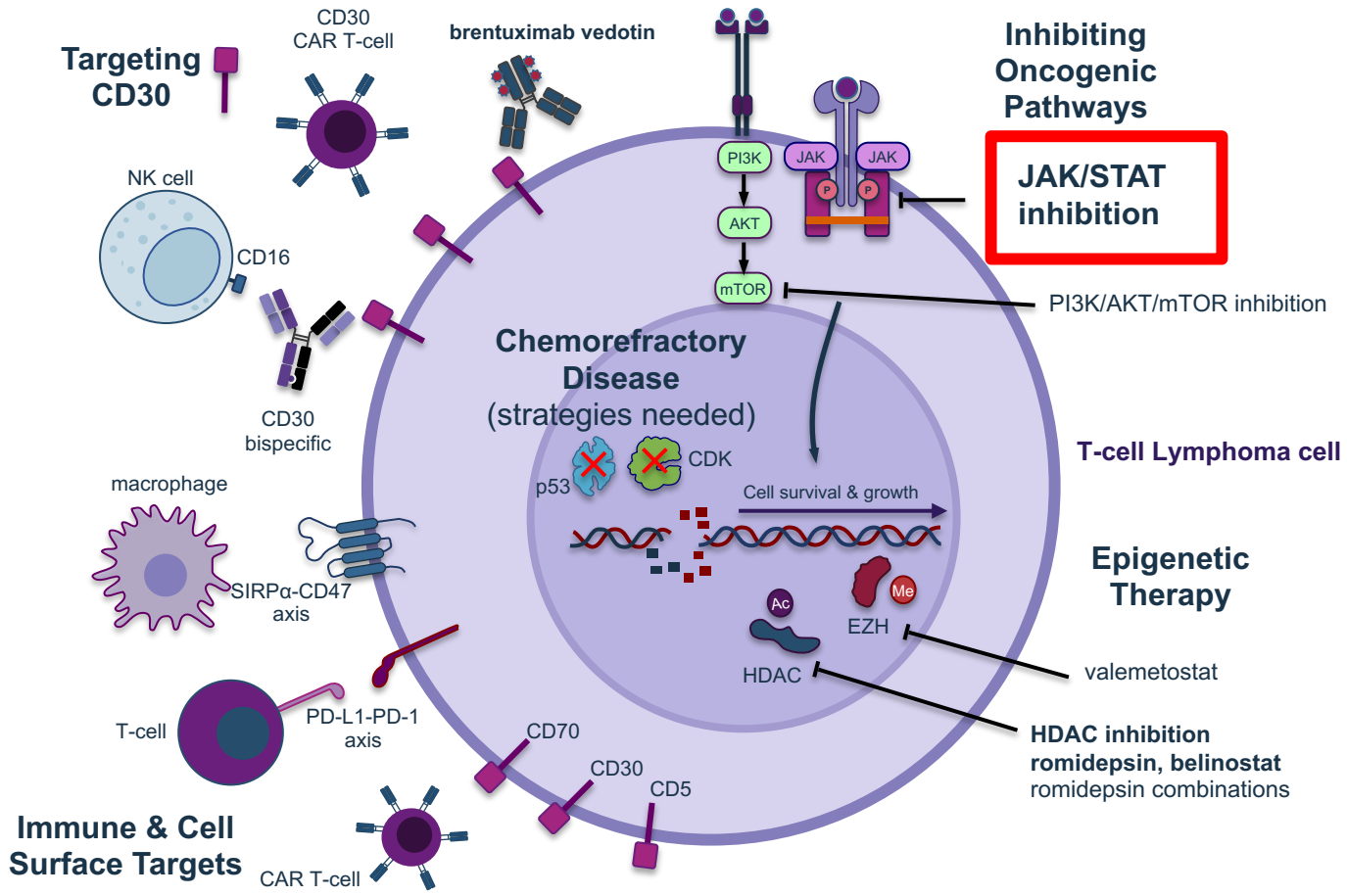
Data cutoff: May 5, 2023.

[a] PFS evaluated by BICR CT-based assessment

Valemetostat is not FDA approved for PTCL

Horwitz et al. ASH 2023. Oral presentation 302.

Other Targets in T Cell Lymphoma: Signaling Targets in PTCL



TCL subtype	% with JAK/STAT activating mutations
ALCL[1]	38%
Extranodal NK/TCL[2]	5.9%
T-PLL[3]	36%
γδ–T-cell lymphoma[2]	33%
MEITL[2]	36.8%
Large granular lymphoma[4]	28-40%
Sezary syndrome[5]	11%

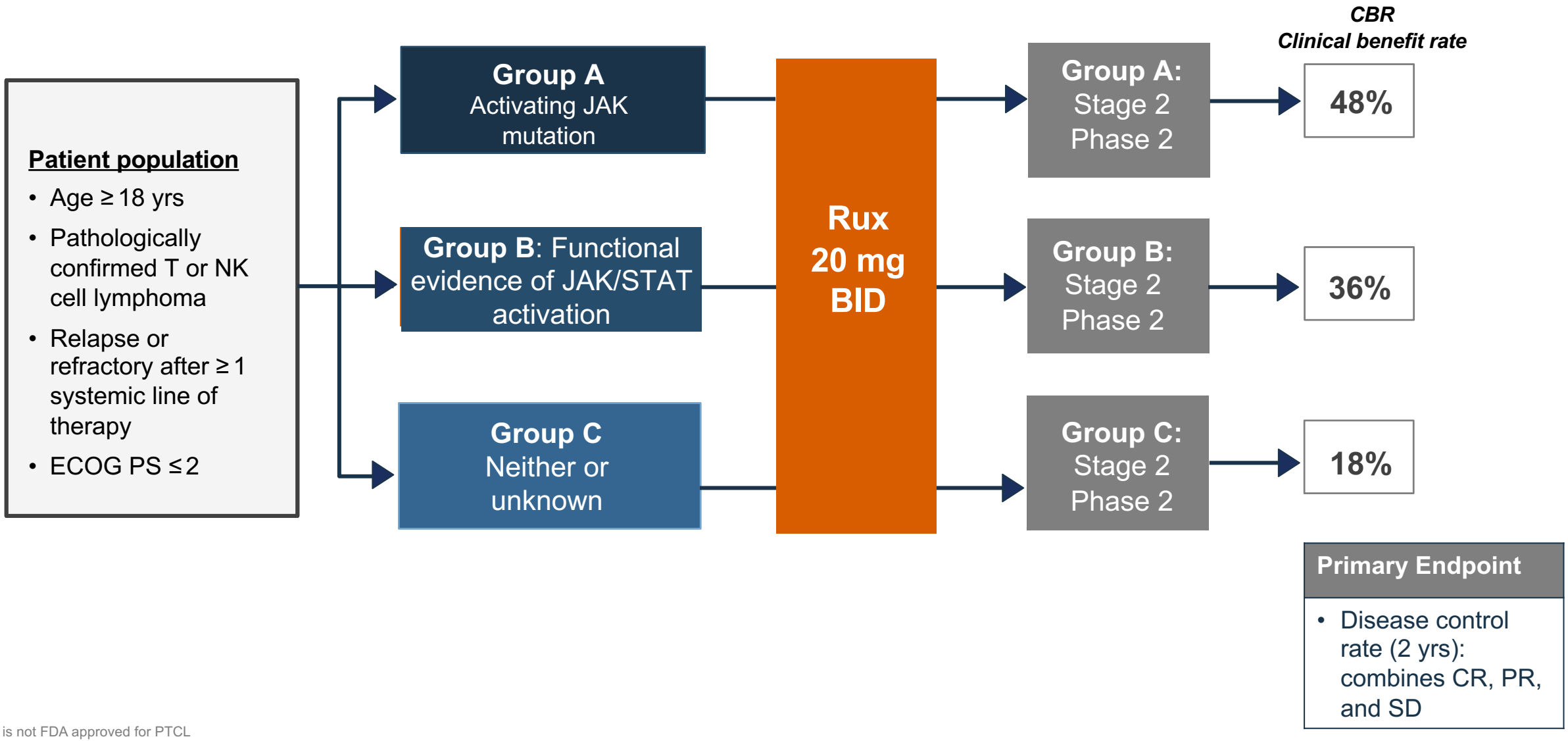
Image Courtesy of Robert Stuver MD

ALCL, anaplastic large cell lymphoma; NK/TCL, natural killer/T-cell lymphoma; MEITL, monomorphic epitheliotropic intestinal T-cell lymphoma; T-PLL, T-cell prolymphocytic leukemia

1. Crescenzo R, et al. *Cancer Cell*. 2015;27(4):516-532. 2. Kucuk C et al. *Nat Comm.* 2015;6:6025. 3. Kiel MJ, et al. *Blood*. 2014 Aug 28;124(9):1460-72. 4. Koskela HL, et al. *N Engl J Med*. 2012;366(20):1905-1913. 5. Kiel MJ, et al. *Nat Commun*. 2015;6:8470.

Phase 2 Multicenter Biomarker-Driven Study: Ruxolitinib

Targeting JAK1/2 Inhibition in R/R T-Cell Lymphomas



Ruxolitinib is not FDA approved for PTCL

Moskowitz AJ, et al. *Blood*. 2021;138(26):2828-2837. ClinicalTrials.gov. NCT02974647.

Phase 2 Multicenter Biomarker-Driven Study: Ruxolitinib

Targeting JAK1/2 Inhibition in R/R T-Cell Lymphomas

Response by Cohort

Cohorts	Total treated, n	Total evaluable for response, n	ORR n (%)	CBR n (%)
Cohort 1	21	21	**7 (33%)**	10 (48%)
Cohort 2	15	14	**4 (29%)**	5 (36%)
Cohort 3	17	17	**2 (12%)**	3 (18%)
Total	53	52	**13 (25%)**	18 (35%)
P (cohorts 1 & 2 vs 3)			***P* = 0.2**	*P* = 0.073

Response by Subtype

Subtype	Evaluable for response, n	ORR n (%)	CBR n (%)
PTCL-NOS	11	**2 (18%)**	2 (18%)
T-PLL	8	**3 (38%)**	4 (50%)
AITL/TFH	9	**3 (33%)**	4 (44%)
T-LGL	5	**2 (40%)**	4 (80%)
ALCL	4	**1 (25%)**	1 (25%)
ATLL	3	**0**	0
CTCL	7	**1 (14%)**	1 (14%)
G/D TCLs	4	**1 (25%)**	1 (25%)
SPTCL	1	**0**	1 (100%)

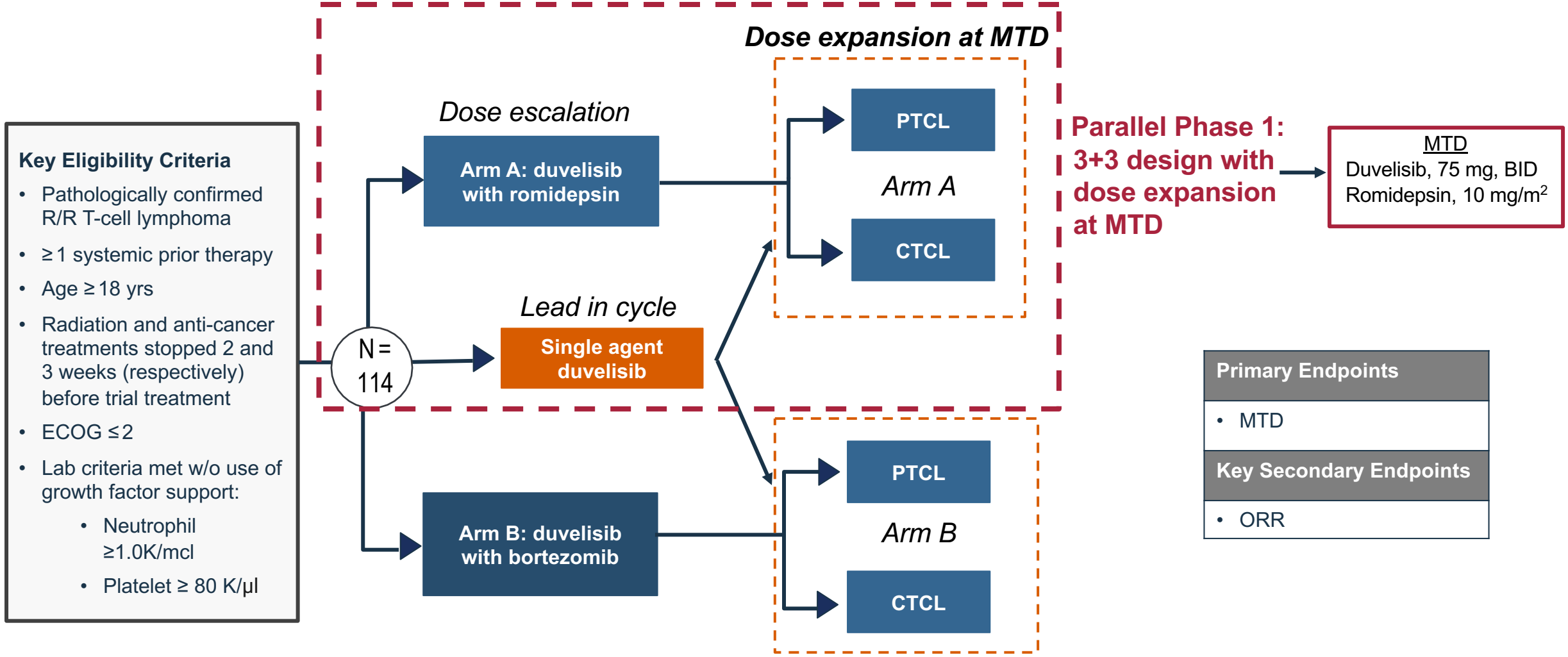
- Adverse events were consistent with the known side effect profile of ruxolitinib and primarily involved cytopenias
- Treatment-related SAEs included herpes simplex virus-1 stomatitis (n = 1), spontaneous bacterial peritonitis (n = 1), febrile neutropenia (n = 3), anemia (n = 1), and herpes zoster (n = 1)

AITL/TFH, angioimmunoblastic T-cell lymphoma with T-follicular helper phenotype; ALCL, anaplastic large cell lymphoma; ATLL, adult T-cell leukemia; CTCL, cutaneous T-cell lymphoma; G/D TCLs, gastro/digestive TCLs including hepatosplenic T-cell lymphoma, onomorphic epitheliotropic intestinal T-cell lymphoma, and primary cutaneous γδ-TCL; T-LGL, T-cell large granular lymphocyte; T-PLL, T prolymphocytic leukemia; SPTCL, subcutaneous panniculitis-like T-cell lymphoma

Ruxolitinib is not FDA approved for PTCL

Moskowitz AJ, et al. *Blood*. 2021;138(26):2828-2837

Phase 1b/2a Study of Duvelisib With Either Romidepsin or Bortezomib in R/R PTCL: *Non-Randomized, Parallel Assignment, Open-Label Trial*



MTD, maximum tolerated dose

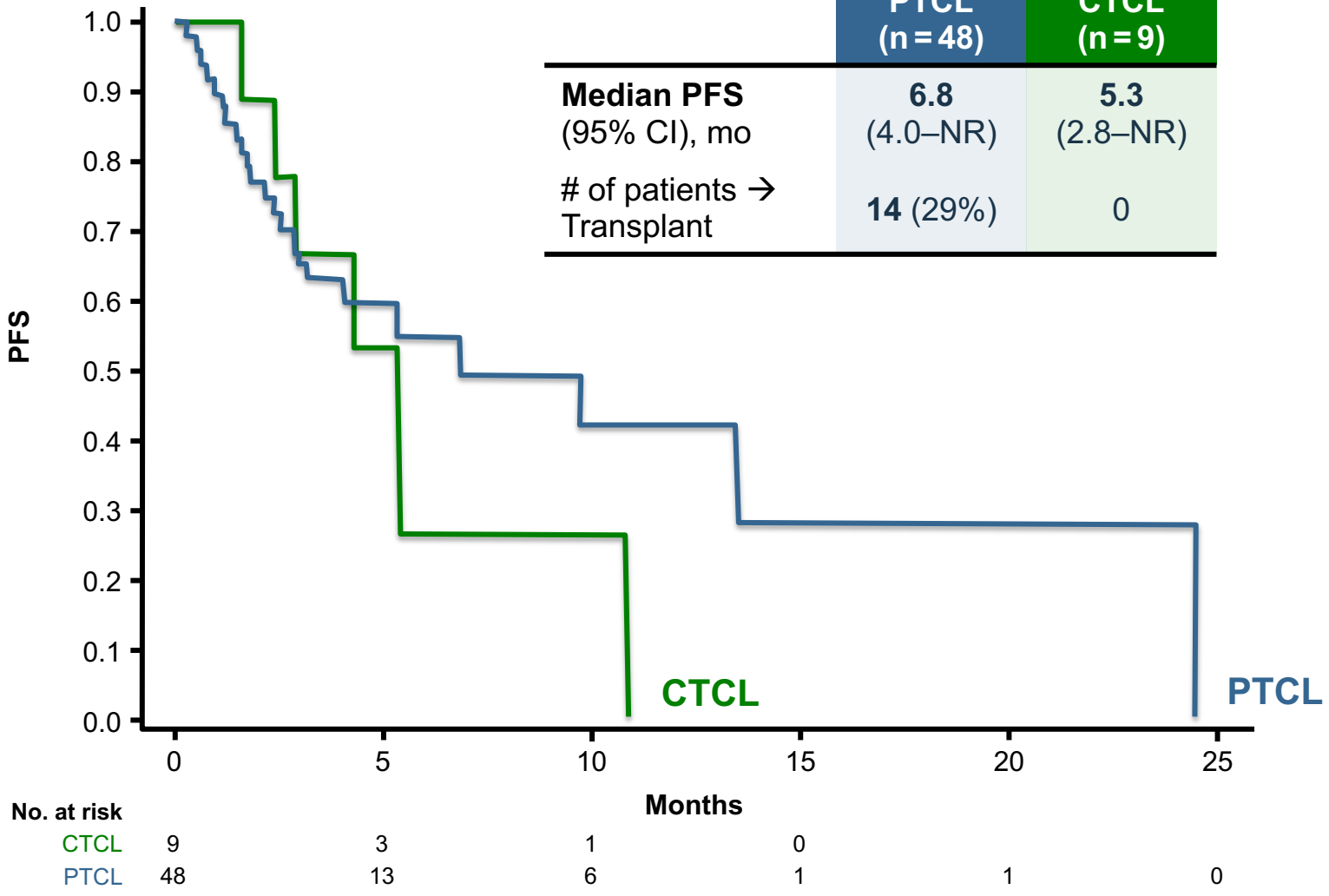
This regimen is not FDA approved for PTCL

ClinicalTrials.gov. NCT02783625. Horwitz SM, et al. *Nat Med*. 2024;30(9):2517-2527.

All patients received prophylaxis against varicella zoster virus (VZV) and pneumocystis jiroveci pneumonia (PJP), and anti-fungal prophylaxis with either nystatin or fluconazole was encouraged but not mandatory.

Arm A: Progression-Free Survival at MTD
(Duvelisib + Romidepsin)

	PTCL (n = 48)	CTCL (n = 9)
Median PFS (95% CI), mo	**6.8** (4.0–NR)	**5.3** (2.8–NR)
# of patients → Transplant	**14** (29%)	0



Grade 3-4 Adverse Events Occurring in ≥ 10% of patients at MTD

Event	Total # of patients at MTD n = 59	
	Grade 3, n (%)	Grade 4, n (%)
Transaminase	8 (14%)	
ALT	7 (12%)	-
AST	3 (5%)	-
Diarrhea	9 (15%)	-
Neutropenia	12 (20%)	9 (15%)
Infections	6 (10%)	-
Rash	7 (12%)	-

All subjects received prophylaxis for PJP and VZV and were monitored for EBV and CMV. Many received nystatin to reduce risk of candidal esophagitis.

This regimen is not FDA approved for PTCL

Horwitz SM, et al. *Nat Med*. 2024;30(9):2517-2527; ASH 2021:Abstract 619.

Examples of Other Targets in PTCL: Immune Therapies

- PD1/PDL1 therapy
  - Efficacy in R/R extra-nodal NK/T-cell lymphomas[1]
  - May be efficacious in primary nodal EBV+ T/NK-cell lymphoma[2]
  - Limited data for the remaining nodal PTCL
  - In PTCL, there is concern about hyperprogression[3-5]
- Bispecific T-cell engagers are another type of novel CD30-based therapy in clinical development
  - CD30/CD16A-bispecific antibody AFM13 is a first-in-class innate cell engager that binds to CD16A on innate immune cells and CD30 on cHL cells
    - Phase 2 REDIRECT trial (NCT04101331)[6]
      - Heavily pretreated patients with CD30-positive R/R PTCL
      - ORR of 32.4% (95% CI, 23.7%–42.1%); CRR of 10.2% (95% CI, 5.4%–18.1%)
    - Phase 1b study of AFM13 with pembrolizumab resulted in ORR of 83%[7]
  - Anti-PD-1/anti-CD3 bispecific antibody ONO-4685 for R/R PTCL (NCT05079282)
- Anti-CD94 antibody DR-01 for large granular lymphocytic leukemia and cytotoxic lymphoma (NCT05475925)

These regimens are not FDA approved for PTCL

1. Marouf A. *Hematol Oncol*. 2023;41(S2):503-503. 2. Wai, et al. *Haematologica*. 2022;107 (8):1864-1879. 3. Rauch, et al. *Blood*. 2019;134 (17):1406-1414. 4. Bennani, et al. *J Immunother Cancer*. 2022;10 (6):e004984.
5. Agbedia, et al. *Blood*. 2022;140 (Suppl 1) (2022):2313-2315. 6. Kim WS, 2023 AACR Annual Meeting; April 14-19, 2023; Orlando, FL. Abstract CT024. 7. Bartlett NL, et al. *Blood*. 2020;136(21):2401–2409.

CAR-T Therapy in T-Cell Lymphoma

Antigen	Frequency in T-cell malignancies, %						Expression in normal tissue	Trial
	PTCL-NOS	AITL	ALCL	NK-T	ATLL	CTCL		
CD5	85	96	26–32	36	85	91	T cells, thymocytes, B1 cells	NCT03081910
CD7	50	57	32–54	79	25	18	T cells, thymocytes, NK cells	NCT02742727; NCT03690011
CD3	60–66	71	32–40	36*	80	91	Mature T cells	
CD30	16	32–50	93	64*	39	18	Activated T and B cells	**NCT02917083; NCT02690545**
TCRBC1	27	34	25	—	—	—	~35% of T cells	NCT03590574
CCR4	34	—	—	—	88	31–100	Tregs, Th2 and Th17 cells, platelets, kidney	NCT04930653; NCT05956041 NCT04256018; NCT05414500 NCT04848064; NCT06235281 NCT04045470
CD4	60	86	63	29*	94	92	CD4* T cells, some monocytes and dendritic cells	NCT03829540
CD37			82				Mature B cells, at a low level in plasma cells, dendritic cells	NCT04136275
CD70			—				T and B cells	NCT06326463

AITL, angioimmunoblastic T-cell lymphoma; ALCL, anaplastic large cell lymphoma; ATLL, adult T-cell leukemia; CAR, chimeraic antigen receptor therapy; CTCL, cutaneous T-cell lymphoma; NK-T, natural killer/T-cell lymphoma; PTCL, peripheral T-cell lymphoma

- NK-CAR, Allo CAR, Myeloid CAR
- Efficacy, safety, fratricide, long-term immunosuppression, resistance – TBD in clinical trials

CTX-130

These regimens are not FDA approved for PTCL
ClinicalTrials.gov

Clinical Trials at Emory for TCL

Clinical Studies:

- Frontline Phase 3 duvelisib or oral azacitadine + CHO(E)P in CD30 - PTCL, AO51902
- CD3 x PD-1 bispecific antibody R Peripheral and Cutaneous Lymphoma, ONO 4685-03
- Phase 3, Randomized, Open-Label Study of ITK Inhibitor Soquelitinib vs MD's Choice SofCare Treatment (Selected Single Agent) R/R PTCL.NOS (Pending)
- Phase 2 Mogamulizumab and extra-corporeal photopheresis in CTCL
- NCI 10335 : Phase 1 Study of Lenalidomide in Combination with EPOCH Chemotherapy for ATLL
- Phase 1/2 Open-Label Multi-Center Study to Characterize the Safety and Tolerability of CFT7455 in Subjects with R/R NHL and MM

Observational Studies:

- BioSpecimen & Clinical INformation in T-Cell Lymphoma (SCIN-TCL)
- Open label, single-cohort, and muti-center phase II study evaluating tumor-specific immunity after extracorporeal photopheresis in patients with Sezary syndrome at single-cell resolution.
- A Prospective, US-based Study Assessing Mogamulizumab-Associated Rash in Patients Diagnosed with Mycosis Fungoides or Sézary Syndrome and Treated with Standard of Care Mogamulizumab
- Navigating Life and Care with Cutaneous T-Cell Lymphoma and Sézary Syndrome in Georgia: A Qualitative Exploration of Patient and Caregiver Experiences

Acknowledgements

- Organizers and Sponsors
- Team at Emory
- Collaborators
- Patients

Q&A