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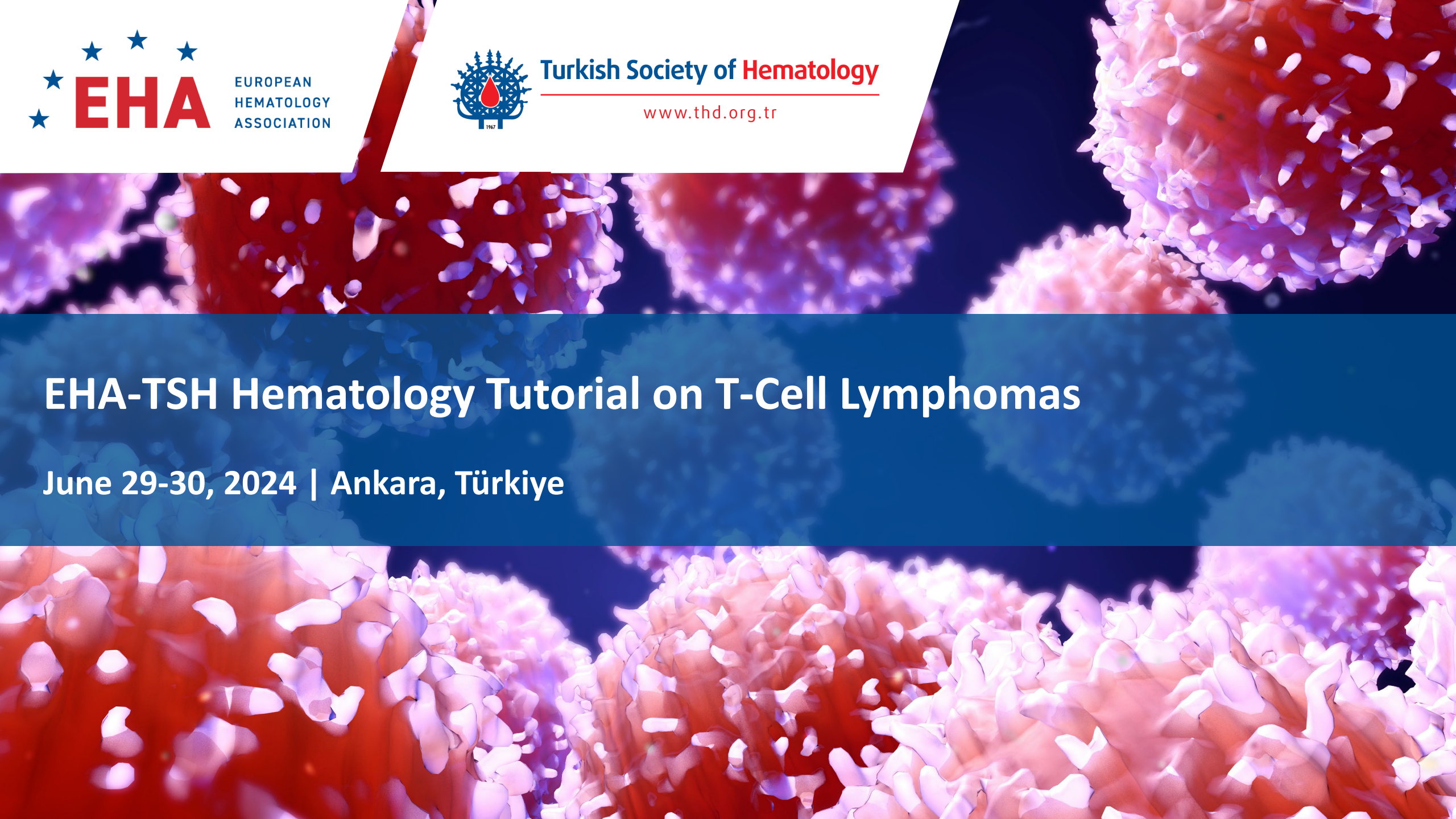


EHA-TSH Hematology Tutorial on T-Cell Lymphomas

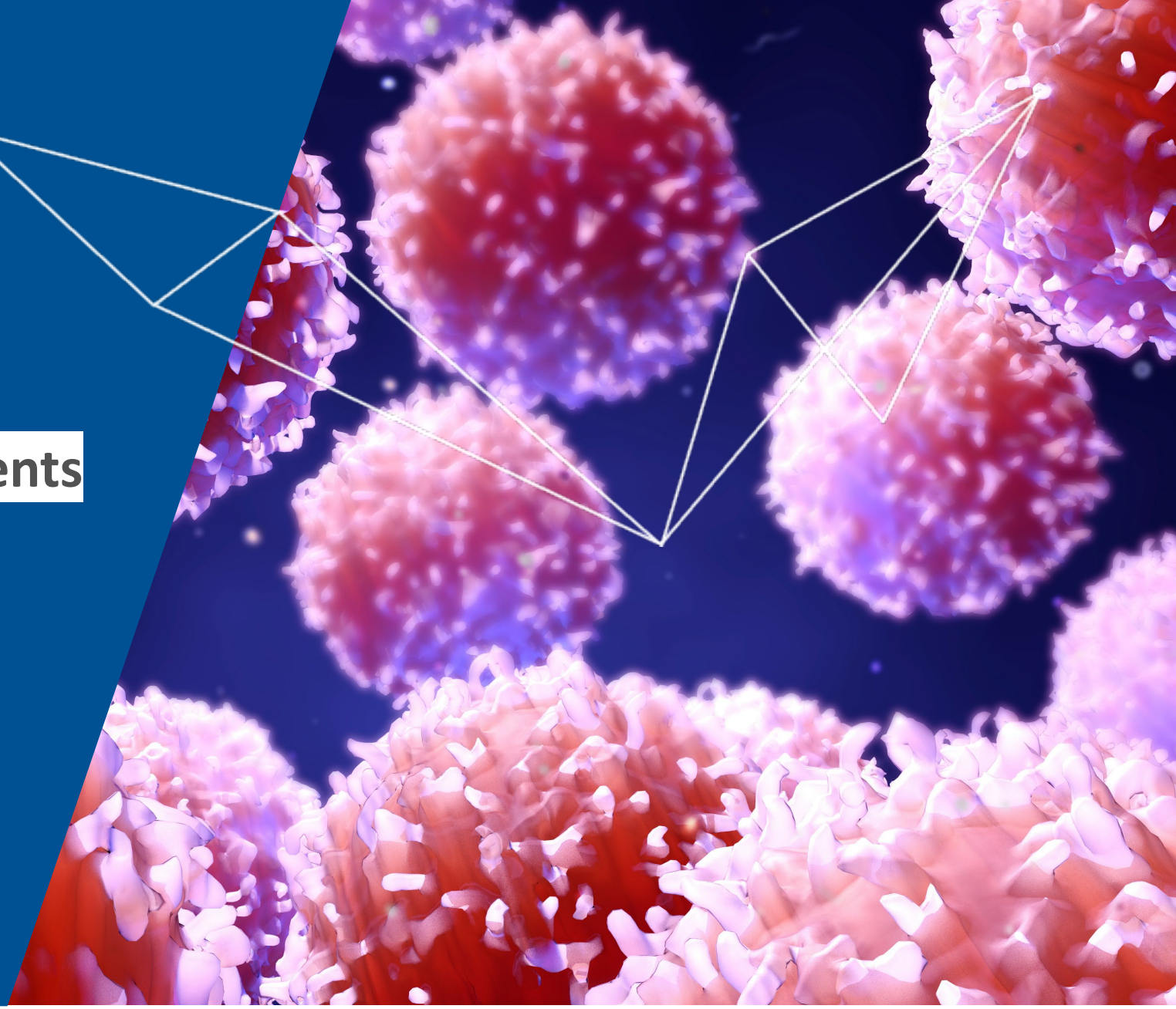
June 29-30, 2024 | Ankara, Türkiye

EHA EUROPEAN HEMATOLOGY ASSOCIATION

SESSION TITLE

How I treat PTCL NOS patients

June 29, 2024



LECTURE TITLE

Treatment of PTCL NOS patients

Elif Birtas Atesoglu

Yeditepe University, Department of Hematology

Istanbul, Turkey

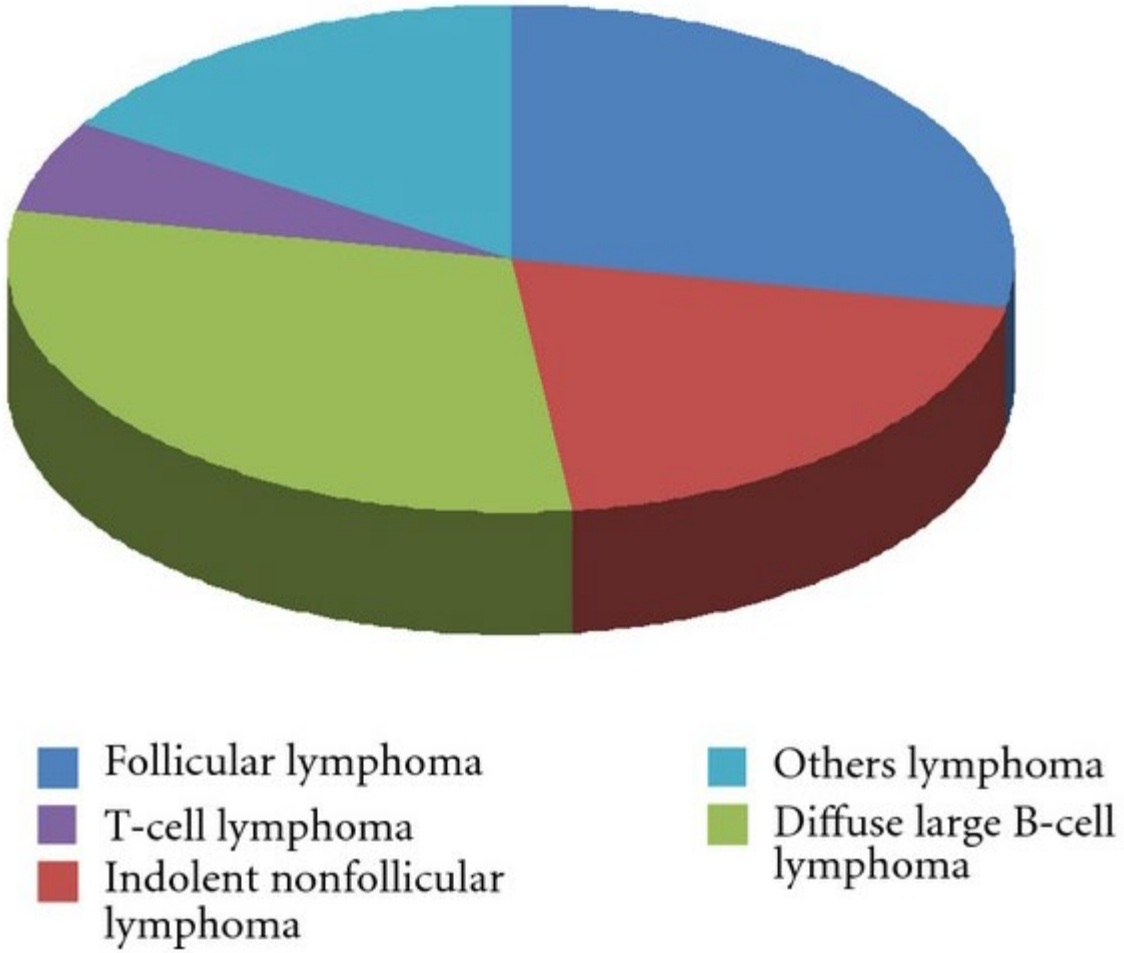
June 29, 2024

DISCLOSURE

- Abbvie, Janssen, Takeda (Advisory board)
- Abbvie, Janssen, Takeda, Astra Zeneca (Honoraria)

PERIPHERAL T CELL LYMPHOMA

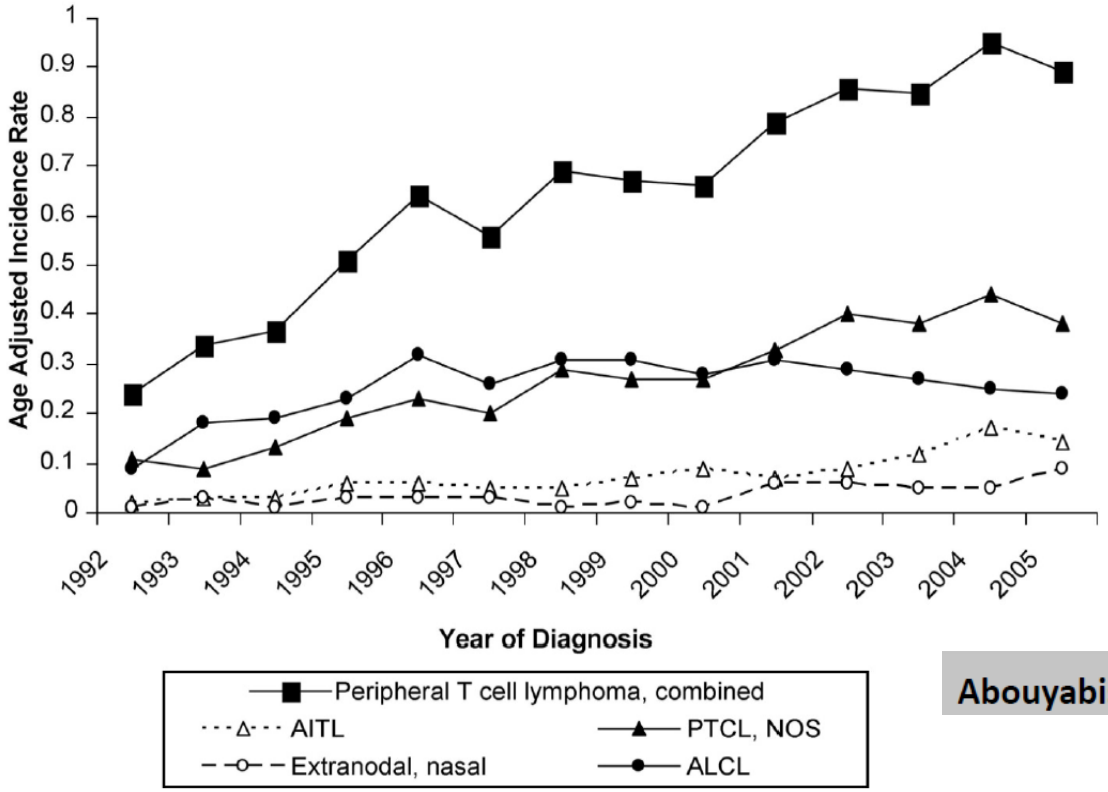
- Peripheral T-cell lymphomas (PTCL) are mature T- and NK-cell lymphomas.
- More than 30 different PTCL subtypes.
- A diverse group of diseases with variable clinical presentations.
- In Western populations PTCL represent 10% of all NHLs.



NODAL PTCL-represent about 60% of all PTCL in Western populations

WHO-HAEM4R	ICC 2022	WHO-HAEM5
Anaplastic large cell lymphoma, ALK-positive	Anaplastic large cell lymphoma, ALK-positive	ALK-positive anaplastic large cell lymphoma
Anaplastic large cell lymphoma, ALK-negative	Anaplastic large cell lymphoma, ALK-negative	ALK-negative anaplastic large cell lymphoma
Nodal lymphomas of T follicular helper origin	Follicular helper T-cell lymphoma	Nodal T-follicular helper (TFH) cell lymphoma
Angioimmunoblastic T-cell lymphoma	Follicular helper T-cell lymphoma, angio-immunoblastic type (angioimmunoblastic T-cell lymphoma)	Nodal TFH cell lymphoma, angioimmunoblastic type
Follicular T-cell lymphoma	Follicular helper T-cell lymphoma, follicular type	Nodal TFH cell lymphoma, follicular type
Nodal peripheral T-cell lymphoma with T follicular helper phenotype	Follicular helper T-cell lymphoma, NOS	Nodal TFH cell lymphoma, NOS
Not listed as an entity, subtype of peripheral T-cell lymphoma, not otherwise specified (PTCL, NOS)	*Primary nodal EBV⁺ T-cell/NK-cell lymphoma*	EBV⁺ nodal T- and NK-cell lymphoma
Peripheral T-cell lymphoma, NOS	Peripheral T-cell lymphoma, NOS	Peripheral T-cell lymphoma, NOS

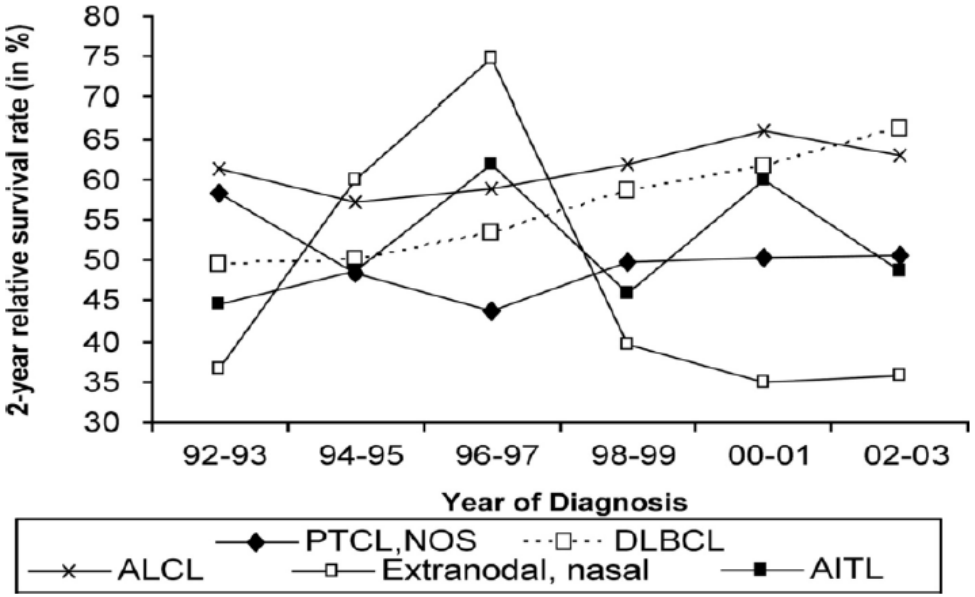
Bisig B. Et al. Haematologica 2023

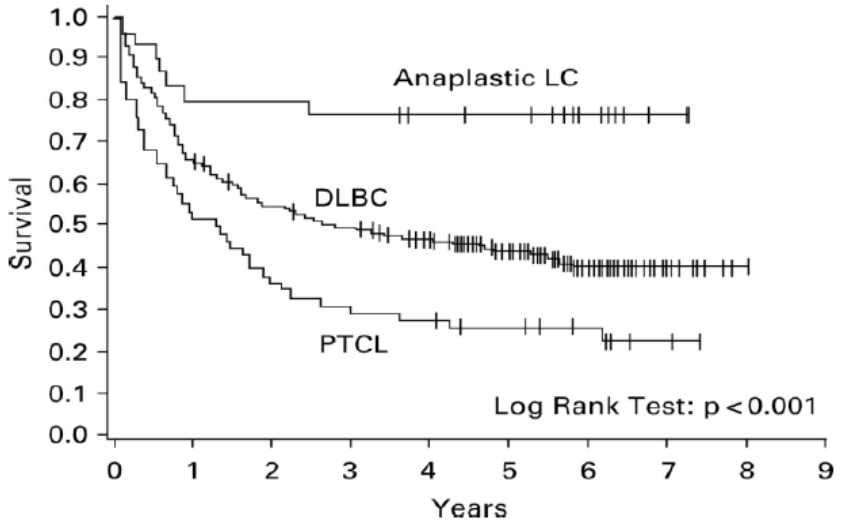


Abouyabis AN, et al. Leuk Lymphoma. 2008 Nov;49(11):2099-107

Study	Study era and design	Sample size	Geographic regions	Classification	Global subtypes distribution (percent of PTCLs globally)		Epidemiology (percent of PTCLs in region)							Median age	Gender	References
							U.S	Sweden	N.A	Europe	Asia	S.A	Australia/ India			
T-cell Project 2.0—Interim results	2018–2021 Prospective	*N* = 648	N.A./ Europe S.A Australia/ India	WHO (2016)	PTCL-NOS	31.3	NR	NR	25.4		NR	31.9	32.3	NR	NR	Federico et al. Hematological Oncology 2021* [7•]
					AITL	13.5			20.6			11.0	16.2			
					ALCL, ALK +	8.8			15.9			8.5	6.6			
					ALCL, ALK-	18.9			11.1			17.9	24.0			
					ENKTL	11.6			12.7			11.5	11.4			
					ATLL	9.9			3.2			14.3	3.0			
					EATL	1.2			1.6			1.6	0			
					MEITL	0.3			1.6			0.3	0			
					HSTCL	1.7			0			1.4	3.0			

OVERALL SURVIVAL OF PTCL COMPARED TO DLBCL

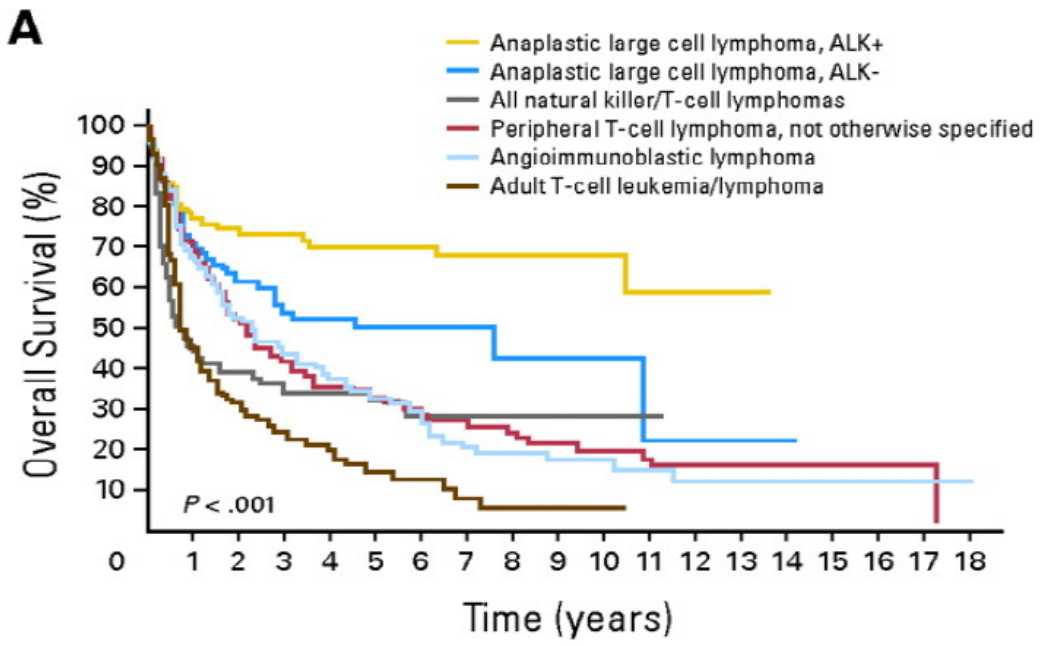




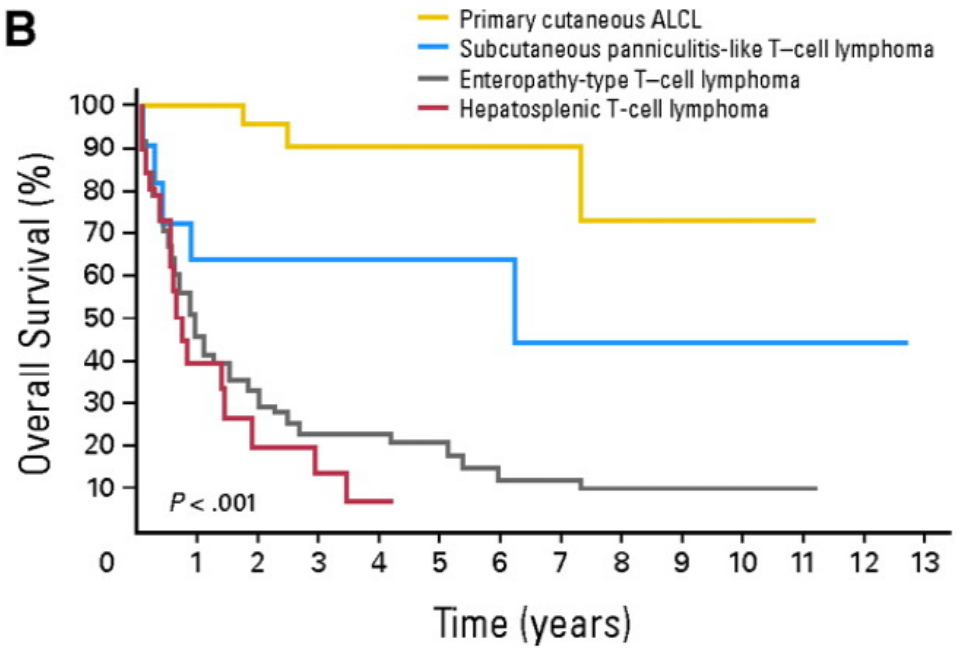
Abouyabis AN, et al. Leuk Lymphoma. 2008 Nov;49(11):2099-107
Armitage JO et al. Ann Oncol 2004;15:1447-1449

OVERALL SURVIVAL BY T-CELL LYMPHOMA TYPE

Common types



Uncommon types



Vose et al. J Clin Oncol 2008;26:4124-4130

PTCL-NOS; Pathology

- Defined as a diagnosis of exclusion for those cases of PTCL lacking specific features that qualify for other specific PTCL subtypes.
- PTCL, NOS is morphologically heterogeneous
- Mostly; predominantly medium-sized or large cells with irregular nuclei and prominent nucleoli.
- Less commonly; a predominance of atypical small cells with irregular nuclei.
- Tumors with a predominance of large cells have a worse outcome.
- **Lennert Lymphoma:**

✓ Prominent infiltrate of epithelioid histiocytes

✓ <10% of PTCL-NOS in historical series

✓ Associated with better prognosis than other PTCL-NOS

✓ Recently, many cases of “Lennert lymphoma” in fact correspond to histiocyte-rich TFH lymphomas.

Bisig B. Et al. Haematologica 2023

PTCL-NOS; Pathology

- Positive for pan-T cell antigens (CD3, CD2, CD5, CD7)
- However, one or several of these (most commonly CD5 or CD7) may show reduced or absent expression.
- CD4+ CD8–: most common
- CD4– CD8+: less frequent
- CD4– CD8– or CD4+ CD8+:uncommon
- > 85% express the αβ TCR, and a minority γδ TCR or TCR-silent
- CD4+ PTCL-NOS lack of TFH immunophenotype (PD1, ICOS, CXCL13, CD10 and BCL6) should be shown.
- CD30 expression is frequent (~30%) and variable.
- In a study of 141 cases of PTCL-NOS; >20% had >50% CD30+ tumor cells.

Bisig B. Et al. Haematologica 2023

CLINICAL FEATURES

- The median age at diagnosis is 60 years
- M/F:2
- Frequent concurrent extranodal involvement, especially of the skin.
- Most patients have:

✓Disseminated disease

✓Constitutional symptoms

✓Intermediate- to high-risk IPI score

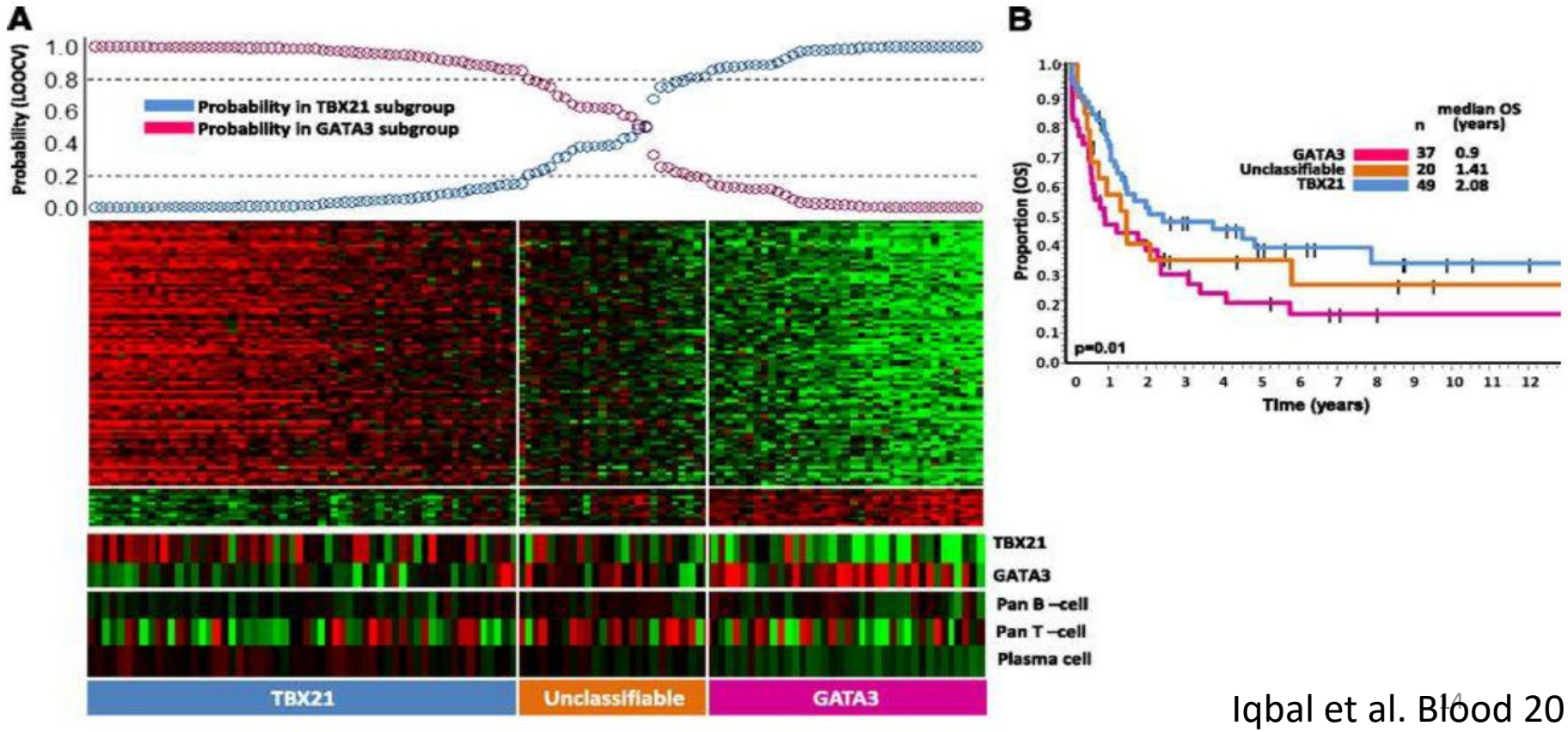
✓Sometimes blood eosinophilia.

- Small minority of patients may have a preceding lymphoproliferative variant of the hypereosinophilic syndrome or CLL

PROGNOSIS

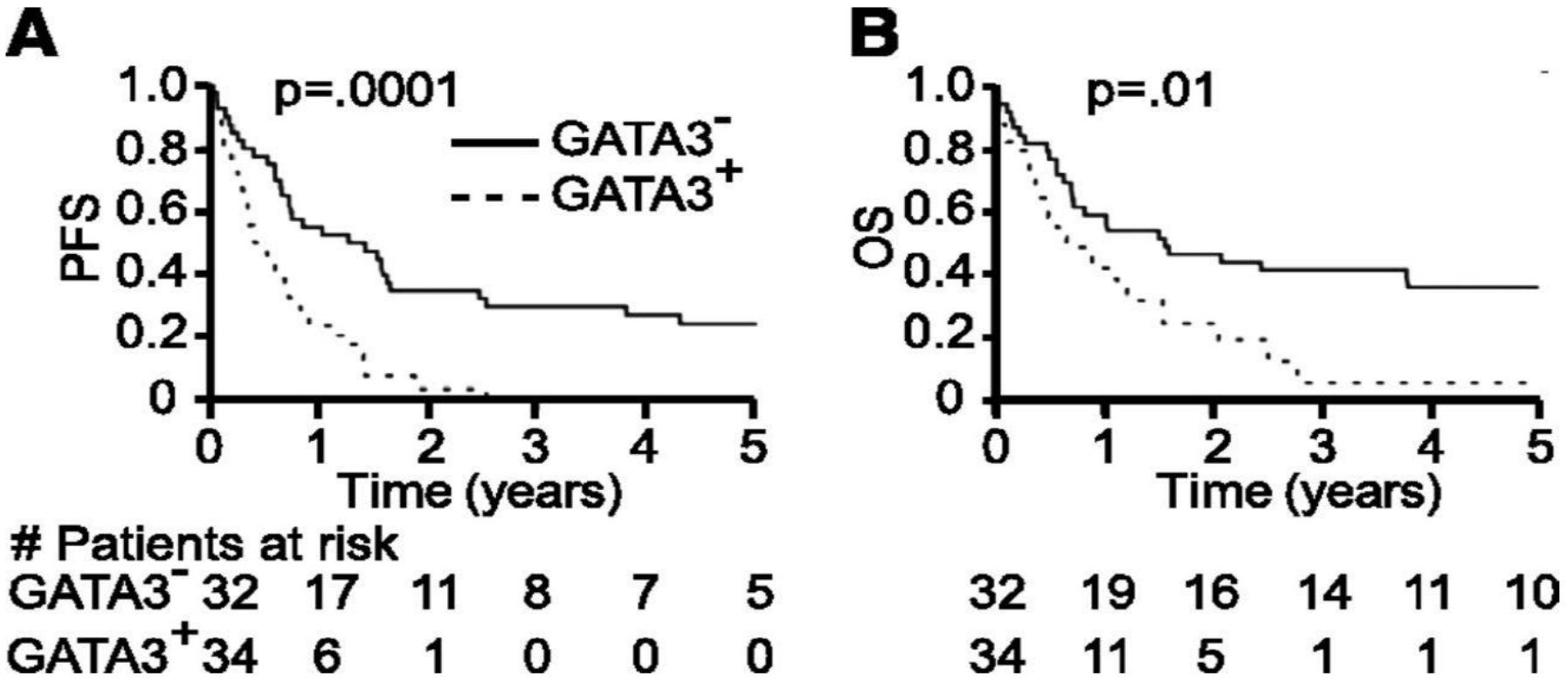
PTCL-NOS –Molecular Subgroups

GEP studies identified two main groups within PTCL-NOS:
1-PTCL-TBX21: characterized by expression of transcription factor T-box 21(TBX21), which is the regulator in TH1 and cytotoxic T-cell differentiation
2-PTCL-GATA3: characterized by overexpression of GATA3, which is the transcriptional regulator in TH2 cell differentiation.



Iqbal et al. Blood 2014

GATA-3 expression identifies a subset of PTCL-NOS with inferior survival

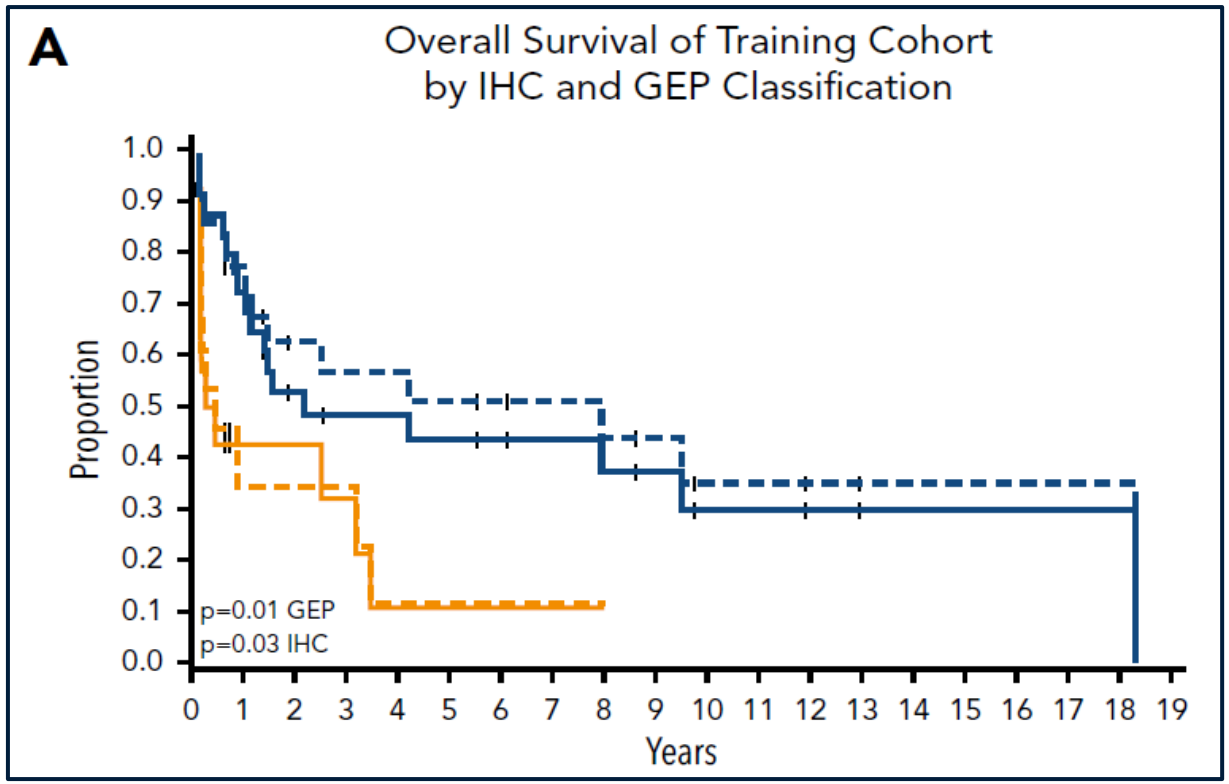


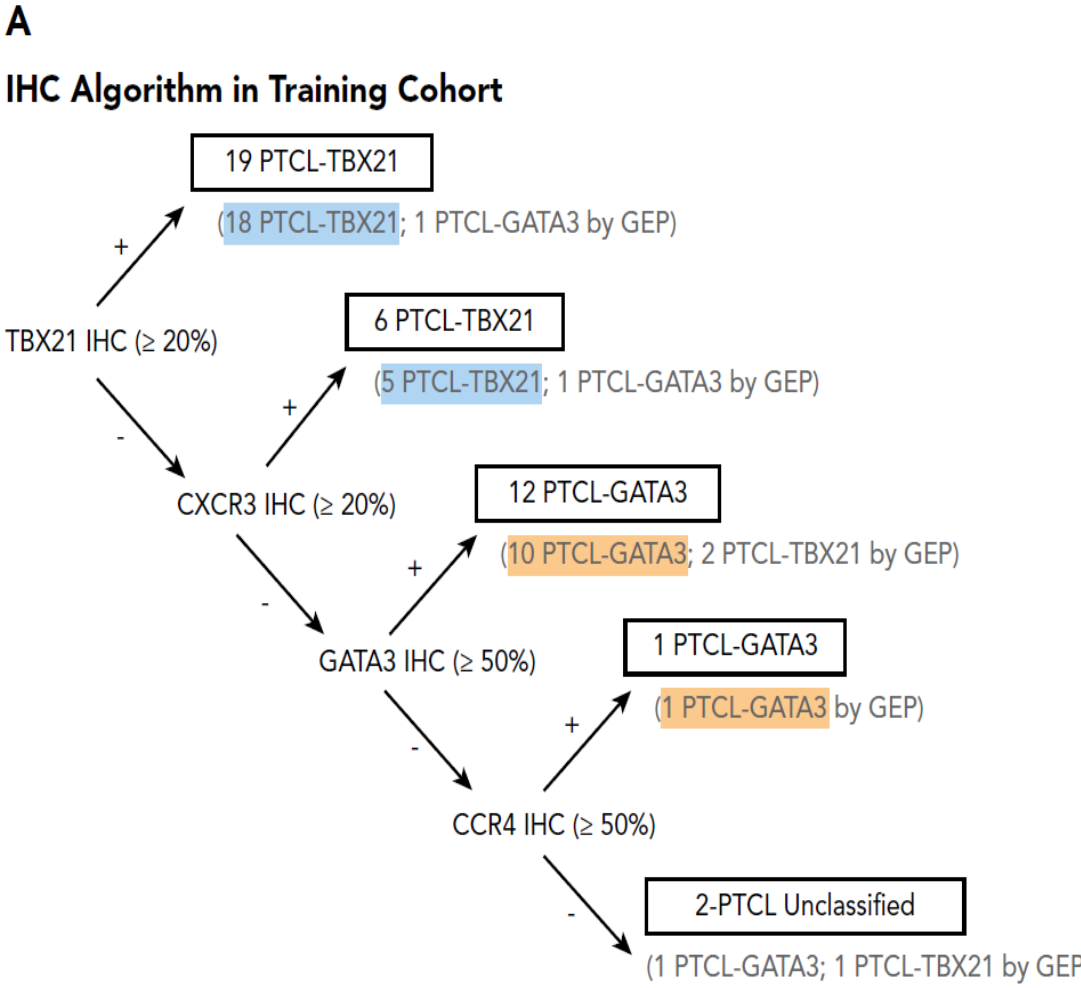
Wang et al. Blood 2014

PTCL-NOS –Molecular Subgroups

Feature	TBX21	GATA3
Frequency	50-60% of PTCL, NOS	30-40% of PTCL, NOS
Defining signature	High expression of TBX21 and its target genes (*CCL3, CXCR3, EOMES, IFNG, ILR2B*)	High expression of GATA3 and its target genes (*CCR4, CXCR7, IL18RA*)
Morphology	Polymorphous	Medium-sized to large tumor cells Little environment
Immunohistochemistry	Cytotoxic subset $TBX21^{+}$ and/or $CXCR3^{+}$	$TBX21^{-}$ and $CXCR3^{-}$ $GATA3^{+}$ and/or $CCR4^{+}$
Pathways	Enrichment of the NF-κB pathway	High MYC and proliferation signatures
Genetics	Relatively lower genomic complexity, mutations in epigenetic modifiers frequent	Higher genomic complexity, recurrent *TP53* alterations, *CDKN2A* and *PTEN* deletions
Outcome	Better than GATA3 except for the subset of cytotoxic cases	Worse than TBX21

Reproducing the molecular subclassification of peripheral T-cell lymphoma–NOS by immunohistochemistry





B

	PTCL-TBX21 by GEP (n=26)	PTCL-GATA3 by GEP (n=14)	Unclassified by GEP (n=9)
PTCL-TBX21 by IHC	23 (88%)	2 (14%)	6 (67%)
PTCL-GATA3 by IHC	2 (8%)	11 (79%)	2 (22%)
Unclassified by IHC	1 (4%)	1 (7%)	1 (11%)

Amador C et al. Blood 2019

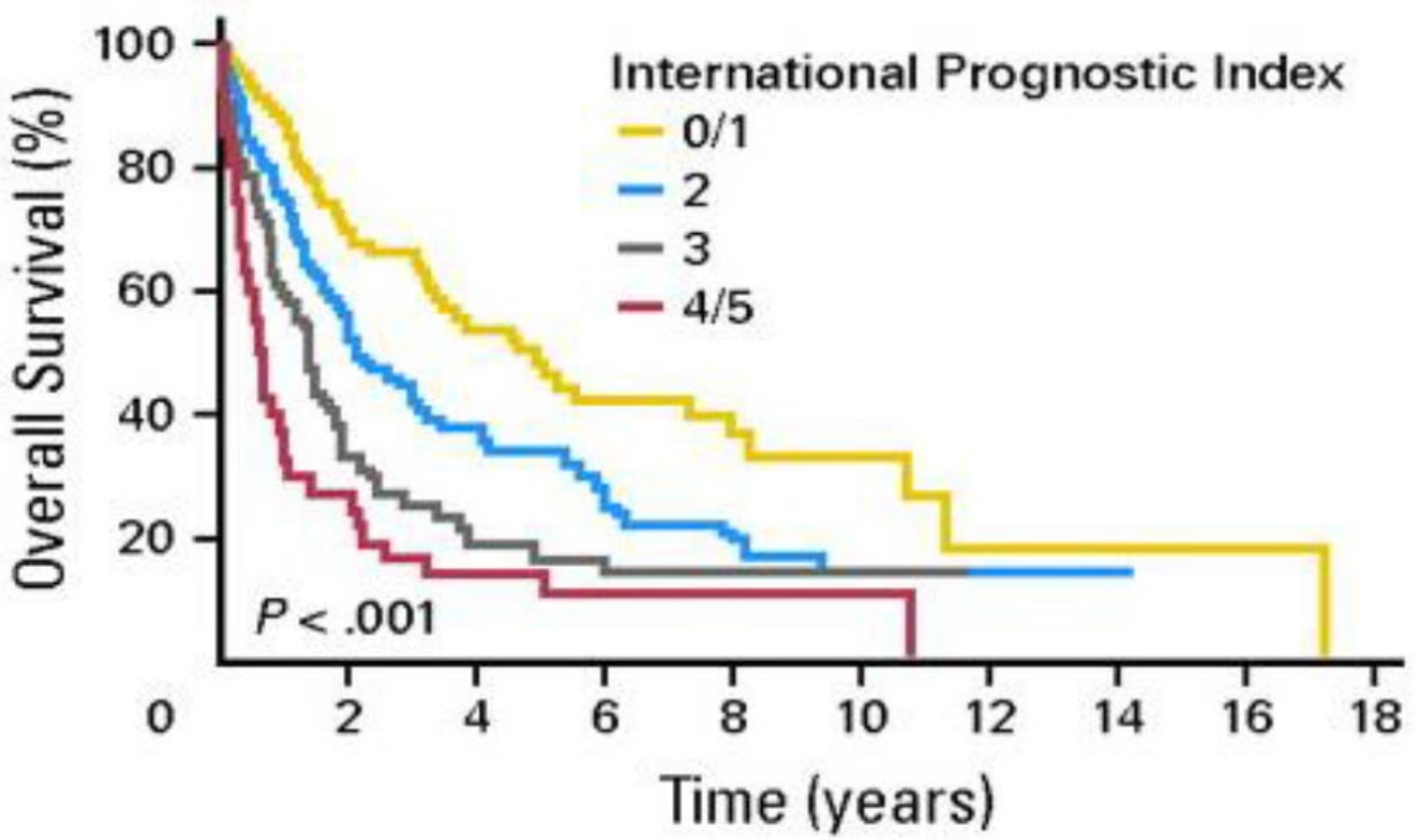
Reproducing the molecular subclassification of peripheral T-cell lymphoma–NOS by immunohistochemistry

Table 2. Univariate and multivariate model of OS

	Univariate				Multivariate			
	n	HR	95% CI	*P*	n	HR	95% CI	*P*
PTCL-GATA3 vs PTCL-TBX21 by IHC	128	2.39	1.55-3.70	<.0001	67	2.75	1.51-5.01	.0009
Sex: male vs female	128	1.09	0.71-1.69	.69				
Morphology								
Monomorphous vs polymorphous	121	1.77	1.14-2.75	.0095				
$CD8^+$ vs $CD8^-$	120	0.75	0.46-1.22	.24				
$CD4^+$ vs $CD4^-$	121	1.24	0.76-2.05	.39				
CTX phenotype vs non-CTX phenotype	70	0.87	0.46-1.63	.65				
IPI factors								
High IPI vs low IPI	74	2.13	1.21-3.74	.0089	67	1.8	1.0-3.24	.05
Age: >60 y vs ≤60 y	124	1.95	1.27-3.01	.0025				
Stage: III/IV vs I/II	85	1.77	0.91-3.44	.092				
High LDH vs normal LDH	78	1.69	0.95-3.02	.074				
Extranodal sites: >1 vs ≤1	77	1.85	1.04-3.29	.035				

Amador C et al. Blood 2019

IPI effectively stratifies patients with PTCL-NOS into risk groups

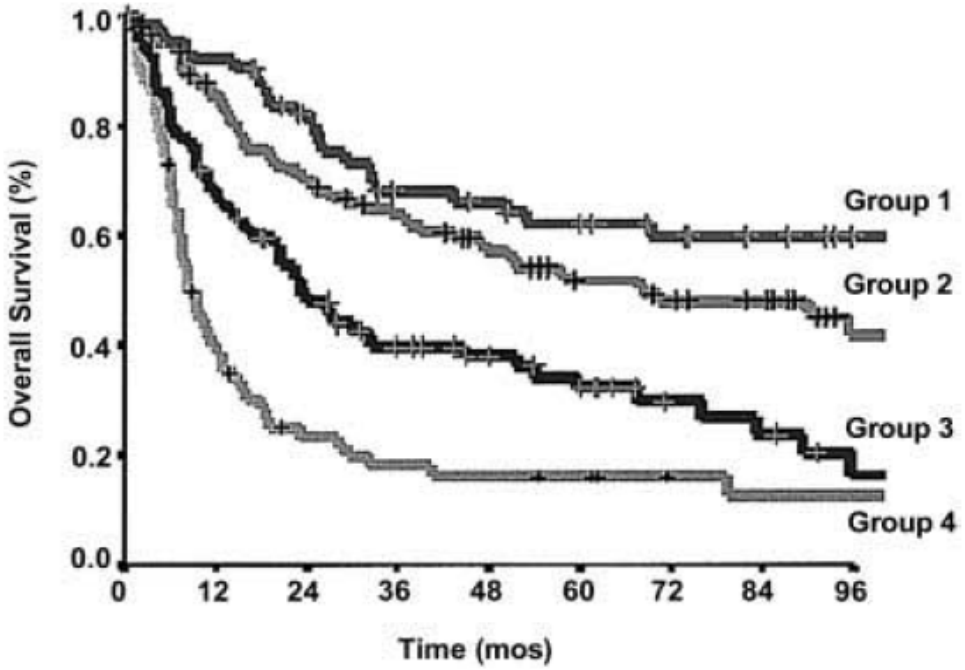


Vose et al. J Clin Oncol 2008

PIT (SPECIFIC FOR PTCL)

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

RISK FACTORS:	RISK GROUPS:	
• Age >60 years	• Group 1	0
• Serum LDH > normal	• Group 2	1
• ECOG Performance Status 2–4	• Group 3	2
• Bone marrow involvement	• Group 4	3 or 4



Gallamini A et al. Blood. 2004;103(7):2474-9.

FIRSTLINE TREATMENT

ANTHRACYCLINE-BASED CT

Table 1. Largest retrospective series including nodal peripheral T-cell lymphomas treated with primarily anthracycline-based chemotherapy.

First author Study	Period of PTCL diagnosis (age for enrollment)	Nodal PTCL subtypes	N	Received CHOP/CHOP-like therapy, %	5-year PFS %	5-year OS %
Vose[7a] International Peripheral T-cell Lymphoma Project	1990-2002 (≥19 yrs)	PTCL-NOS	340	80	20	32
		AITL	243	82	18	32
		ALK⁻ ALCL	72	95	36	49
		ALK⁺ ALCL	87	88	60	70
Ellin[8] Swedish Registry	2000-2009 (≥18 yrs)	PTCL-NOS	256	84 (All)[b]	21	28
		AITL	104		20	32
		ALK⁻ ALCL	115		38	31
		ALK⁺ ALCL	68		63	79
Brink[9] Netherlands Cancer Registry	1989-2018 (18-65 yrs)	PTCL-NOS	692	NR[c]	NR	32
		AITL	294			44
		ALK⁻ ALCL	89			52
		ALK⁺ ALCL	139			72

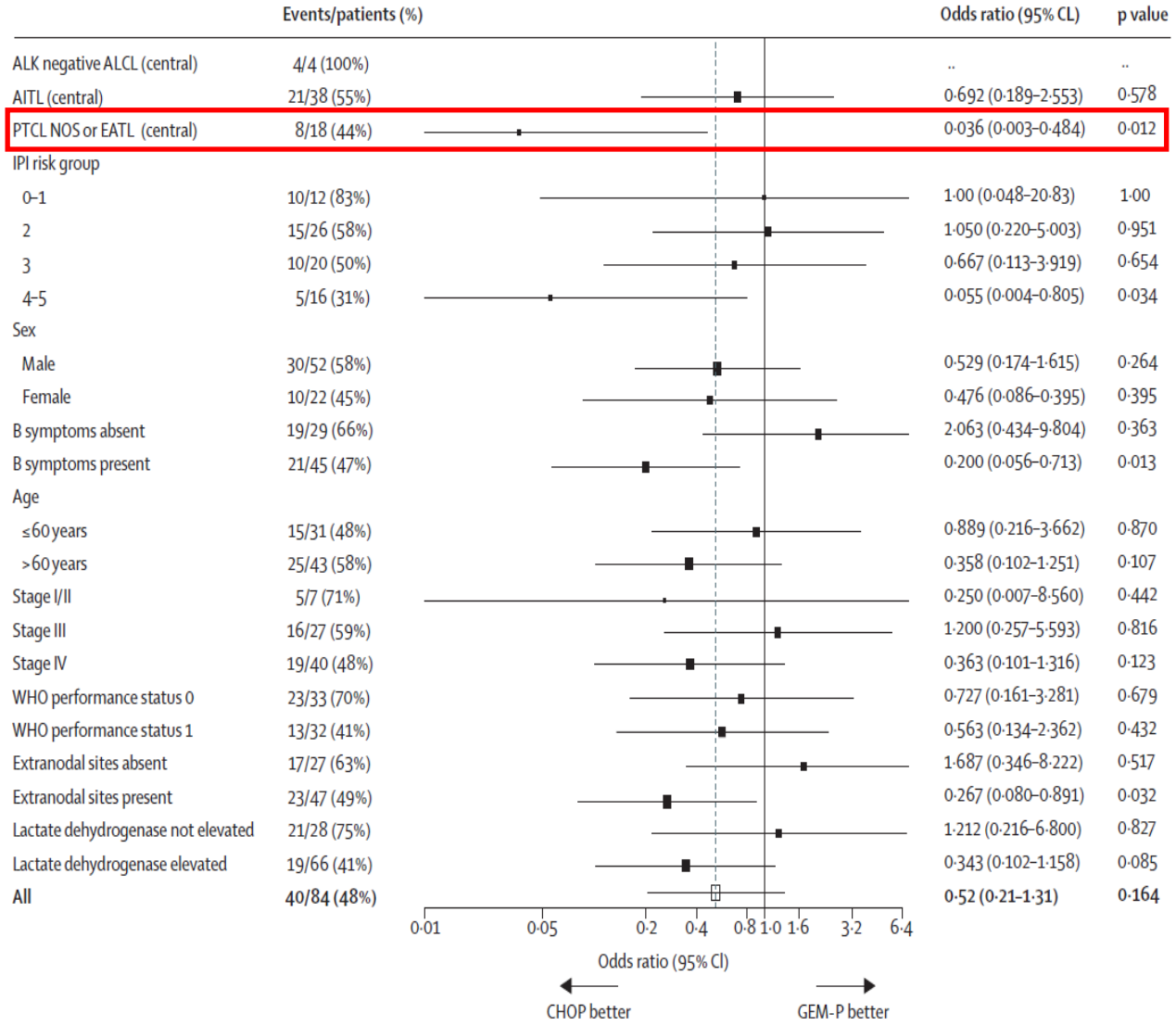
- Given their only recent recognition, primary nodal EBV⁺ T/NK-cell lymphoma and TFHL other than AITL, are combined in the PTCL-NOS subgroup

Ngu HS, Savage KJ. Haematologica 2023

CHOP versus GEM-P in previously untreated patients with peripheral T-cell lymphoma (CHEMO-T): a phase 2, multicentre, randomised, open-label trial

CHOPX6 vs GEM-PX4
PTCL-NOS :26% vs 23%

	CHOP (six cycles; n=43)	GEM-P (four cycles; n=44)
Overall response	28 (75·7)	25 (67·6)
Complete response or unconfirmed complete response*	23 (62·2)	17 (45·9)
Partial response	5 (13·5)	8 (21·6)
Stable disease	2 (5·4)	3 (8·1)
Progressive disease	4 (10·8)	6 (16·2)
Progressive disease assessed clinically	3 (8·1)	3 (8·1)
Not done or not assessable	6	7



Gleeson M et al. Lancet Haematol 2018

+/- Anthracycline in induction treatment

- 412 pts
- **39% PTCL,NOS**
- 20% AITL

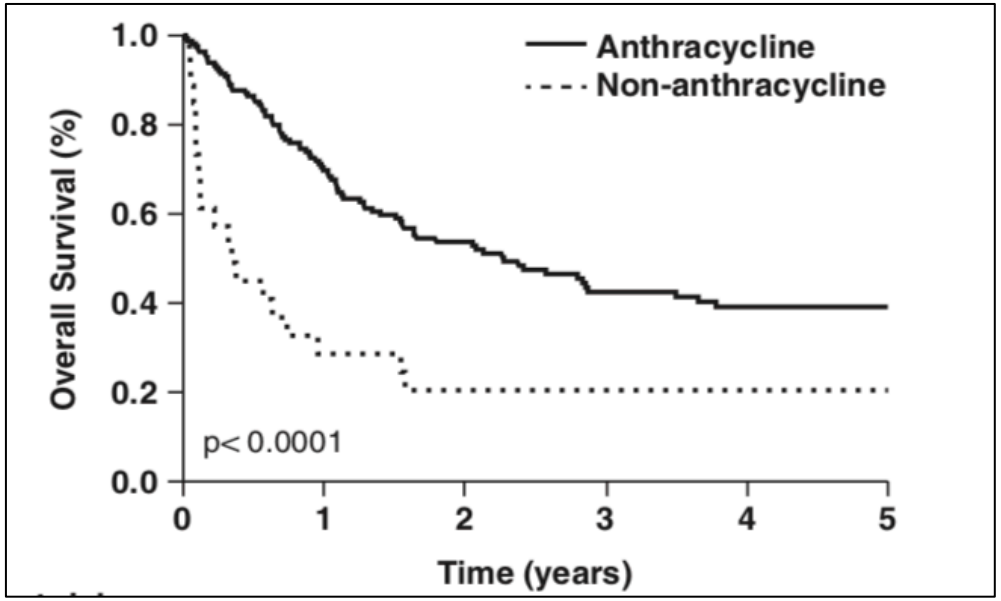


Table 4. Multivariate analysis for progression-free and overall survival

	Progression-free survival		*Overall survival*	
	HR (95% CI)	*P-value*	*HR (95% CI)*	*P-value*
All histologies				
IPI ⩾3	2.5 (1.8–3.5)	<0.0001	3.9 (2.7–5.9)	<0.0001
Nonanthracycline	2.2 (1.4–3.3)	0.001	2.9 (1.9–4.4)	<0.0001
PTCL-NOS/AITL histologies				
IPI ⩾3	3.0 (1.5–5.1)	<0.0001	4.5 (2.6–8.6)	<0.0001
Nonanthracycline	1.8 (1.0–3.1)	0.04	2.9 (1.7–4.8)	0.0004

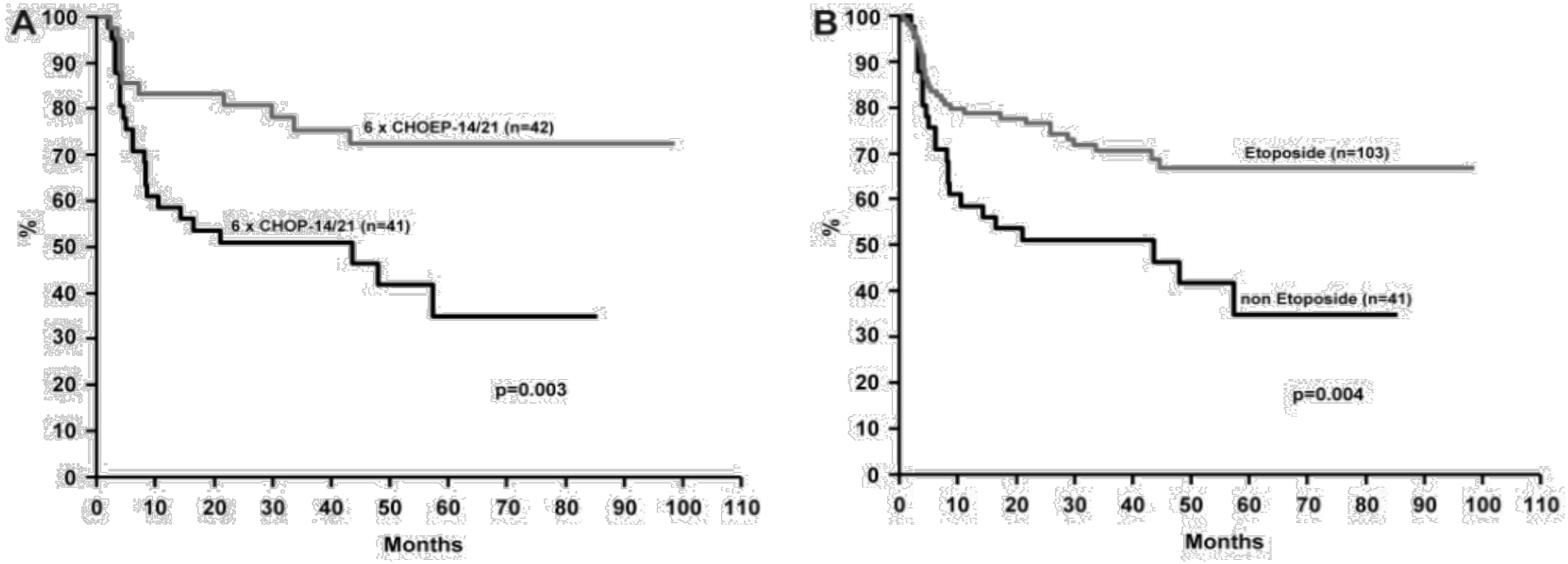
Briski R et al. Blood Cancer J 4:e214, 2014

Treatment and prognosis of mature T-cell and NK-cell lymphoma: an analysis of patients with T-cell lymphoma treated in studies of the German High-Grade Non-Hodgkin Lymphoma Study Group

Norbert Schmitz,[1] Lorenz Trümper,[2] Marita Ziepert,[3] Maike Nickelsen,[1] Anthony D. Ho,[4] Bernd Metzner,[5] Norma Peter,[6] Markus Loeffler,[3] Andreas Rosenwald,[7] and Michael Pfreundschuh[8]

CHOP+X (ETOPOSIDE)

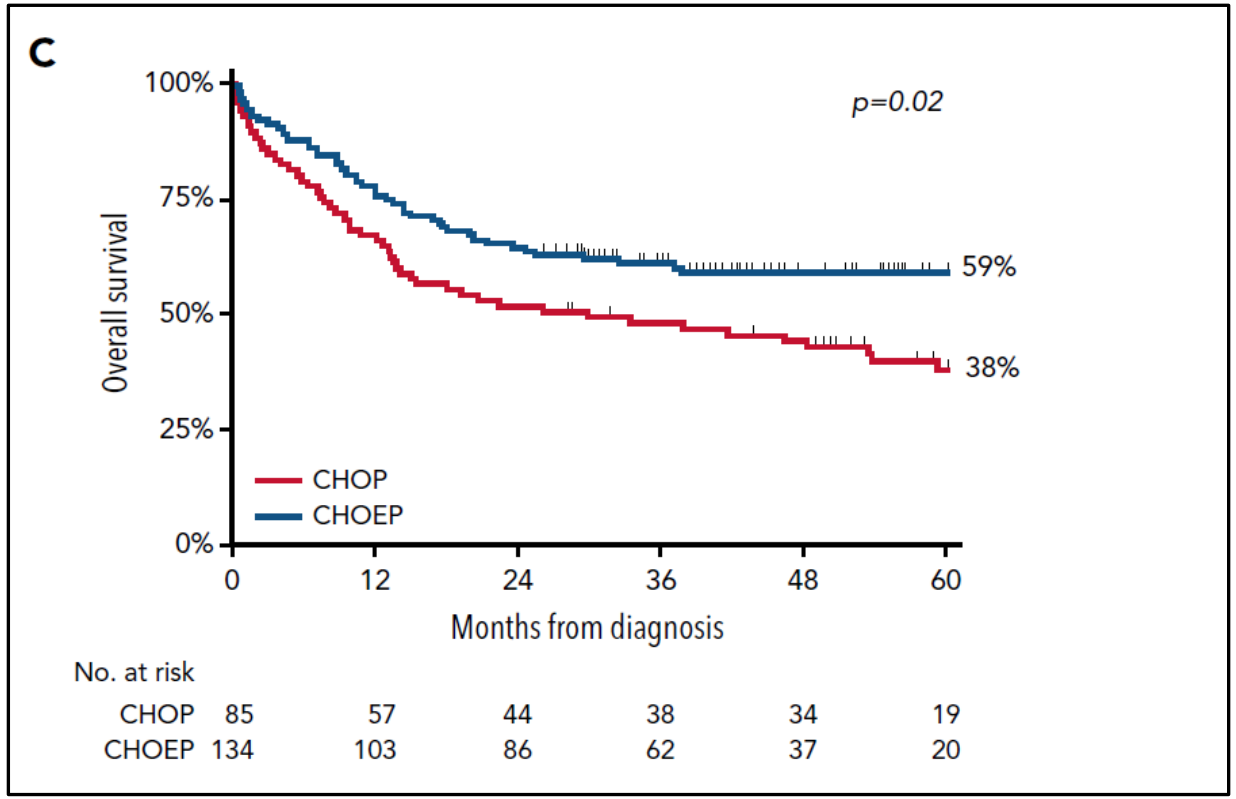
EFS of pts <60 years and with normal LDH

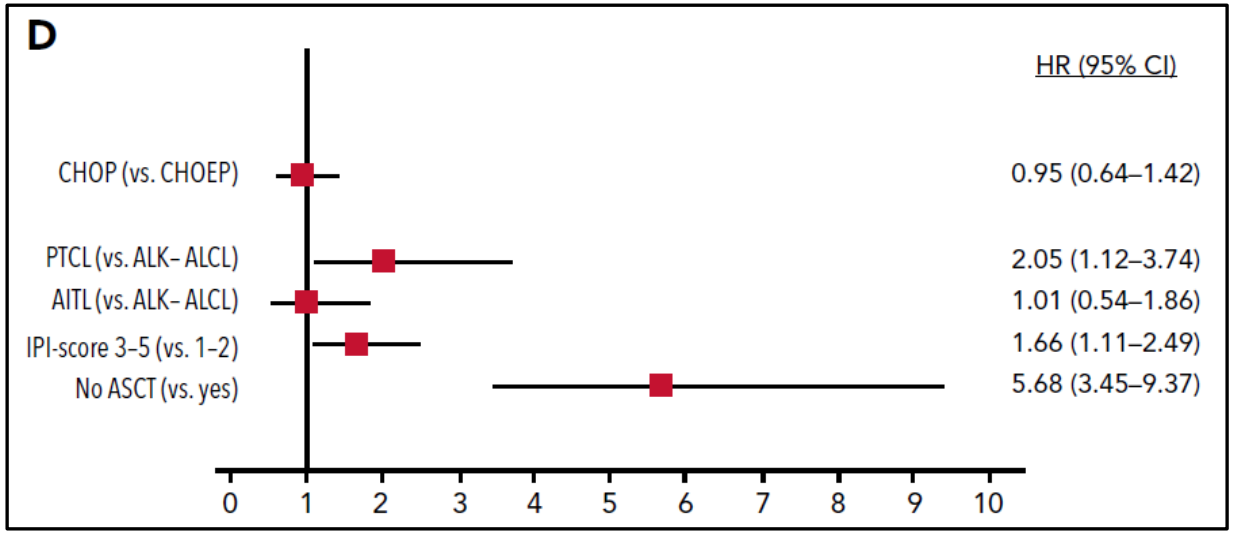


- ✓ CHOEP improves the EFS of young Pts with normal LDH, but not OS (P=0.176)
- ✓ In Pts >60 years the addition of etoposide (CHOEP) didn't yield any advantage, mainly due to added toxicities
- ✓ The significant benefit from etoposide was predominantly seen in the good prognosis ALK+ ALCL lymphoma group with a 3 year EFS of 57.1% with CHOP versus 91.2% with CHOEP (*p*= 0.012);

Blood. 2010;116(18):3418-3425

Impact of etoposide and ASCT on survival among patients aged <65 years with stage II to IV PTCL: a population-based cohort study





ALK- ALCL, AITL, PTCL-NOS

Brink M et al. Blood. 2022;116(18):3418-3425

Dose-adjusted EPOCH chemotherapy for untreated peripheral T-cell lymphomas: a multicenter phase II trial of West-JHOG PTCL0707

- 41 PTCL pts
- 51% PTCL-NOS
- ORR:71,4% CR:47,6%
- Hematological toxicity frequent.
- Febrile neutropenia 9%

Characteristic	N (%)	% PFS at 2 years	P	%OS at 2 years	P
Pathology					
PTCL-NOS	21 (51.2)	47.1		61.9	
AITL	17 (41.5)	55.2		88.2	
ALK (+) ALCL	2 (4.9)	100.0		50.0	
ALK (-) ALCL	1 (2.4)	100.0	0.629	100.0	0.244

Maeda Y et al. Haematologica 2017

The ECHELON-2 Trial: 5-year results of a randomized, phase III study of brentuximab vedotin with chemotherapy for CD30-positive peripheral T-cell lymphoma☆

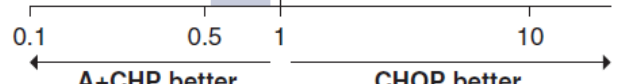
CHOP+X (BV)

- ❑CD30 + (≥10%) PTCL
- ❑A+CHP vs CHOP
- ❑226 vs 226
- ❑PTCL-NOS: 13% vs 19%

Horwitz S et al. Ann Oncol 2022

PFS

ITT subgroups	Event/N A+CHP	Event/N CHOP	Hazard ratio (95% CI)
PFS per investigator	94/226	125/226	0.70 (0.53-0.91)
IPI score			
0-1	14/52	27/48	0.42 (0.22-0.81)
2-3	59/141	79/145	0.72 (0.51-1.01)
4-5	21/33	19/33	1.14 (0.61-2.15)
Age, years			
<65	51/157	74/156	0.64 (0.45-0.92)
≥65	43/69	51/70	0.68 (0.45-1.04)
Sex			
Male	60/133	79/151	0.84 (0.60-1.17)
Female	34/93	46/75	0.44 (0.28-0.69)
Baseline ECOG status			
0	36/84	56/93	0.63 (0.41-0.96)
1	38/90	50/86	0.61 (0.40-0.93)
2	20/51	19/47	0.99 (0.52-1.88)
Disease stage			
I	3/12	2/9	2.15 (0.22-20.88)
II	12/30	18/37	0.93 (0.43-1.99)
III	26/57	36/67	0.63 (0.37-1.05)
IV	53/127	69/113	0.66 (0.46-0.95)
Disease indication			
ALK-positive sALCL	7/49	16/49	0.40 (0.17-0.98)
ALK-negative sALCL	46/113	61/105	0.58 (0.40-0.86)
ATLL	2/4	2/3	0.69 (0.10-4.94)
AITL	19/30	12/24	1.41 (0.64-3.11)
EATL	1/1	2/2	Not estimable
PTCL-NOS	19/29	32/43	0.79 (0.43-1.43)
sALCL	53/162	77/154	0.55 (0.39-0.79)
Non-sALCL	41/64	48/72	0.96 (0.63-1.47)



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Turkish Society of Hematology
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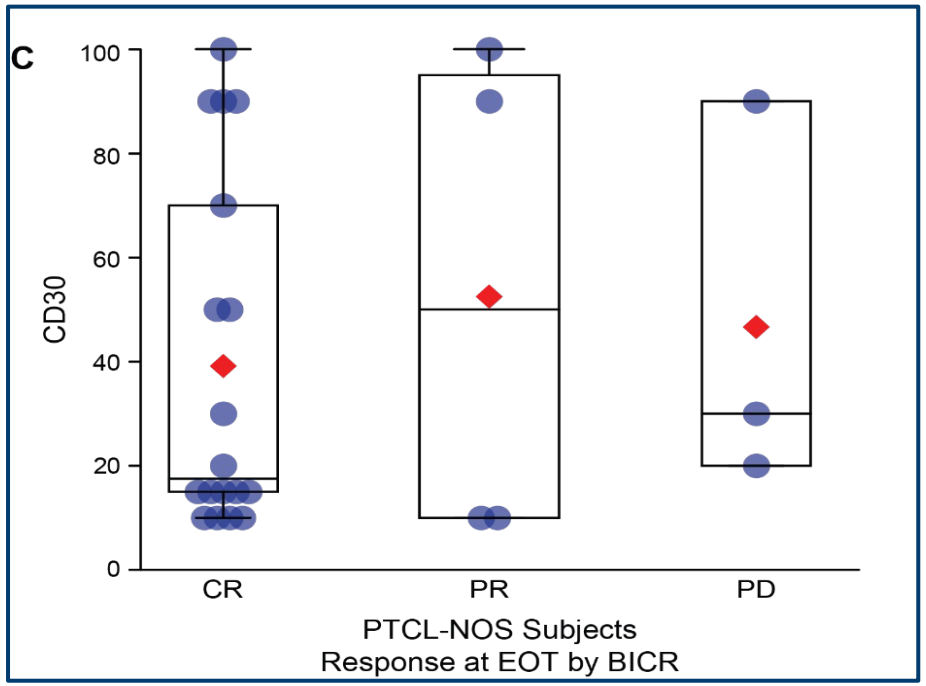
The ECHELON-2 Trial: 5-year results of a randomized, phase III study of brentuximab vedotin with chemotherapy for CD30-positive peripheral T-cell lymphoma☆

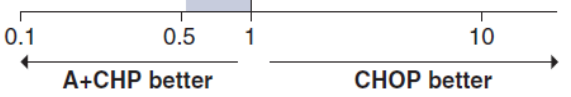
CHOP+X (BV)



Horwitz S et al. Ann Oncol 2022

OS

ITT subgroups	Event/N A+CHP	Event/N CHOP	Hazard ratio (95% CI)
Overall survival	68/226	89/226	0.72 (0.53-0.99)
IPI score			
0-1	8/52	13/48	0.58 (0.24-1.39)
2-3	40/141	59/145	0.61 (0.41-0.91)
4-5	20/33	17/33	1.23 (0.64-2.34)
Age, years			
<65	37/157	44/156	0.79 (0.51-1.23)
≥65	31/69	45/70	0.62 (0.39-0.98)
Sex			
Male	41/133	59/151	0.73 (0.49-1.08)
Female	27/93	30/75	0.68 (0.40-1.16)
Baseline ECOG status			
0	25/84	38/93	0.59 (0.35-0.99)
1	25/90	38/86	0.54 (0.33-0.90)
2	18/51	13/47	1.42 (0.69-2.93)
Disease stage			
I	2/12	2/9	1.34 (0.12-14.81)
II	7/30	14/37	0.66 (0.26-1.68)
III	18/57	22/67	0.70 (0.37-1.33)
IV	41/127	51/113	0.73 (0.48-1.10)
Disease indication			
ALK-positive sALCL	5/49	10/49	0.48 (0.16-1.40)
ALK-negative sALCL	34/113	39/105	0.71 (0.44-1.12)
ATLL	2/4	3/3	0.70 (0.11-4.27)
AITL	12/30	8/24	1.01 (0.40-2.55)
EATL	1/1	2/2	Not estimable
PTCL-NOS	14/29	27/43	0.75 (0.37-1.48)
sALCL	39/162	49/154	0.66 (0.43-1.01)
Non-sALCL	29/64	40/72	0.76 (0.46-1.23)



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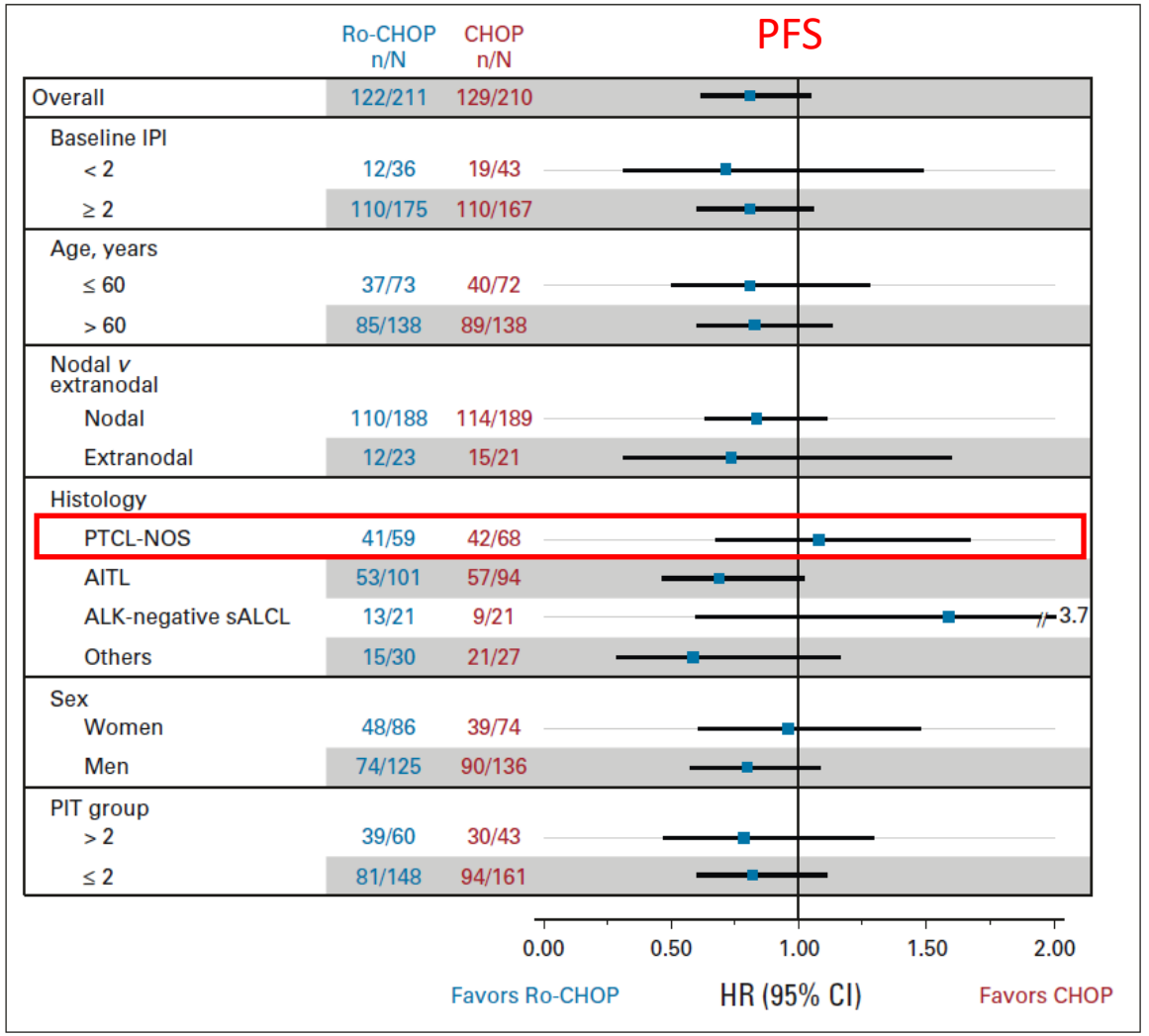
Romidepsin Plus CHOP Versus CHOP in Patients With Previously Untreated Peripheral T-Cell Lymphoma: Results of the Ro-CHOP Phase III Study (Conducted by LYSA)

CHOP+X (ROMIDEPSIN)

Parameter	Ro-CHOP (n = 211)	CHOP (n = 210)	Total (N = 421)
Median age, years (range)	65 (26-80)	65 (25-81)	65 (25-81)
Age group, years			
≤ 60	73 (34.6)	72 (34.3)	145 (34.4)
> 60	138 (65.4)	138 (65.7)	276 (65.6)
Sex			
Male	125 (59.2)	136 (64.8)	261 (62.0)
Female	86 (40.8)	74 (35.2)	160 (38.0)
Histologic diagnosis (local pathology)			
AITL	101 (47.9)	94 (44.8)	195 (46.3)
PTCL-NOS	59 (28.0)	68 (32.4)	127 (30.2)
ALCL ALK–negative type	21 (10.0)	21 (10.0)	42 (10.0)
Others	30 (14.2)	27 (12.9)	57 (13.5)



Bachy E et al. J Clin Oncol 2021

Alemtuzumab and CHOP-14 (or CHOEP-14) versus CHOP-14 (or CHOEP-14)

- Phase III studies
- 1-in younger pts (CHOEP-14, 18-65 years; ACT-1 trial) + Auto-SCT
- 2-in older pts (CHOP-14, >65 years; ACT-2 trial)
- ACT-2, 3-yr EFS: A-CHOP:27% vs CHOP:24% (p=0.248) and A-CHOP associated with significant toxicity
- ACT-1, 3-yr EFS: A-CHOP 35% vs CHOP:26%

d'Amore F et al. Blood. 2018;132(Suppl 1):998.
Wulf GG et al. Leukemia. 2021;35(1):143-155.

Role of consolidative Autologous transplant in front-line treatment of PTCL-NOS

Up-Front Autologous Stem-Cell Transplantation in Peripheral T-Cell Lymphoma: NLG-T-01

Francesco d'Amore, Thomas Relander, Grete F. Lauritzsen, Esa Jantunen, Hans Hagberg, Harald Anderson, Harald Holte, Anders Österborg, Mats Merup, Peter Brown, Outi Kuittinen, Martin Erlanson, Bjørn Østenstad, Unn-Merete Fagerli, Ole V. Gadeberg, Christer Sundström, Jan Delabie, Elisabeth Ralfkiaer, Martine Vornanen, and Helle E. Toldbod

VOLUME 30 · NUMBER 25 · SEPTEMBER 1 2012

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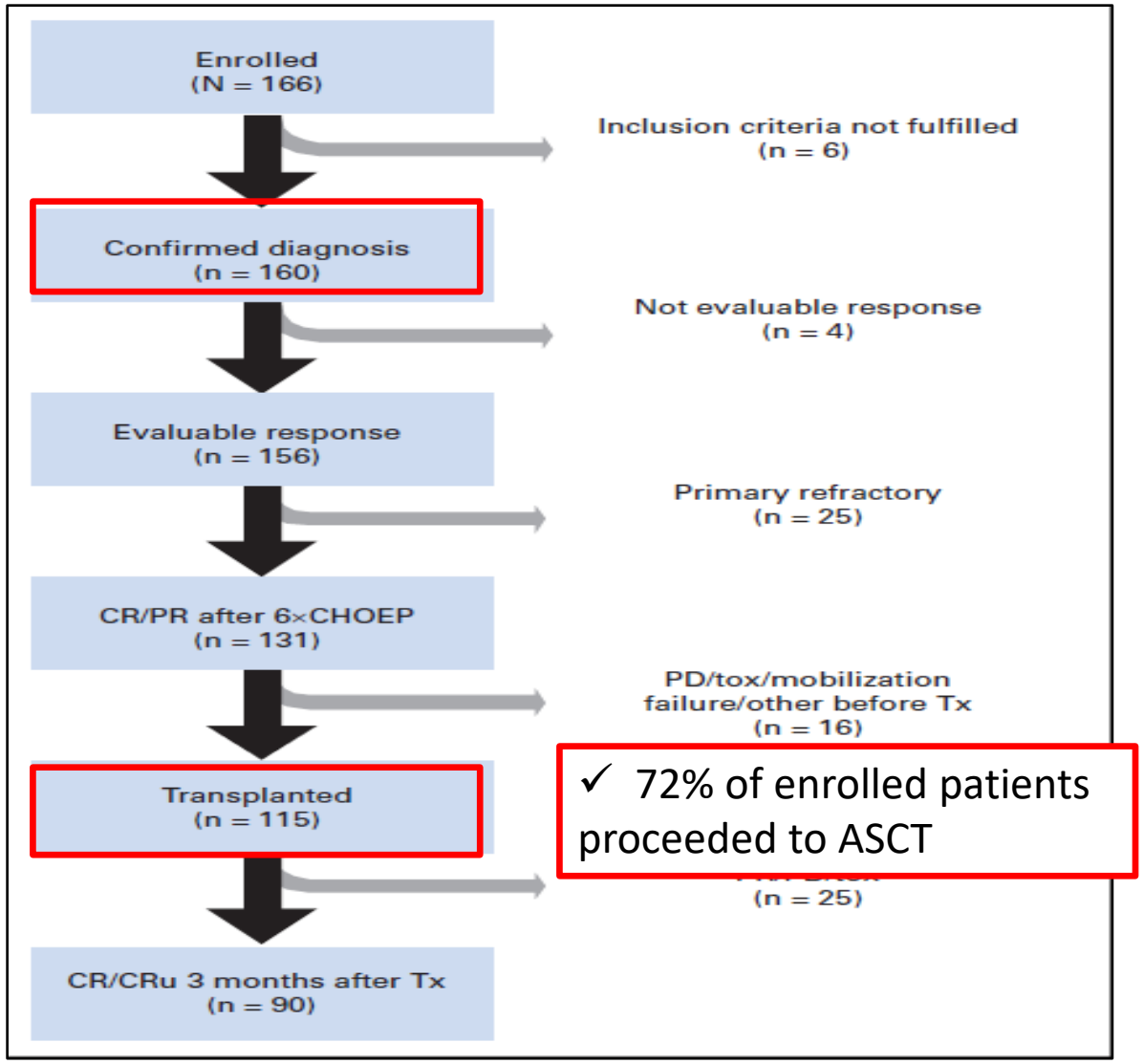

✓ 72% of enrolled patients proceeded to ASCT

- ✓ Biweekly CHOEP (CHOP for patients age >60)
- ✓ If CR or PR consolidation with ASCT
- ✓ Intention to Treat analysis

Up-Front Autologous Stem-Cell Transplantation in Peripheral T-Cell Lymphoma: NLG-T-01

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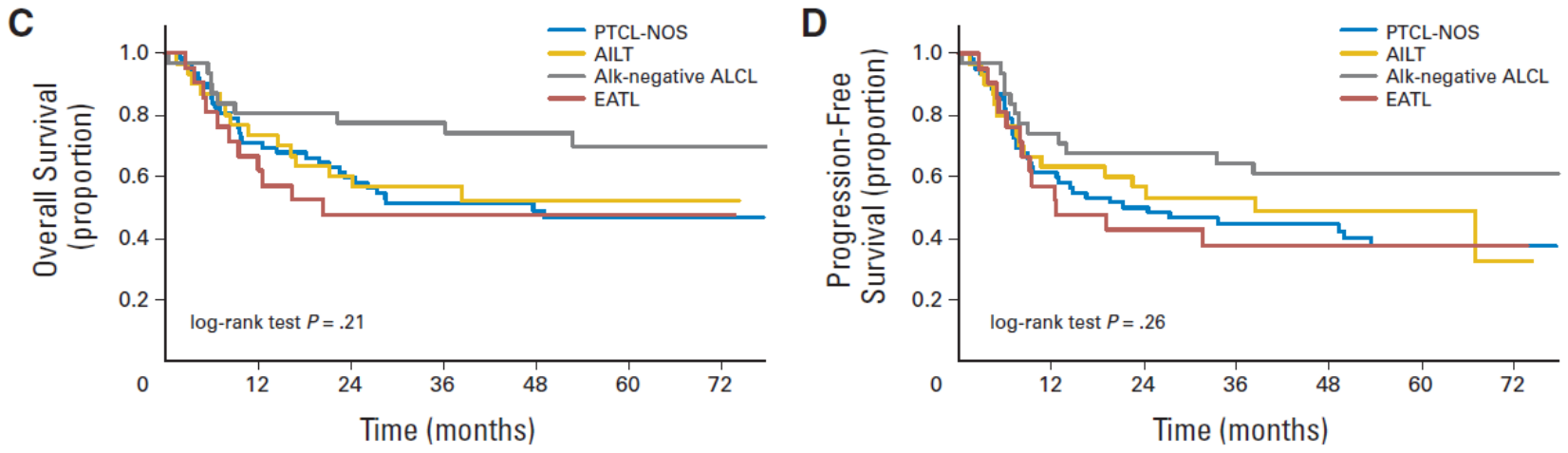


5 yr OS:51%
5 yr PFS:44%

Histology	5-yr OS	95% CI
ALCL	70%	50%-83%
AILT	52%	33%-69%
EATL	48%	26%-67%
PTCL-NOS	47%	34%-59%

Meta-analysis CHOP 5y OS (Abouyaby, 2011)
56.5 %
36.5 %
21 %
34%

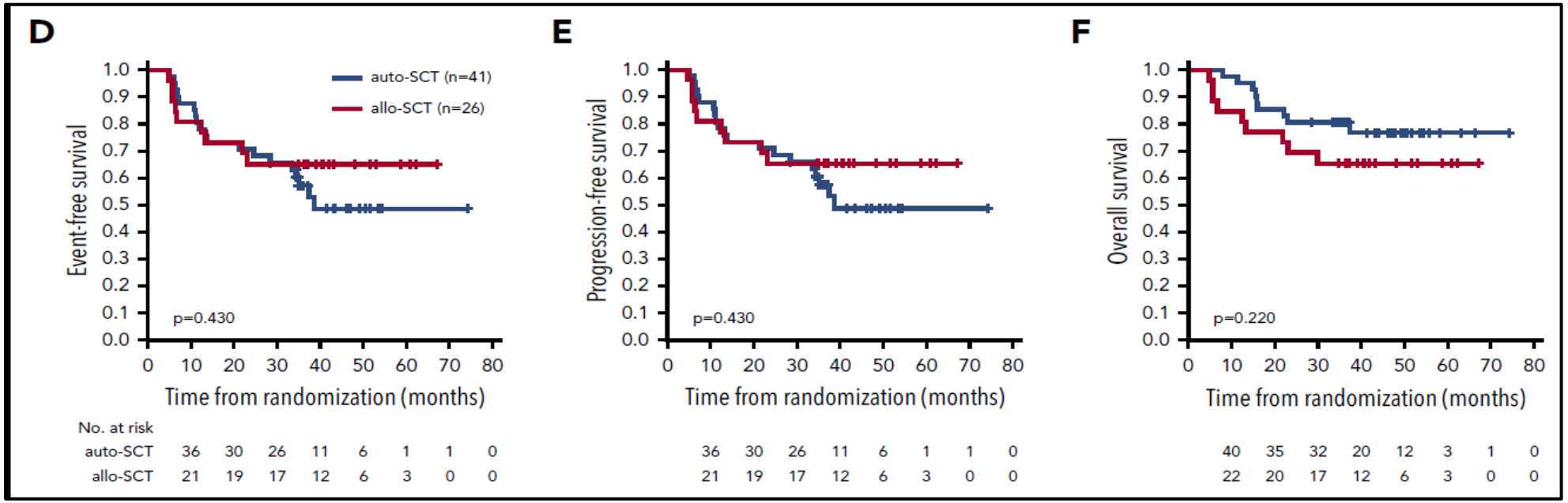
Histology	5-yr PFS	95% CI
ALCL	61%	42%-76%
AILT	49 %	30%-65%
EATL	38 %	18%-57%
PTCL-NOS	38 %	25%-50%

A randomized phase 3 trial of autologous vs allogeneic transplantation as part of first-line therapy in poor-risk peripheral T-NHL

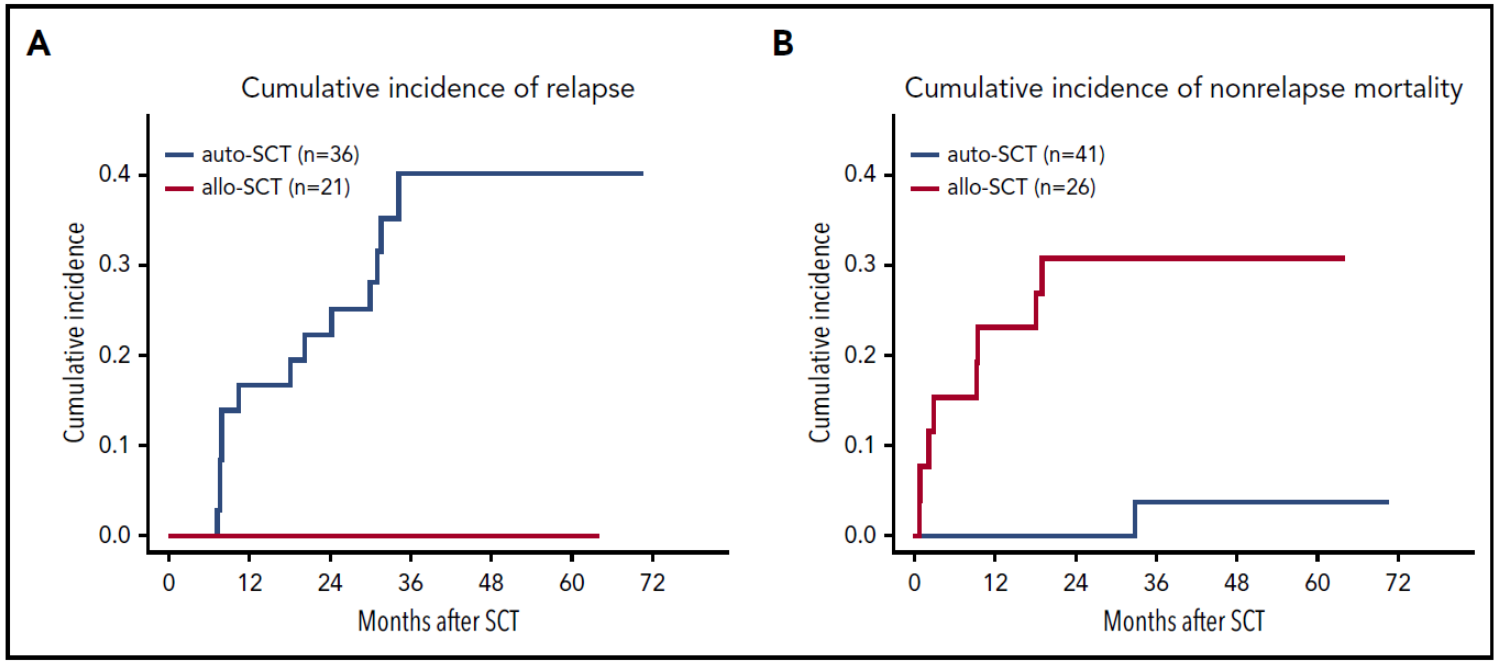
- CHOEPX4+DHAPX1→
- AutoSCT vs AlloSCT
- Out of 103 pts:
- 41 AutoSCT, 26 AlloSCT
- MAC AlloSCT

	Randomized patients				Transplant recipients			
	Auto-SCT (n = 54)		Allo-SCT (n = 49)		Auto-SCT (n = 41*)		Allo-SCT (n = 26)	
Histology								
Reviewed	54†	(100)	46	(94)	41‡	(100)	25	(96)
Peripheral T-cell lymphoma, not otherwise specified (PTCL-NOS)	16	(30)	15	(33)	11	(27)	8	(32)
Angioimmunoblastic T-cell lymphoma	17	(33)	20	(43)	16	(40)	12	(48)
Anaplastic large cell lymphoma ALK-negative	9	(17)	5	(11)	8	(20)	3	(12)
Extranodal NK/T-cell lymphoma, nasal type	0	(0)	1	(2)	0	(0)	0	(0)
Enteropathy-associated T-cell lymphoma (EATL) types I and II	3	(6)	0	(0)	3	(8)	0	(0)
Hepatosplenic T-cell lymphoma	2	(4)	1	(2)	1	(2)	1	(4)
Subcutaneous panniculitis-like PTCL	1	(2)	0	(0)	0	(0)	0	(0)
Primary cutaneous γ/δ T-cell lymphoma	0	(0)	1	(2)	0	(0)	0	(0)
T-cell lymphoma, further specification not possible	1	(2)	1	(2)	1	(2)	1	(4)
Other entities	3§	(6)	2‖	(4)	0	(0)	0	(0)

Schmitz N et al. Blood 2021



Median Observation:42 mo



Schmitz N et al. Blood 2021

Autologous Stem-Cell Transplantation As First-Line Therapy in Peripheral T-Cell Lymphomas: Results of a Prospective Multicenter Study

Peter Reimer, Thomas Rüdiger, Eva Geissinger, Florian Weissinger, Christoph Nerl, Norbert Schmitz, Andreas Engert, Hermann Einsele, Hans Konrad Müller-Hermelink, and Martin Wilhelm

VOLUME 27 · NUMBER 1 · JANUARY 1 2009

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Table 1. Clinical Characteristics of Patients at Diagnosis

Characteristic	No. of Patients (N = 83)	%
Histology		
NOS	32	39
AIL	27	33
ALK-negative ALCL	13	16
Intestinal	5	6
Nasal type	4	5
Hepatosplenic	2	2
Age, years		
Median	46.5	
Range	30-65	
Sex		
Male	51	61
Female	32	39
Ann Arbor stage		
I	5	6
II	16	19
III	25	30
IV	37	45

- 6XCHOP→CR or PR→ASCT
- CR:32(39%)
- PR:33(40%)
- 55(66%) underwent ASCT
- **<u>Reasons for not receiving ASCT:</u>**
- -Progressive dis (24 pts)
- -Patient request (2 pts)
- -TRM (1 pt)
- -Other (1 pt)

Autologous Stem-Cell Transplantation As First-Line Therapy in Peripheral T-Cell Lymphomas: Results of a Prospective Multicenter Study

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Median follow-up time:33 months

TRM:%3,6

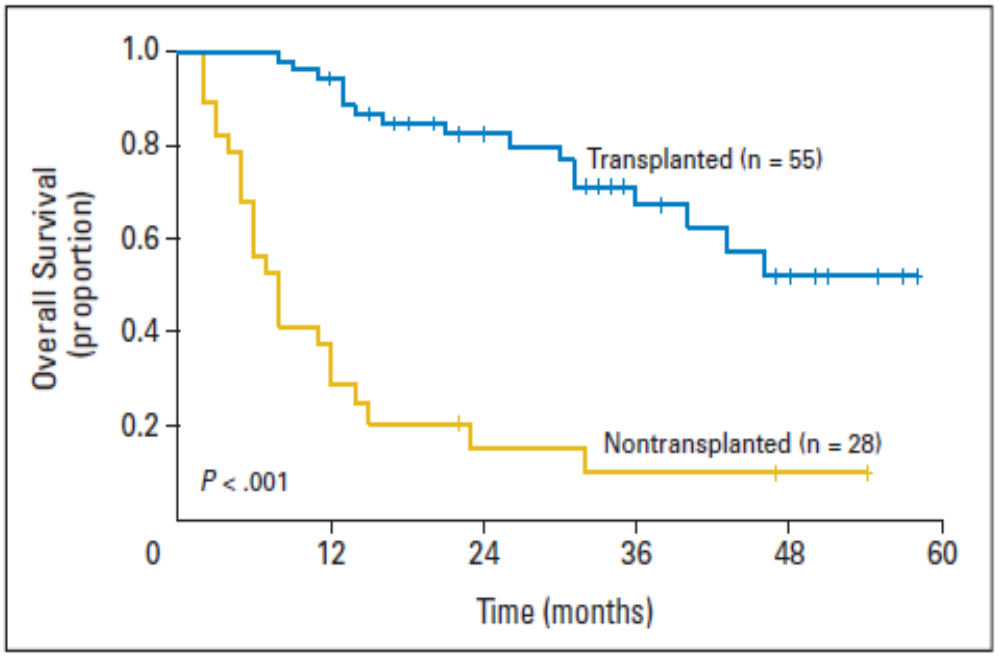
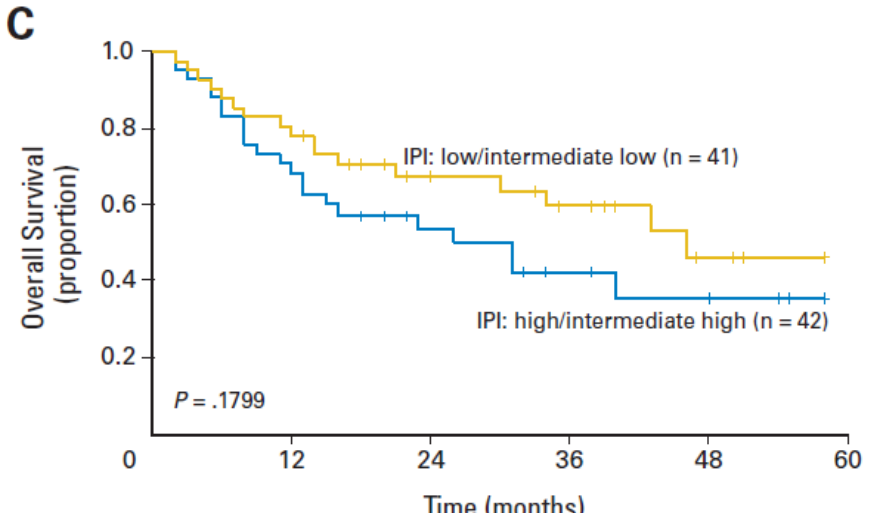
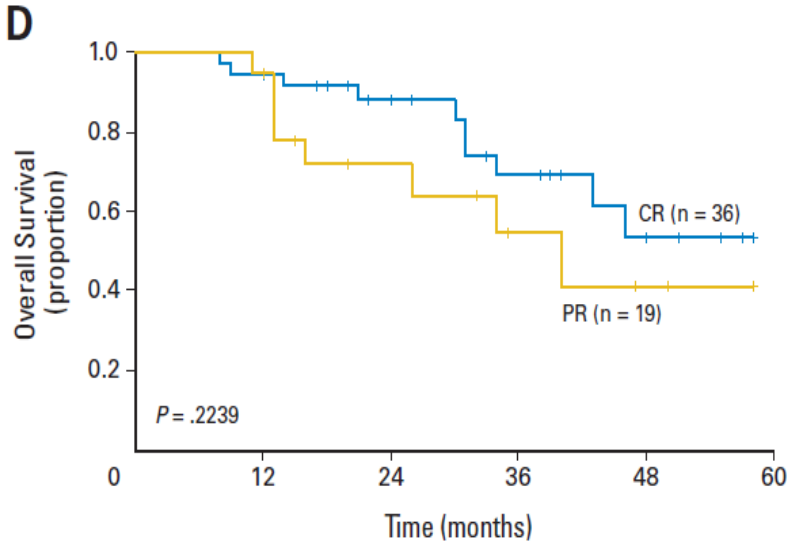


Fig 2. Overall survival in patients who did and did not receive transplantation.





- ❑ 3-year OS:71% ASCT vs 11% no ASCT
- ❑ 22/55(40%) patients experienced relapse after autoSCT
- ❑ Median time to relapse:11.5 months

The Role of Autologous Stem Cell Transplantation in Patients With Nodal Peripheral T-Cell Lymphomas in First Complete Remission: Report From COMPLETE, a Prospective, Multicenter Cohort Study

Cancer 2019;125:1507-1517

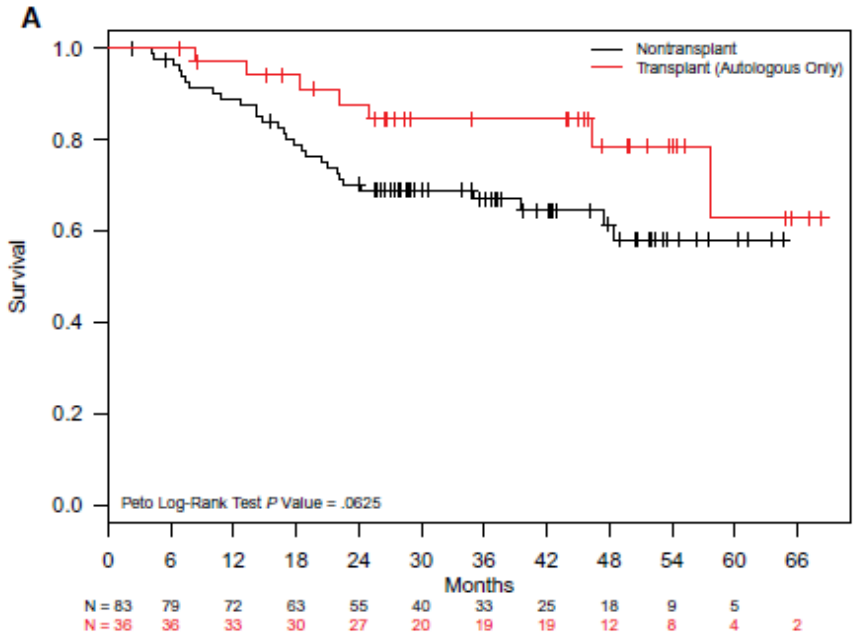
- ✓ 499 pts
- ✓ 213 pts in CR
- ✓ **119 pts with nodal PTCL**
- ✓ -ALK- PTCL
- ✓ -AITCL
- ✓ -PTCL-NOS
- ✓ **36 pts ASCT**
- ✓ **83 pts non-ASCT**
- ✓ **Reasons for non-ASCT:**
- ✓ -physician decision 55%
- ✓ -PTCL subtype 21%
- ✓ -Pateint age/comorbidities (14%)
- ✓ -Others

TABLE 1. Characteristics of Patients With PTCL in First Complete Remission

Characteristic	Non-ASCT (n = 83)	ASCT (n = 36)	*P*
Age			
<65 y, No. (%)	39 (47)	23 (64)	.09
≥65 y, No. (%)	44 (53)	13 (36)	
Mean ± SD, y	64.5 ± 13.9	57.5 ± 12.6	
Range, y	24-89	23-75	
Sex, No. (%)			
Female	28 (34)	8 (22)	.21
Male	55 (66)	28 (78)	
Race, No. (%)			
White	65 (78)	30 (83)	.32
Black	11 (13)	4 (11)	
Asian	3 (4)	0	
Other/unavailable	4 (5)	2 (6)	
ECOG performance status, No. (%)			
0-1	79 (95)	35 (97)	.61
2	4 (5)	1 (3)	
3	0	0	
Histologic subtype, No. (%)			
AITL	18 (22)	17 (47)	.01
ALK-negative ALCL	26 (31)	4 (11)	.02
PTCL NOS	39 (47)	15 (42)	.59
Ann Arbor stage, No. (%)			
I/II	30 (36)	3 (8)	.01
III/IV	53 (64)	33 (92)	
Bone marrow involvement, n/N (%)	11/40 (28)	8/13 (62)	.03
IPI score, No. (%)			
0-2	59 (71)	23 (64)	.44
3-4	24 (29)	13 (36)	
PIT score, No. (%)			
1	18 (22)	9 (25)	.23
2	38 (46)	15 (42)	
3	22 (27)	6 (17)	
4	5 (6)	6 (17)	
First-line chemotherapy			
Anthracycline-containing, No. (%)	54 (71)	25 (71)	.97
No. of cycles, mean ± SD	4.8 ± 2.3	4.9 ± 1.9	.71

The Role of Autologous Stem Cell Transplantation in Patients With Nodal Peripheral T-Cell Lymphomas in First Complete Remission: Report From COMPLETE, a Prospective, Multicenter Cohort Study

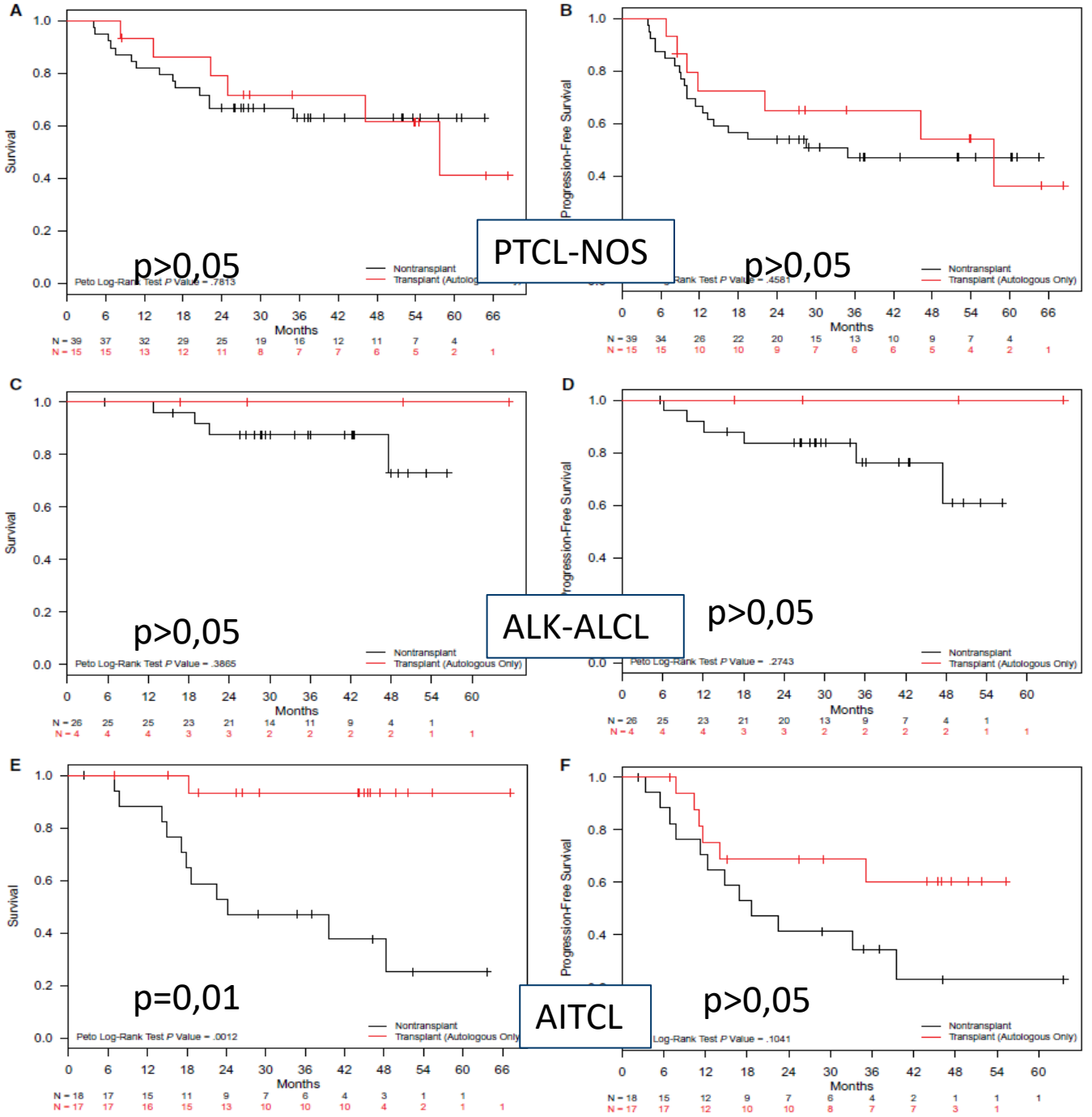
Cancer 2019;125:1507-1517.



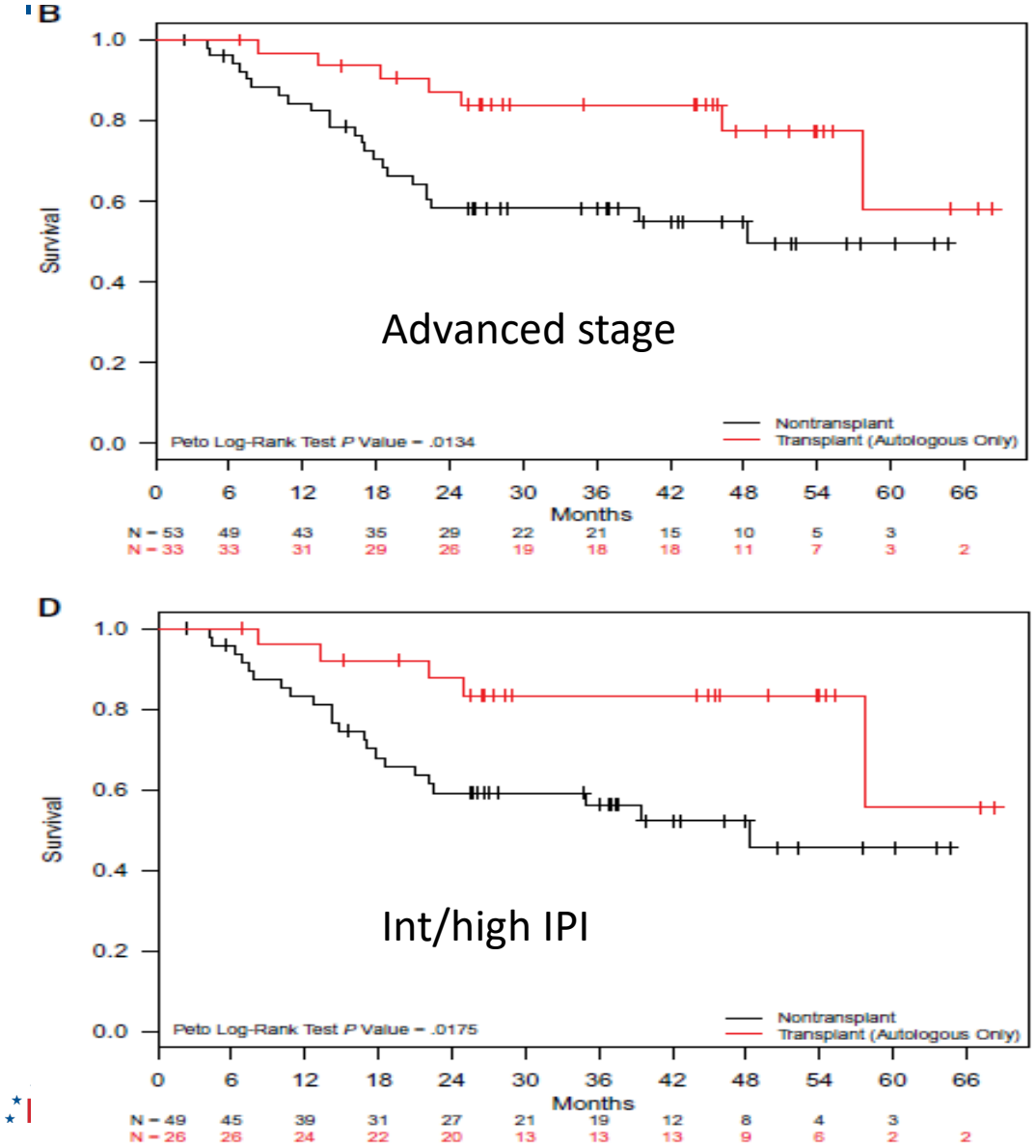
Median FU: 2.8 years

<u>2-year OS:</u>

- ✓ 87.8% for the ASCT group
- ✓ 70.2% for the non-ASCT group.



The Role of Autologous Stem Cell Transplantation in Patients With Nodal Peripheral T-Cell Lymphomas in First Complete Remission: Report From COMPLETE, a Prospective, Multicenter Cohort Study



Patients with
-AITL
-Advanced-stage disease
-Intermediate-to-high IPI
might benefit from consolidative ASCT in CR1

Table 2. Selected large studies evaluating consolidative autologous stem cell transplant in nodal peripheral T-cell lymphomas.

First author Study type[a]	Benefit of auto-SCT	Response prior to auto-SCT CR/PR, %	Outcome of intent to auto-SCT (*vs.* no auto-SCT)		Outcome after auto-SCT (*vs.* no auto-SCT)		Comment auto-SCT
			PFS, %	OS, %	PFS, %	OS, %	
Reimer[108]/ Wilhelm[109] Phase II	Maybe	62/20[e]	3-yr, 36[e] 5-yr, 39	3-yr, 48 5-yr, 44	NR	3-yr, 71 (*vs.* 11)* 5-yr, 57 (*vs.* 23)*	5-yr analysis: 28 additional patients analyzed (on protocol)
D'Amore[38] Phase II NLG-01	Maybe	53/31	5-yr, 44	5-yr, 51	NR	5-yr, 61 (*vs.* 28)*	No auto-SCT group includes those with no response/PD
Abramson[41,b] USA multicenter	Yes (UVA)[f] No (CR)	61/12	NR	NR	3-yr, 58 (*vs.* 30)*	3-yr, 74 (*vs.* 53)	No PFS/OS benefit of auto-SCT in MVA All CR: no PFS/OS benefit of auto-SCT
Ellin[8,c] Swedish Registry	Yes	NR	Auto-SCT MVA*	Auto-SCT MVA*	NR	NR	PFS*/OS* benefit in 'intent to auto-SCT' group <70 yr (not adjusted for response)
Cederleuf[42] Swedish/Danish	No	CR (All by design)	NR	NR	2-yr, 66 (*vs.* 67)	2-yr, 76 (*vs.* 80)	MVA: no OS benefit
Fossard[40] LYSA	No	CR/PR 57	5-yr, 46 (*vs.* 40.5)	59 (*vs.* 60)	NR	NR	No PFS/OS benefit using propensity score matching MVA: no PFS/OS benefit
Park[110] COMPLETE	No	CR (All by design)	NR	NR	*P*=0.23	2-yr, 88 (*vs.* 70)	Improved OS with auto-SCT in IPI score 2-4
Janikova[111] CLSG	No	NR	5-yr, 46 (*vs.* 41)	5-yr, 59.5 (*vs.* 49)	NR	NR	Adjusted by IPI score: no PFS/OS benefit with auto-SCT
Garcia-Sancho[112,d] GELTAMO/FIL	Yes	CR (All by design)	NR	NR	5-yr, 63 (*vs.* 49)*	5-yr, 74 (*vs.* 62)	All CR: PFS*/OS* benefit in MVA
Brink[9] Netherlands Registry	Yes	NR	NR	NR	NR	Landmark 5-yr, 78 (*vs.* 45)* CR: 5-yr, 82 (*vs.* 47)*	MVA: improved OS*

Ngu HS, Savage KJ. Haematologica 2023

Role of stem cell transplant in CD30^{+} PTCL following frontline brentuximab vedotin plus CHP or CHOP in ECHELON-2

Supplemental Table 3. Patients Achieving CR on the A+CHP Arm: Summary of PFS by Consolidative SCT

	ALK– sALCL N=76		Non-sALCL N=38		Combined N=114	
	SCT (n=27)	No SCT (n=49)	SCT (n=11)	No SCT (n=27)	SCT (n=38)[a]	No SCT (n=76)
Estimated PFS at 3 years, % (95% CI)	85.0 (64.9-94.1)	62.4 (46.4-74.8)	70.1 (32.3-89.5)	41.7 (22.4-59.9)	80.4 (62.9-90.2)	54.9 (42.4-65.8)
Estimated PFS at 5 years, % (95% CI)	75.6 (46.6- 90.2)	51.5 (31.6- 68.3)	56.1 (19.5-81.5)	35.7 (17.0-55.0)	65.3 (38.7-82.6)	46.4 (32.3-59.3)
Univariate, HR (95% CI)	0.35 (0.13-0.98)		0.46 (0.15-1.41)		0.36 (0.17-0.77)	

Savage KJ et al. Blood Advances 2022

Role of stem cell transplant in CD30^{+} PTCL following frontline brentuximab vedotin plus CHP or CHOP in ECHELON-2

Supplemental Table 6. Patients Achieving CR on the CHOP Arm: Summary of PFS by Consolidative SCT

	ALK– sALCL N=53		Non-sALCL N=44		Combined N=97	
	SCT (n=13)	No SCT (n=40)	SCT (n=16)	No SCT (n=28)	SCT (n=29)	No SCT (n=68)
Estimated PFS at 3 years, % (95% CI)	58.6 (26.7-80.6)	62.7 (45.2-76.0)	73.7 (44.1-89.2)	42.9 (24.6-60.0)	67.2 (46.3-81.5)	54.1 (41.2-65.3)
Estimated PFS at 5 years, % (95% CI)	58.6 (26.7-80.6)	55.7 (35.2-72.1)	43.0 (8.8-74.6)	42.9 (24.6-60.0)	48.9 (21.6-71.6)	50.9 (37.4-62.9)
Univariate, HR (95% CI)	0.67 (0.24-1.89)		0.57 (0.22-1.47)		0.63 (0.32-1.24)	

Savage KJ et al. Blood Advances 2022

R/R PTCL-NOS TREATMENT

R/R PTCL-NOS TREATMENT

- Despite advances in the front-line setting a large proportion of PTCL patients have lymphoma relapse or have primary refractory disease.
- The only established curative treatment is SCT.
- Studies of PTCL-NOS have elucidated the GATA3 and TBX21 molecular subtypes, BUT how this informs treatment decisions remains unknown

The outcome of peripheral T-cell lymphoma patients failing first-line therapy: a report from the prospective, International T-Cell Project

Monica Bellei,[1] Francine M. Foss,[2] Andrei R. Shustov,[3] Steven M. Horwitz,[4] Luigi Marcheselli,[1] Won Seog Kim,[5] Maria E. Cabrera,[6] Ivan Dlouhy,[7] Arnon Nagler,[8] Ranjana H. Advani,[9] Emanuela A. Pesce,[1] Young-Hyeh Ko,[10] Virginia Martinez,[6] Silvia Montoto,[11] Carlos Chiattone,[12] Alison Moskowitz,[4] Michele Spina,[13] Irene Biasoli,[14] Martina Manni[1] and Massimo Federico;[1] on behalf of the International T-cell Project Network

Haematologica 2018
Volume 103(7):1191-1197

- ✓ The International T-cell Project is an international prospective cohort study
- ✓ Out of 937 patients who received first-line treatment:
- ❑ 436 (47%) were identified as refractory
- ❑ 197 (21%) as relapsed
- ❑ 304 (32%) patients remained in complete remission
- ✓ Median time from the end of treatment to relapse was 8 months (range 2-73)

Median FU:38 mo

Table 1. Main characteristics at diagnosis of 436 refractory and 197 relapsed patients, and of all 937 patients analyzed.

Parameter	Refractory (n=436)		Relapsed (n=197)		All (n=937)	
	N	%	N	%	N	%
Median age (range), years	59 (18-89)	58 (21-88)	56 (18-89)			
Age, >60 years, N, %	203	47	90	46	401	43
Sex, male, N, %	273	63	136	69	579	62
ECOG-PS, >1, N, %	143	33	31	16	214	23
Serum LDH, > ULN, N, % [578]	234	54	82	42	404	43
Ann Arbor staging, III-IV, N, % [591]	325	75	128	65	605	65
ENS, >1, N, % [568]	148	34	43	22	250	27
Serum albumin, <3.5 g/dL, N, % [562]	204	47	70	36	359	38
NLR, >6.5, N, % [598]	125	29	48	24	231	25
PIT, high-risk (2-4), N, % [503]	172	39	52	26	283	30
IPI, high-risk (3-5), N, % [551]	184	42	53	27	294	31
Histology subtype						
PTCL, NOS	185	42	83	42	346	37
AITL	70	16	42	21	154	16
ALCL, ALK -	60	14	22	11	140	15
ALCL, ALK +	21	5	14	7	77	8
NKTCL	35	8	21	11	109	12
Other	65	15	15	8	80	9
1st line therapy						
CHT +/- RT	422	97	174	88	844	90
RT alone	2	<1	1	<1	18	2
CHT/consolidation HCT	12	3	22	11	75	8
Response to 1st line therapy						
CR	-	-	170	86	474	51
PR	137	31	27	14	164	18
<PR	299	69	-	-	299	32

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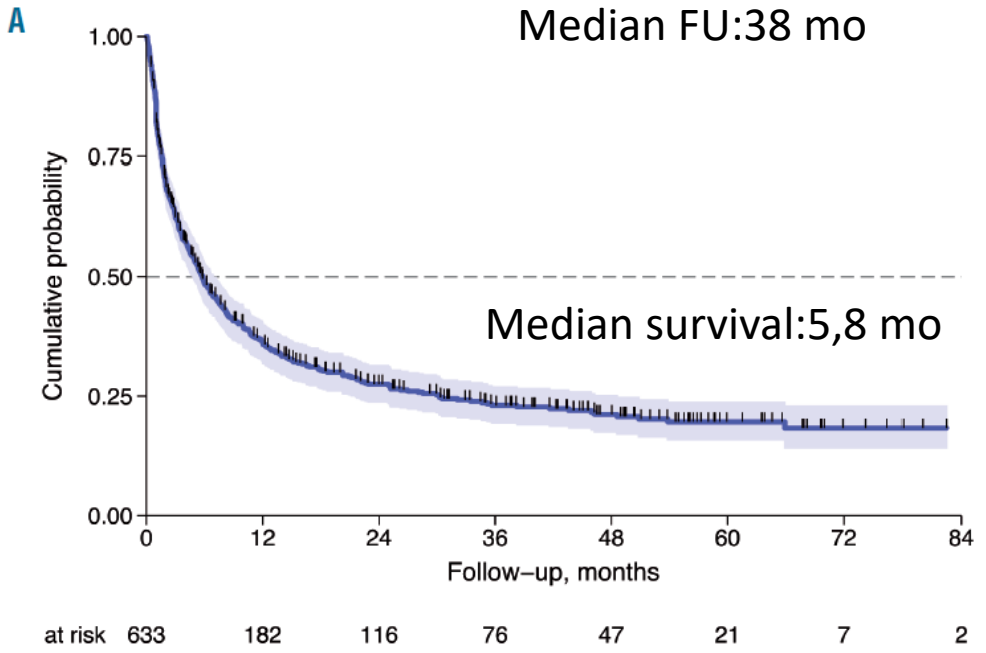
The outcome of peripheral T-cell lymphoma patients failing first-line therapy: a report from the prospective, International T-Cell Project

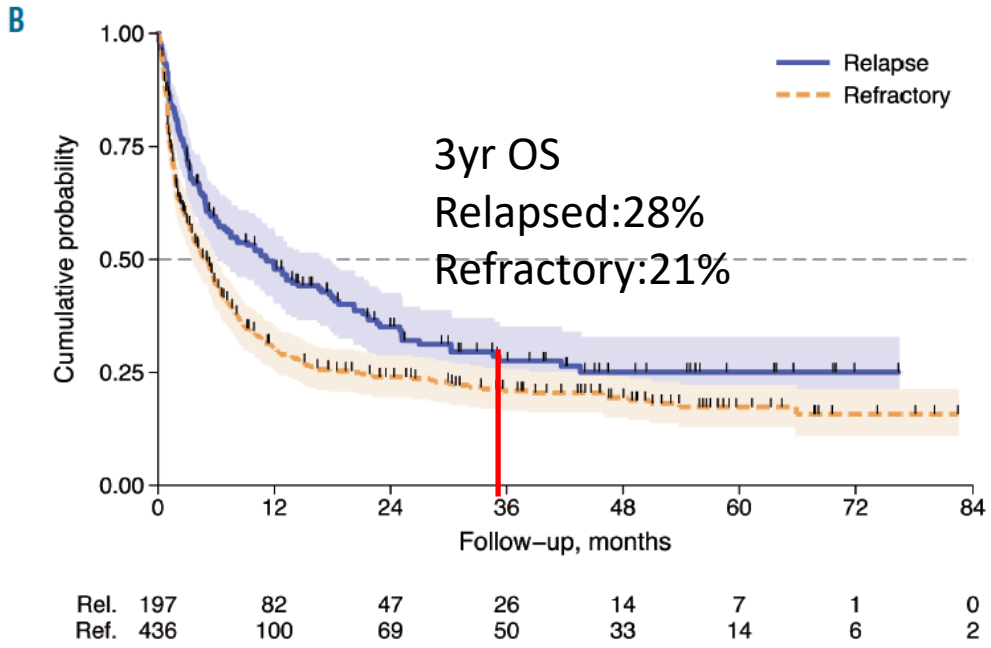
Haematologica 2018
Volume 103(7):1191-1197

Table 2. Details of treatment and events for the refractory/relapsed patients (n=633).

Parameter	Refractory (n=436)		Relapsed (n=197)		All (n=633)	
	N	%	N	%	N	%
Type of event						
Relapse after CR	-	-	170	86	170	27
Relapse after PR	-	-	27	14	27	4
Unsatisfactory PR	137	31	-	-	137	22
Refractory (<PR)	299	69	-	-	299	47
Timing of events						
Refractory	436	69	-	-	436	69
Early relapse (≤ 12 months)	-	-	125	20	125	20
Late relapse (>12 months)	-	-	72	11	72	11
HCT as Salvage						
HCT, yes	42	9	57	29	99	16
No HCT (eligible for HCT)	-	-	124	63		
No HCT (CR/PR not eligible for HCT)	125	29	16	8		
No HCT (<PR not eligible for HCT)	269	62	-	-		
No HCT (*whichever the reason*)	394	91	140	71	534	84

CR: complete remission; PR: partial remission; Unsatisfactory PR: PR requiring immediate treatment after initial therapy; HCT: hematopoietic cell transplantation.





Relapsed pts:

- ✓ 92% eligible for HCT
- ✓ 29% received HCT
- ✓ 63% was eligible for HCT but not received HCT

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Table 3. Univariate Cox regression analysis for SAR.

Status	3-year SAR%(95%CI)	HR (95%CI)
Relapse	28 (21-35)	1.00
Refractory	21 (17-25)	1.43 (1.16-1.76)
Early relapse (≤ 12 months)	23 (16-32)	1.00
Late relapse (> 12 months)	34 (21-48)	0.57 (0.41-0.79)
Not eligible to HCT <PR	7 (3-11)	1.00
Not eligible to HCT (CR/PR)	30 (21-38)	0.43 (0.34-0.55)
Eligible HCT (CR/PR)	27 (19-36)	0.45 (0.35-0.58)
HCT	48 (37-58)	0.22 (0.16-0.30)
No HCT at salvage	18 (14-22)	1.00
HCT at salvage	48 (37-58)	0.36 (0.26-0.48)

CR: complete remission; PR: partial remission; SAR: survival after relapse; HCT: hematopoietic cell transplantation; HR: Hazard Ratio; CI: Confidence Interval

Hematopoietic Cell Transplantation for Systemic Mature T-Cell Non-Hodgkin Lymphoma

Table 1. Patient Characteristics

Characteristic	Autologous HCT No.	Autologous HCT %	Allogeneic HCT No.	Allogeneic HCT %	P
Histology†					.04
Anaplastic large-cell lymphoma‡	61	53	51	40	
Peripheral T-cell lymphoma, unspecified	39	34	63	50	
Angioimmunoblastic T-cell lymphoma	15	13	12	10	
No. of lines of therapy prior to transplantation					
Median	2		3		.002
1	19	17	18	14	< .001
2	55	48	38	30	
≥ 3	39	34	55	43	
Unknown	2	2	7	6	

Table 2. Treatment- and Transplantation-Related Characteristics

Characteristic	Autologous HCT No.	Autologous HCT %	Allogeneic HCT No.	Allogeneic HCT %	P
Chemotherapy sensitivity					< .001
Sensitive	99	86	75	60	
Resistant	9	8	37	29	
Untreated	0		2	2	
Unknown	7	6	12	10	
Disease status at transplantation					.001
CR1	40	35	18	14	
CR2+	24	21	20	16	
PIF, sensitive	16	14	23	18	
PIF, other	6	5	23	18	
Relapse, sensitive	17	15	21	17	
Relapse, other	10	9	18	14	
Missing	2	2	3	3	
Conditioning regimen (allogeneic)	N/A				
Myeloablative			74	59	
NST/RIC			45	36	
Unknown			7	5	

Smith SM et al. J Clin Oncol 2013

Hematopoietic Cell Transplantation for Systemic Mature T-Cell Non-Hodgkin Lymphoma

Table 3. Univariate Outcomes of Patients With HCT

	All Patients							Patients Beyond CR1						
	AutoHCT		Myeloablative		NST/RIC			AutoHCT		Myeloablative		NST/RIC		
Variable	%	95% CI (%)	%	95% CI (%)	%	95% CI (%)	*P*	%	95% CI (%)	%	95% CI (%)	%	95% CI (%)	*P*
Nonrelapse mortality														
At 100 days	2	0 to 6	19	11 to 29	18	8 to 30	< .001	3	1 to 8	21	12 to 32	20	9 to 33	< .001
At 1 year	7	3 to 13	29	19 to 40	27	15 to 40	< .001	4	1 to 10	30	19 to 42	27	14 to 41	< .001
At 3 years	11	6 to 17	32	22 to 43	27	15 to 40	< .001	6	2 to 13	34	22 to 46	27	14 to 41	< .001
Relapse/progression														
At 1 year	34	26 to 43	29	19 to 40	38	24 to 52	.5694	46	35 to 57	33	22 to 45	39	24 to 53	.2978
At 3 years	43	33 to 52	32	21 to 43	40	26 to 54	.3282	53	41 to 64	37	25 to 49	42	27 to 56	.1627
Progression-free survival														
At 1 year	58	49 to 67	42	31 to 53	36	22 to 49	.0113	50	38 to 60	37	25 to 49	34	20 to 49	.1813
At 3 years	47	37 to 56	36	25 to 47	33	20 to 47	.1834	41	29 to 52	29	18 to 41	32	18 to 46	.3449
Overall survival														
At 1 year	68	59 to 76	49	37 to 60	59	44 to 72	.0266	62	50 to 72	43	30 to 55	58	41 to 71	.0701
At 3 years	59	49 to 68	39	28 to 51	52	36 to 66	.0356	53	40 to 64	31	20 to 44	50	33 to 64	.0349

Abbreviations: autoHCT, autologous hematopoietic cell transplantation; CR1, first complete remission; NST, nonmyeloablative stem-cell transplantation; RIC, reduced-intensity conditioning.

Smith SM et al. J Clin Oncol 2013

Outcome of allogeneic transplantation for mature T-cell lymphomas: impact of donor source and disease characteristics

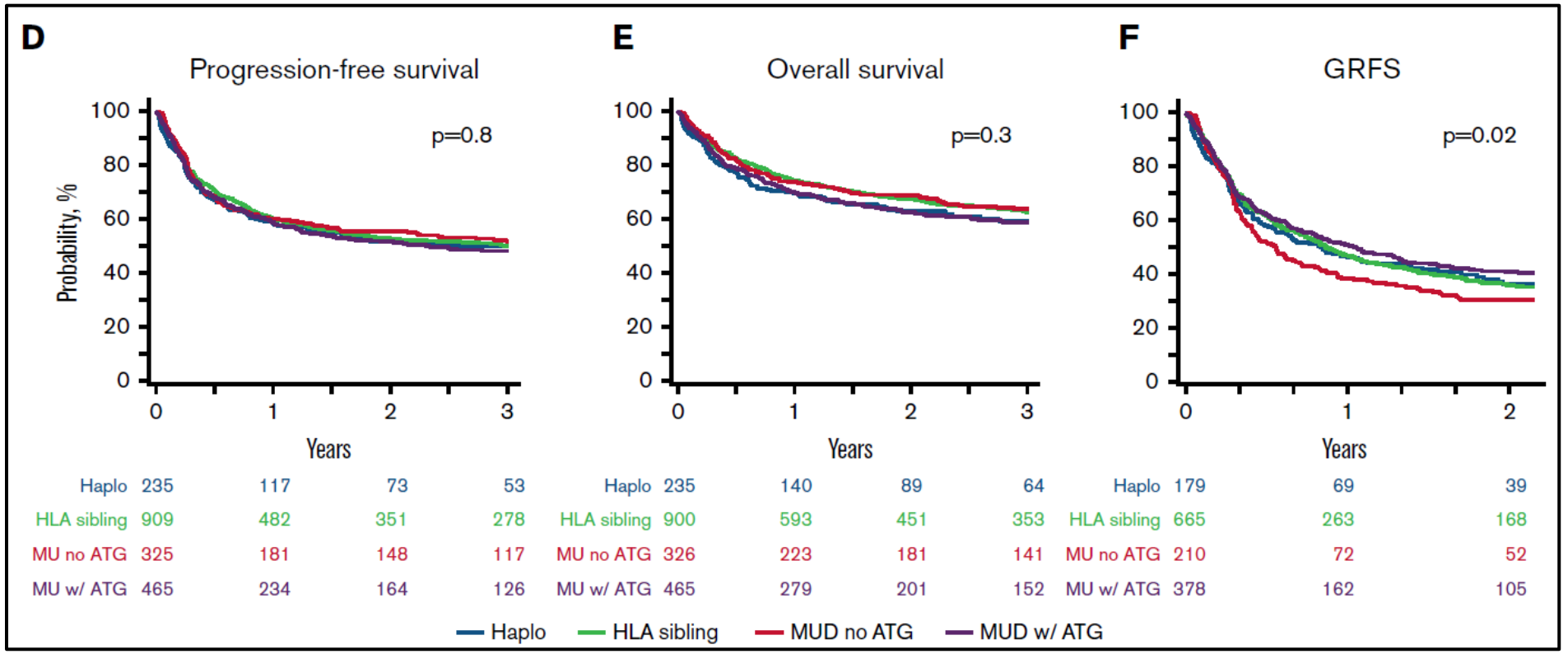
- Combined retrospective registry study from EBMT and CIBMTR: 1,942 PTCL undergoing allo-SCT between 2008 and 2018 primarily with R/R disease

Table 1. Patient characteristics

	Haplo-HCT	MSD HCT	MUD TCD+	MUD TCD−	*P*
Disease status					.84
CR	120 (51)	451 (51)	238 (52)	161 (51)	
PR	74 (32)	252 (29)	124 (27)	96 (30)	
Resistant/Untreated	39 (17)	177 (20)	93 (20)	60 (19)	
Missing data	4	31	13	9	
HCT-CI					
≥3	52 (28)	191 (30)	105 (35)	95 (37)	.08
Missing data*	52	280	164	72	
Chemotherapy lines					
Median (IQR), n	2 (1.8-3)	2 (1-3)	2 (1-3)	2 (2-3)	.34
1 line†	31 (23)	89 (26)	57 (29)	19 (21)	
2 lines†	47 (34)	109 (32)	62 (32)	32 (34)	
≥3 lines†	58 (43)	143 (42)	76 (39)	42 (45)	
Missing data‡	101	570	273	233	
Female donor/male recipient	61 (26)	254 (28)	52 (11)	45 (14)	<.001
Histology					.14
AITL	68 (29)	270 (30)	155 (33)	101 (31)	
ALCL§	58 (24)	170 (19)	82 (18)	75 (23)	
PTCL	111 (47)	471 (51)	231 (49)	150 (46)	
Prior autologous HCT	78 (33)	336 (37)	195 (42)	132 (41)	.09
Follow-up, median (range) [IQR], months	24 (1-113) [13-48]	43 (1-128) [17-72]	35 (1-132) [13-63]	49 (1-134) [24-72]	

Hamadani M et al. Blood Advances 2022

Outcome of allogeneic transplantation for mature T-cell lymphomas: impact of donor source and disease characteristics



- 3-yr PFS:48-52%; 3-yr OS:59-64%
- Significant predictors of inferior OS and PFS were active disease status at HCT and decreased PS.
- AITL was associated with significantly reduced relapse risk and better PFS compared with PTCL-NOS.

Hamadani M et al. Blood Advances 2022

SALVAGE CHEMOTHERAPY

CT	ORR %	CR %	Median PFS (mo)
GDP	69	19	4 mo
Bendamustin	50	28	DoR 3.5 mo
ICE	70	35	6 mo
ESHAP	32	18	2.5 mo

Mak et al. Clin Oncol. 2013; 31:1970–1976.

Pralatrexate in Patients With Relapsed or Refractory Peripheral T-Cell Lymphoma: Results From the Pivotal PROPEL Study

- n: 111 pts
- Median prior lines:3
- PTCL unspecified:53%
- The median DoR was 10.1 months
- The median PFS was 3.5 months
- The median OS was 14.5 months
- The most common AEs were mucositis, nausea, thrombocytopenia,and fatigue.

Table 3. Response Analyses by Key Subsets

Parameter	No.	%	IWC Response Rate No.	IWC Response Rate %	95% CI
Region					
North America	85	78	27	32	22 to 43
Europe	24	22	5	21	7 to 42
Age, years					
< 65	70	64	19	27	17 to 39
≥ 65	39	36	13	33	19 to 50
Prior systemic therapy					
1 regimen	23	21	8	35	16 to 57
2 regimens	29	27	7	24	10 to 44
> 2 regimens	57	52	17	30	18 to 43
Prior transplant					
Yes	18	17	6	33	13 to 59
No	91	83	26	29	20 to 39
Prior methotrexate					
Yes	21	19	5	24	8 to 47
No	88	81	27	31	21 to 41
Histology					
PTCL NOS	59	54	19	32	21 to 46
Angioimmunoblastic	13	12	1	8	0 to 36
Anaplastic LC	17	16	6	35	14 to 62
Transformed MF	12	11	3	25	5 to 57
Other	8	7	3	38	9 to 76

Abbreviations: IWC, International Workshop Criteria; PTCL, peripheral T-cell lymphoma; NOS, not otherwise specified; LC, large cell; MF, mycosis fungoides.

O'Connor OA et al. J Clin Oncol 2011

Objective responses in relapsed T-cell lymphomas with single-agent brentuximab vedotin

Table 1. Demographics and baseline disease characteristics by diagnosis

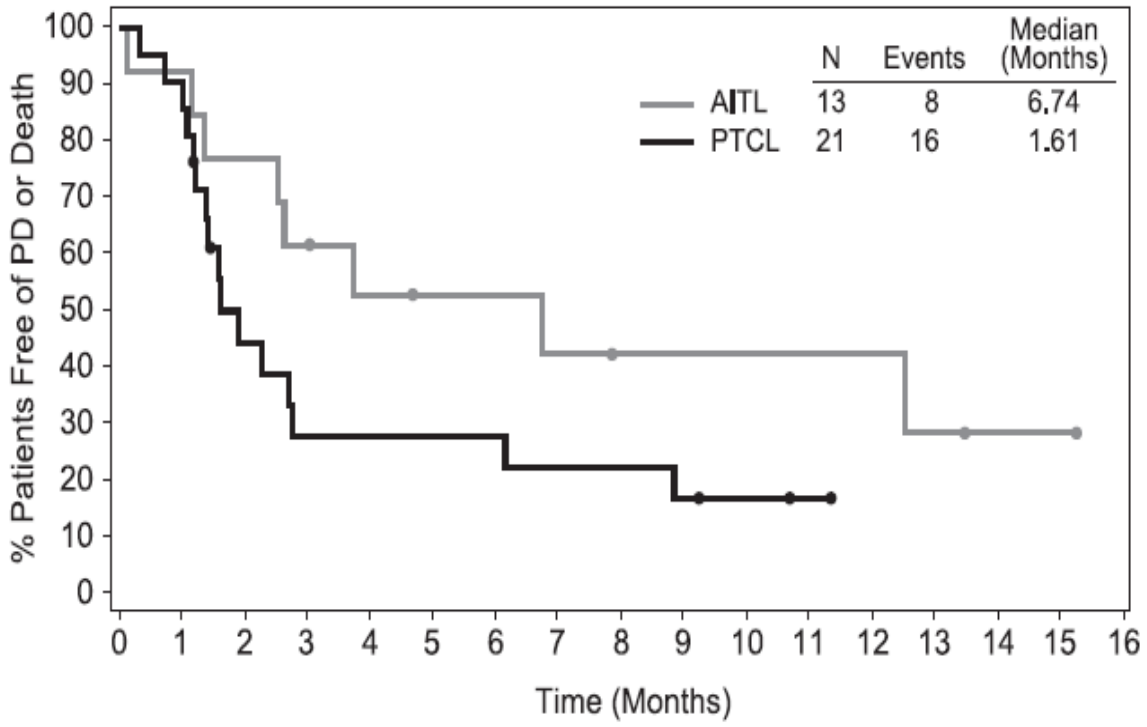
Demographics and characteristics	AITL, n = 13	PTCL, n = 22	All treated patients, N = 35
CD30 expression*			
Positive	9 (69)	17 (77)	26 (74)
Negative	2 (15)	4 (18)	6 (17)
NA or missing	2 (15)	1 (5)	3 (9)
Disease status relative to most recent prior therapy, n (%)			
Refractory	9 (69)	13 (59)	22 (63)
Relapsed	4 (31)	9 (41)	13 (37)
Disease status relative to frontline therapy, n (%)			
Refractory	9 (69)	17 (77)	26 (74)
Relapsed	4 (31)	5 (23)	9 (26)
Median number of prior cancer-related systemic therapy (min, max)	3 (1, 4)	2 (1, 9)	2 (1, 9)

Table 2. Best clinical response

	AITL, n = 13	PTCL-NOS, n = 21	Total, N = 34
Best clinical response, n (%)*			
CR	5 (38)	3 (14)	8 (24)
PR	2 (15)	4 (19)	6 (18)
SD	3 (23)	3 (14)	6 (18)
PD	3 (23)	11 (52)	14 (41)
Objective response rate, n (%)	7 (54)	7 (33)	14 (41)
95% CI for objective response rate†	25.1, 80.8	14.6, 57	24.6, 59.3
Disease control rate, n (%)‡	10 (77)	10 (48)	20 (59)

Horwitz SM et al. Blood 2014

Objective responses in relapsed T-cell lymphomas with single-agent brentuximab vedotin



- Median DOR:
- All patients: 7.6 months
- AITL: 5.5 months
- PTCL-NOS:7.6 months
- No correlation between response and CD30 expression
- CRs or PRs in 9 of 14 patients with little to no detectable CD30 expression (≤15% CD30 expression) by central review.

Horwitz SM et al. Blood 2014

Novel Agents

Table 3. Approved novel agents for the treatment of relapsed/refractory peripheral T-cell lymphomas: global perspective.

Agent	Type of agent	Study phase	Country approval	PTCL subtype(s)	ORR/CR %	Median DoR in months	Median PFS in months	Median OS in months
Pralatrexate[51]	DHFR inhibitor	II	USA/Canada	PTCL/tMF	29/11	10.1	3.5	14.5
Brentuximab vedotin[66]	ADC CD30	II	Global	ALCL	86/57	12.6[a]	13.3	Not reached*
Romidepsin[50,71, b*]	HDAC inhibitor	II	USA/Canada (de-listed)	PTCL AITL	25/15 27/19	17[b] -	4 -	11.3 -
Belinostat[72]	HDAC inhibitor	II	USA	PTCL AITL	26/11 45.5	13.6 -	1.6 -	7.9 -
Chidamide[73]	HDAC inhibitor	II	China	PTCL AITL	28/14 50/40	9.9	2.1	21.4
Forodesine[113]	PNP inhibitor	II	Japan	PTCL	25/10	10.4	1.9	15.6
Mogamulizumab[114,c]	CCR4 antibody	II	Japan	CCR4+ PTCL[c] (2014)	34/17	NR	2.0	14.2
Crizotinib[67]	ALK inhibitor	II	USA 1-21 yr	ALK+ ALCL	88/81	NR	NR	NR

Ngu HS, Savage KJ. Haematologica 2023

T follicular helper phenotype predicts response to histone deacetylase inhibitors in relapsed/refractory peripheral T-cell lymphoma

Table 2. Response to romidepsin as single agent or combinations in TFH vs non-TFH phenotype relapsed/refractory PTCL

	TFH (n = 76)		Non-TFH (n = 51)		
Response	ORR, n/total (%)	CR, n/total (%)	ORR, n/total (%)	CR, n/total (%)	*P**
Overall (n = 127)	43/76 (56.5)	22/76 (28.9)	15/51 (29.4)	10/51 (19.6)	.0035
Single agent (n = 97)	32/59 (54.2)	15/59 (25.4)	12/38 (31.5)	8/38 (21.0)	.0371
Combinations (n = 30)	11/18 (61.1)	7/18 (38.8)	3/12 (25.0)	2/12 (16.6)	.0717

Ghione P et al. Blood Advances 2020

SUMMARY

- Front-line treatment for PTCL is anthracycline-containing chemotherapy regimens (e.g., CHOP or CHOEP in younger patients) or BV-CHP in CD30-expressing subtypes based on ECHELON-2.
- High-dose chemotherapy and ASCT have been used as a consolidation strategy in eligible patients with chemosensitive disease and it leads to improvement in outcomes based on several studies.
- However, attainment of CR prior to transplant is prognostic for improved OS.
- There is no standard therapy for relapsed and refractory setting.
- Enrollment in a clinical trial when possible is recommended.
- Salvage therapy should be considered as palliative therapy or a bridge to transplant.
- Recent large series reported favorable outcomes in patients who underwent allogeneic transplant with the potential curative nature of allogeneic transplant.
- Pralatrexate, the ORR for PTCL-NOS was 32% and the median duration of response was 10.1 months.

THANK YOU...