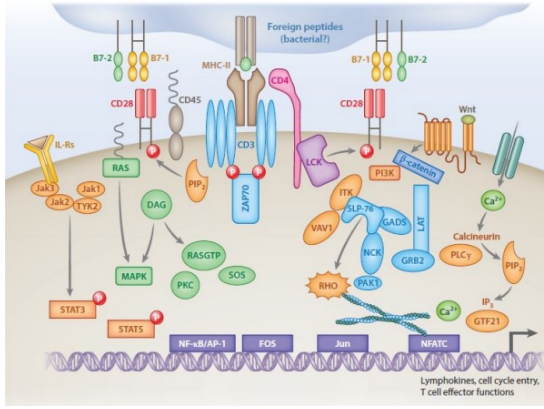
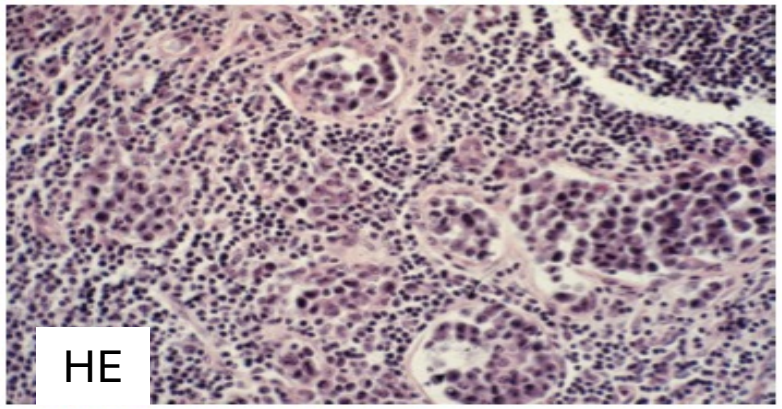


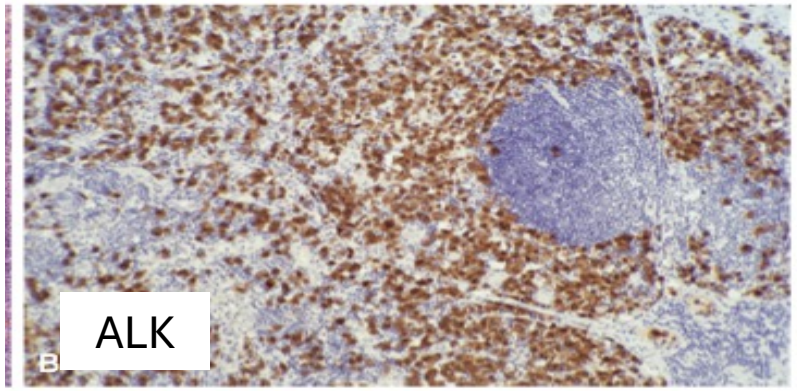
Linfomas T periféricos
¿Que hacer en segunda línea?


HE

Danielle Leao

LEX

03 abril 2025

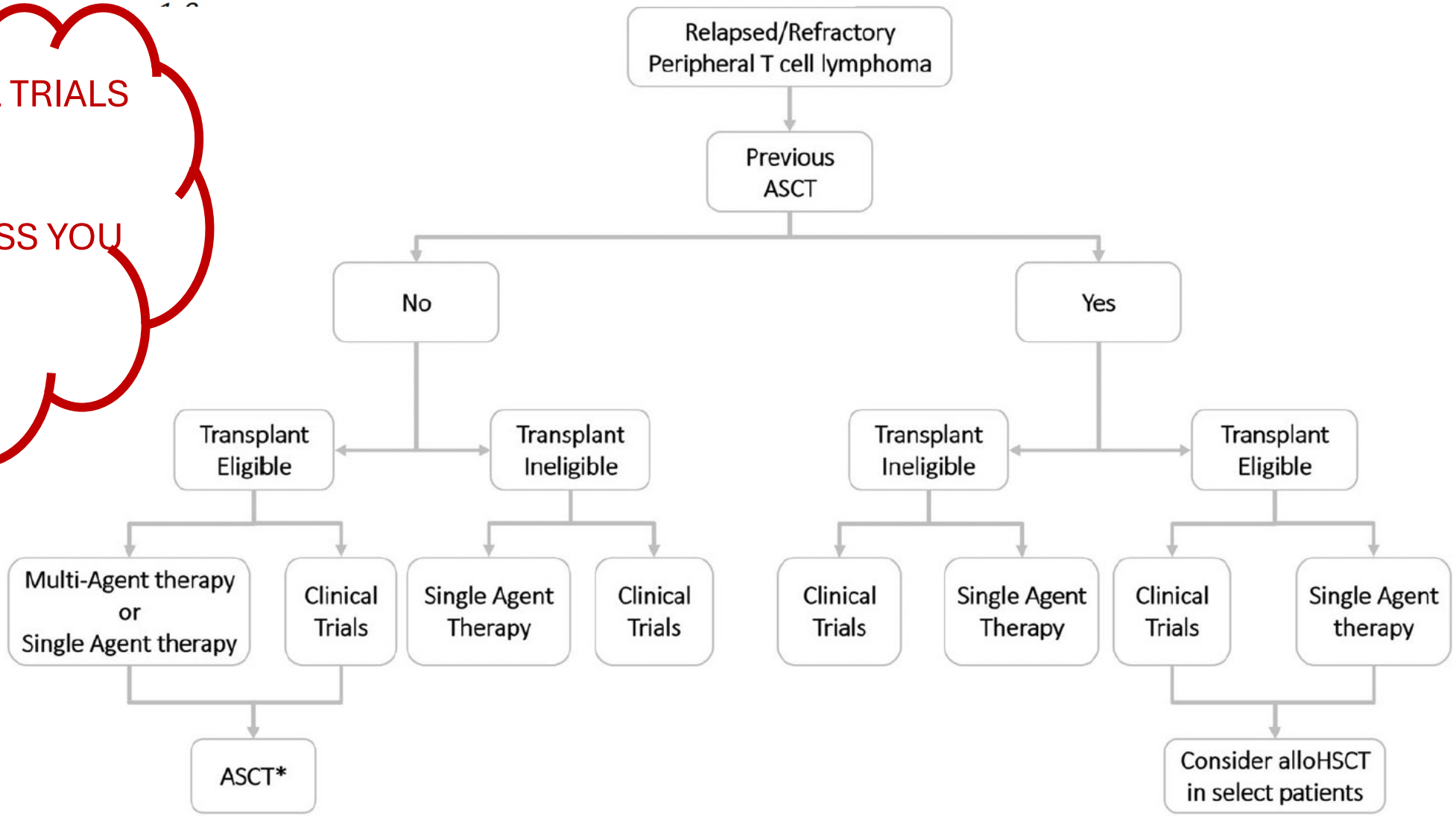

ALK

How to Sequence Therapies in Peripheral T Cell Lymphoma

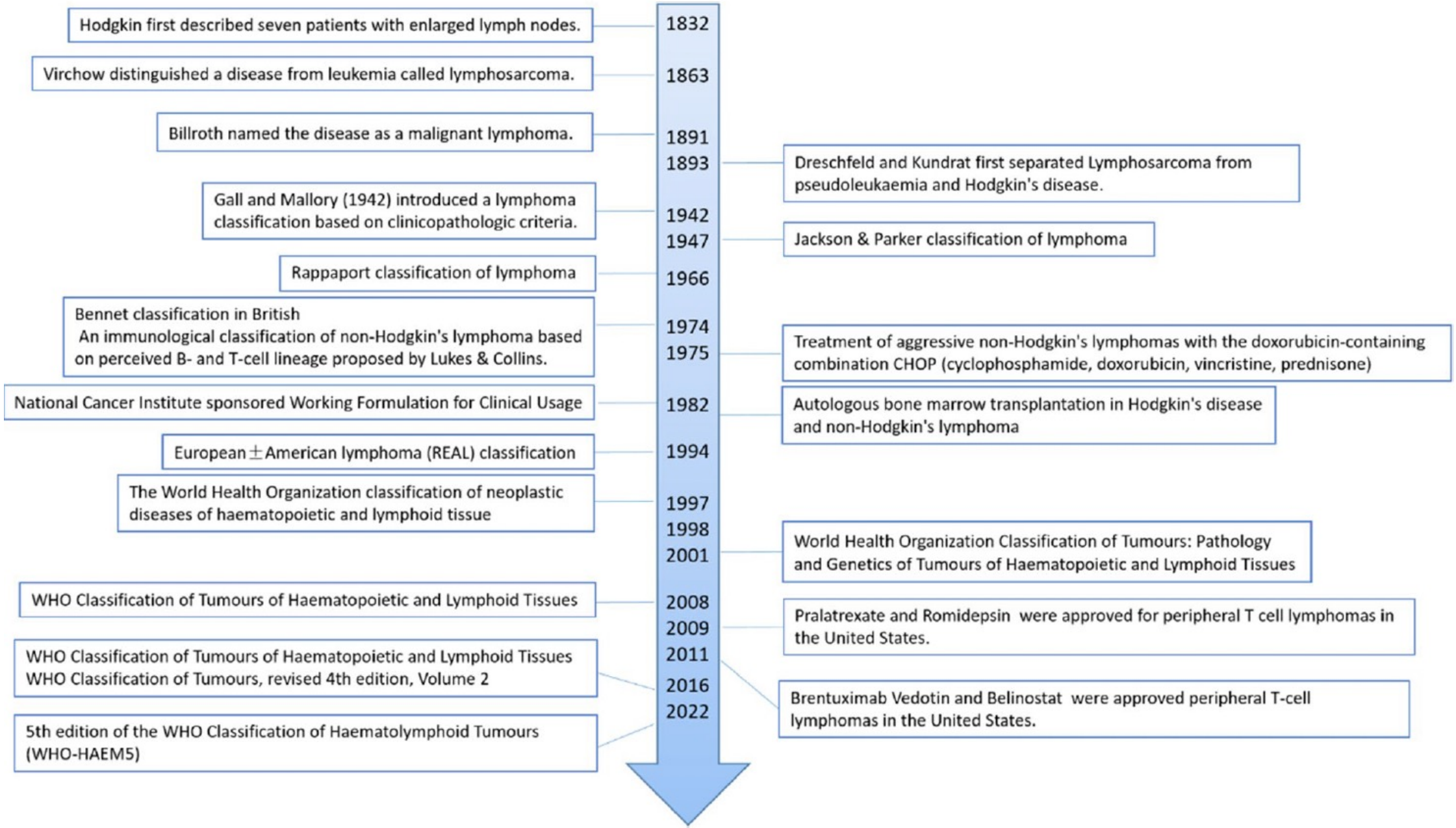
CLINICAL TRIALS

GOD BLESS YOU

BYE



Kitsada Wudhikarn &N. Nora Bennani Curr. Treat. Options in Oncol. (2021)

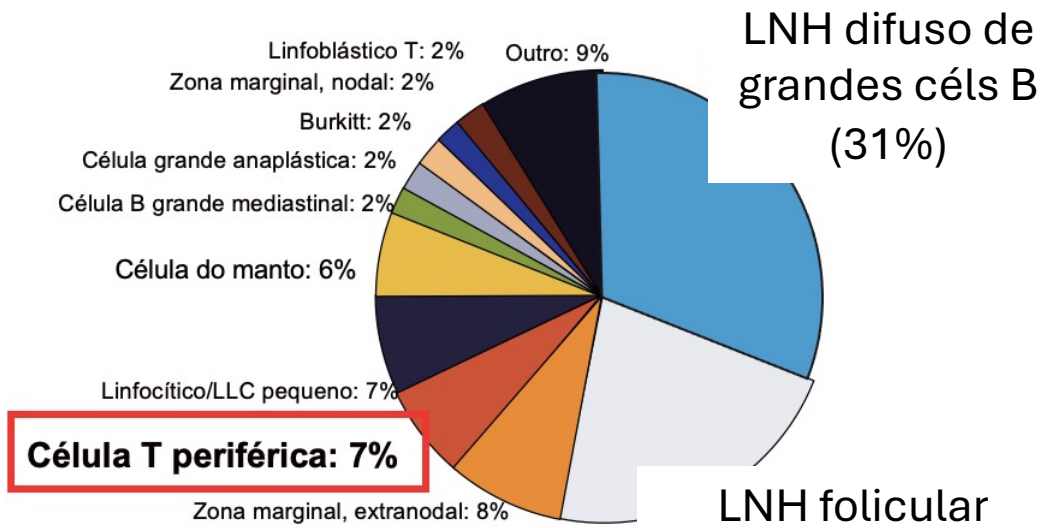


Luan et al. Molecular Cancer (2024)

LNH de células T periféricas

- Células T maduras (post-tímicas):
  - Desafío diagnóstico
  - Manifestación agresiva
  - Resultados desfavorables
  - Recurrencias frecuentes

- 20% de los LNH agresivos:
  - Predominio en hombres
  - Edad media: 55-61 años
  - Estadios avanzados
  - Frecuente IPI de alto riesgo



Adapt. Swerdlow et al, 2016
*Mina & Pro, Blood Rev 2021

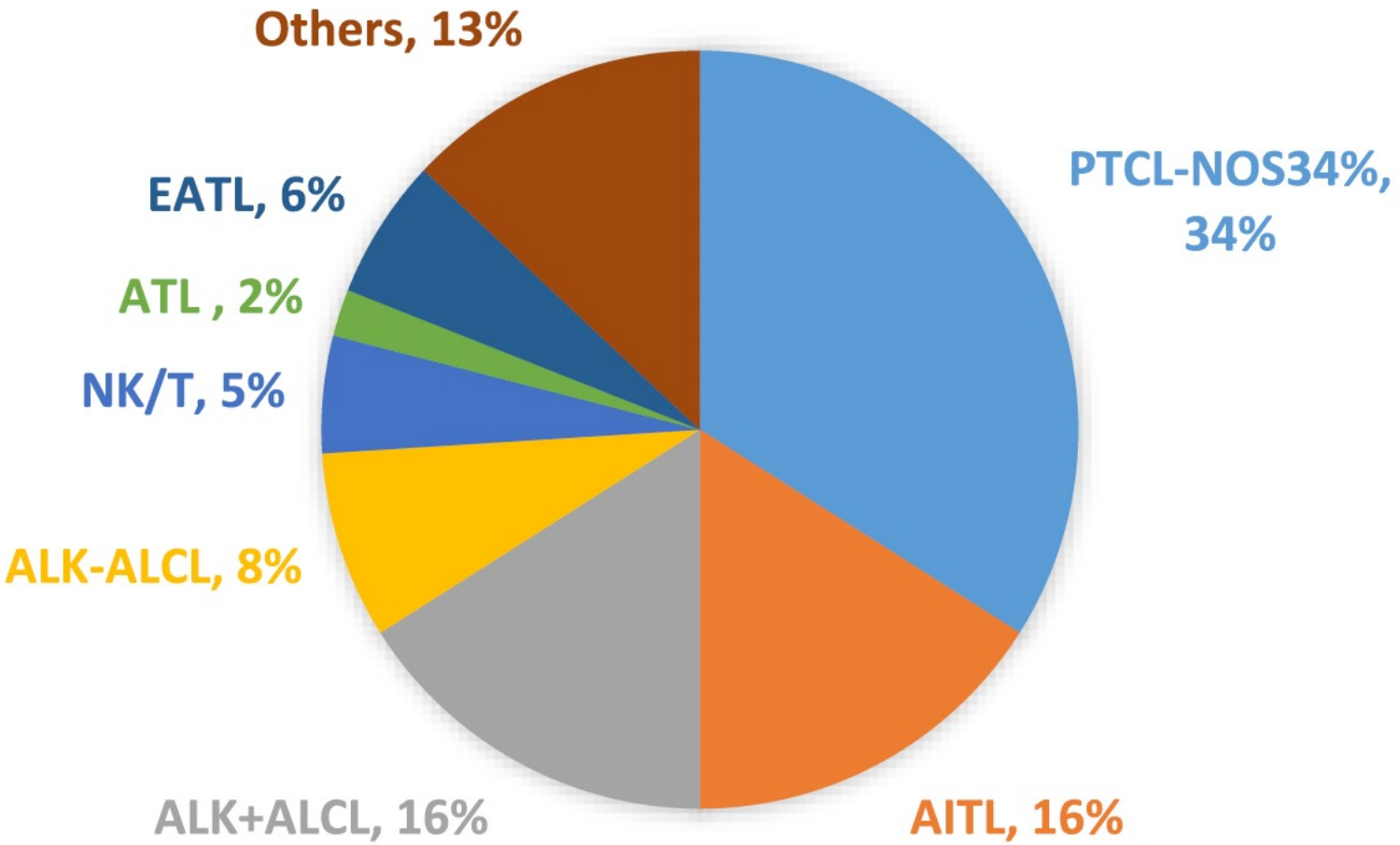


Fig. 2 Incidence of different Peripheral T-cell lymphoma subtypes according to IPTCLP [7]

Luan et al. Molecular Cancer (2024)

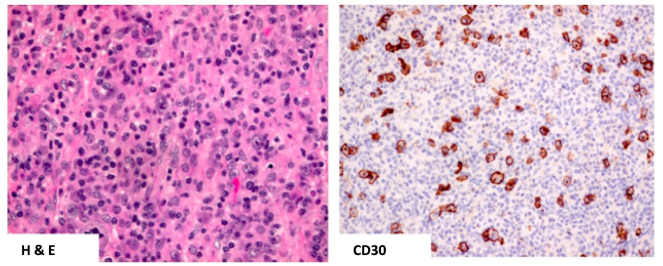


Figure 2. CD30$^+$ PTCL-NOS. H&E staining demonstrates predominantly small- to medium-size lymphocytes with pleomorphism and the absence of hallmark cells. Only scattered tumor cells demonstrate CD30 positivity compared with ALCL.

HAPGOOD and SAVAGE, Blood 20

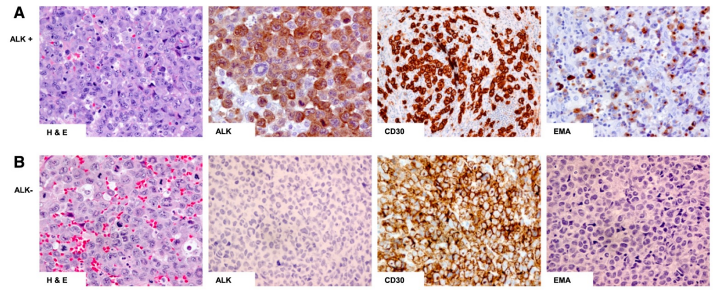
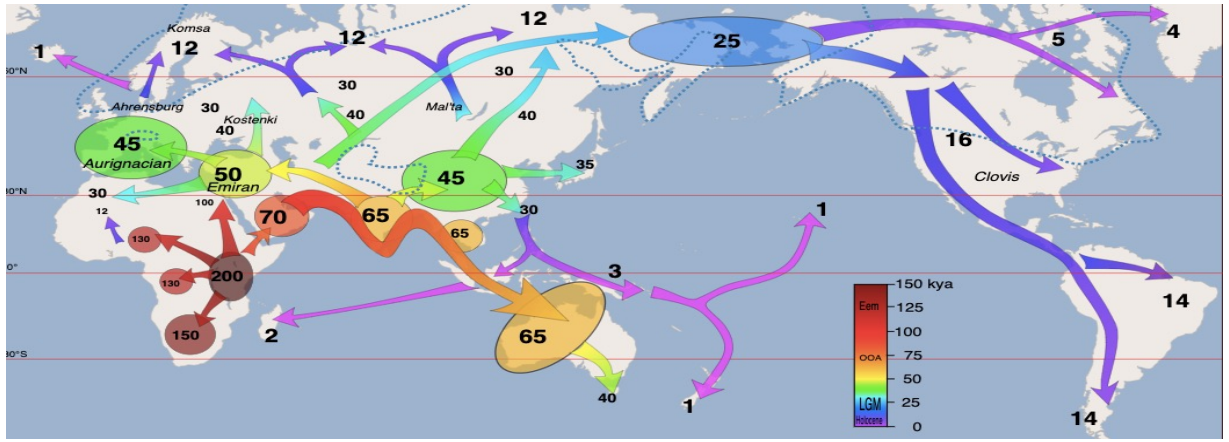


Figure 1. Hematoxylin and eosin (H&E) and immunohistochemical staining of ALCL. (A) ALK+: Hallmark cells demonstrated by H&E staining and tumor cells positive for ALK, CD30, and epithelial membrane antigen (EMA); (B) ALK−: Hallmark cells demonstrated by H&E staining and tumor cells positive for CD30 but negative for ALK and EMA staining.

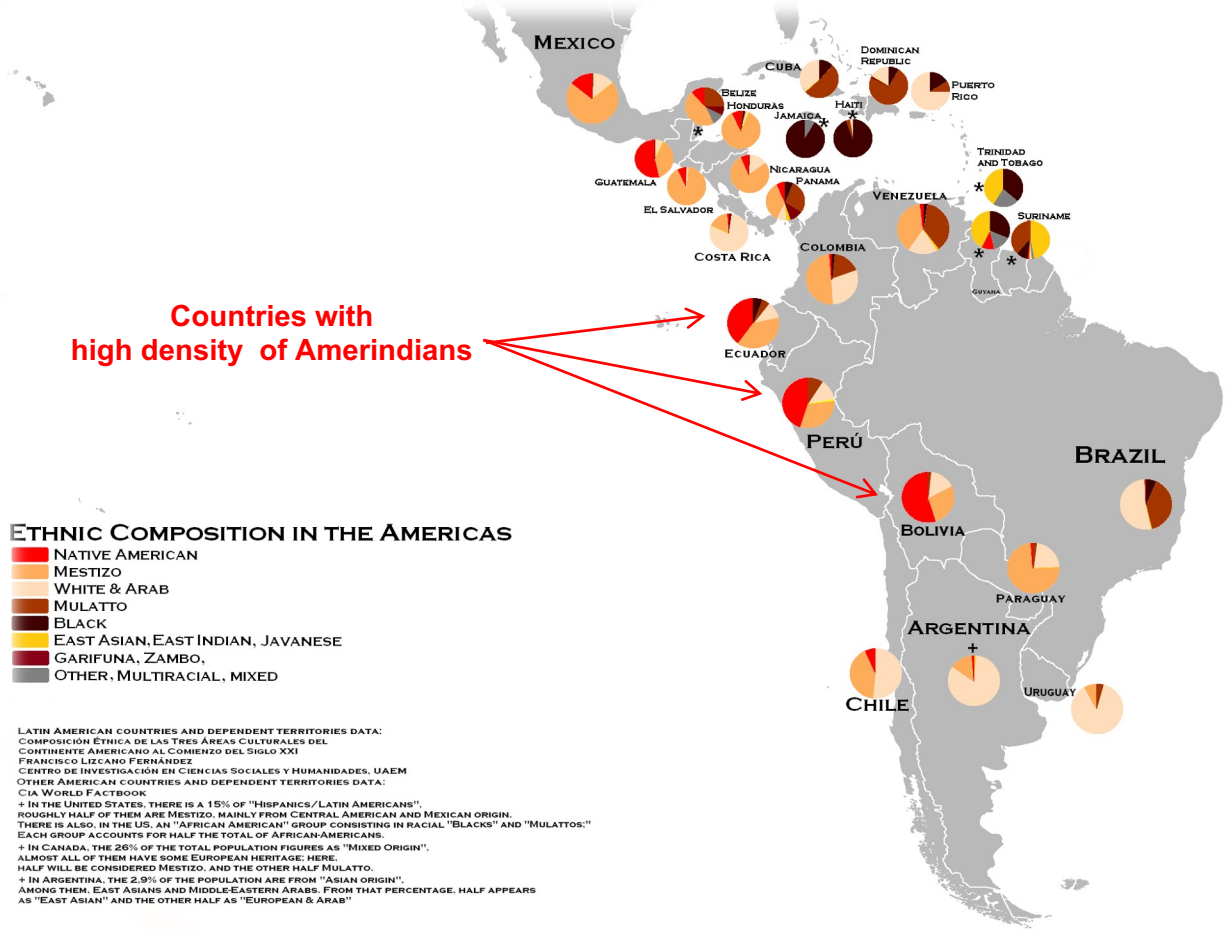
Asian Origin of South American Amerindians (*Origin population*)



File:Early migrations mercator.svg
Created: 31 December 2017

Cortesia Dr Chiattone e
Brazilian T-Cell lymphoma Group

Latin America Ethnic Composition

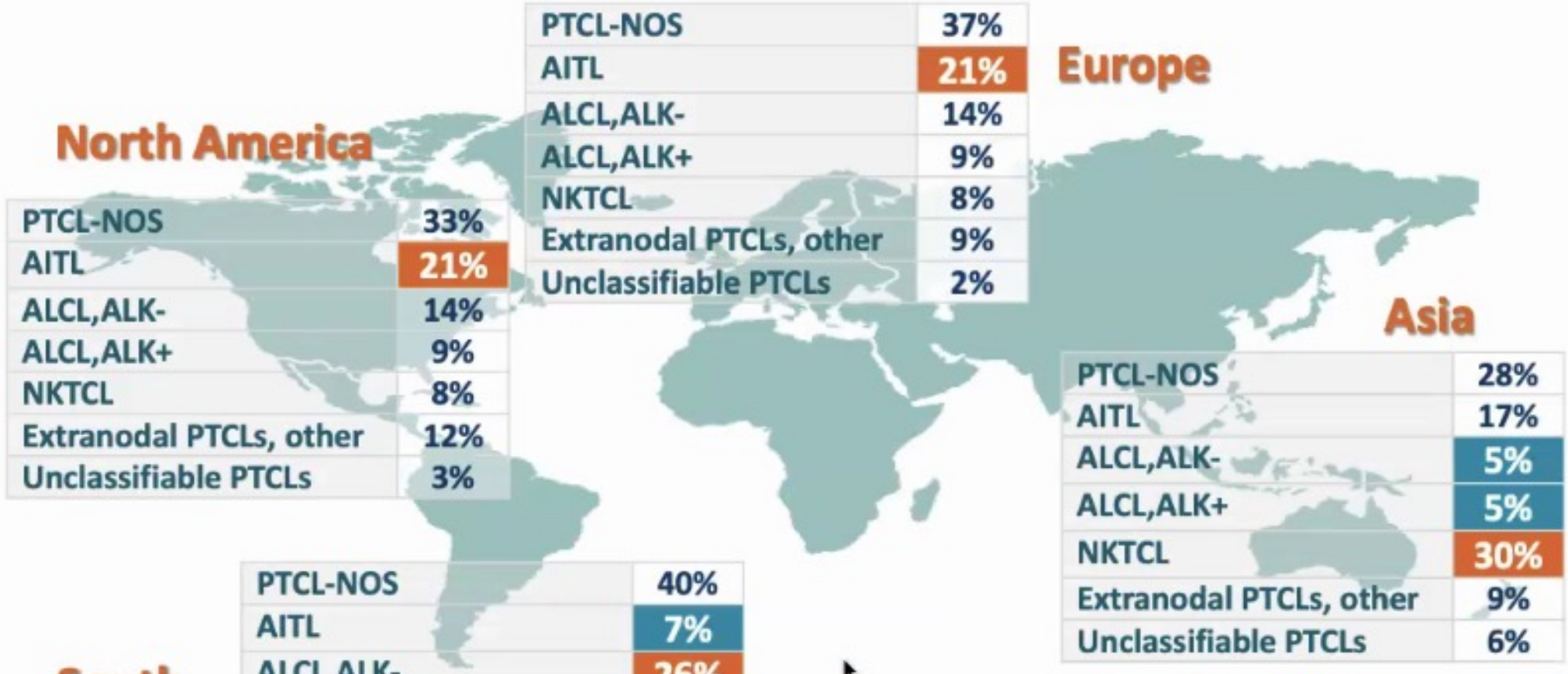


Sources: figure: enacademic.com
Homburger et al., 2015 PLOS Genetics

International T-cell Project 1.0

updated on december 2019
(N=1553)

Subtypes by geographic area



North America

PTCL-NOS	33%
AITL	21%
ALCL,ALK-	14%
ALCL,ALK+	9%
NKTCL	8%
Extranodal PTCLs, other	12%
Unclassifiable PTCLs	3%

Europe

PTCL-NOS	37%
AITL	21%
ALCL,ALK-	14%
ALCL,ALK+	9%
NKTCL	8%
Extranodal PTCLs, other	9%
Unclassifiable PTCLs	2%

Asia

PTCL-NOS	28%
AITL	17%
ALCL,ALK-	5%
ALCL,ALK+	5%
NKTCL	30%
Extranodal PTCLs, other	9%
Unclassifiable PTCLs	6%

South America

PTCL-NOS	40%
AITL	7%
ALCL,ALK-	26%
ALCL,ALK+	8%
NKTCL	11%
Extranodal PTCLs, other	6%
Unclassifiable PTCLs	2%

Blood 1997; 89:3909
JCO 2008; 26:4124

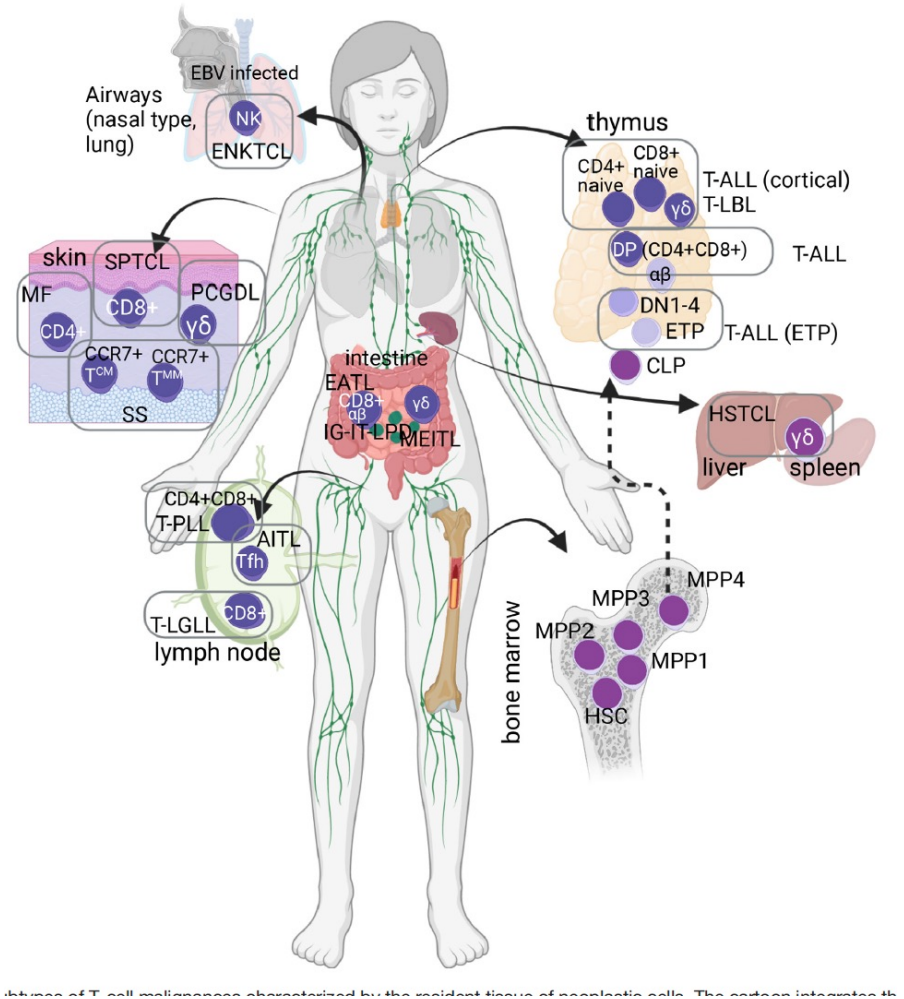
More frequent

Frequency of Histological Subtypes

Histological Subtypes	n= 689	%
PTCL-NOS	208	30
ALCL, ALK negative	125	18
ATLL	100	15
ENKTL	83	12
AITL	75	11
ALCL, ALK positive	44	6.5
HSTCL	16	2.5
EATCL	12	1.5
LGLL	11	1.5
ALCL, BIA	7	1.2
Aggressive NK_TCL	5	0.5
SPTCL	2	0.2
Indolent_TCL of GIT	1	0.1

Cortesia Dr Chiattone e
Brazilian T-Cell lymphoma Group

Subtypes of T-cell malignances characterized by the resident tissue of neoplastic cell



Bigas A et al.
Experimental Hematology
2021

Linfomas T periféricos

Subclasificación

- Nodales
- Extranodales
- Cutáneos
- Leucémicos

 # WHO-HAEM5 (2022) #

1. Lesões Tumor-like com predominância de céls T
2. Neoplasias de células T y NK maduras
3. Neoplasias de células precursoras linfoideas

WHO HAEM5-Allagio R et al. Leukemia 2022;36:1720)

TABLE 1 Updates in classification of more common PTCL subtypes.

2017 WHO Fourth Edition	2022 WHO Fifth Edition	Molecular and Genomic Information	Prognosis and Survival
PTCL-NOS	PTCL-NOS	GATA3 and TBX21 subtypes	Reduced 5-year OS (19%) of GATA3 subtype compared with TBX-21 subtype (38%). TBX21-PTCL-NOS with cytotoxic signature (*DNMT3A* mutations) worse prognosis.
Angioimmunoblastic T-cell lymphoma	Nodal TFH lymphoma, angioimmunoblastic type	*TET2*, *DNMT3A*, $IDH2^{R172K}$ $RHOA^{G17Val}$	Mutations in epigenetic regulators may predict response to epigenetic therapies.
Follicular T-cell lymphoma nodal	Nodal TFH lymphoma, follicular type	*TET2*, *DNMT3A*, *RHOAG17Val*, t(5;9) ITK:SYK translocation (20%)	
PTCL with TFH phenotype	Nodal TFH cell lymphoma, NOS	*TET2*, *DNMT3A*, and $RHOA^{G17Val}$	
Anaplastic large cell lymphoma	Anaplastic large cell lymphoma, ALK+ Anaplastic large cell lymphoma, ALK-	t(2;5) (NPM1-ALK) *DUPSP22-IRF4*, *TP63*	ALK+ favorable prognosis ALK- less favorable - *DUPSP22* 5-year OS 40–90% - *TP53* 5-year OS 0–17% - Triple negative intermediate prognosis
Previously listed under PTCL-NOS	Primary nodal EBV+ lymphoma	Upregulation of NF-κB, IFNγ, JAK/STAT3, low genomic instability	Worse prognosis than extranodal NK/T lymphoma (median OS 4.6 vs. 14.7 months)

Am J Hematol. 2024;

ESCORES PROGNÓSTICOS

INTERNATIONAL PROGNOSTIC INDEX[a]

ALL PATIENTS:
• Age >60 years
• Serum LDH > normal
• ECOG Performance Status 2–4
• Stage III or IV
• Extranodal involvement >1 site

INTERNATIONAL INDEX, ALL PATIENTS:	
• Low	0 or 1
• Low-intermediate	2
• High-intermediate	3
• High	4 or 5

AGE-ADJUSTED INTERNATIONAL PROGNOSTIC INDEX[a]

PATIENTS ≤60 YEARS:
• Stage III or IV
• Serum LDH > normal
• ECOG Performance Status 2–4

INTERNATIONAL INDEX, PATIENTS ≤60 YEARS:	
• Low	0
• Low-intermediate	1
• High-intermediate	2
• High	3

PROGNOSTIC INDEX FOR PTCL-U (PIT)[b]

RISK FACTORS:
• Age >60 years
• Serum LDH > normal
• ECOG Performance Status 2–4
• Bone marrow involvement

PROGNOSTIC RISK:	
• Group 1	0
• Group 2	1
• Group 3	2
• Group 4	3 or 4

PROGNOSTIC INDEX FOR PTCL-U (modified-PIT)[c]

RISK FACTORS:
• Age >60 years
• Serum LDH > normal
• ECOG Performance Status 2–4
• Ki-67 ≥80%

PROGNOSTIC RISK:	
• Group 1	0 or 1
• Group 2	2
• Group 3	3 or 4

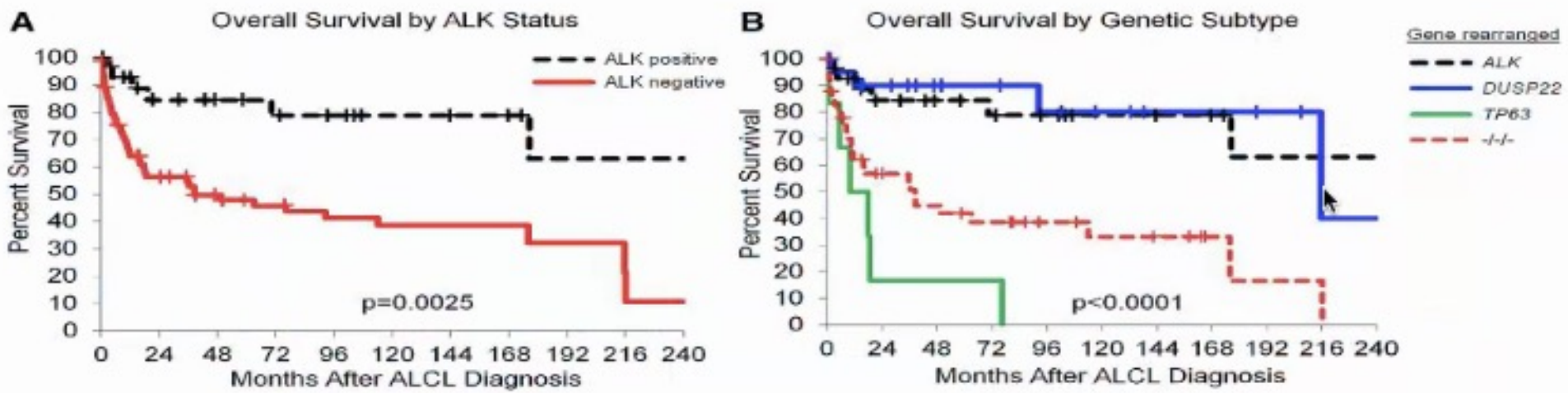
INTERNATIONAL T-CELL LYMPHOMA PROJECT[d]

RISK FACTORS:
• Age >60 years
• ECOG Performance Status 2–4
• Platelet count (<150 x 10^9/L)

• Group 1	0
• Group 2	1
• Group 3	2
• Group 4	3

NCCN guidelines,

Anaplastic Large Cell Lymphoma
Prognostic impact of
DUSP22 and TP63 rearrangements



Parrilla Castellar ER, et al. Blood. 2014;124(9):1473-80.

Striking Association of Lymphoid Enhancing Factor (LEF1) Overexpression and *DUSP22* Rearrangements in Anaplastic Large Cell Lymphoma

Aishwarya Ravindran, MBBS, Andrew L. Feldman, MD,* Rhett P. Ketterling, MD,† Surendra Dasari, PhD,‡ Karen L. Rech, MD,* Ellen D. McPhail, MD,* Paul J. Kurtin, MD,* and Min Shi, MD, PhD**

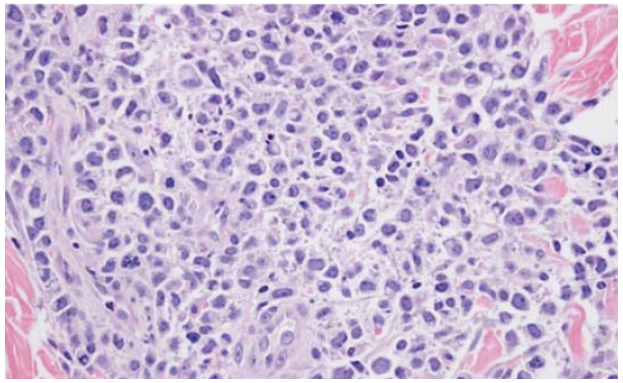
TABLE 2. The PPV and NPV of LEF1-high Positive Expression for *DUSP22* Rearrangement in ALK-negative ALCL

	ALK-negative ALCL		
LEF1 Expression	***DUSP22*-rearranged**	***DUSP22*-nonrearranged**	**Predictive Values**
LEF1-high positive*	15	1	PPV = 93.8%
LEF1-low positive/ negative*	1	24	NPV = 96.0%
	Sensitivity = 93.8%	Specificity = 96.0%	

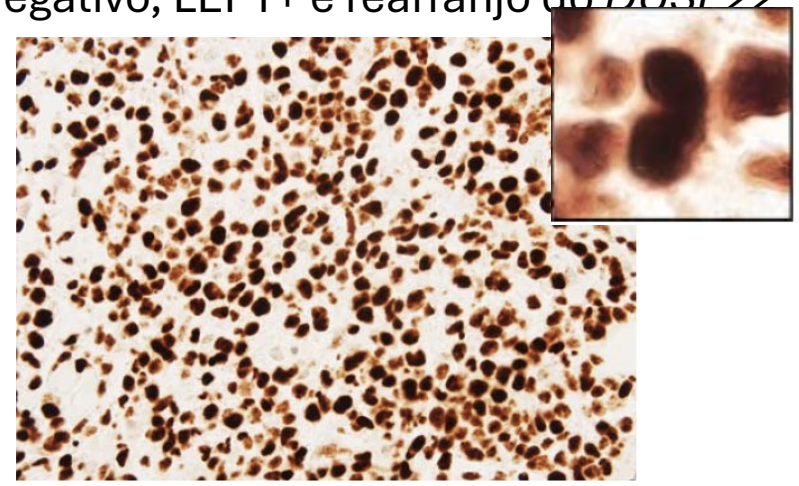
*LEF1-high positive was defined as 3+ LEF1 staining in > 75% of tumor cells. Otherwise, it was defined as LEF1-low positive/negative.
NPV indicates negative predictive value; PPV, positive predictive value.

LNH Anaplásico de células T (ALCL) ALK negativo

- 30% -Rearranjo do *DUSP22* → SG 5 anos: 90%
- 8% - Rearranjo do *TP63* → SG 5 anos: 42%
- 62% Triplo negativo → SG 5 anos: 17%



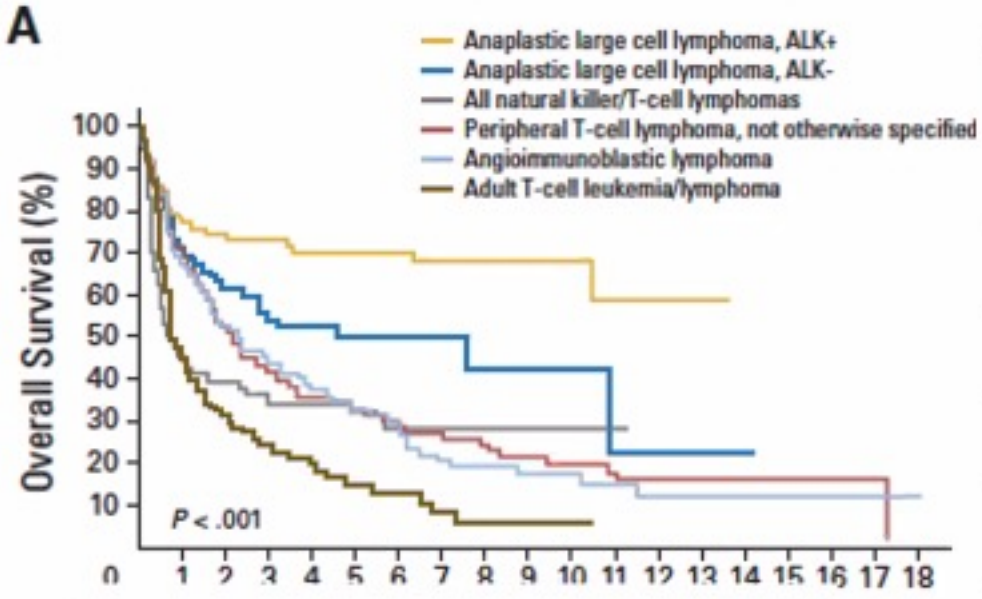
LNH Anaplásico de células T, ALK negativo, LEF1+ e rearranjo do *DUSP22*

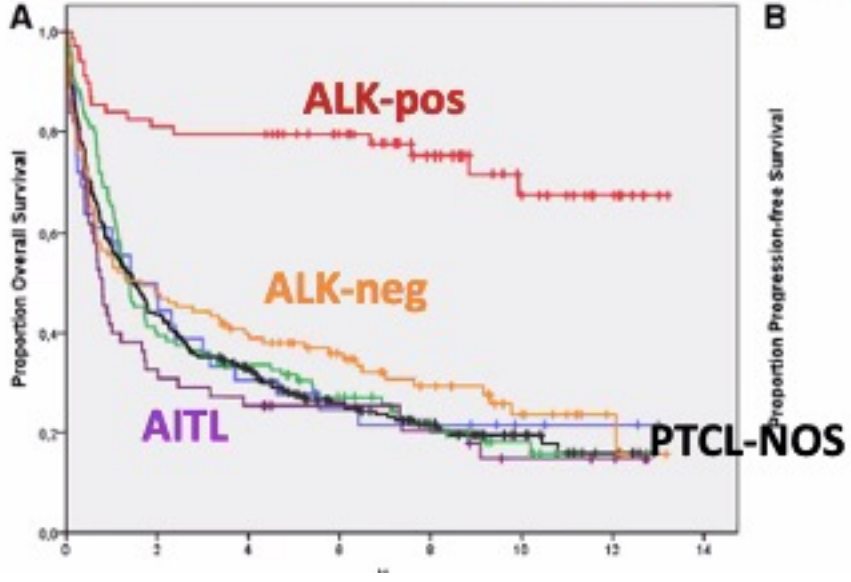


Lymphoide Enhancer-binding Factor (LEF1): Maturação de células T
Dual–specific Phosphatase 22 (DUSP22): supressor tumoral

Ravindran et al, Am J Surg Pathol 2021

Outcomes of most PTCL subtypes is poor



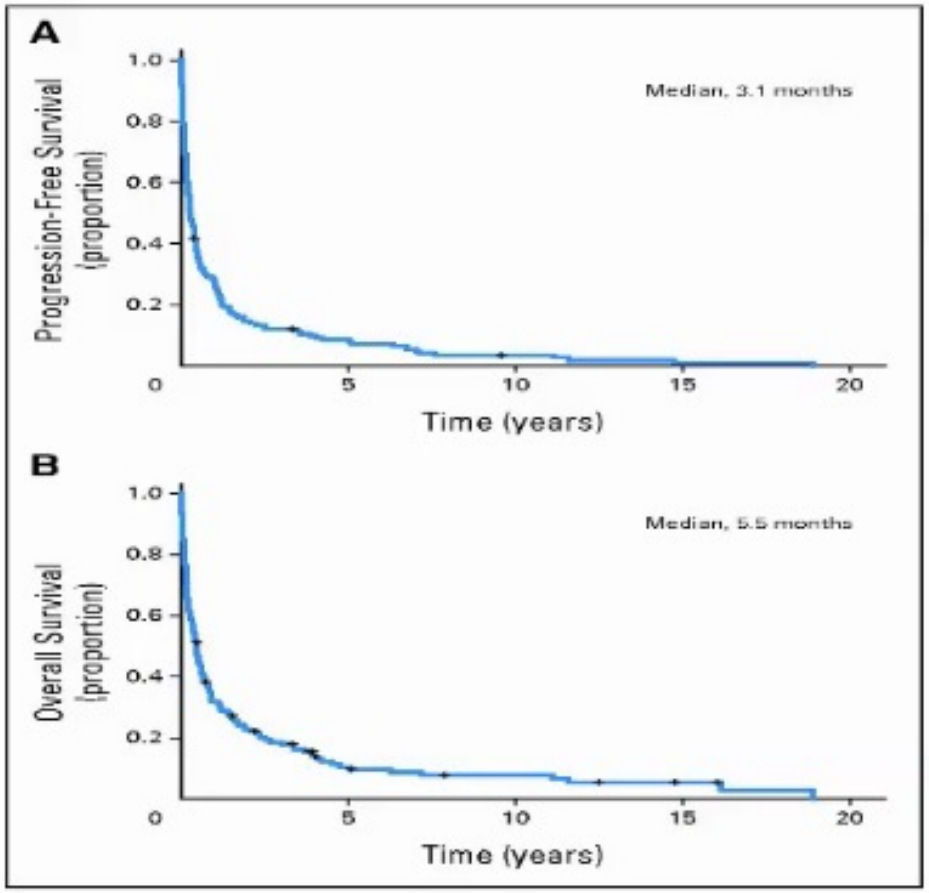


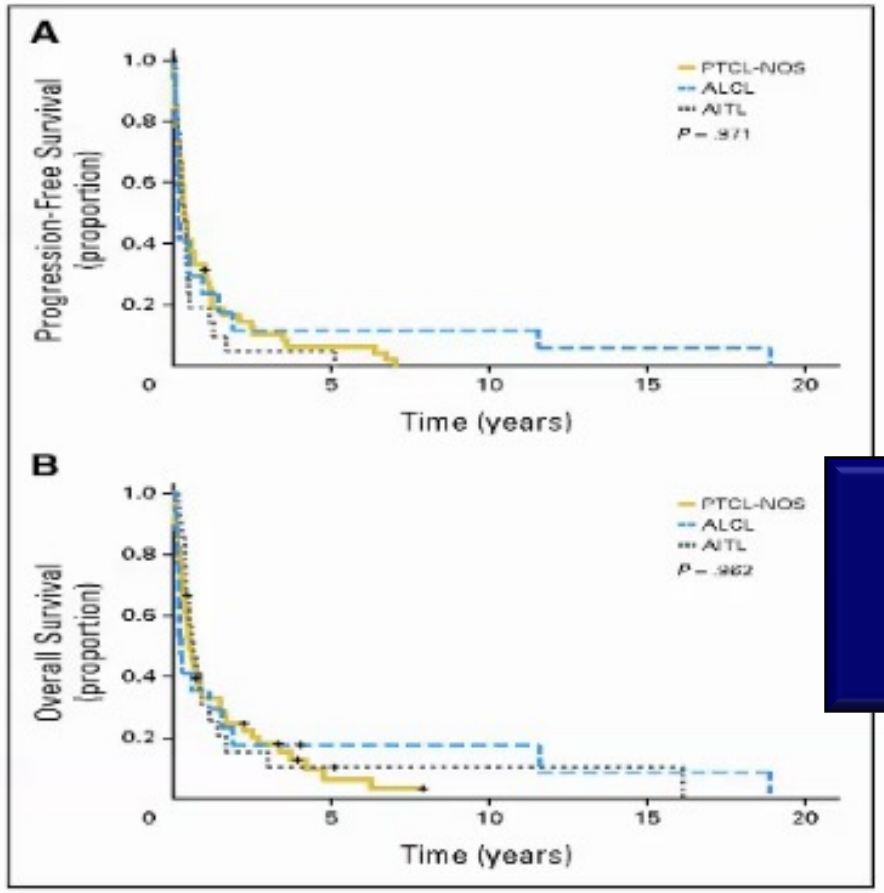
PTCL (ITLP)	5 y PFS	5 y OS
ALK-pos ALCL	60%	70%
ALK-neg ALCL	36%	49%
PTCL-NOS	20%	32%
AITL	18%	32%

PTCL(Swedish)	5 y PFS	5 y OS
ALK-pos ALCL	63%	79%
ALK-neg ALCL	31%	38%
PTCL-NOS	21%	28%
AITL	20%	31%

Vose et al. JCO 2012; Ellin et al. Blood 2014

First Relapse or Progression of PTCL





WITH Chemotherapy

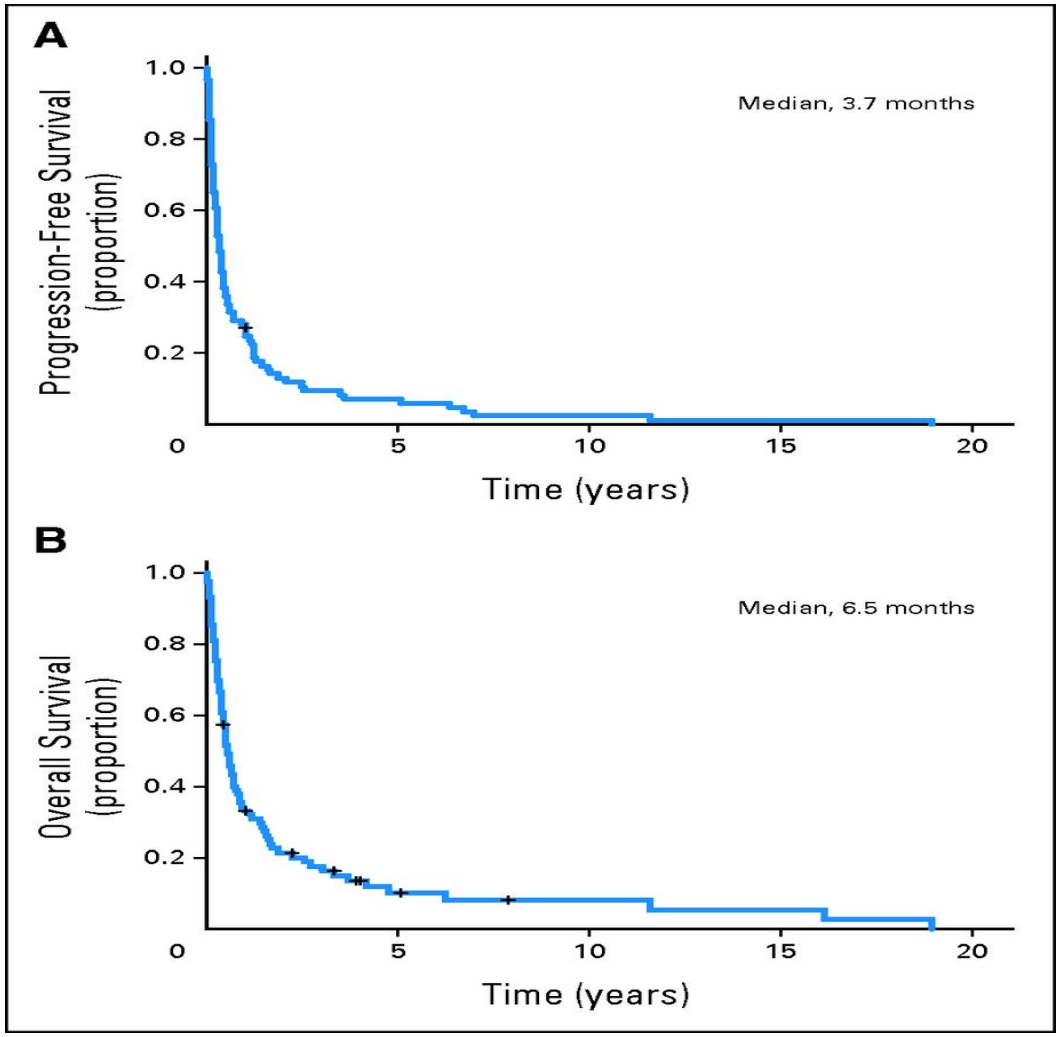
2nd PFS = 3.7 months

OS 2nd Relapse = 6.5 months

PTCL – peripheral T-cell lymphoma; PTCL-NOS – PTCL not otherwise specified;
ALCL – anaplastic large cell lymphoma; AITL - angioimmunoblastic T-cell lymphoma

Mak V et al. JCO 2013;31:1970-1976

PTCL After First Relapse: *Very Poor Overall Survival*



Mak V et al. JCO 2013;31:1970-1976

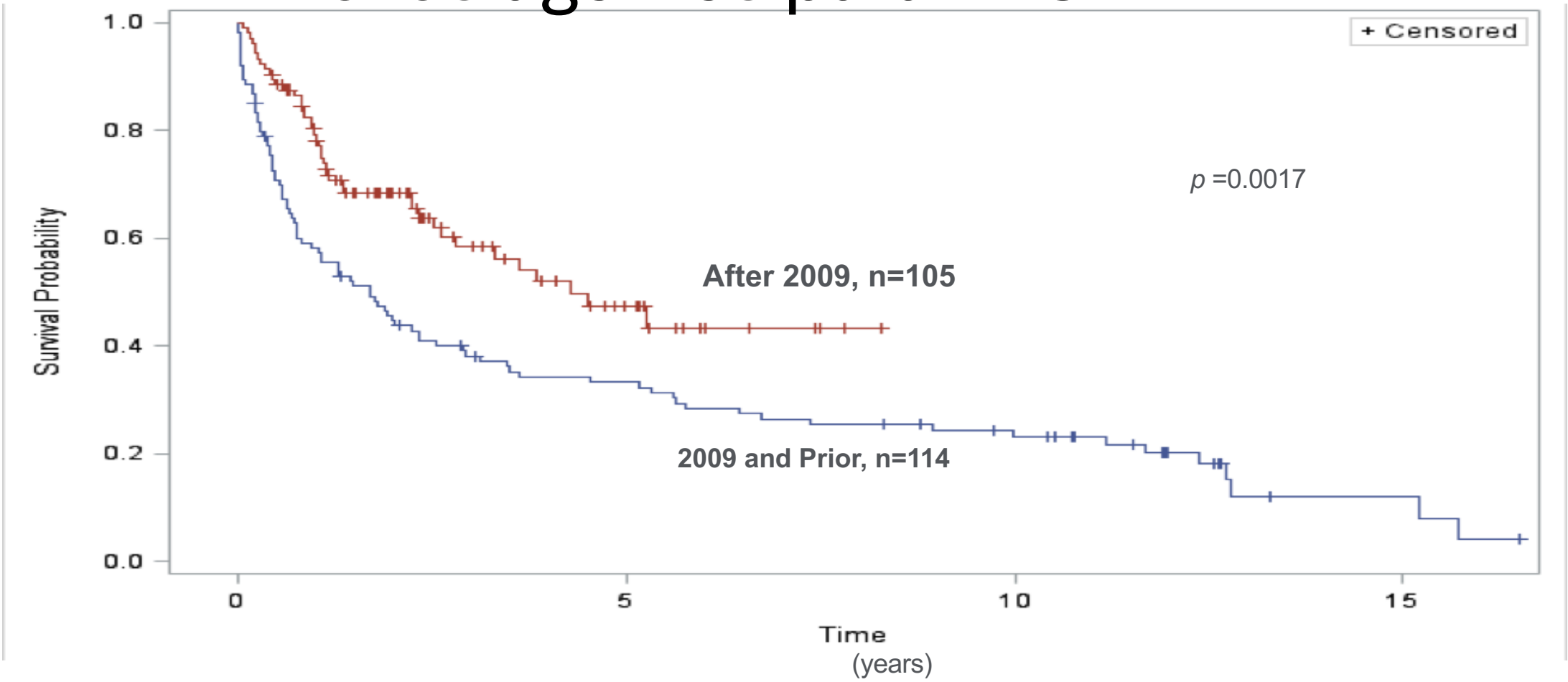
2nd PFS (median, 3.7 months) of patients treated with chemotherapy (n = 89) with R/R PTCL

2nd PFS = 3.7 months

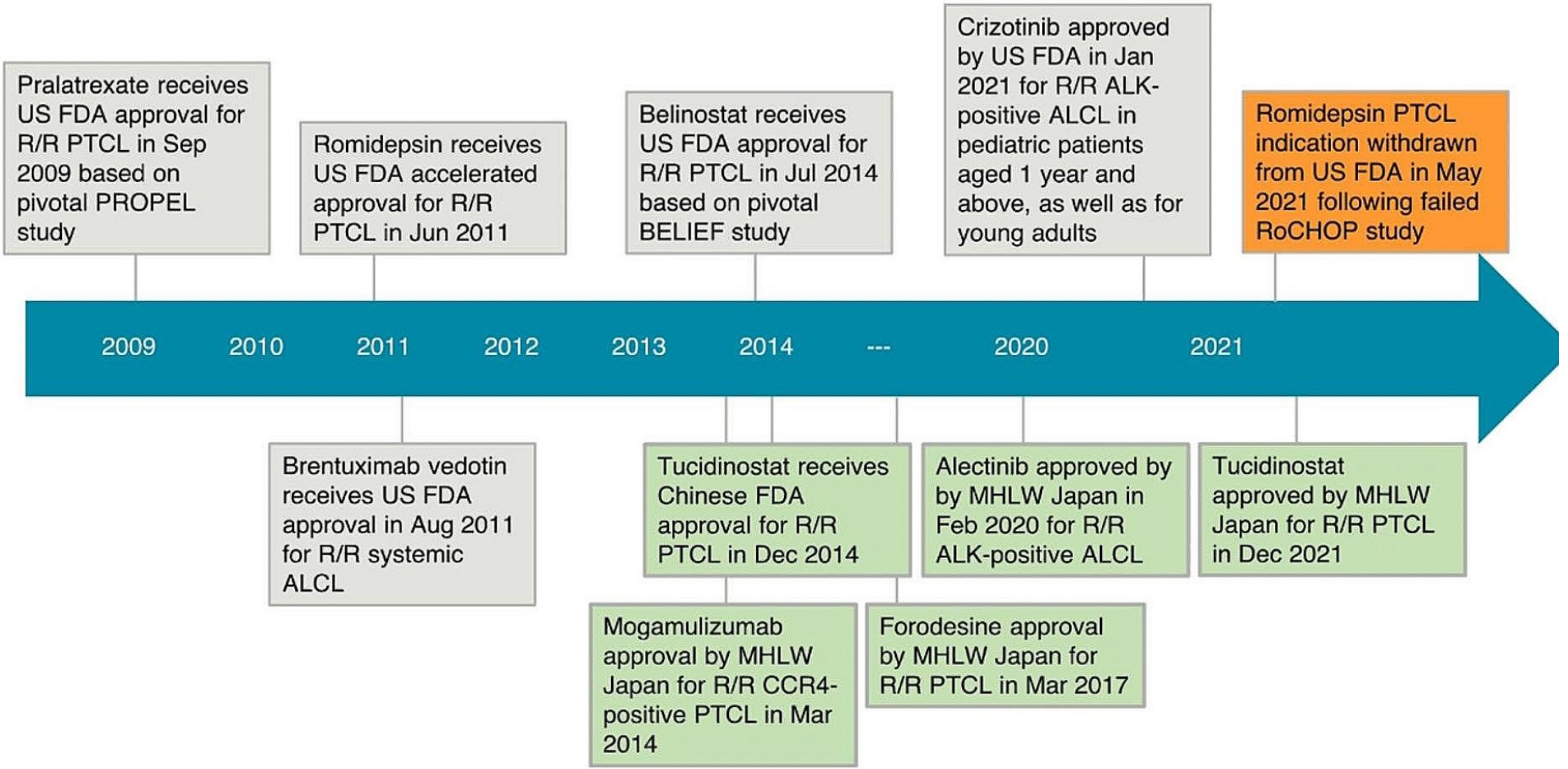
OS (median, 6.5 months) after first relapse or progression of PTCL.

Overall Survival from 2nd Relapse = 6.5 months

Melhora da Sobrevida após aprovação de novos agentes para PTCL RR



Ma et al., 2020. Hematol Oncol

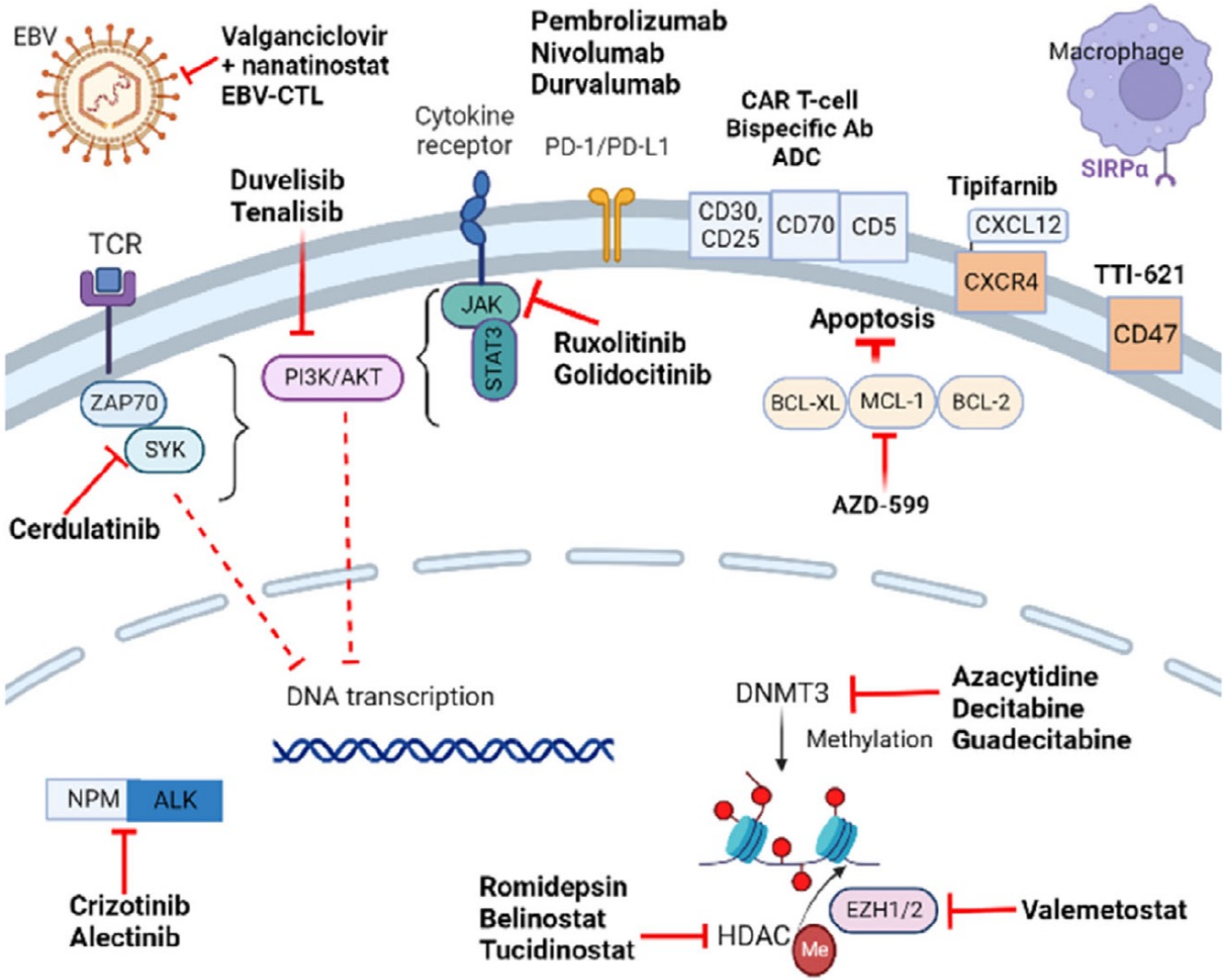


Chang et al. Journal of Hematology & Oncology 2024

ANNUAL CLINICAL UPDATES IN HEMATOLOGICAL MALIGNANCIES

AJH WILEY

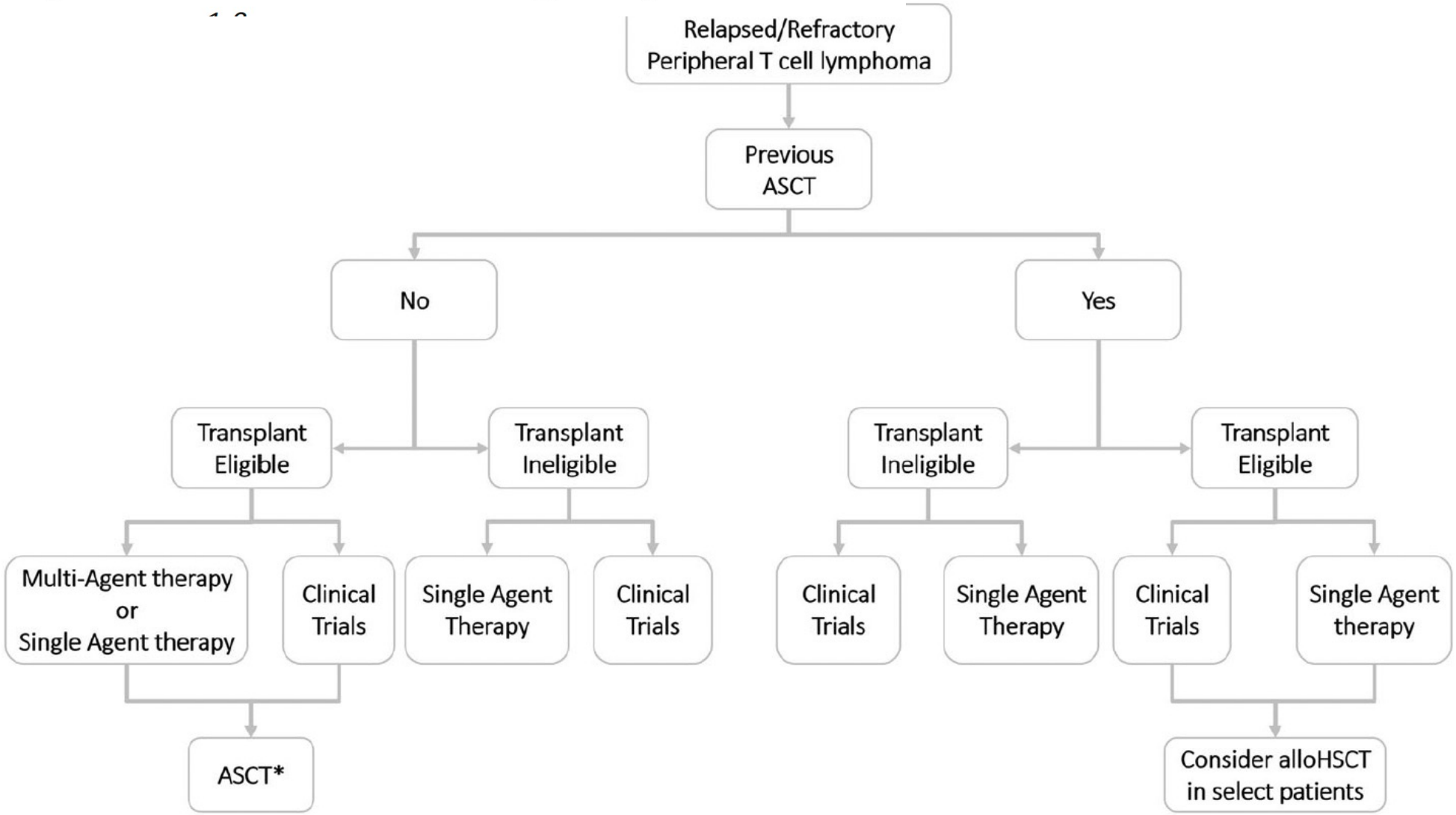
Aggressive T-cell lymphomas: 2024: Updates on diagnosis, risk stratification, and management



Shin Yeu Ong [1,2] | Jasmine M. Zain [1]

Am J Hematol. 2024;

How to Sequence Therapies in Peripheral T Cell Lymphoma



Kitsada Wudhikarn &N. Nora Bennani Curr. Treat. Options in Oncol. (2021)

CHALLENGES FOR CAR-T CELL THERAPY IN T-CELL NHL

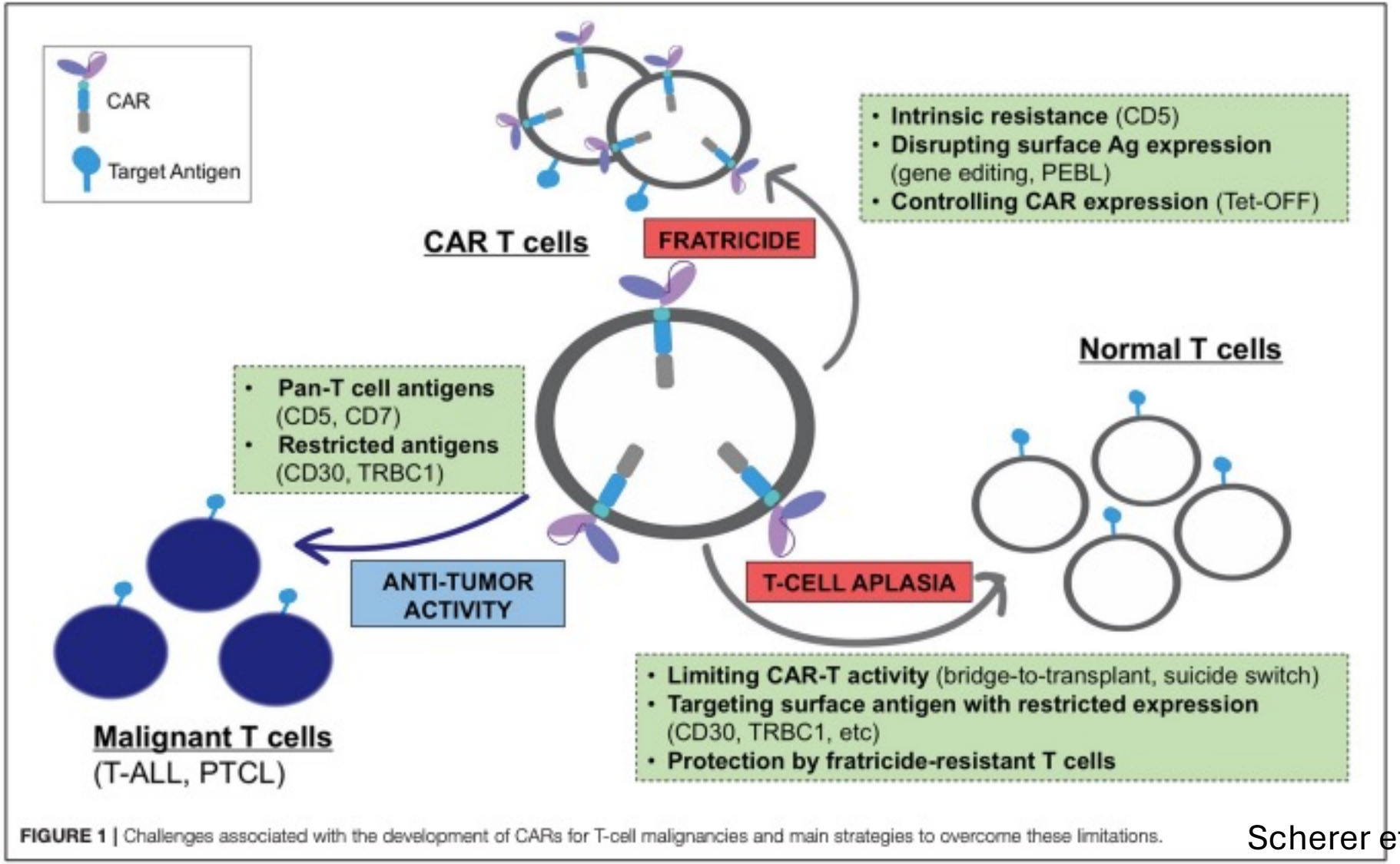


FIGURE 1 | Challenges associated with the development of CARs for T-cell malignancies and main strategies to overcome these limitations.

Scherer et al. Front Onc 2019;

Evidence for autologous/allogeneic SCT in R/R PTCL: from retrospective studies and registry data.

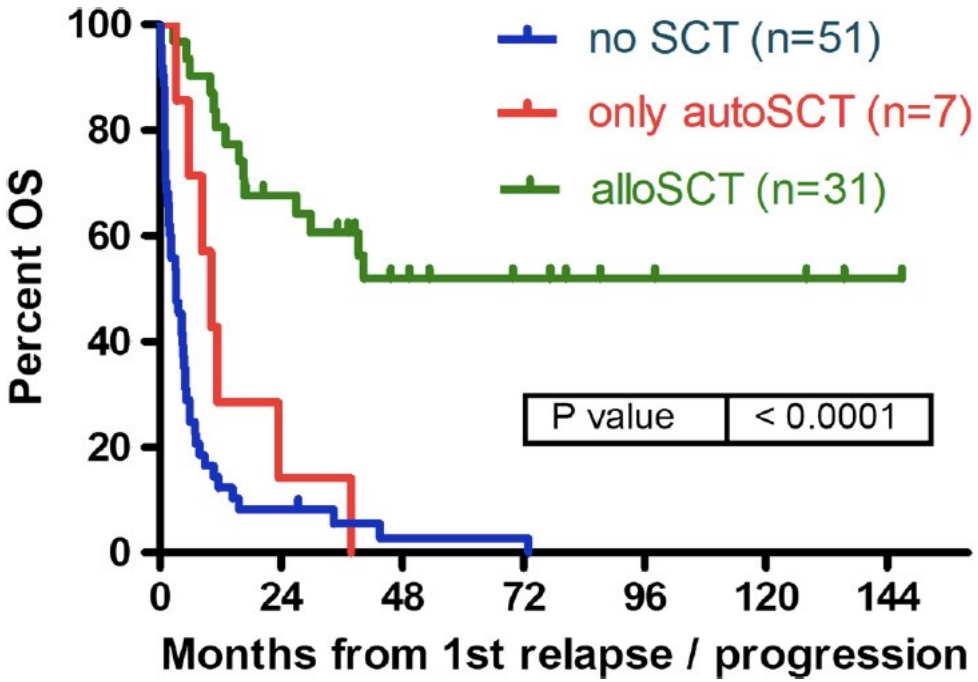
Study	Patients	Follow-up	3-Year OS	3-Year PFS	TRM	Key Findings
EBMT/CIBMTR Collaboration	~2,000 Haplo-SCT (ptCY), MSD, MUD TCD+/TCD–	Median 38 months	~60%	~50%	N/A	- AITL outcomes superior to non-AITL - No donor source outcome differences - Active disease/poor performance predict worse outcomes - Infections caused 19% of deaths
U.S. Multicenter Analysis	508	2-year, 5-year	59.1% (2y), 50.8% (5y)	45.8% (2y), 39.5% (5y)	11.2% (1y), 22% (3y)	- AITL trended toward better 5y PFS - Disease status at transplant critical: 3y PFS 57% (CR) vs. 36% (refractory) - 3y OS: 68% (CR) vs. 49% (refractory)
Meta-Analysis (30 trials)	880 (Allo-SCT), 885 (Auto-SCT)	2001–2020	50% (Allo-SCT), 55% (Auto-SCT)	N/A	33–40% (Allo-SCT), 6–17% (Auto-SCT)	- Allo-SCT survival advantage in chemo-refractory patients - Auto-SCT data confounded by inclusion of first-remission patients
Retrospective Comparisons	N/A	N/A	N/A	N/A	33–40% (Allo-SCT), 6–17% (Auto-SCT)	- No clear allo-SCT benefit over auto-SCT due to high TRM - TRM rates reflect outdated practices; modern protocols likely better

Foley and Mehta-Shah, Curr Oncol Rep. 2023

Allo transplant – RR PTLC

The impact of stem cell transplantation on the natural course of peripheral T-cell lymphoma: a real-world experience

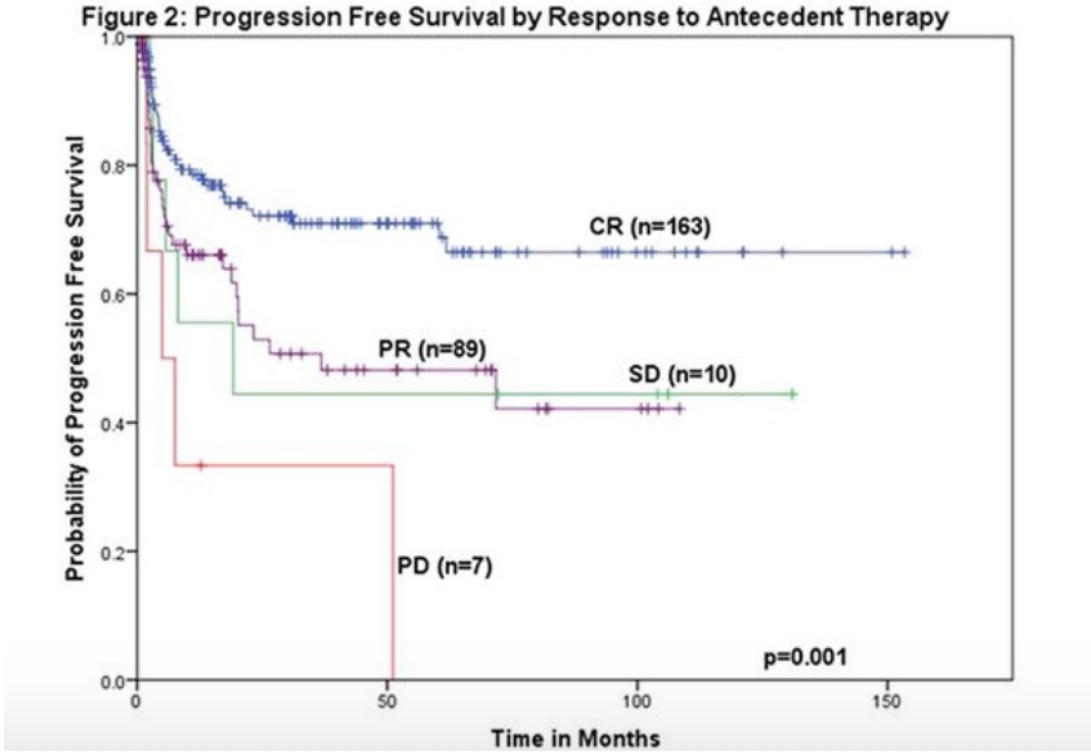
Sarah Rohlfing[1,2] · Sascha Dietrich[1] · Mathias Witzens-Harig[3] · Ute Hegenbart[1] · Stefan Schönland[1] · Anthony D. Ho[1] · Peter Dreger[1]



Rolfing et al., Ann Hematol 2018

Successful Treatment of Mature T-Cell Lymphoma with Allogeneic Stem Cell Transplantation: The Largest Multicenter Retrospective Analysis

Neha Mehta-Shah, MD, Stephanie Teja, Yu Tao, MD, Amanda F. Cashen, MD, Anne Beaven, MD, Onder Alpdogan, MD, Pierluigi Porcu, MD, Mackenzie Wiggin, Kevin W Song, MD, Musa Alzahrani, Parastoo B. Dahi, MD, Alison J. Moskowitz, MD, Steven M. Horwitz, MD, Eric D. Jacobsen, MD

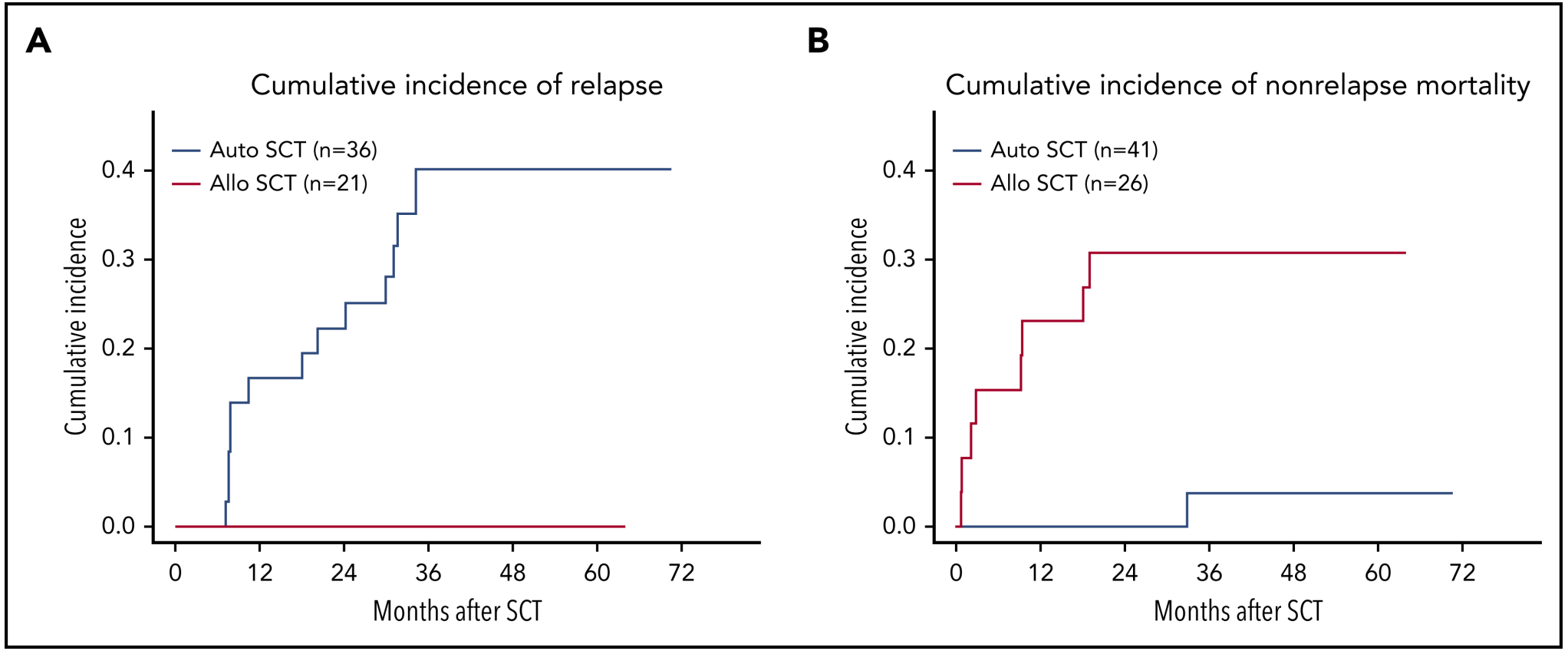


Mehta-Shah et al, ASH 2017

Comment on Schmitz et al, page 2646

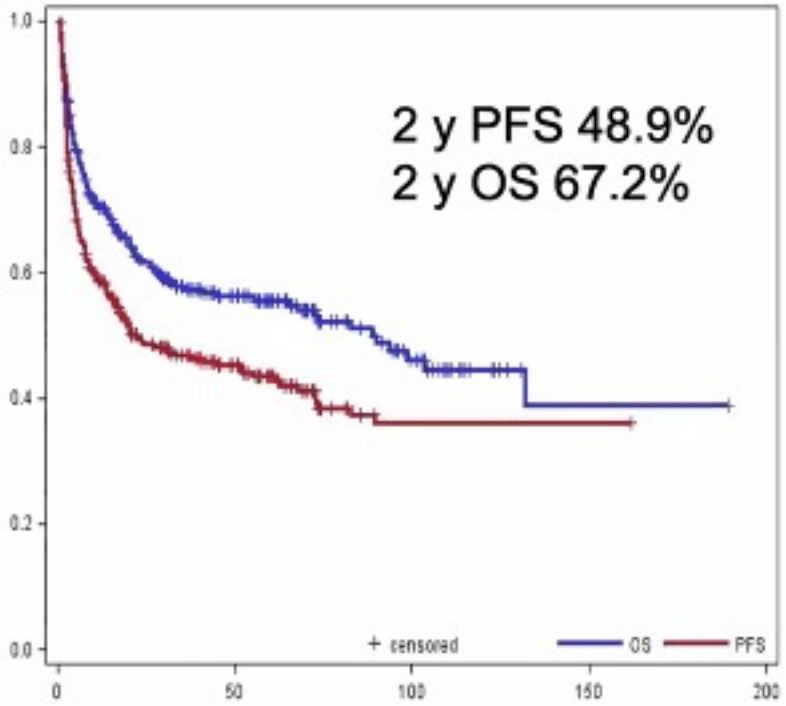
Outcomes for PTCL: which pathway to success?

Julie M. Vose | University of Nebraska Medical Center



Julie M. Vose,Blood, 2021,

Allogeneic SCT in PTCL/CTCL



PTCL subtype Total n=301	2 y PFS
AITL (n=50)	60.3%
PTCL-NOS (n=82)	60.3%
ALCL n=10	25%
6 month TRM	9.2%

SOHO, 2020

State of the Art & Next Questions: T-cell Lymphoma

SOHO Highlights
Kerry J. Savage MD MSc FRCP(C)
Professor of Medicine, University of British Columbia
Medical Oncologist, BC Cancer

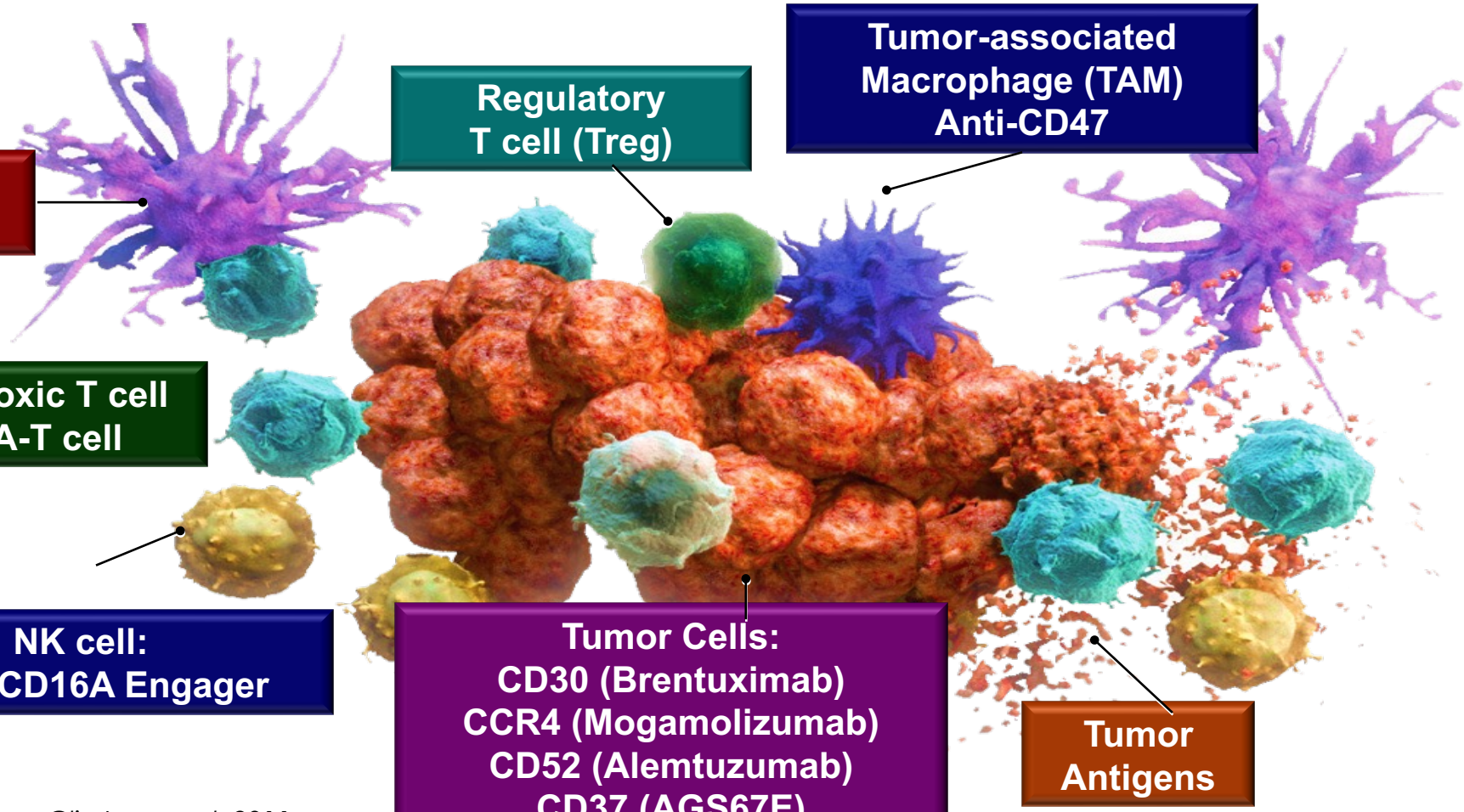
Courtesy of N. Mehta-Shah T-cell forum 2018

Transplant in R/R PTCL

- Survival Rates:
  - Allo-SCT: 50–60% 3-year OS; auto-SCT: ~55% 3-year OS (bias: patient selection, etc).
- Graft Sources: No significant outcome differences: haplo-SCT, MSD, or MUD.
- Key Prognostic Factors:
  - Disease status at transplant (CR > PR > refractory).
  - Histology (AITL has better outcomes).
- TRM: allo-SCT (33–40%) vs. auto-SCT (6–17%) (modern protocols may improve it)
- Clinical Practice:
  - Auto-SCT recommended in first remission for eligible patients.
  - Allo-SCT is salvage therapy for R/R disease after achieving disease control.

Foley and Mehta-Shah, Curr Oncol Rep. 2023

TARGETS IN RR PTCL



BI-ESPECÍFICO

CD38, BCL2, PDGFR alfa/beta

Warrington R, et al . *Allergy Asthma Clin Immunol*. 2011.
Smyth MJ, et al. *Nat Rev Clin Oncol*. 2016.
Melero I, et al. *Nat Rev Cancer*. 2014.

AJH WILEY

Aggressive T-cell lymphomas: 2024: Updates on diagnosis, risk stratification, and management

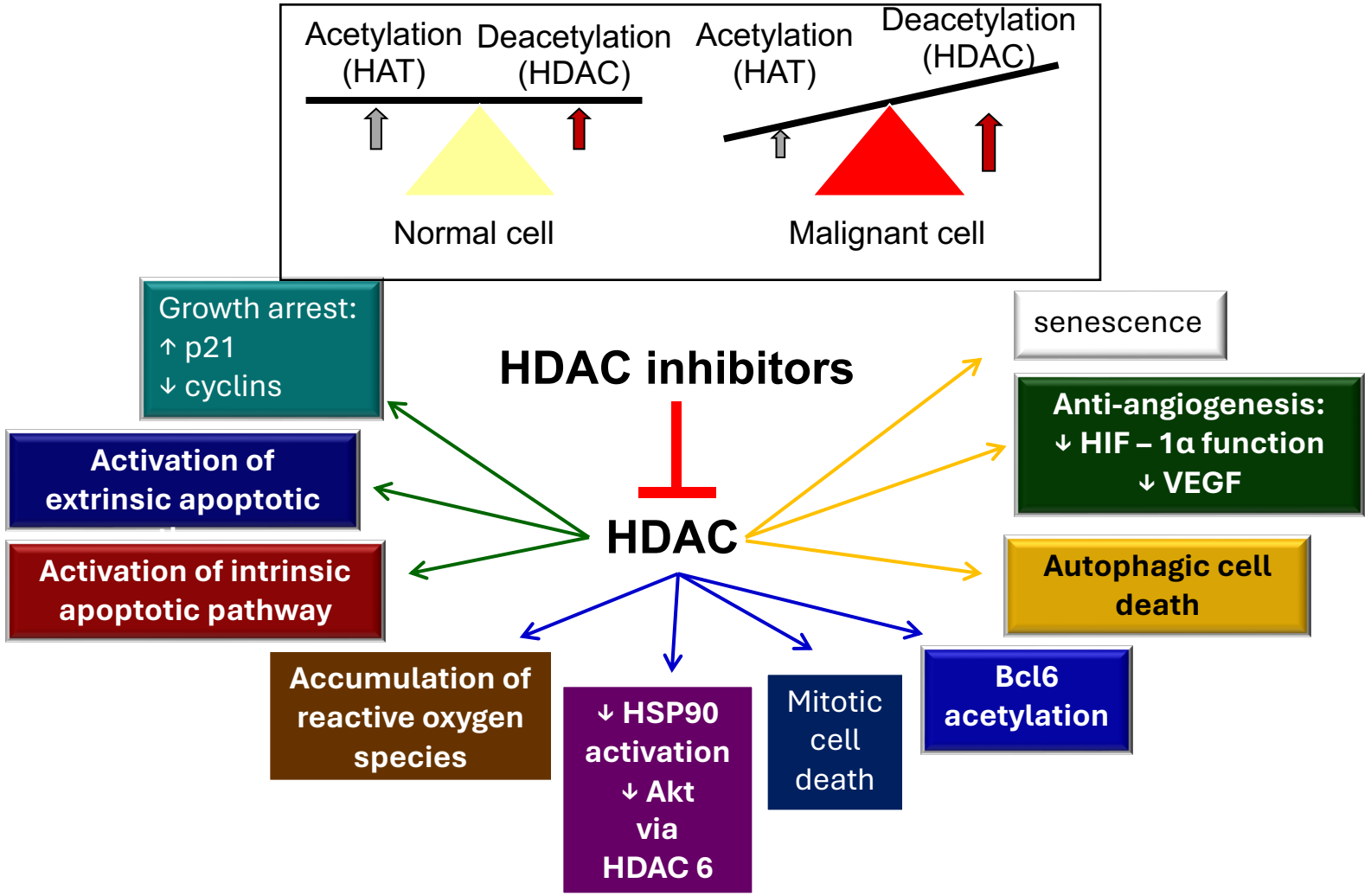
TABLE 3 FDA-approved novel agents for relapsed/refractory peripheral T-cell lymphoma.

Agent	N in pivotal trial	Subtype	ORR/CR	Response by histology ORR/CR	Outcomes
Pralatrexate[104]	109	All subtypes	29%/11%	PTCL-NOS 32% ALCL- 35%	DOR = 10.1 months (1–22.1)
Romidepsin[105]	130	All subtypes	25%/15%	AITL-30/19	DOR = 28 months (1–48) Median OS = 11.3 months Time to CR = 3.7 months
Belinostat[106]	129	All subtypes	26%/11%	AITL-46%/18% ENKTL-50%	DOR = 13.6 months (4.5–29.4)
Brentuximab Vedotin[103]	58	ALCL	86%/59%		DOR = 13.2 months (5.7–26.3) OS = 70% at 1 year, 64% at 4 years
Mogamulizumab[107]	27	ATLL	50%/31%	Approved for CTCL in the US and CCR4+ PTCl in Japan	Median PFS 5.2 months
Chidamide[108]	79	PTCL	28%/14%	Approved in China	Median PFS 2.1 months, OS 21.4 months
Crizotinib[109]	26	ALK+ ALCL	88/83		

Shin Yeu Ong[1,2] | Jasmine M. Zain[1]

Am J Hematol. 2024;

THE DIVERSE BIOLOGICAL EFFECTS OF HDAC INHIBITORS



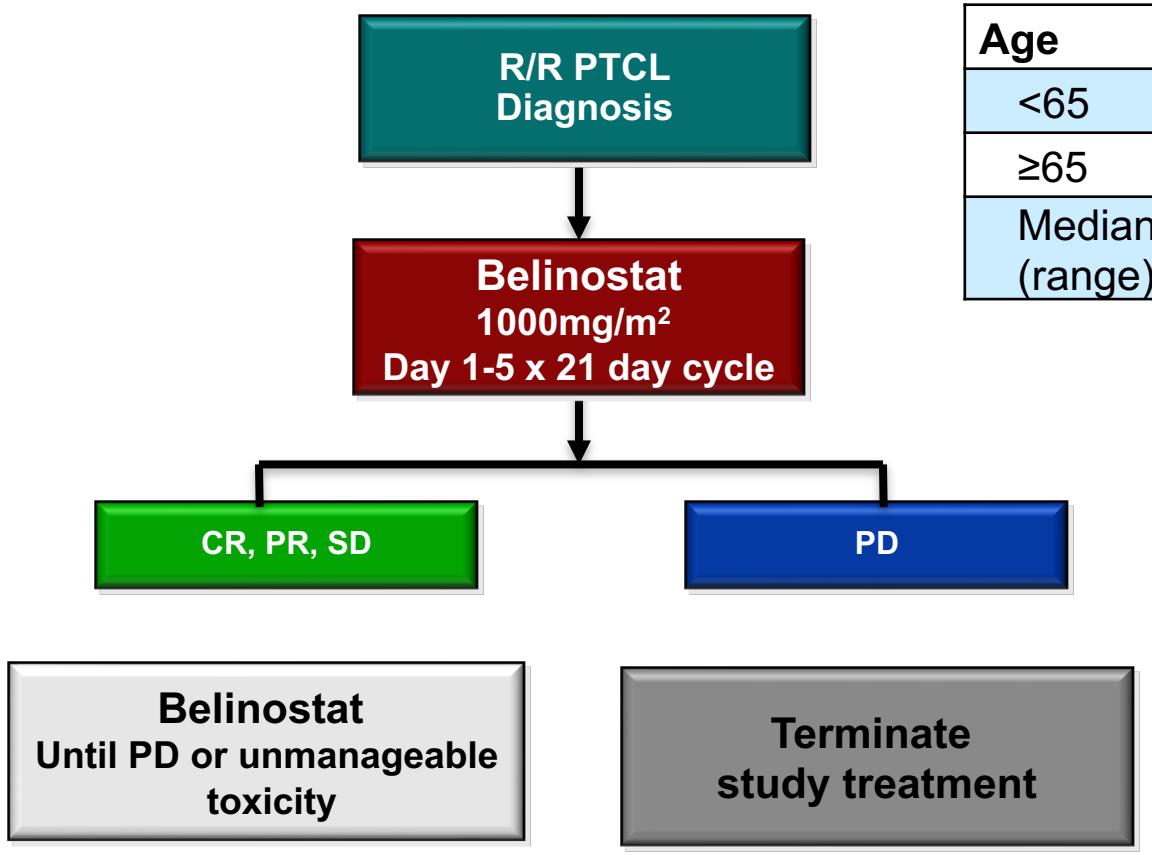
Xu WS et al. Oncogene. 2007

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

Owen A. O'Connor, Steven Horwitz, Tamás Masszi, Achiel Van Hoof, Peter Brown, Jeannette Doorduijn, Georg Hess, Wojciech Jurczak, Poul Knoblauch, Shanta Chawla, Gajanan Bhat, Mi Rim Choi, Jan Walewski, Kerry Savage, Francine Foss, Lee F. Allen, and Andrei Shustov

VOLUME 33 · NUMBER 23 · AUGUST 10 2015

JOURNAL OF CLINICAL ONCOLOGY



Age	
<65	67 (52)
≥65	62 (48)
Median, yr (range)	63 (29-81)

O'Connor et al; JCO 2015

R/R PTCL , Relapsed and/or Refractory Peripheral T Cell Lymphoma; CR, complete response; PR, partial response; SD, stable disease; PD progressive disease

PHASE II BELINOSTAT STUDY: BELINOSTAT IN R/R CTCL OR PTCL

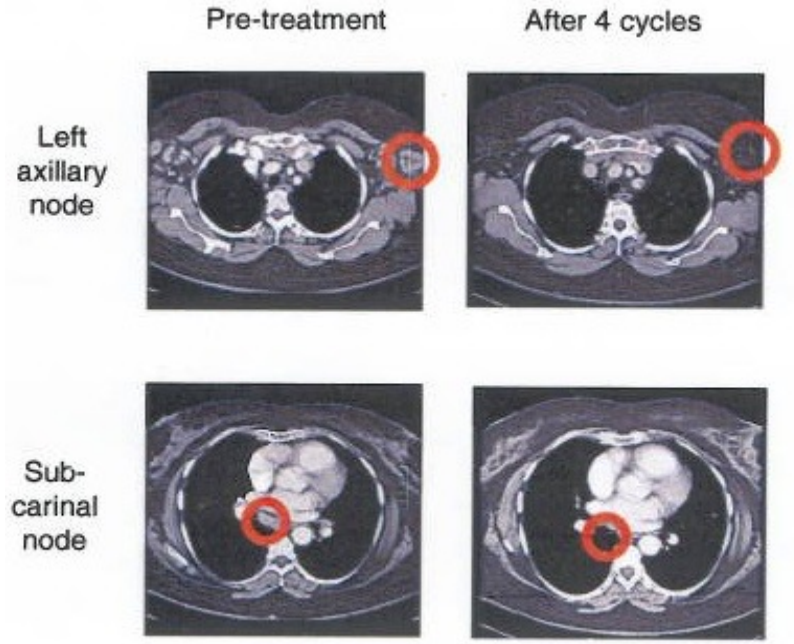
- CTCL or PTCL
- Failed ≥1 prior systemic therapy

(N=53; 48 evaluable: 29 CTCL, 19 PTCL)

- **CTCL and PTCL arms analyzed separately**

Belinostat 1000 mg/m² IV Days 1-5 q21d x 2 → **Belinostat up to 6 more cycles* or until PD**

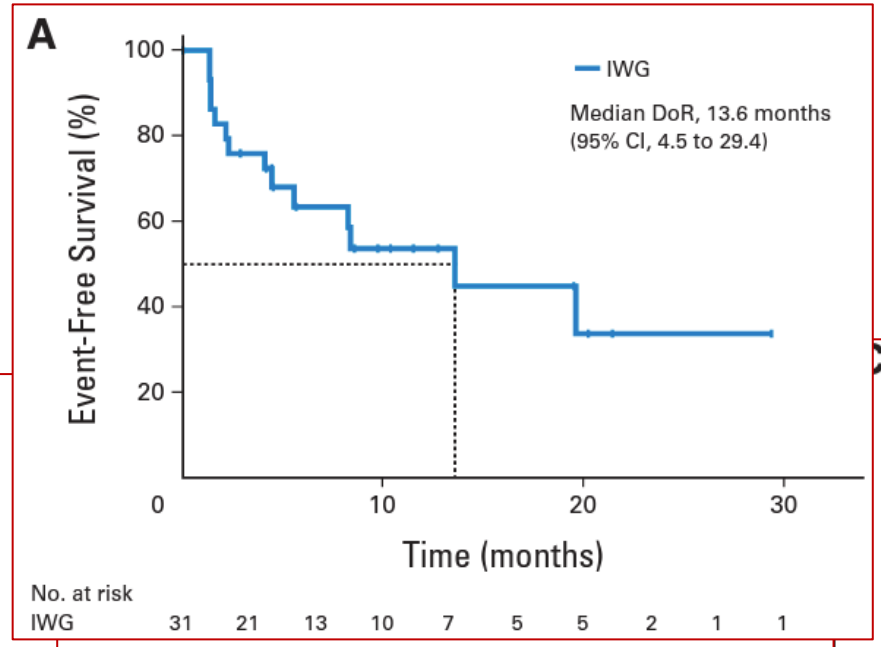
Prior Therapy for PTCL	N = 129 n (%)
Median number of therapies (range)	2 (1-8)
Systemic therapy	**129 (100)**
CHOP or CHOP-like	125 (96)
Stem cell transplant	**29 (23)**
Autologous	27 (21)
Allogeneic	2 (2)
Radiation therapy	**28 (22)**

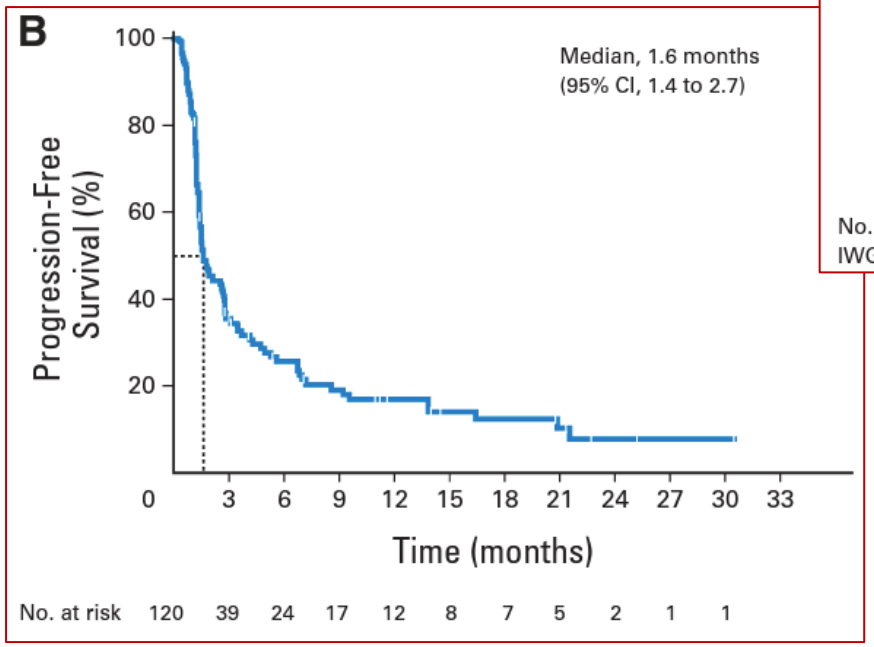


CT Scan in a Patient With PTCL-NOS Achieving a CR

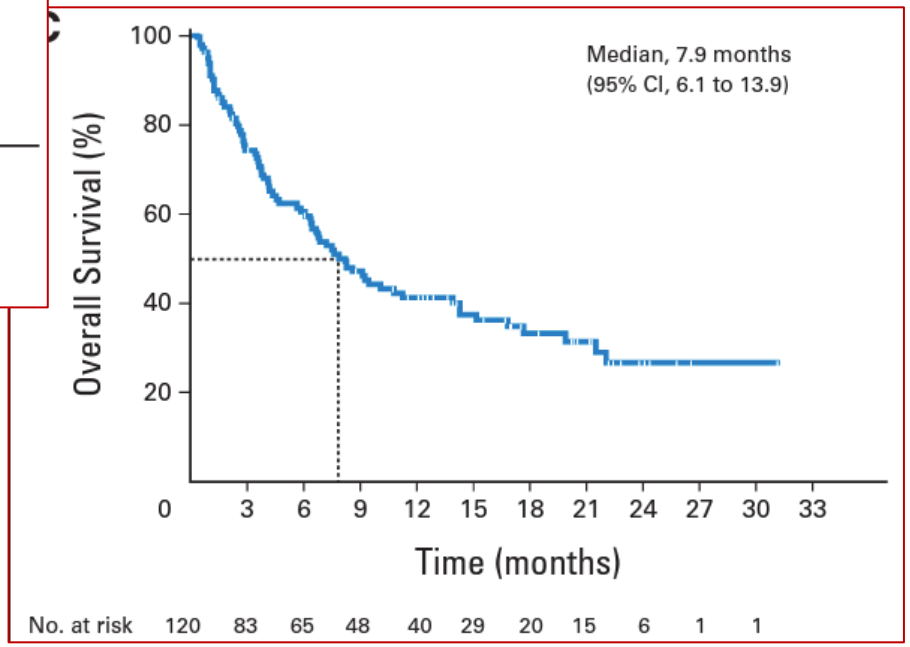
O'Connor et al; JCO 2015

Estudo BELIEF – Belinostat – fase 2





N= 120
TRG 26%
(11% RC)



O'Connor et al; JCO 2015

BELIEF - BELINOSTAT PHASE 2

O. A. O'Connor et al., JCO, 2015;

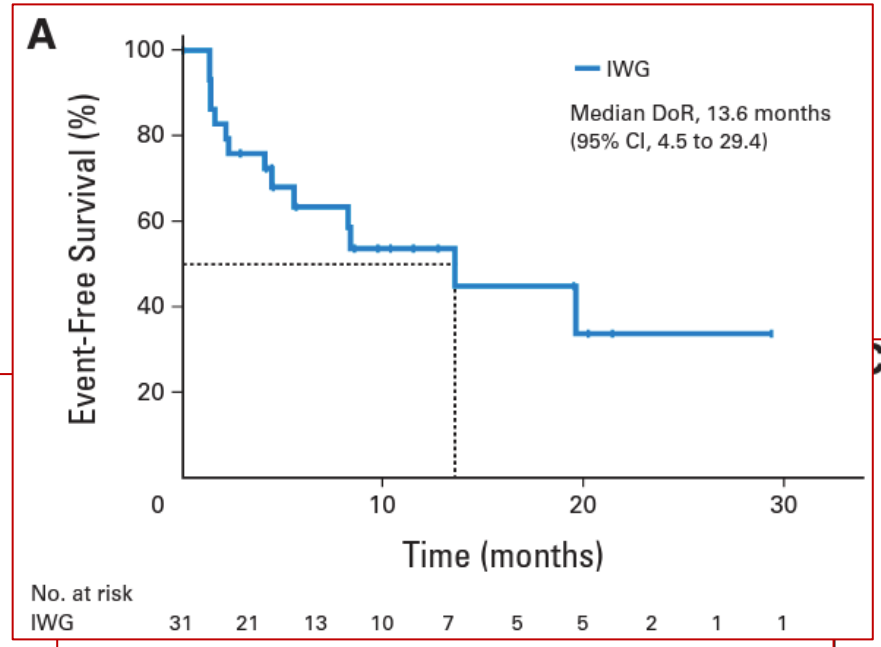
	Efficacy Analysis Set (N=120)	
Response	**n (%)**	**(95% CI)**
ORR	**31 (26)**	**(18-35)**
CR	13 (11)	(6-18)
PR	18 (15)	
SD	18 (15)	
PD	48 (40)	
NE	23 (19)	

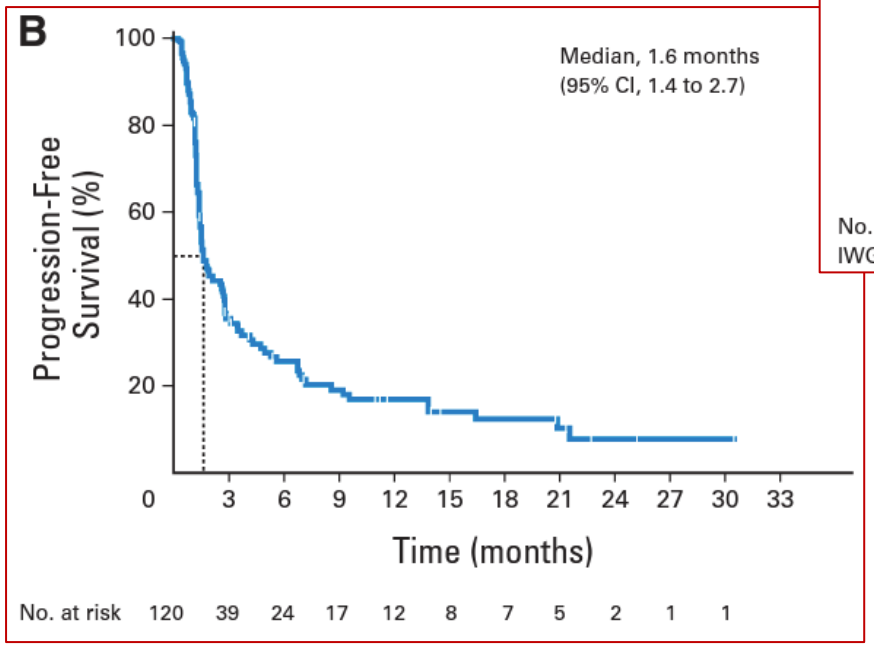
BELIEF: Response Rate by CPRG Lymphoma Diagnosis

O. A. O'Connor et al; 2015; JCO

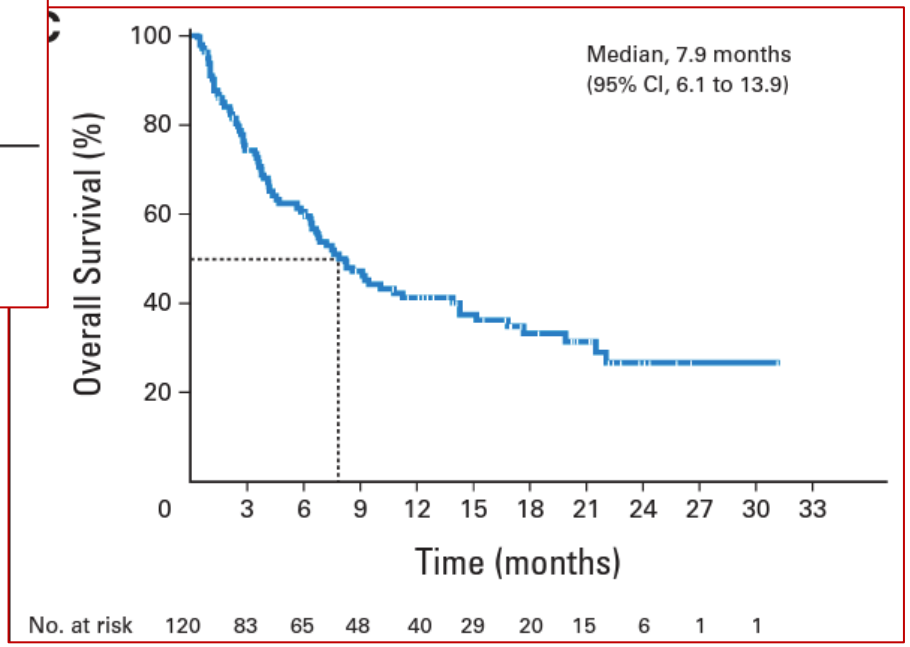
	Subset	Responders
CPRG lymphoma diagnosis	**n (%)**	**n (%)**
PTCL, NOS	77 (64)	18 (23)
AITL	22 (18)	10 (46)
ALCL, ALK-negative	13 (11)	2 (15)
ALCL, ALK-positive	2 (2)	0 (0)
Enteropathy-associated TCL	2 (2)	0 (0)
Extranodal NK/TCL, nasal type	2 (2)	1 (50)
Hepatosplenic TCL	2 (2)	0 (0)

Estudo BELIEF – Belinostat – fase 2





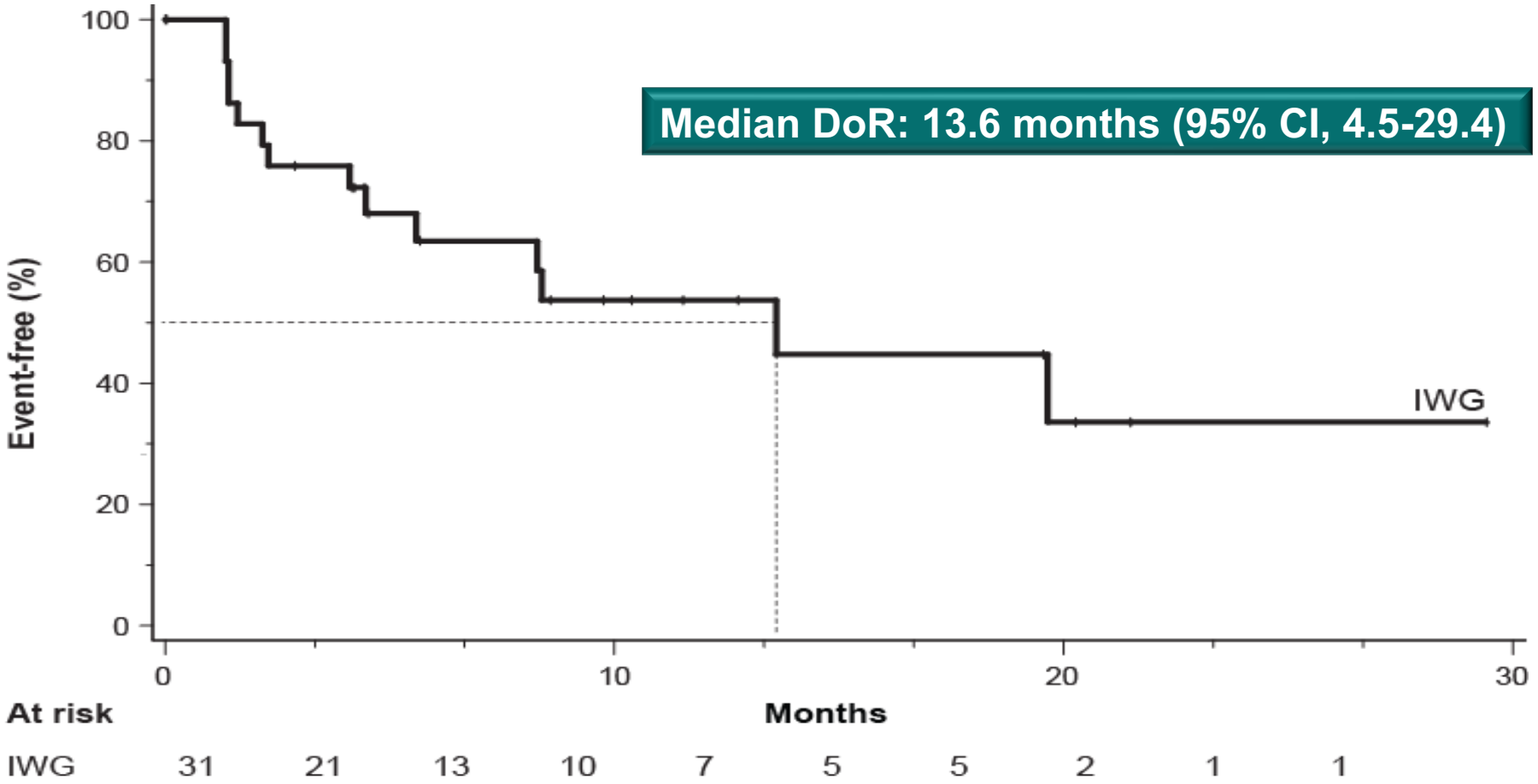
N= 120
TRG 26%
(11% RC)



O'Connor et al; JCO 2015

BELIEF: DURATION OF RESPONSE (DOR) PER CENTRAL REVIEW (IWG CRITERIA)

O. A. O'Connor et al; 2015; JCO



BELINOSTAT SAFETY REVIEW: Toxicity

- The most common toxicities associated with belinostat
  - Nausea (43%) and vomiting (29%)
  - fatigue (35%)
  - constipation (16%)
  - diarrhea (17.6%)
  - anorexia (11.9%)
  - fever (14.5%)
  - dyspnea (7.8%)
  - hypersensitivity or injection site reactions (7.6%).
  - Cardiac abnormalities largely consisted of QTc prolongations and were present in 4.3% of cases

BELINOSTAT SAFETY REVIEW: Toxicity

- 190 grade 3/4 toxicities were reported among 512 patients.
- Grade 3/4 infection occurred in five patients (1%)
- Hematologic AEs of any grade occurred in 26.6% of patients
  - Thrombocytopenia (7.0%)
  - Anemia (12.7%)
  - Lymphopenia (3.9%).
  - Neutropenia was rare (2.5%)

** Most patients had underlying cytopenias that preceded treatment.

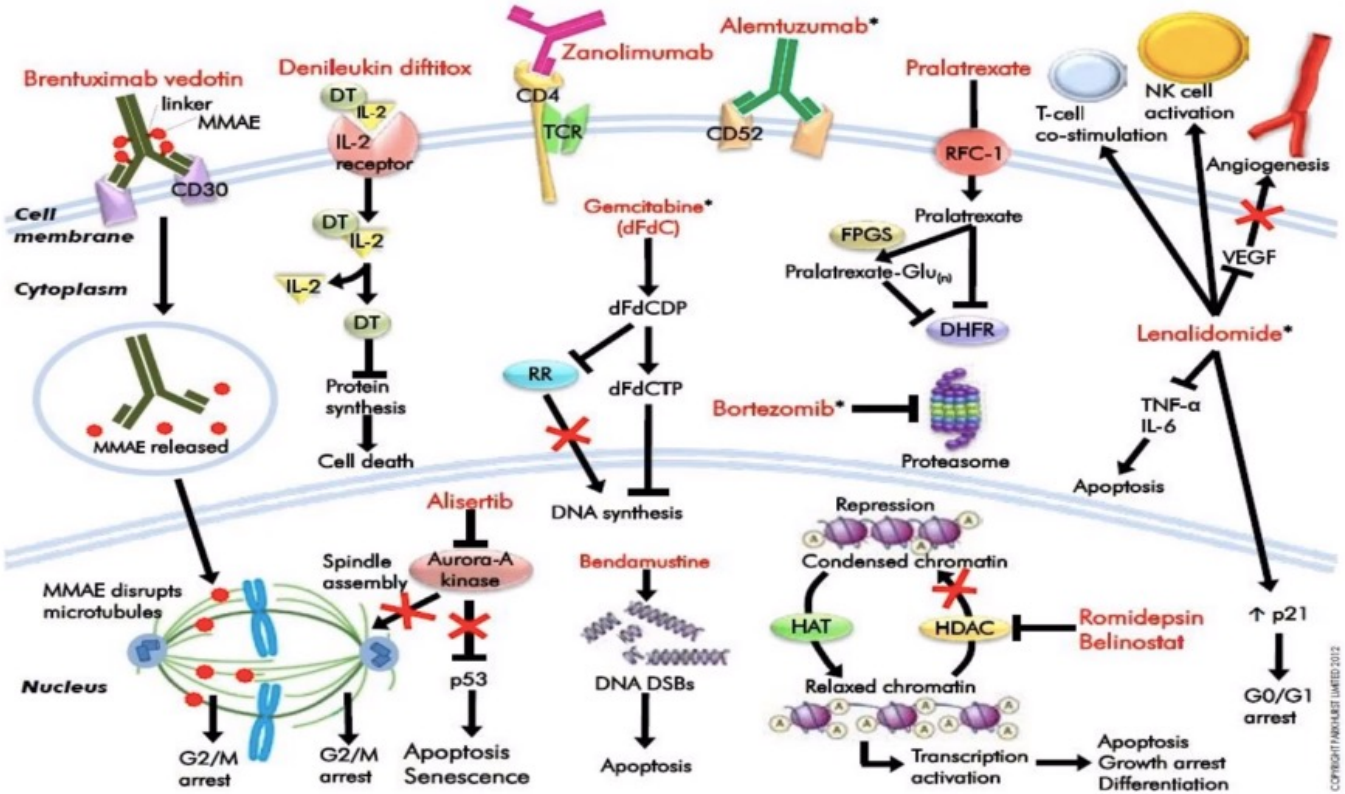
BELINOSTAT REVIEW: Results

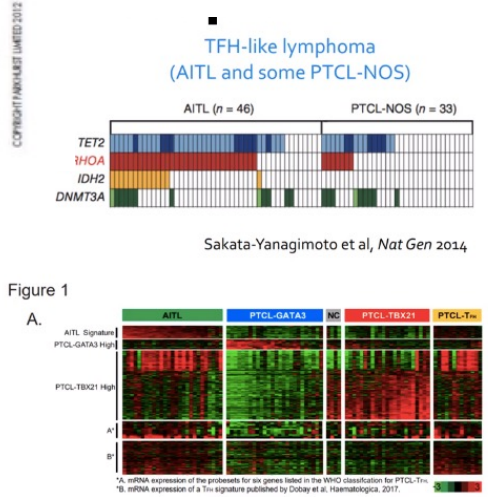
Table 3 Summary of efficacy analysis

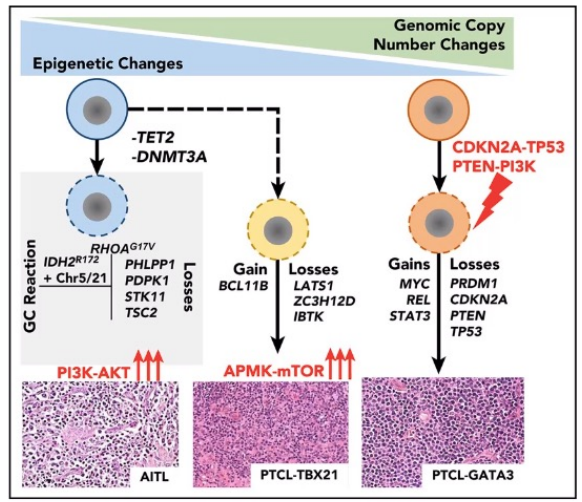
Study	Study type	PTCL (n)	ORR (n)	CR (n)	PR (n)	DOR	Dose	Discontinue for AE
O'Connor et al (BELIEF)[22]	Phase II	120	31	13	18	13.6 months	87.6% at target dose	16
Foss et al[21]	Phase II	24	6	2	4	109 days	Dose exposure: 7,450–83,415 mg over 3–182 days Median of ten doses	3
Reimer et al[23]	Case report	1[a]	1[a]	1[a]	–	39 months (ongoing)	28 cycles	Treated with maintenance, then discontinue in CR
Total		144	37	15	22			
%			25.7	10.4	15.3			

Note: [a]Case report was not included in response calculations.
Abbreviations: AE, adverse event; CR, complete response; DOR, duration of response; ORR, overall response rate; PR, partial response; PTCL, peripheral T-cell lymphoma.

How to improve efficacy of Targeted therapies in PTCL?







GAP 2019
Innovation & Collaboration to Transform Patient Care

REVIEW

Biomarker-driven management strategies for peripheral T cell lymphoma

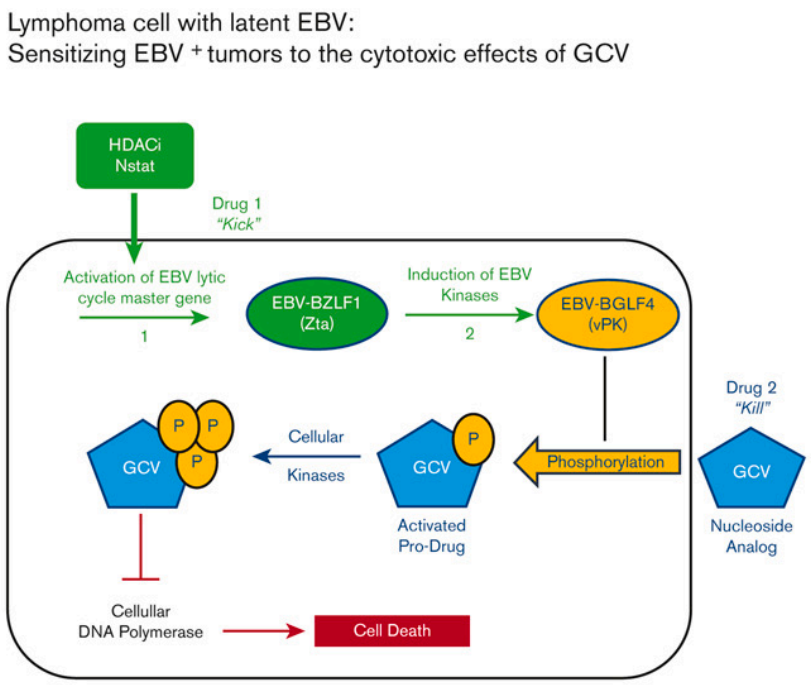
Novel agents and combinations under investigation in PTCL

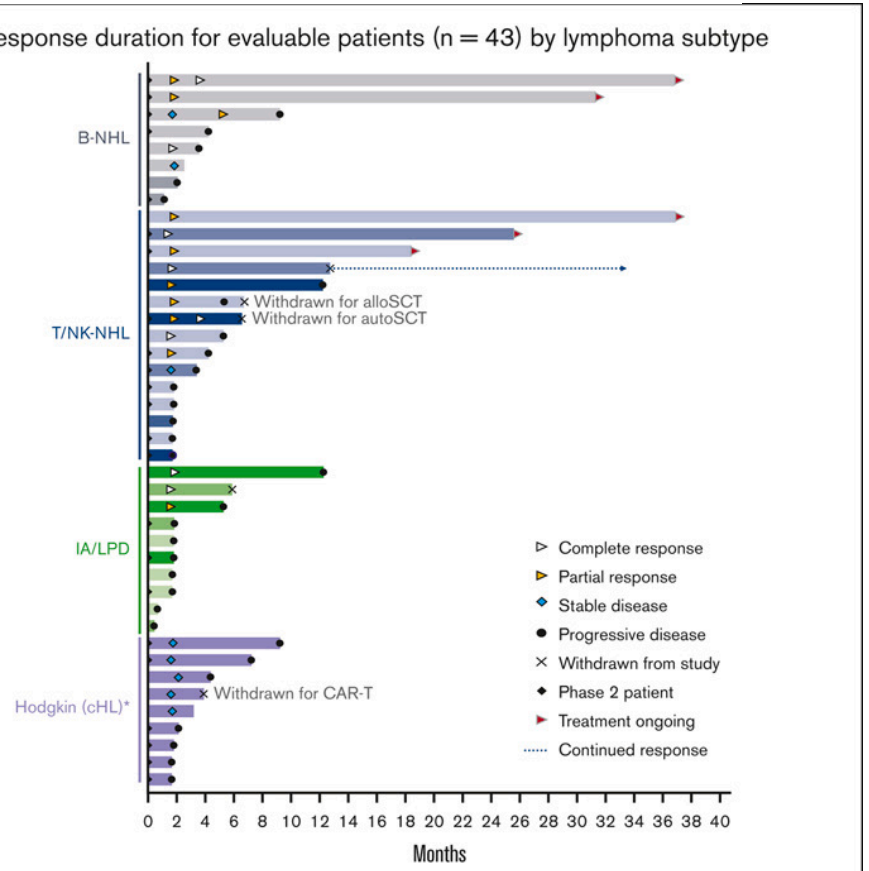
Relapsed/ refractory	Azacitadine vs. investigator's choice	Randomized phase 3 study for patients with R/R AITL	III
	Pembrolizumab + romidepsin	A phase I/II study of pembrolizumab (MK-3475) in combination with romidepsin in patients with R/R PTCL	I/II
	Pembrolizumab + pralatrexate	A phase 1/2 study of pembrolizumab plus pralatrexate for treatment of R/R PTCL	I/II
	Durvalumab ± lenalidomide	A phase 1/2 trial of durvalumab given as a single agent or in combination with lenalidomide in patients with R/R PTCL, including CTCL	I/II
	Durvalumab ± pralatrexate, romidepson, azacitadine	Phase 1/2a study in patients with R/R PTCL	I/II
	Pembrolizumab ± pralatrexate and decitabine	Novel immuno-epigenetic-based platform for patients with PTCL and CTCL: an international phase Ib study of pembrolizumab combined with decitabine and pralatrexate	Ib
	BGB-A317 (tislelizumab)*PD-1 mAb*		II
	Copanlisib + romidepsin		IB
	YY-20394*PI3K-δ inhibitor*		I
	Pralatrexate + romidepsin		I/II
	DS-3201b*EZH2* inhibitor		I
	IDH2 (AG-221)		I/II
	Ruxolitinib*JAK* inhibitor		II
	AZD4205*JAK* inhibitor		I/II
	Cerdulatinib*SYK/JAK* inhibitor		I/II
	Venetoclax*BCL-2* inhibitor		II
	Tipifarnib		II
	MEDI-570 *ICOS mAb*		I
	Daratumumab*CD38 mAb*		II
	ATLCAR.CD30 T cells		II
	AMF13		II
	AMF13		I
	AUTO4*TRBC1* targeted CAR-T cells		I/II

Mulvey and Ruan Journal of Hematology & Oncology (2020)

blood advances

Targeted therapy with nanatinostat and valganciclovir in recurrent EBV-positive lymphoid malignancies: a phase 1b/2 study





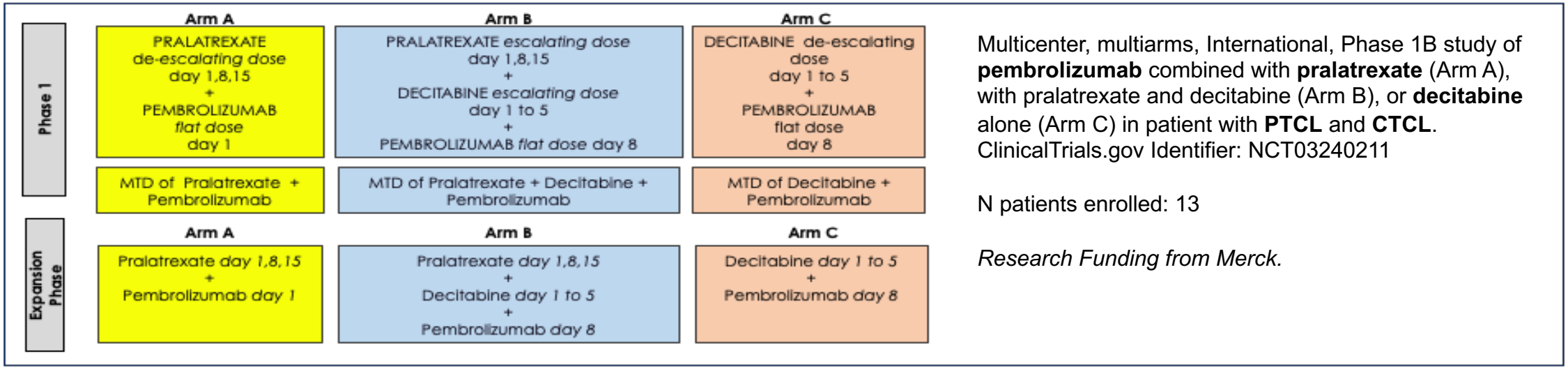
RP2D:
Nanatinostat 20 mg QD; 4 days on/3 days off
Valganciclovir 900 mg QD

alloSCT, allogeneic hematopoietic stem cell transplant; autoSCT, autologous hematopoietic stem cell transplant; B-NHL, B-cell non-Hodgkin lymphoma; CAR-T; chimeric antigen receptor T-cell therapy; cHL, classical Hodgkin lymphoma; EBV, Epstein–Barr virus; GCV, ganciclovir; HDACi, histone deacetylase inhibitor; IA/LPD, immunodeficiency-associated lymphoproliferative disorder; Nstat, nanatinostat; QD, once daily; RP2D, recommended Phase 2 dose; T/NK-NHL, T-cell/natural killer cell non-Hodgkin lymphoma.

*Data for one patient with cHL and a partial response not shown, as the patient withdrew from the study at the time of the first post-treatment assessment and was lost to follow-up.

Haverkos et al
Blood Adv 2023

Novas plataformas imuno-epigenéticas



Multicenter, multiarms, International, Phase 1B study of **pembrolizumab** combined with **pralatrexate** (Arm A), with pralatrexate and decitabine (Arm B), or **decitabine** alone (Arm C) in patient with **PTCL** and **CTCL**. ClinicalTrials.gov Identifier: NCT03240211

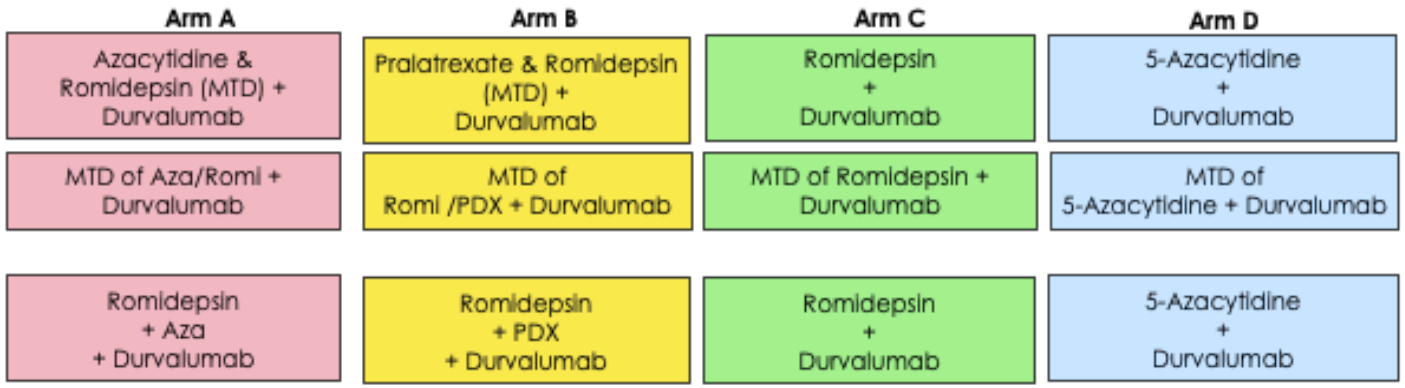
N patients enrolled: 13

Research Funding from Merck.

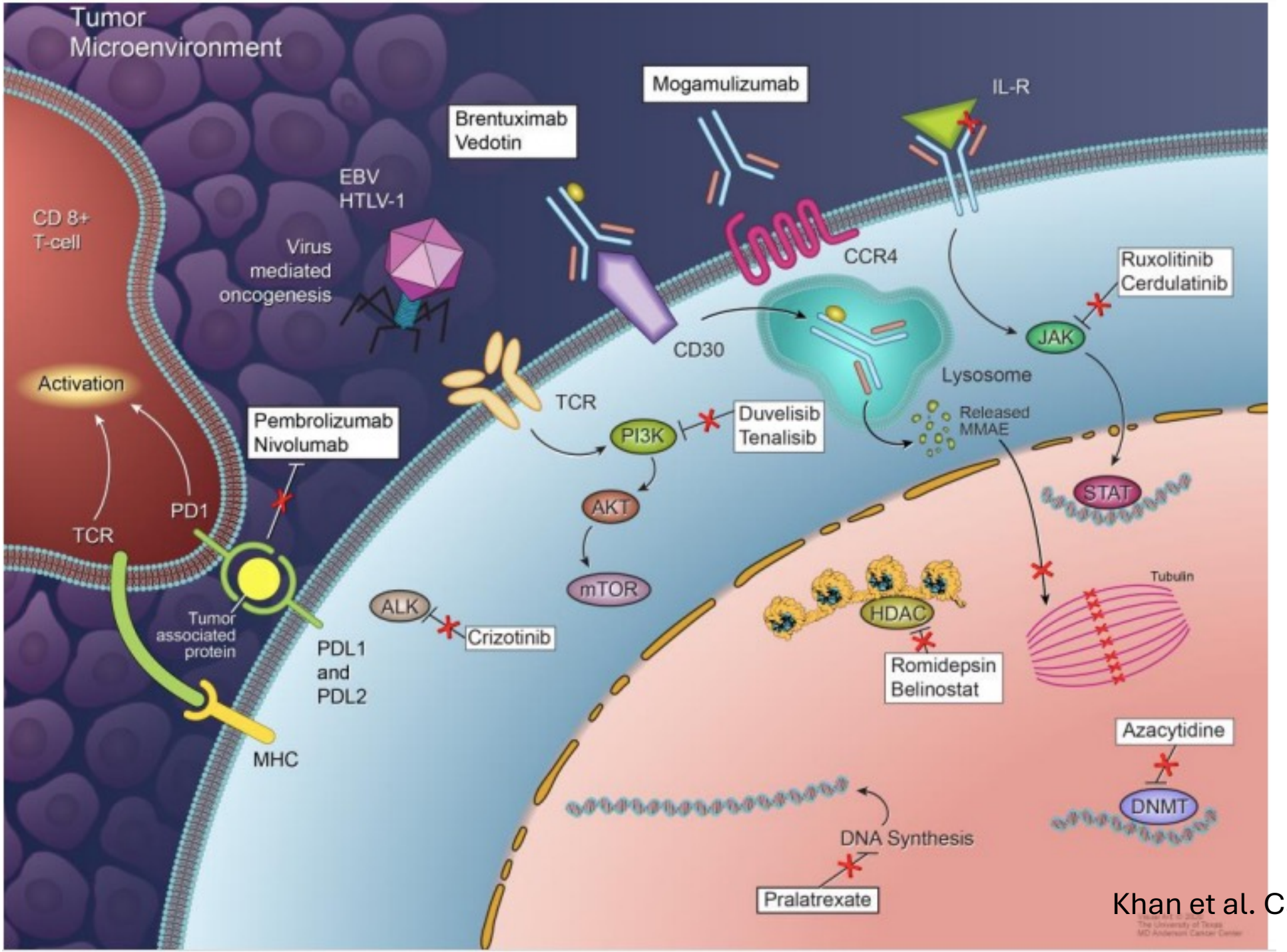
Phase 1/2A study of durvalumab combined with oral 5-azacytidine + romidepsin (Arm A), pralatrexate + romidepsin (Arm B), romidepsin alone (Arm C), or oral 5-azacytidine alone (Arm D) for the treatment of patients with PTCL. ClinicalTrials.gov Identifier: NCT03161223

N patients enrolled: 5

Research funding from Celgene



Marchi E et al., AACR 2020
Marchi E et al., ASCO 2020



Khan et al. Cancers 2021

CONCLUSIONES – PTCL

- Entidades muy agresivas, poco comprendidas y de mal pronóstico
- Creciente comprensión de la biología: terapias dirigidas
- Nuevos agentes aislados o en combinación buscando mayor eficacia
- Diversos agentes con múltiples mecanismos de acción en estudio
- En el futuro: uso de biomarcadores predictivos pre-tratamiento podrán guiar el tratamiento
- Estudios clínicos, por supuesto… **PERO QUE VENGAN A LATINOAMÉRICA**

Adapt. Mina & Pro, Blood Rev 2021; Kallan & Armitage, Expert Rev Hematol. 2020; Hapgood et al. Intern Med J 2021

GRACIAS!

OBRIGADA!

THANK YOU!