



SINTOMA²⁶

14 A 16 DE MAIO | HOTEL INTERCONTINENTAL | SÃO PAULO

PARCERIA **soho**
society of hematologic oncology

APOIO INSTITUCIONAL Faculdade **bp**

GERENCIAMENTO
E PRODUÇÃO

RV+
EVENTOS

Linfomas T Periféricos em 2026: Biologia, Fenótipos TFH e Estratégias Terapêuticas

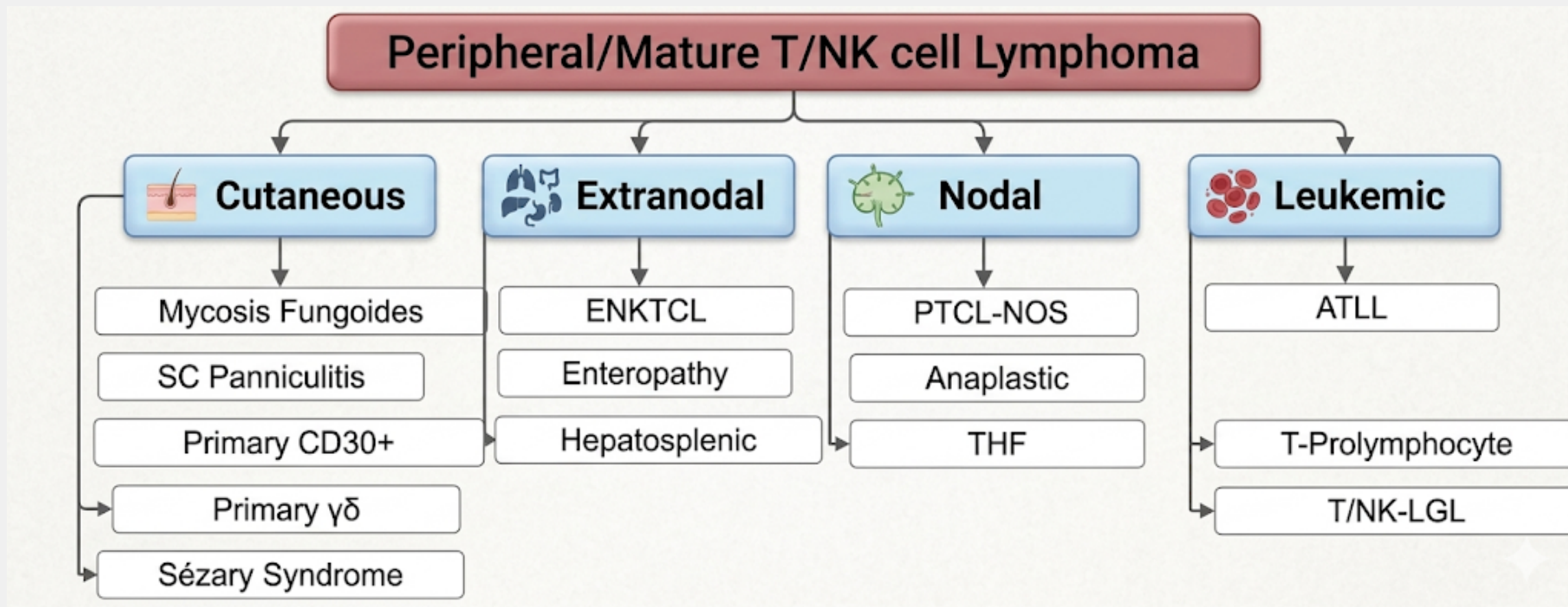


JULIANA PEREIRA

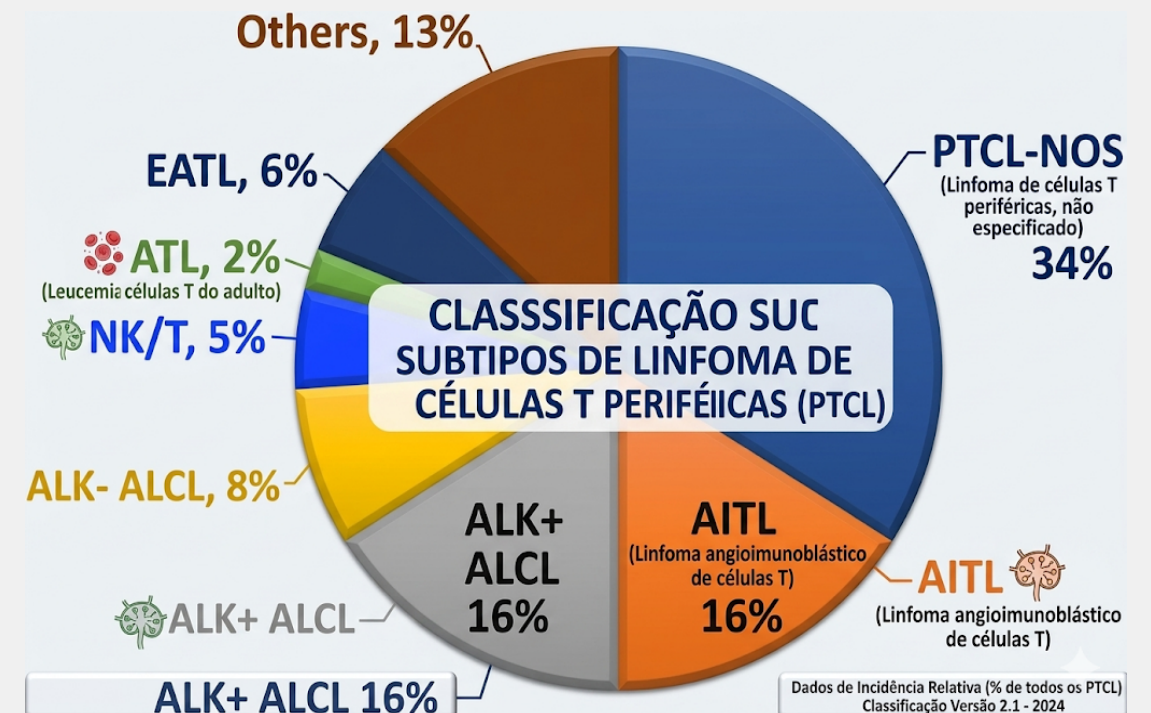
Professora Associada Disciplina de Hematologia FMUSP



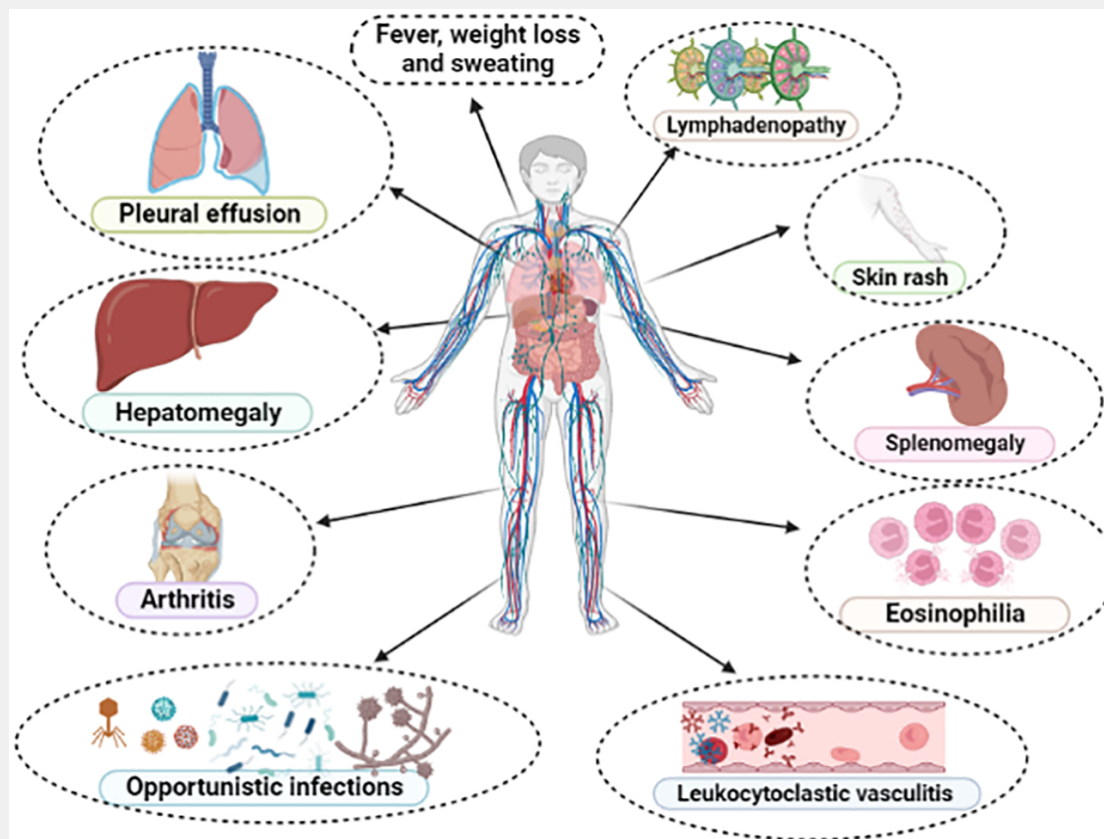
- Biologia dos Linfoma de Células T Periféricas
- Linfoma de Células T de Fenótipo T-Helper Folicular
- Estratégias Terapêuticas em Linfoma de Células T Periféricas



- 10 a 15% NHL
- Differences among geographic areas
 - 20% Asia (HTLV-1 e EBV)
 - 20 to 25% LNH in Latin America
- HC-FMUSP/ICESP (124 nPTCL 2000 to 2018)
 - ALCL ALK-: 39.5% (49/124)
 - PTCL,nos: 31.4% (39/124)
 - ALCL ALK+: 18.5% (23/124)
 - T-Helper Follicular: 10.4% (13/124)

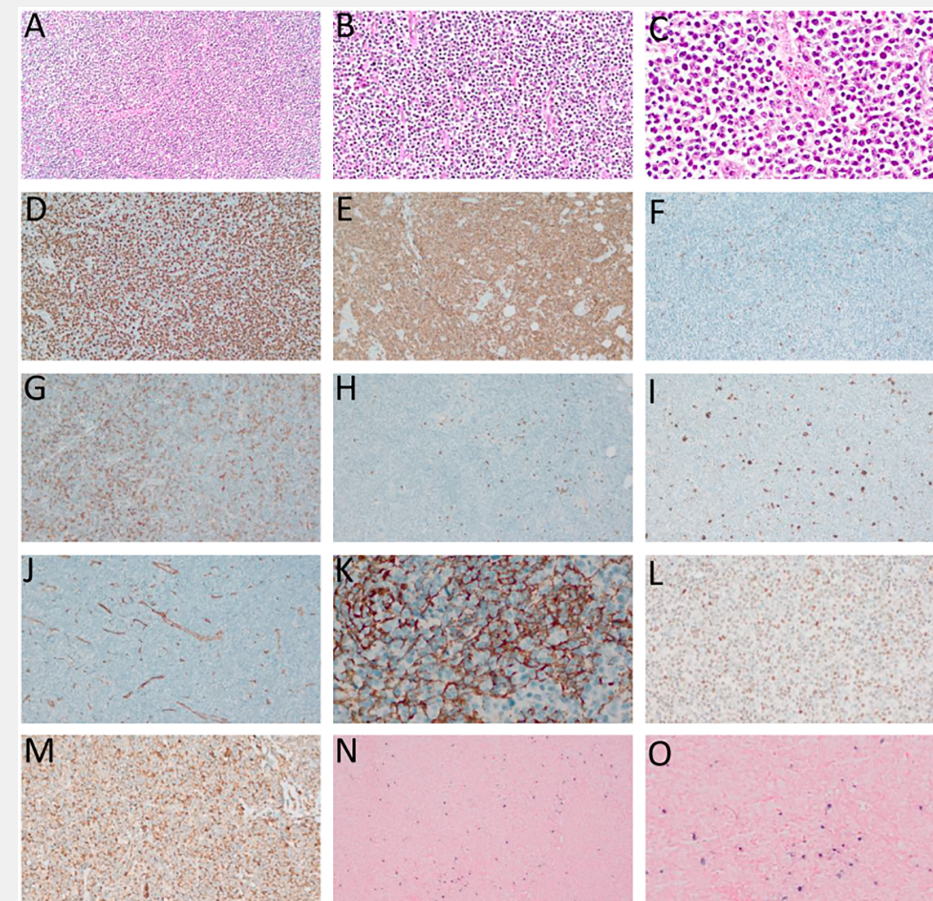


Clinical Aspects T-Helper Follicular Phenotype

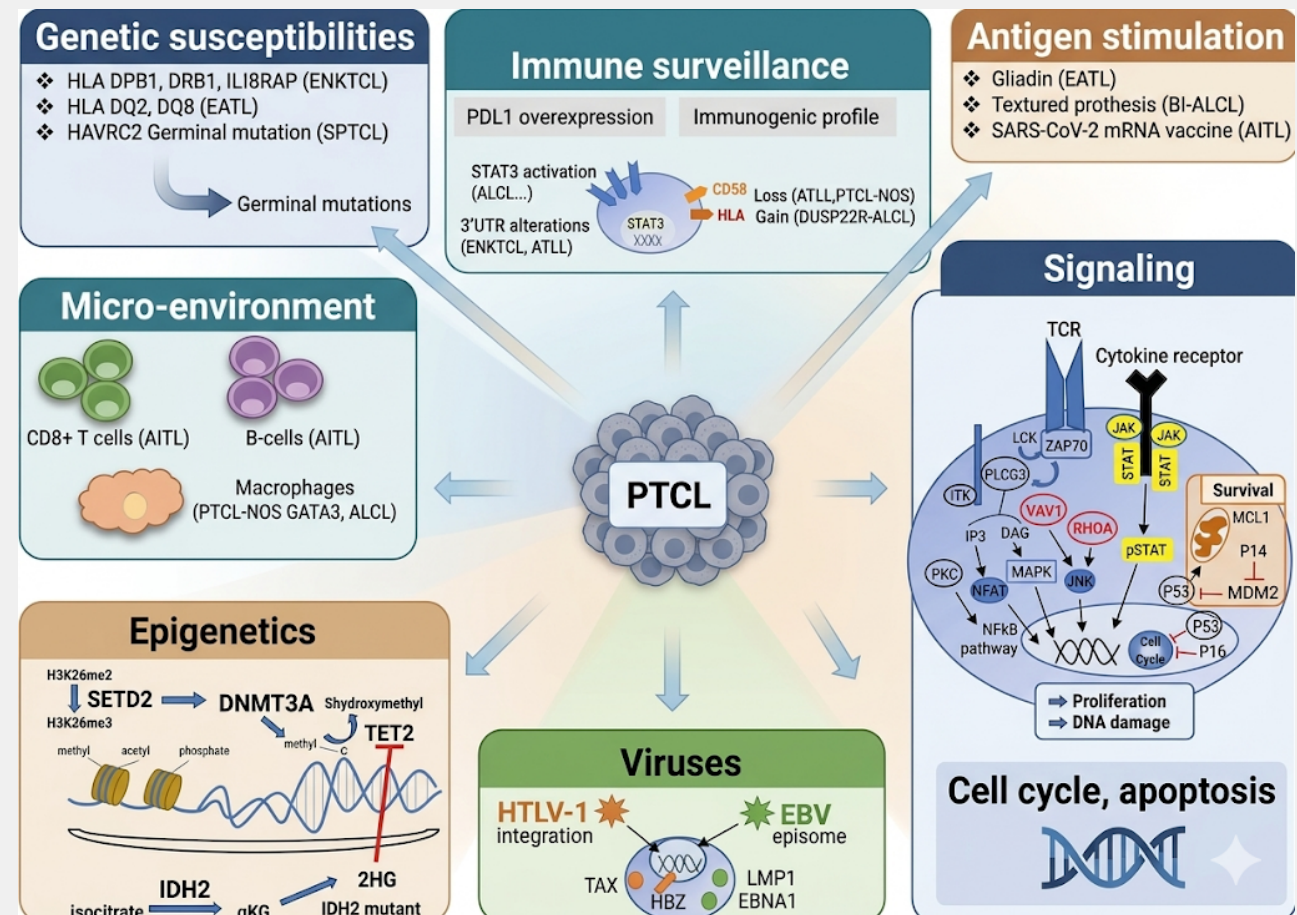


Frequently Challenging

- Incisional or Excisional Biopsy Preferable
- Clinicopathological correlation, image, symptoms and Lab data
- Morphology, Aberrant T cell Phenotypes
- Presence of mutagenic mutations
- Presence of virus (EBV, HTLV1)
- TCR Clonality
- THF: THF Markers



- Genetic susceptibility
- Microenvironment
- Epigenetics
- Immune surveillance
- Antigen stimulation
- Virus
- Cell cycle and apoptosis genes



- Complex Kariotype +7q e + 7p – CDK6 and CARD11

- **Subtype Gata-3, CCR4**

Myc hyperexpression, PI3K activation

Higher genomic complexity (17p, PETEN)

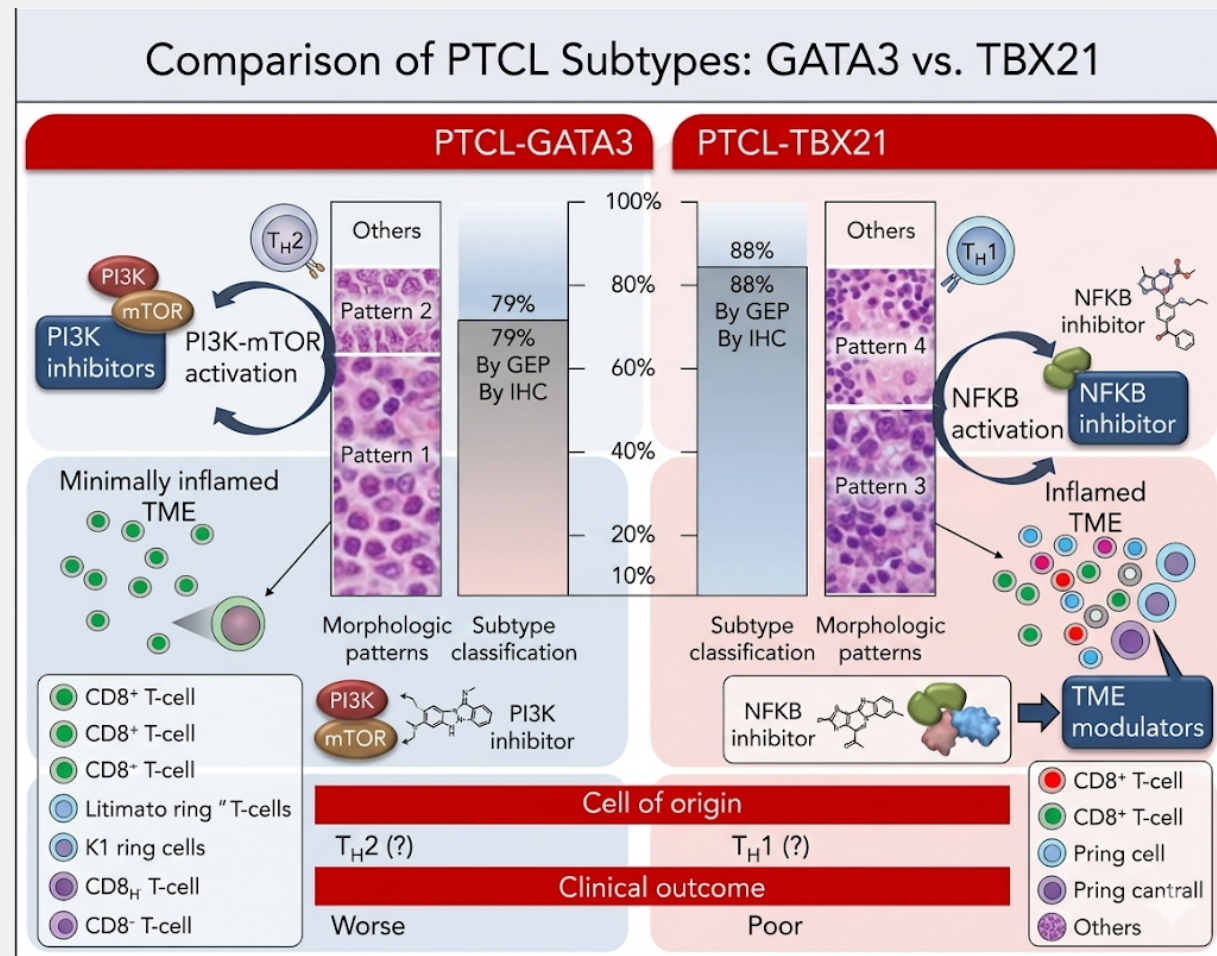
Minimally inflamed

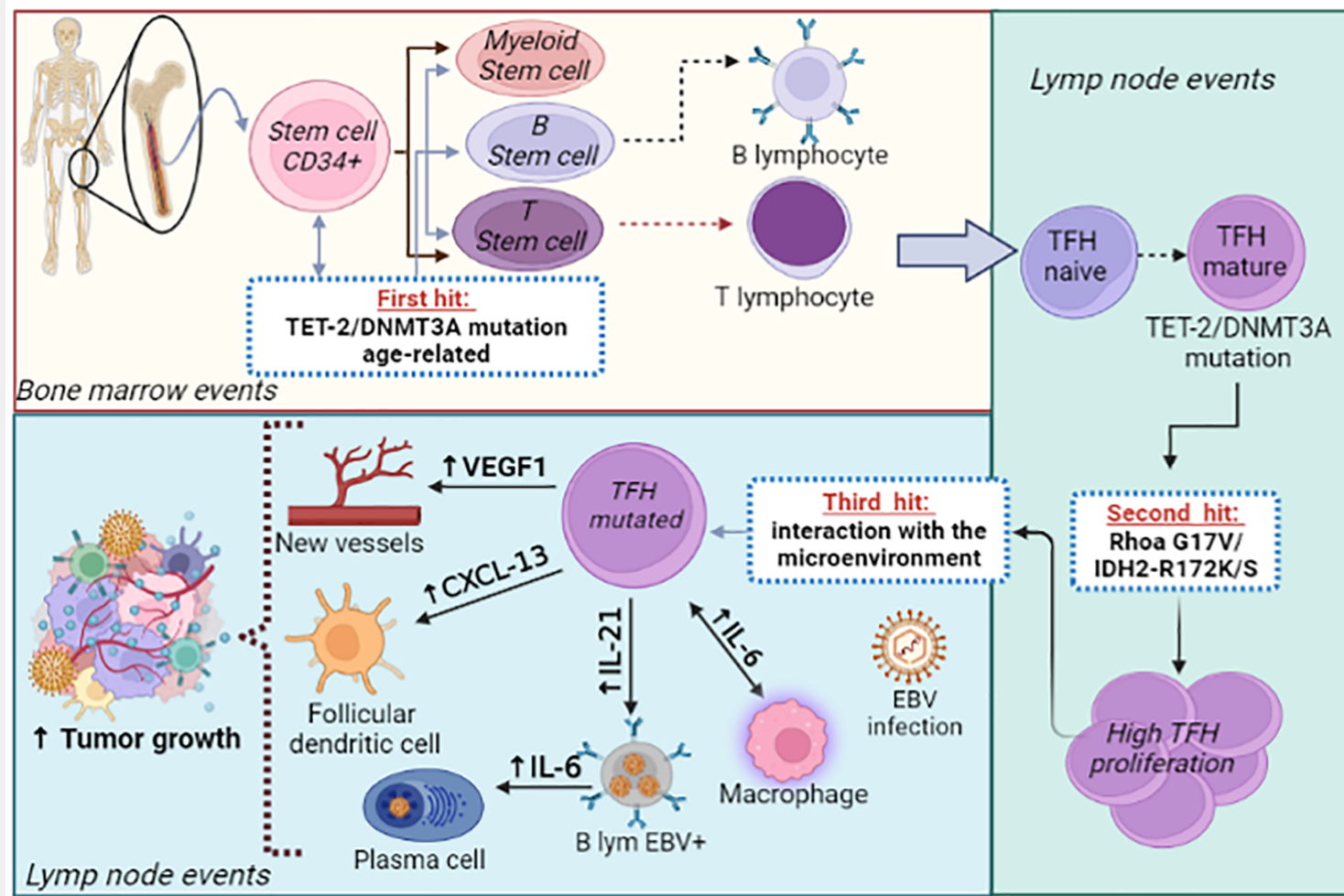
- **Subtype TBX21, CXCR3**

NF-kB activation

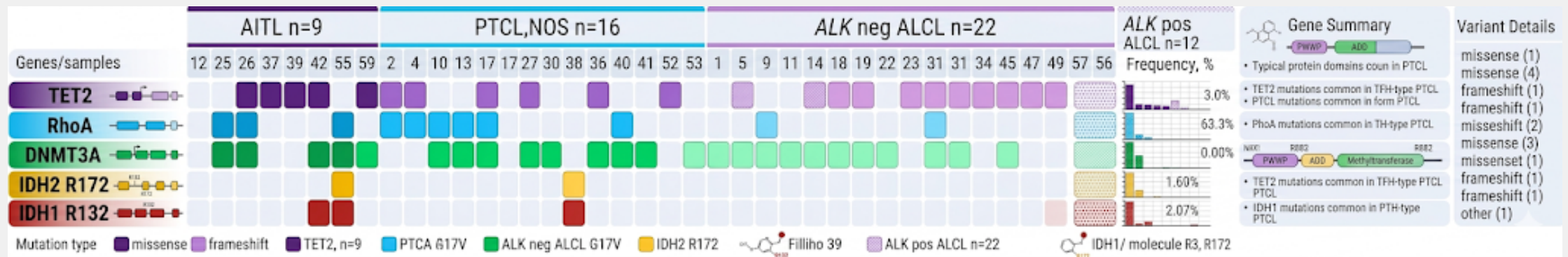
Mut in epigenetic regulators (TET2, DNMT3A)

Highly Inflamed





IDH-1, IDH-2, RHOA, TET-2 and DNMT3A Mutations in nPTCL



- CD30+: BV-CHOP
- CD30-: CHOP/CHOEP
- CHOEP (ALCL ALK+, normal DHL)
- ASCT 1L

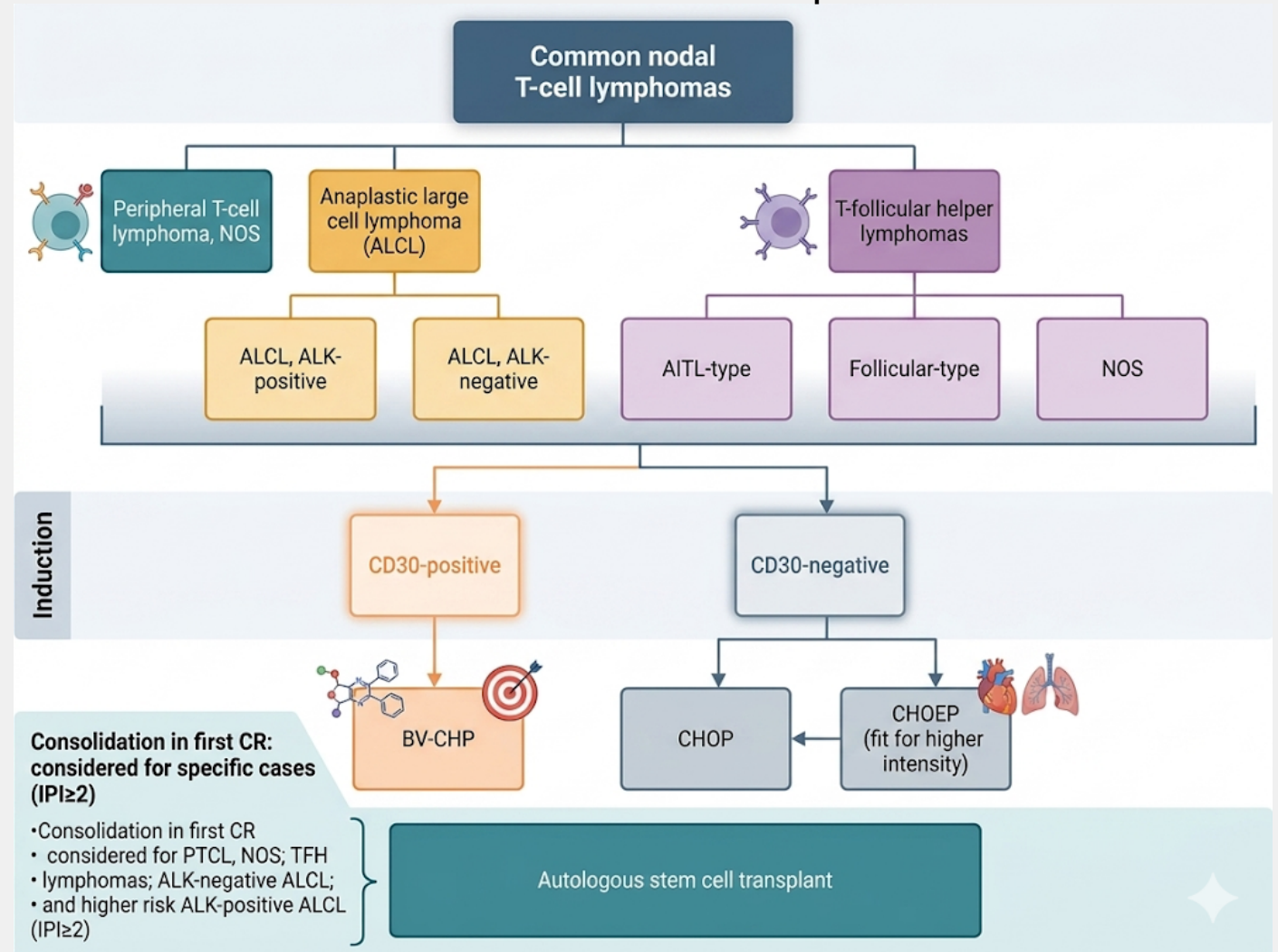
PTCL, nos

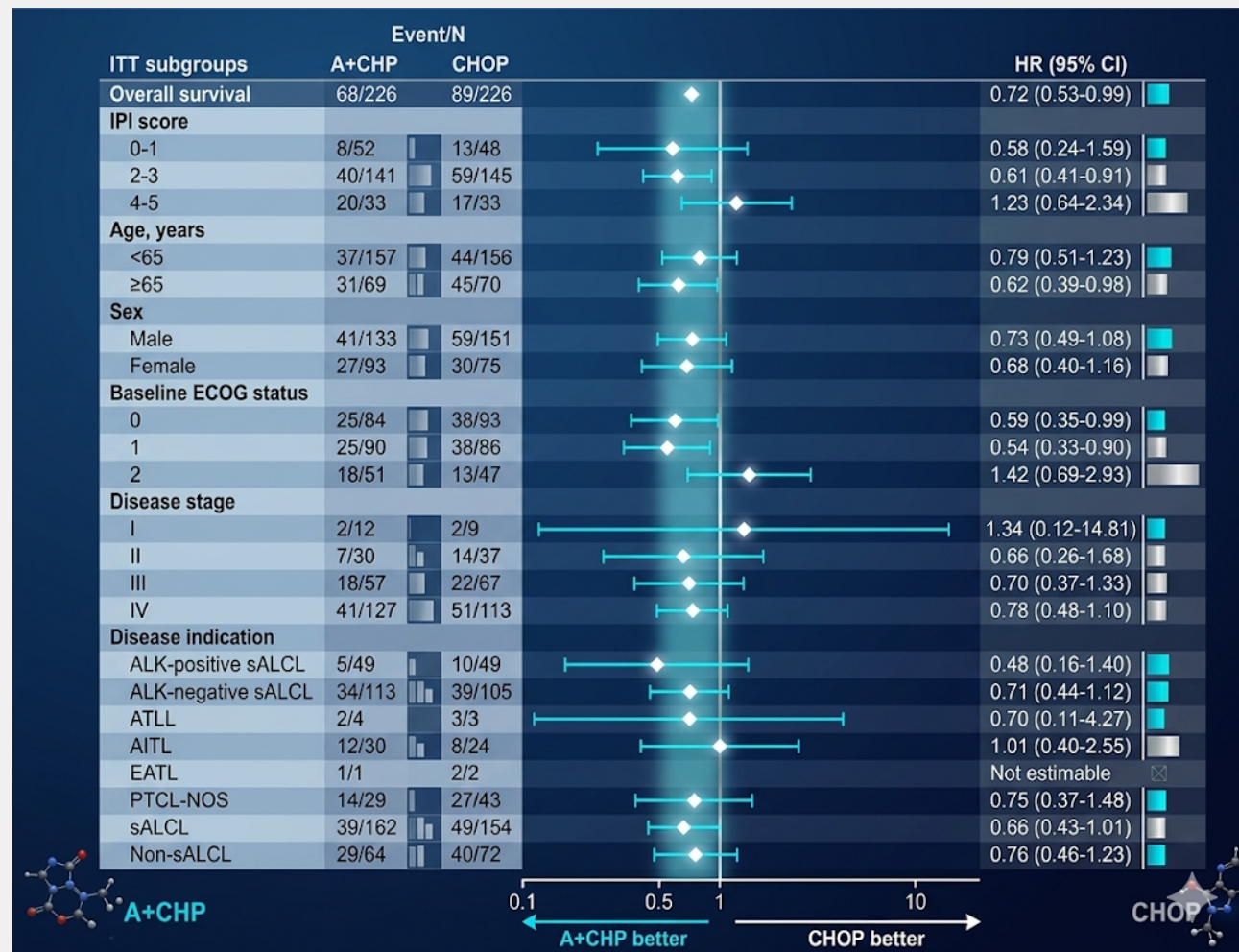
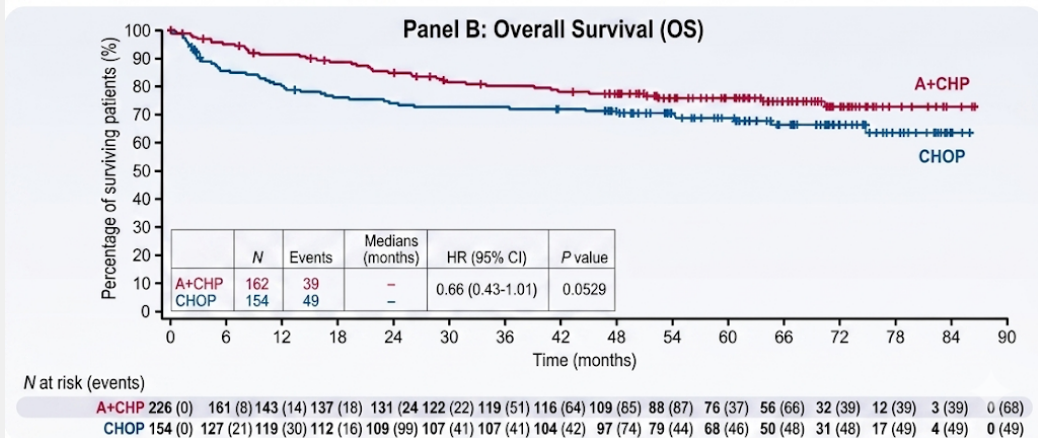
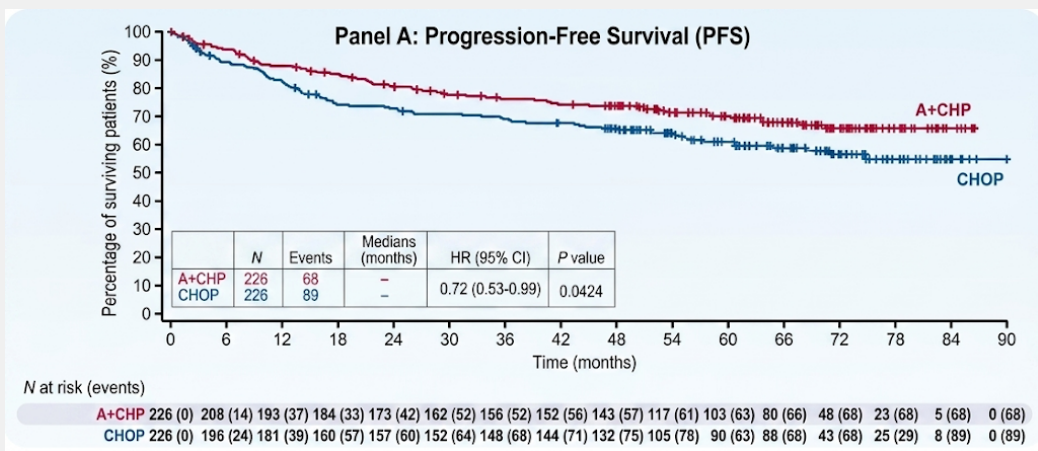
THF

ALCL ALK-

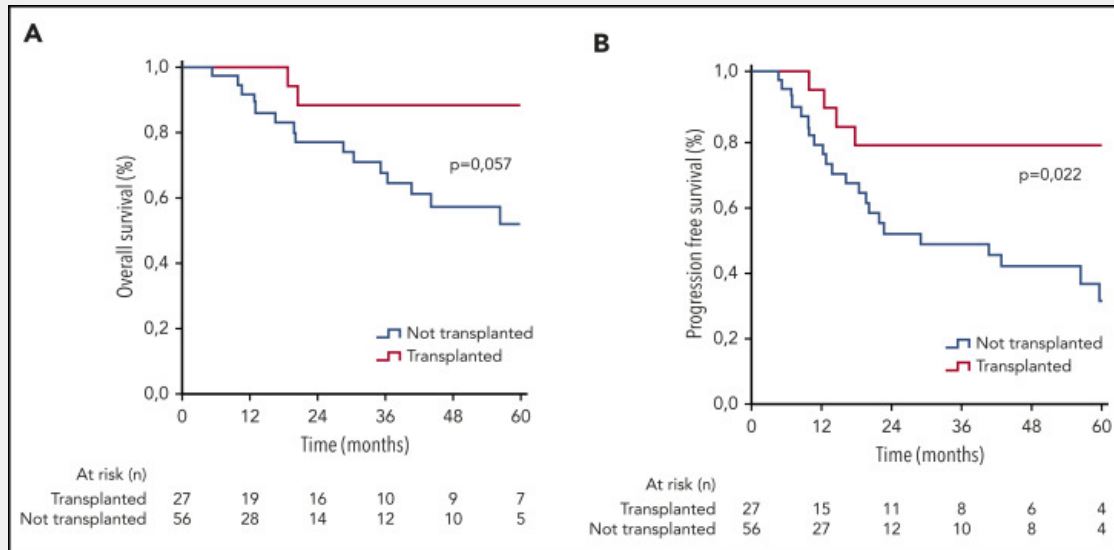
ALCL ALK+ (Bulky, IPI ≥ 2) ?

Clinical Trial whenever possible

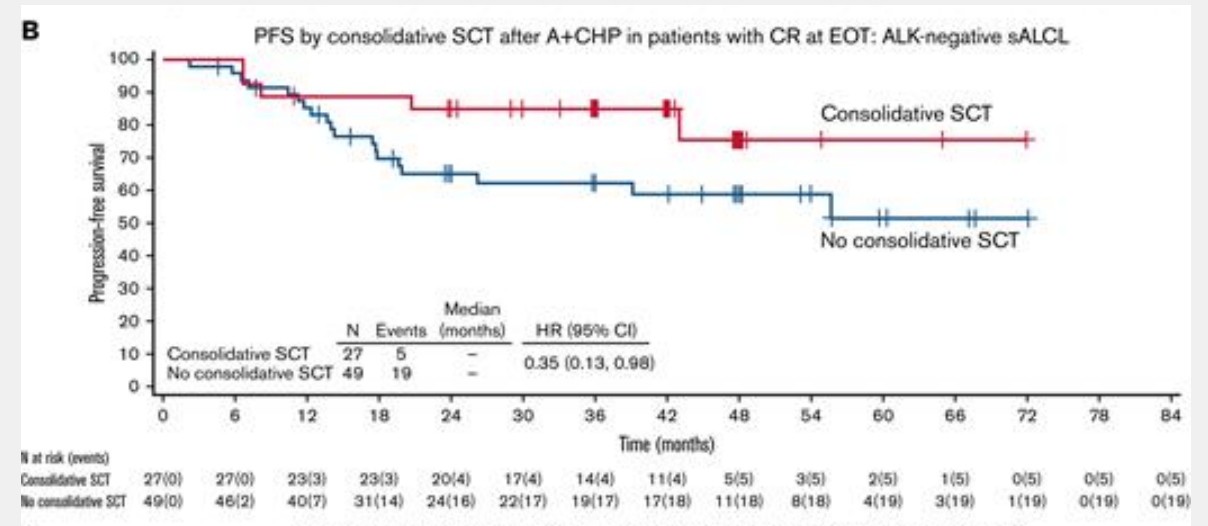




Consolidation with ASCT in AITL in RC1

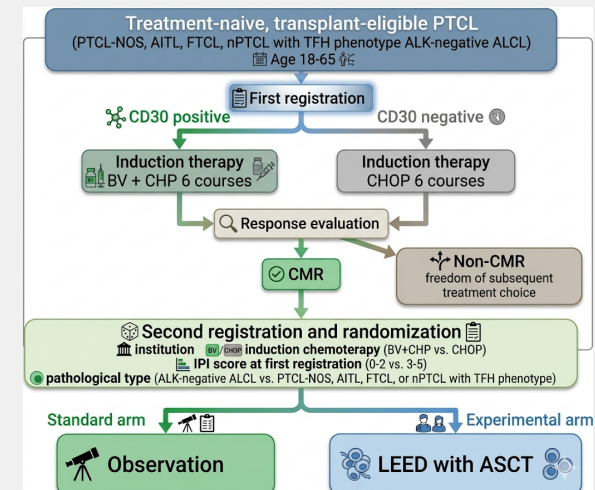


Unclear if benefit for low risk IPI and rearranged DUSP22



282 Patients (International Prospective T-Cell Project)

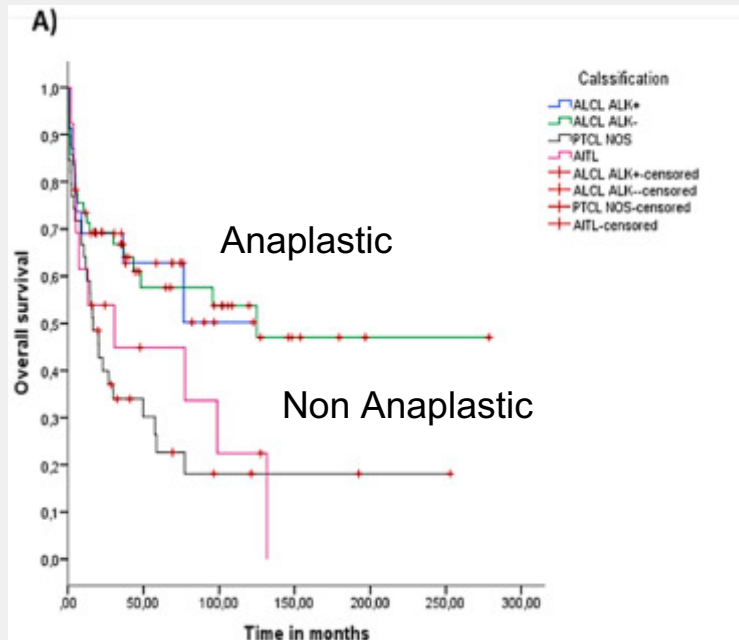
30% Improvement in PFS



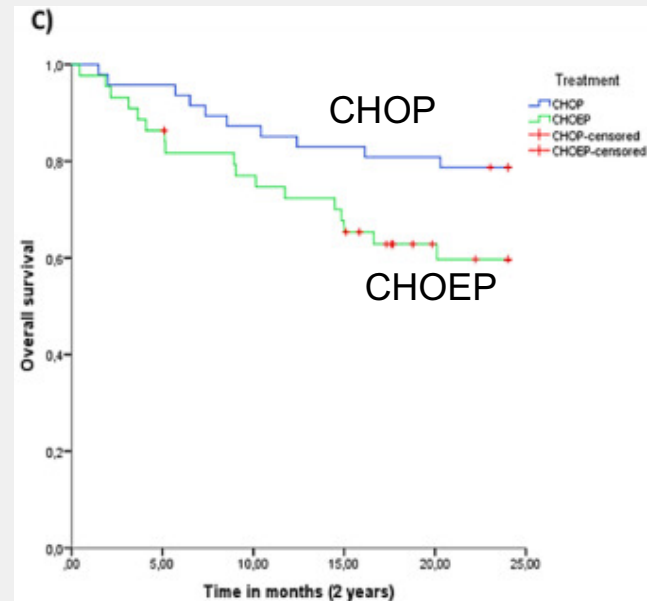
Author	Study design	Population	Therapeutic strategies	Outcomes
Schmitz N, 2010	Retrospective	289 nMTCL (28 AITL)	CHOP vs CHOEP	3y EFS: 50.0 vs 67.5% (for AITL)
Ellin F, 2014	Retrospective	755 nMTCL (104 AITL)	CHOP vs CHOEP	3y EFS: 23.0 vs 40.0% (for AITL)
Lage L, 2022	Retrospective	124 nMTCL (134 AITL)	CHOP vs CHOEP	3y PFS: 69.7 vs 25.0% (for all nMTCL)
Brink MI, 2022	Prospective, Phase II	1427 nMTCL (294 AITL)	CHOP plus alemtuzumab	2y EFS: 48%
Gallamini A, 2007	Prospective, Phase II	46 nMTCL (17 AITL)	CHOP plus bevacizumab	1y EFS: 44% (57% for AITL)
Ganjoon K, 2014	Prospective, Phase II	80 nMTCL (67 AITL)	CHOP plus lenalidomiab	1y PFS: 42% for AITL
Lemonnier F, 2022	Prospective, Phase II	335 AITL	CHOP plusP vs R-CHOP	2y PFS: 45.0 vs 40.0%
Meewez E, 2019	Prospective, Phase II	452 MTCL (> 70% ALCL)	BV-CHP vs CHOP	Median PFS: 48.2 vs 20.8 months
Horwitz S, 2019	Prospective, Phase II	25 R/R nMTCL (20 nMTCL-TFH)	5-azacytidine plus romidepsin	Median PFS: 8.0 months
Ruarn J, 2021	Prospective, Phase II	21 nMTCL (16 nMTCL-TFH)	5-azacytidine plus CHOP	1y PFS: 56.8% (61.1% for AITL)
Bachy E, 2022	Prospective, Phase II	421 MTCL	CHOP vs Romidepsin plus CHOP	Median PFS: 10.2 vs 12.0 months
HC-FMUSP-ICESP	Retrospective	124 nMTCL	CHOP vs CHOEP	<ul style="list-style-type: none"> ■ Median OS 20.8 months CHOP vs 17.9 months CHOEP, p=0.050 ■ Median PFS 18.7 months CHOP and 9.48 months CHOEP, p<0.001 ■ 2-y PFS 67.5% CHOP and 12.7% CHOEP, p<0.0001

Up-front Therapy With CHOP Plus Etoposide in Brazilian nPTCL Increased Toxicity and No Survival Benefit Compared to CHOP Results of a Real-Life Study

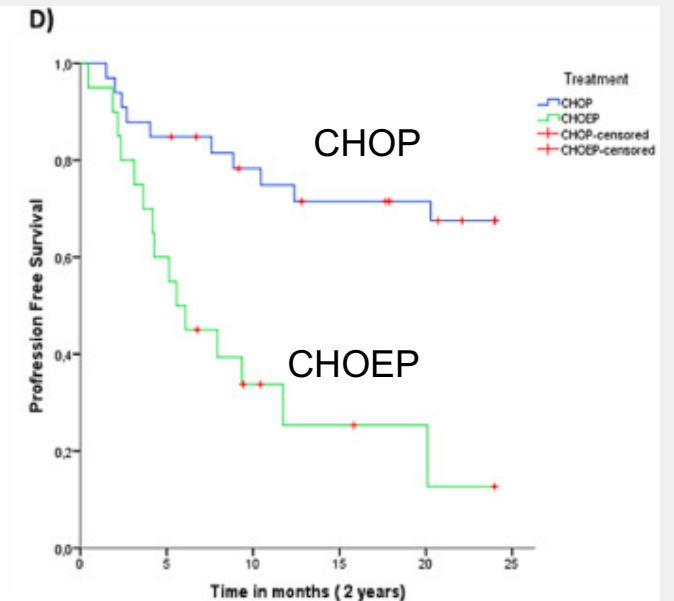
Overall Survival



Overall Survival

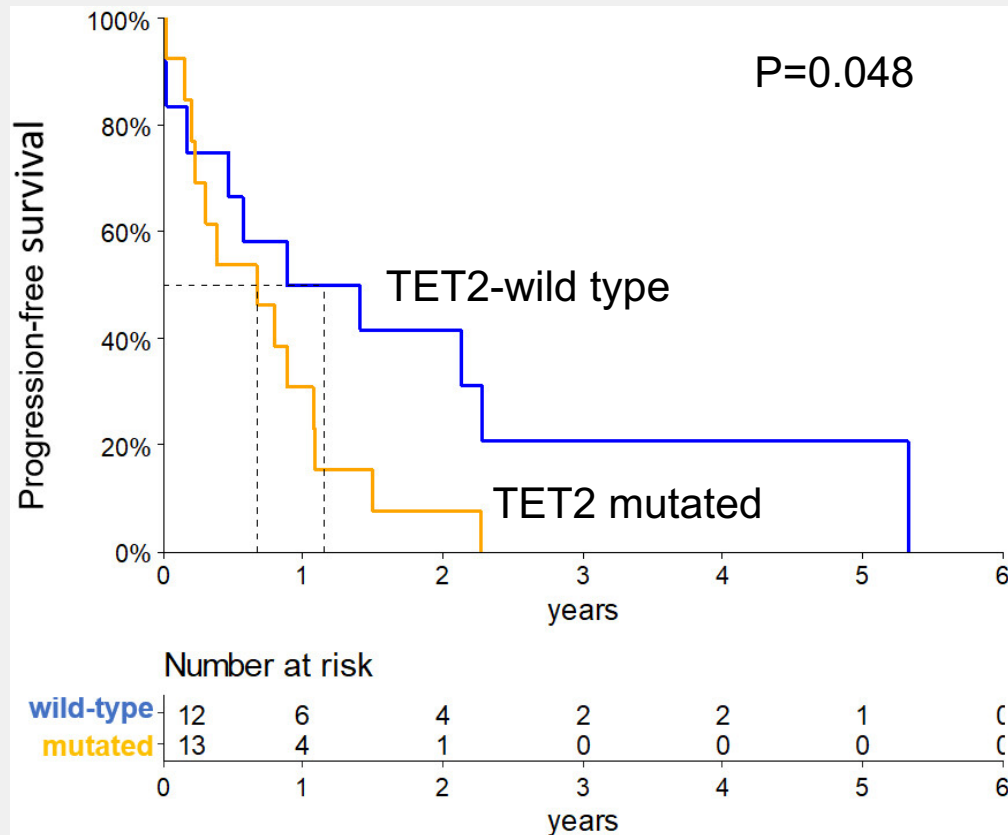


Progression-free Survival

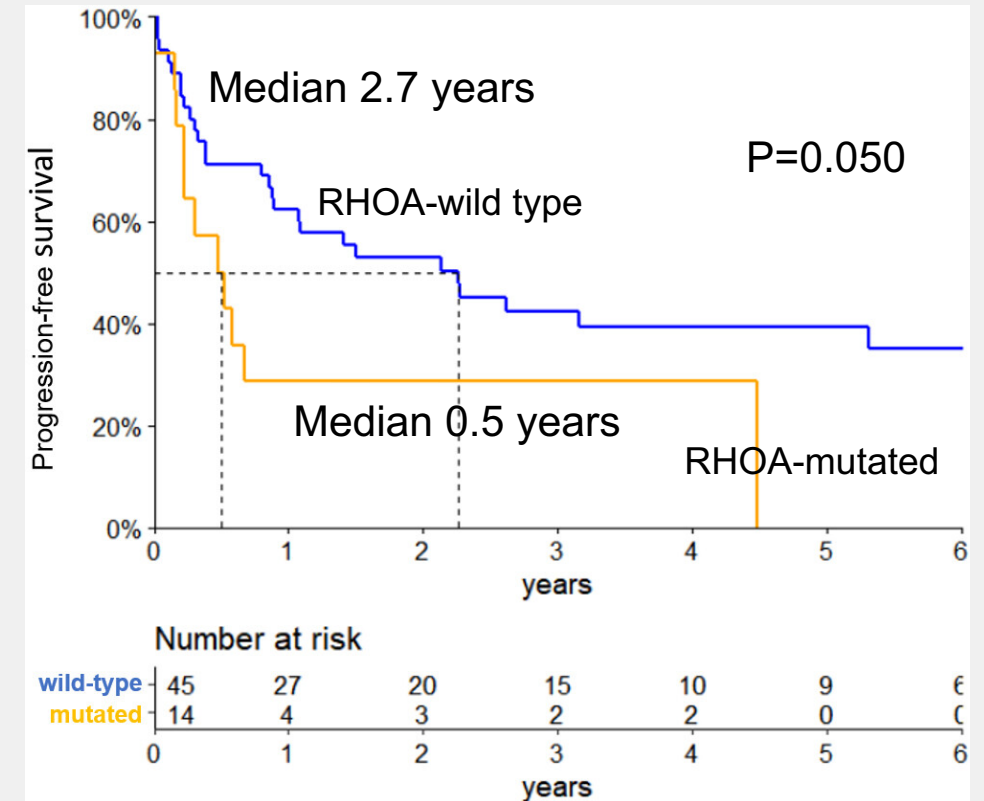


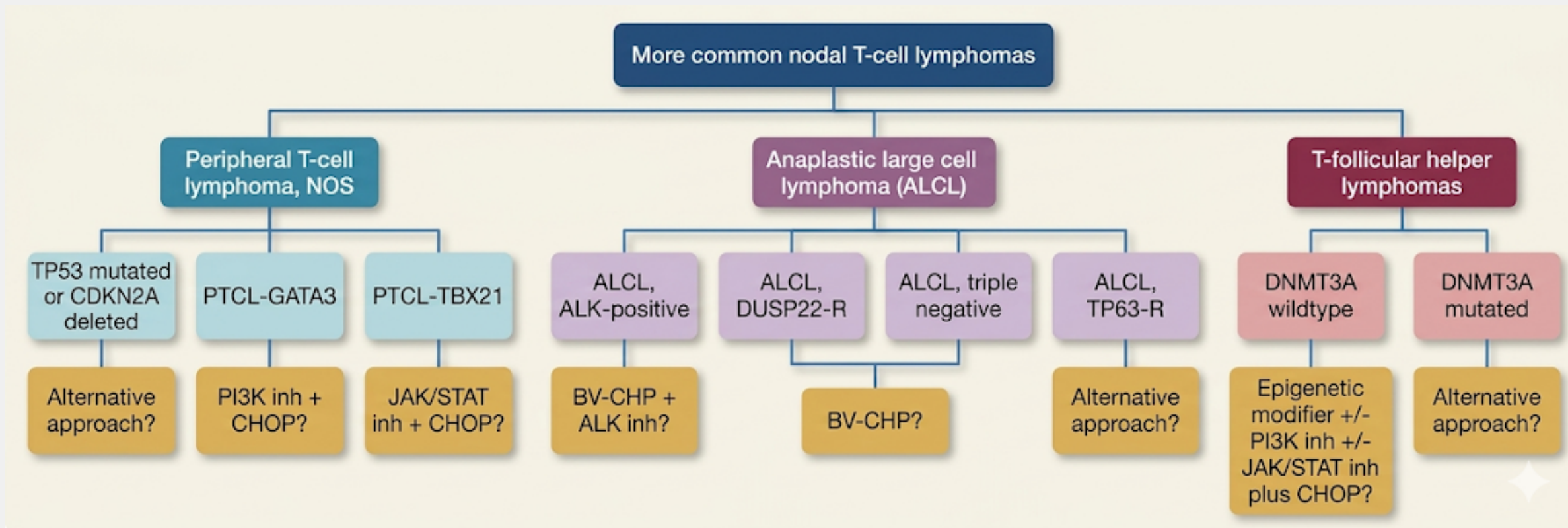
PFS vs mutational status of the *TET-2* and *RHOA* genes in Brazilian patients with PTCL, NOS and AITL

Progression Free Survival
N (25)



Progression Free Survival
N (59)





- nTHF (TET2, DNMT3A, RHOA, IDH2)

CD38 (Daratumumab)

CCR4 (Mogamulizumab)

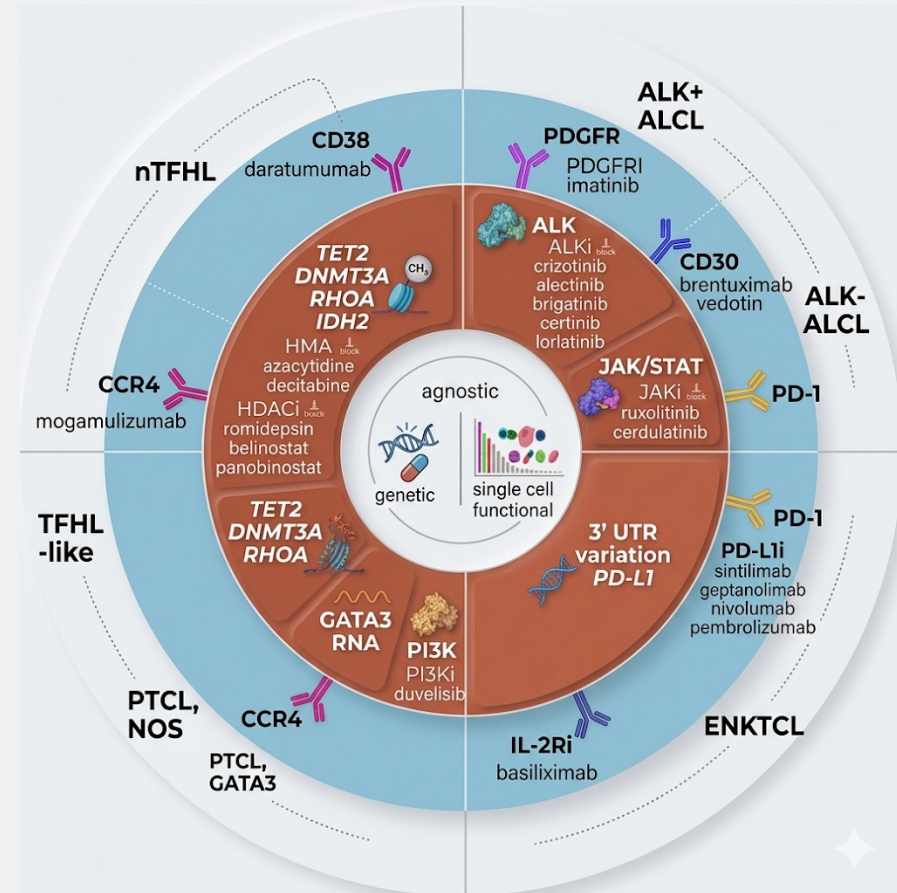
HMA (Azacytidine, decitabine)

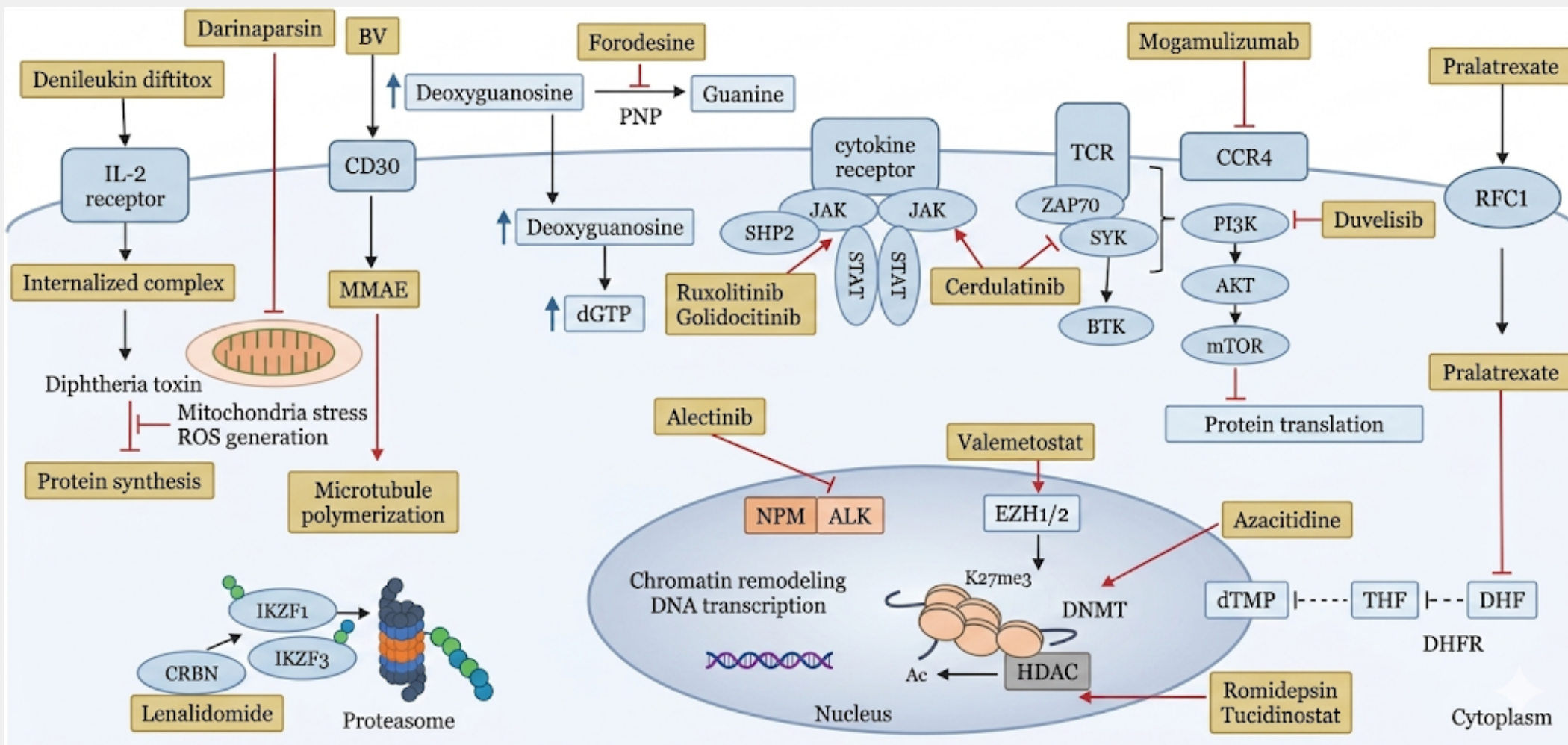
HDACi (Romidepsin, Belinostat, Panabinostat)

- PTCL,nos

GATA3 (Mogamulizumab)

TBX21 (PI3Ki, Duvelisib)





- Retrospective study
- 1143 PTCL in 14 sites

ChT/AlloHSCT

BV Monotherapy

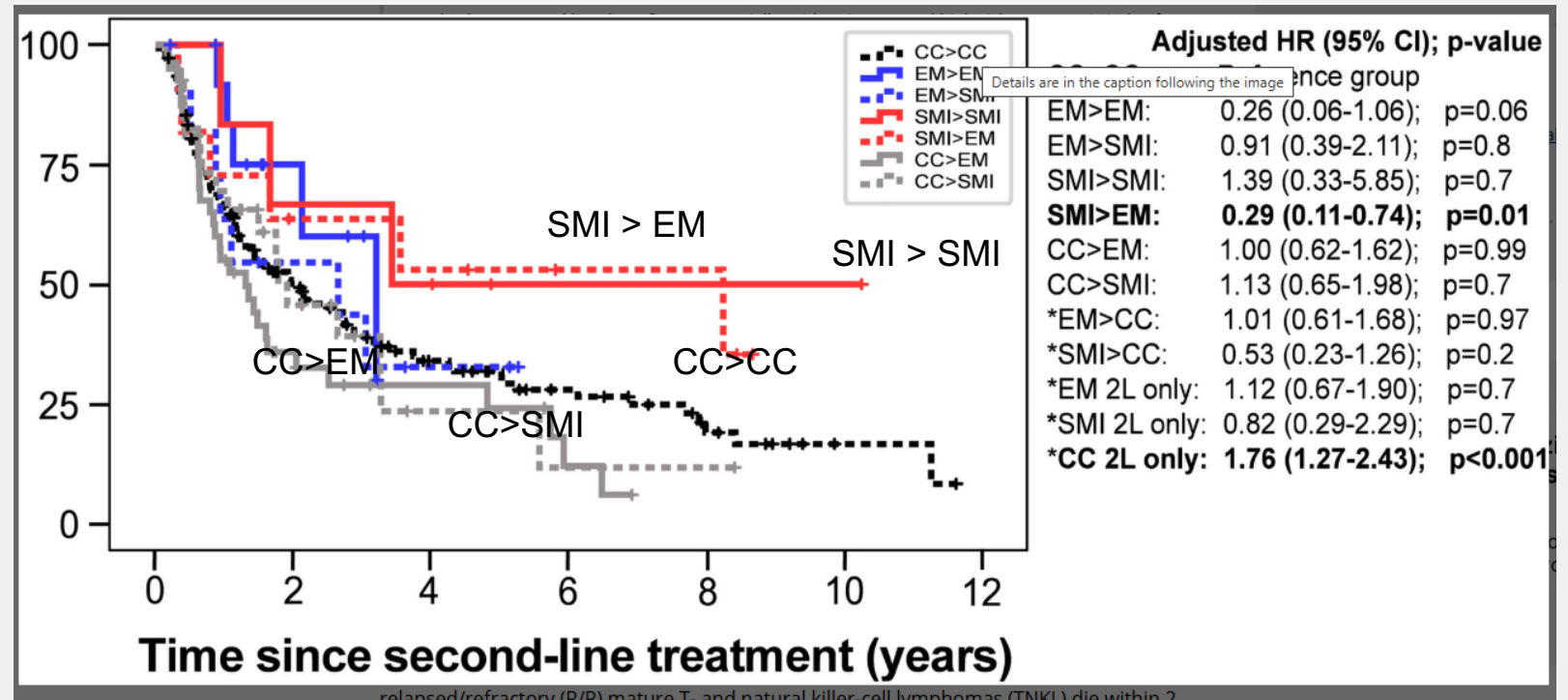
Romidepsin

Belinostat

Pralatrexate

Bendamustine

- Median PFS: 3.1 mo
- Median OS: 5.5 mo

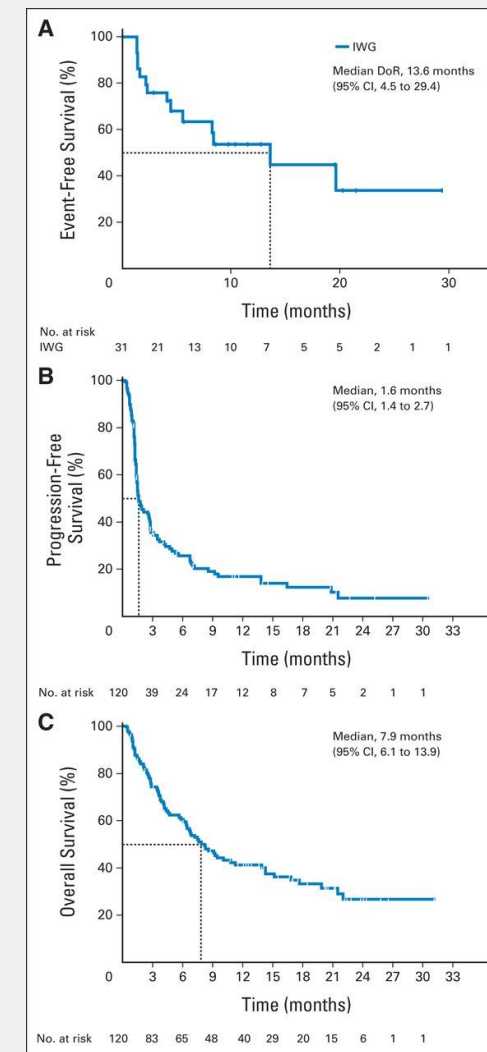
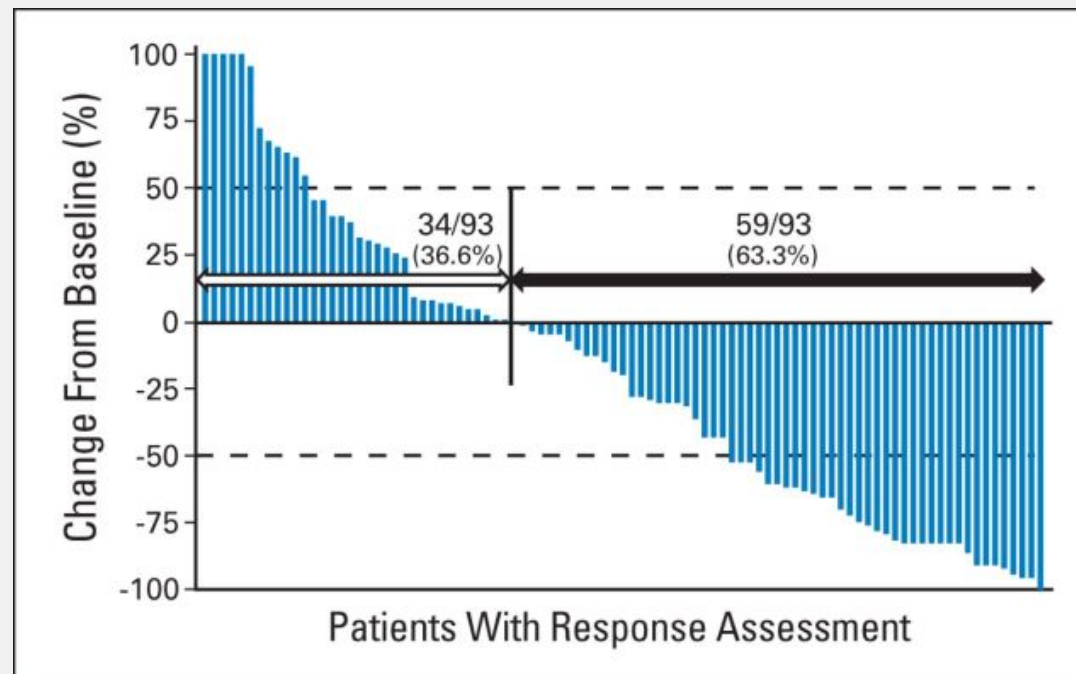


Agent	Target/MOA	Phase	ORR/CRR	PFS (months)	OS (months)	Note
Romidepsin	HDAC inhibitor	II	25 / 15%	4	11.3	
Tucidinostat	HDAC inhibitor	II	46 / 11%	5.6	22.80	
Valemetostat	EZH1/2 inhibitor	II	44 / 14%	5.5	17.0	
Azacitinine	DNA methyltransferase inhibitor	III	31/12% at 3 months	5.6	18.4	Nodal THF lymphomas
Lenalidomide	Immunomodulatory	II	26 / 8%	4	12	
Duvelisib	PI3K inhibitor	II	48 / 33%	3.5	12.4	
Ruxolitinib	JAK1/2 inhibitor	II	27 / 7%	2.8	26.2 ²	ORR 37% for PTCL JAK/STAT mutations, 36% PTCL with up-regulated pSTAT3.
Golidocitinib	JAK1 inhibitor	II	44 / 24%	5.6	19.4	
Cerdulatinib	SYK/JAK inhibitor	IIa	36 / 21%	3.3	N/A ²	
Pralatrexate	Folate analogue	II	29 / 11%	3.5	14.5	
Forodesine	PNP inhibitor	II	25 / 10%	1.9	15.6	Refractory patients were not included
Alectinib	ALK inhibitor	II	80 / 60%	12-mo: 58%	12-mo: 70%	ALK-positive ALCL
Darinaparsin	Organic arsenical	II	19 / 9%	3.3	17.4	
Brentuximab vedotin x2	ADC	II	86 / 67%	20	NR¹	ALCL
Brentuximab vedotin x2	ADC	II	41 / 24%	2.6	N/A²	CD30-positive PTCL and AITL
Mogamulizumab	Anti-CCR4 mAb	II	34 / 17%	2.0	14.2	Refractory patients were not included
Denileukin difitox	IL-2 fusion toxin	II	41 / 6%	2.1	11.8	

Belinostat in Patients With Relapsed or Refractory PTCL: Results of the Pivotal Phase II BELIEF (CLN-19) Study

- PTCL ≥ 1L: N=120
- 1.000 mg/m² D1-D5 21/21
- ORR: 25.8% / RC: 10.8%
- ORR in PTCL: 23.3%
- ORR in AITL 45.5%
- Median PFS: 1.6 mo
- Median OS: 7.8 mo
- Median DoR: 13.6 mo

IC95% 4,5 a 29.4 mo



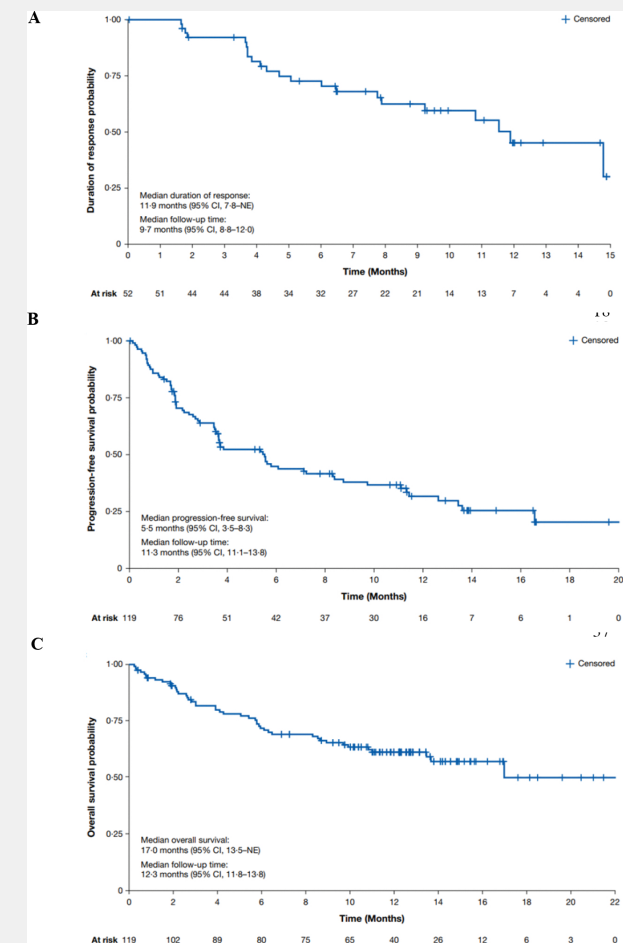
Valemetostat for Patients With Relapsed or Refractory Peripheral T-Cell Lymphoma: An Open-Label, Single-Arm, Multicenter, Phase 2, VALENTINE-PTCL01 Study

EZH2 and EZH1 Inhibitor - prevents trimethylation of histone H3 at lysine 27 (H3K27me3)

- N=115 PTCL, 42 AITL, 41 PTCL, nos, 22 ATLL
- Valemetostat 150 or 200 mg/day
- Mediana follow up 12.3 mo
- ORR in R/R PTCL: 43.7% (95% CI, 34.6%-53.1%), CR 14.3%
- ORR in R/R ATL (n=14): 57.1% (95% CI, 28.9%-82.3%)

EHA 2021, Abstract S218

- Median DoR: 11.9 mo
- Median PFS 5.5 mo
- Median OS 17 mo



Duvelisib in Patients with Relapsed/Refractory Peripheral T-Cell Lymphoma: Final Results from the Phase 2 PRIMO Trial (NCT03372057)

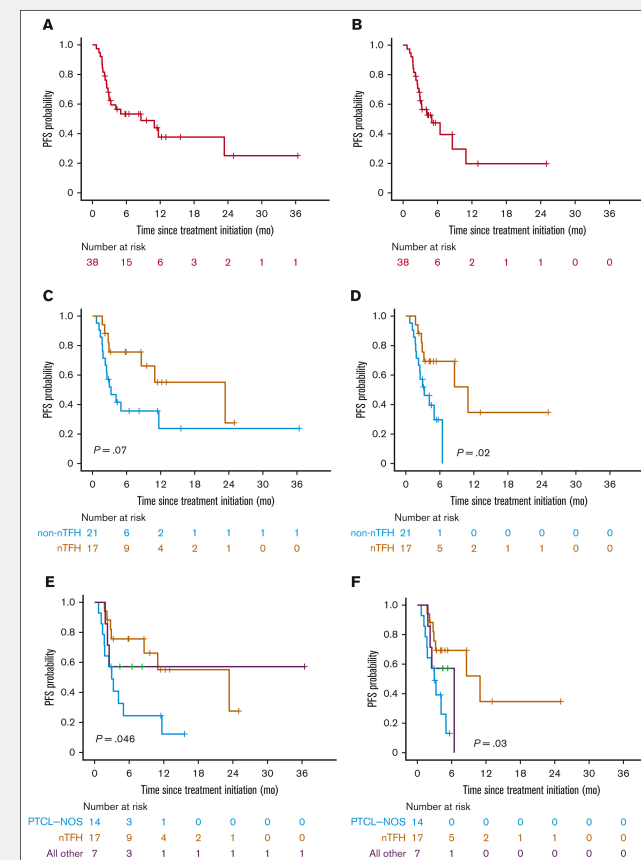
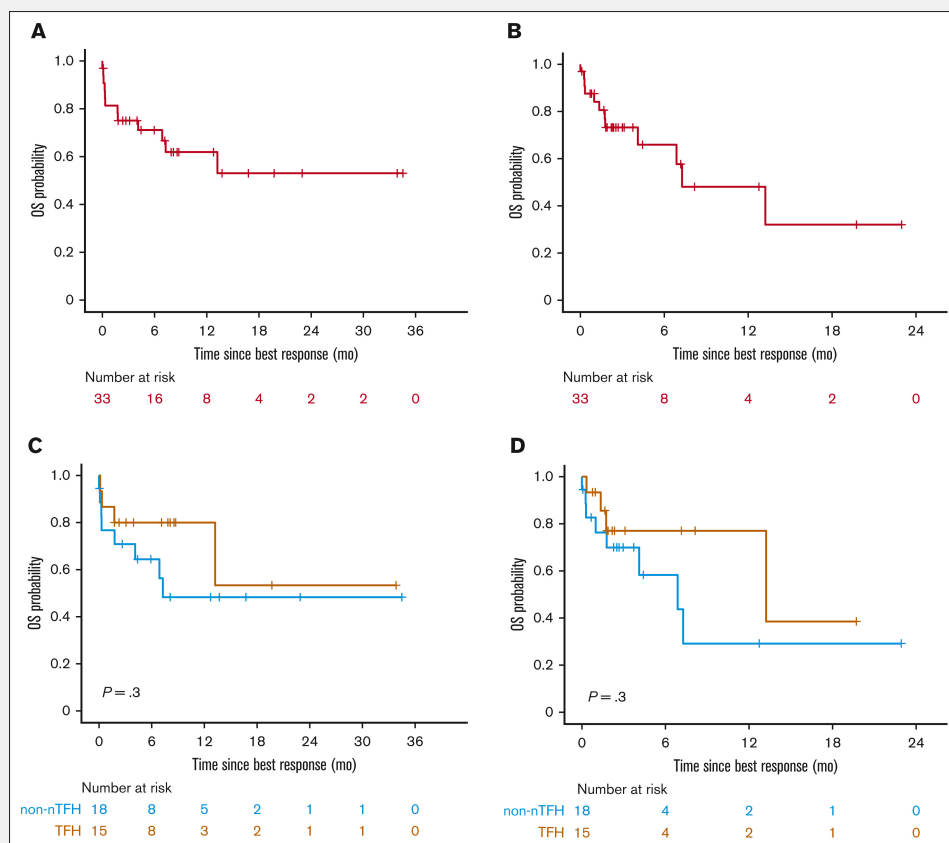
- US, EU, UK, and Japan
- Duvelisib: 75 mg BID for 2 cycles followed by 25 mg BID until PD or unacceptable toxicity
- Primary endpoint: ORR
- 123 R/R PTCL: 53 PTCL-NOS, 37 AITL, 20 ALCL
- Median follow-up for PFS: 6.24 mo
- ORR: 48%, CR: 33%, mPFS: 3.45 mo, mDOR: 7.89 mo, and mOS: 12.35 mo
- ORR: 49.1% (PTCL-NOS), 62.2% (AITL), 15.0% (ALCL)
- mPFS: 3.45 mo (PTCL-NOS), 8.34 mo (AITL), 1.64 mo (ALCL)
- mOS: 11.04 mo (PTCL-NOS), 18.07 mo (AITL), 6.34 mo (ALCL)
- mDOR: 7.39 mo (PTCL-NOS), 11.70 mo (AITL), 1.97 mo (ALCL)
- 15% received SCT

Adverse Events

- 4 (3.3%) fatal treatment-related
 - Cryptococcosis, EBV associated lymphoproliferative disorder, pneumonitis, and sepsis
- AEs of special interest (Grade ≥ 3) included: ALT/AST elevation 24.4%, neutropenia
 - 17.9%, infections
 - 13.0%, cutaneous reactions
 - 10.6%, diarrhea
 - 9.8%, pneumonia
 - 4.1%, pneumonitis

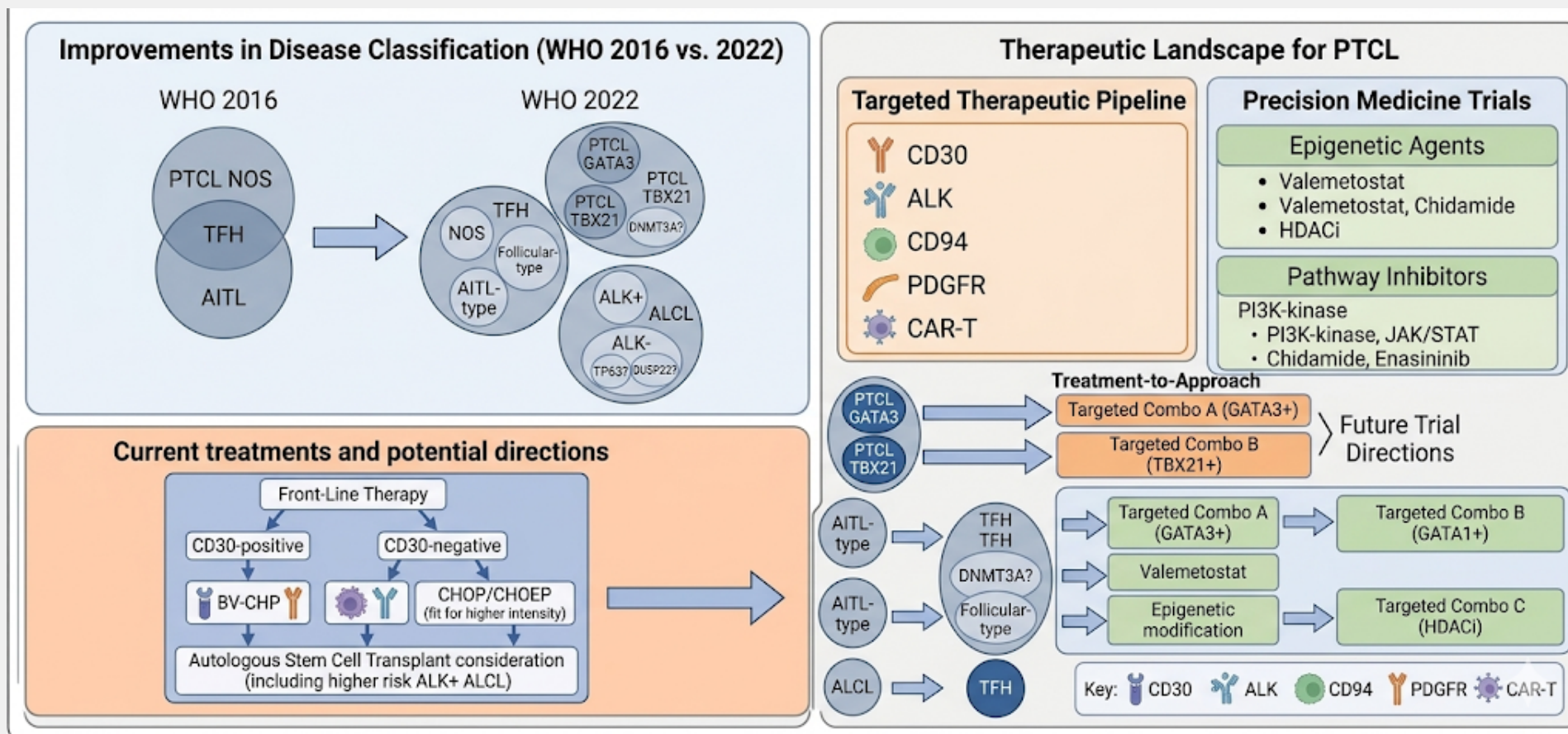
Real-world use of the duv/romi combination confirms its efficacy, tolerability, and safety for patients with R/R PTCL.

The duv/romi combination offers a novel strategy to bridge eligible patients with R/R PTCL to allogeneic transplantation



Poor prognosis, Challenges for clinical trials, important differences among subtypes

- Clinical Trial whenever possible



- Diagnosis of PTCL remains challenging
- The knowledge of the PTCL biology is improving
- New targets has been uncovered
- PTCL Treatment remains as a medical unmet need
- New drugs have been promissor in phase 1/2 but has failed in expansions phase

Obrigado(a)!

Nome e Sobrenome

Cargo/ Função

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PTCL subtype	Praletrexate	Brentuximab (For CD30+)	Romidepsin (HDAC inhibitor)	Belinostat (HDAC inhibitor)	Duveslisib
PTCL,nos	32%	33%	29%	23%	48.1
AITL	8%	54%	30%	46%	66.7%
ALCL	29%	85%	24%	15%	13.3%