4th edition
Unmet challenges in high risk hematological malignancies: from benchside to clinical practice
Turin, March 26-27, 2026
Starhotels Majestic

How I treat high risk T-cell lymphomas

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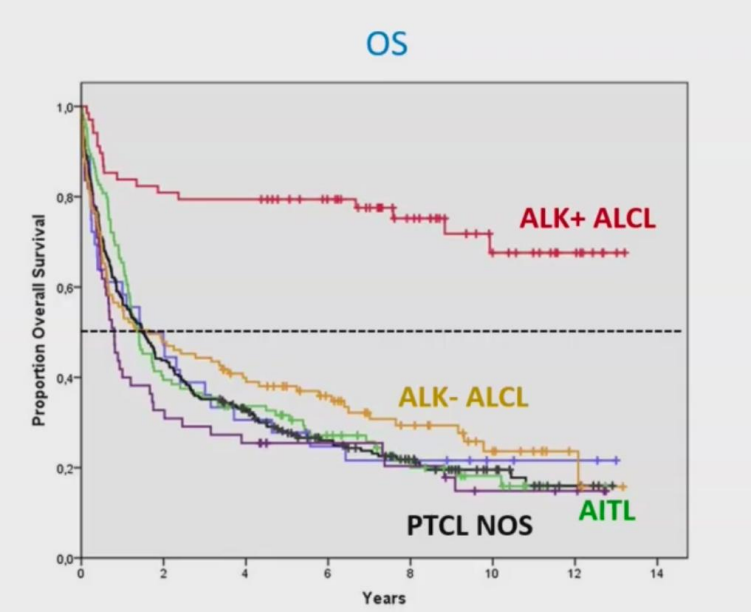
Disclosures of Annalisa Chiappella

Company name	Advisory board	Lecture fees/Educational Events
Abbvie	x	
Incyte	x	
Gilead-Sciences/Kite Pharma Inc.	x	x
Sobi	x	
Eli Lilly		x

PTCL

- PTCL are a group of mature, post-thymic, T-cell, and NK-cell lymphoproliferative disorders
- 15% to 20% of aggressive lymphomas and 10% of NHLs
- Clinical and biological diversity with >30 different subtypes
- Molecular characterization has led to identification of specific subtypes and has contributed to discovery of novel pathway-directed therapies
- Poor outcomes with standard treatments, except for ALK+ ALCL



Fredrik Ellin et al. Blood 2014;124:1570-1577

Outline of the discussion

✓ First line treatment

- Common subtypes of PTCL (PTCL, NOS; ALCL; TFHs)
  - The role of etoposide and consolidation with stem cell transplantation
  - The role of novel pathway-directed and subtype-specific therapies
- Uncommon subtypes of PTCL (EATL, HSTCL) and Extranodal NK-T cell lymphoma

✓ Relapsed/refractory

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- ✓ **Relapsed/refractory**

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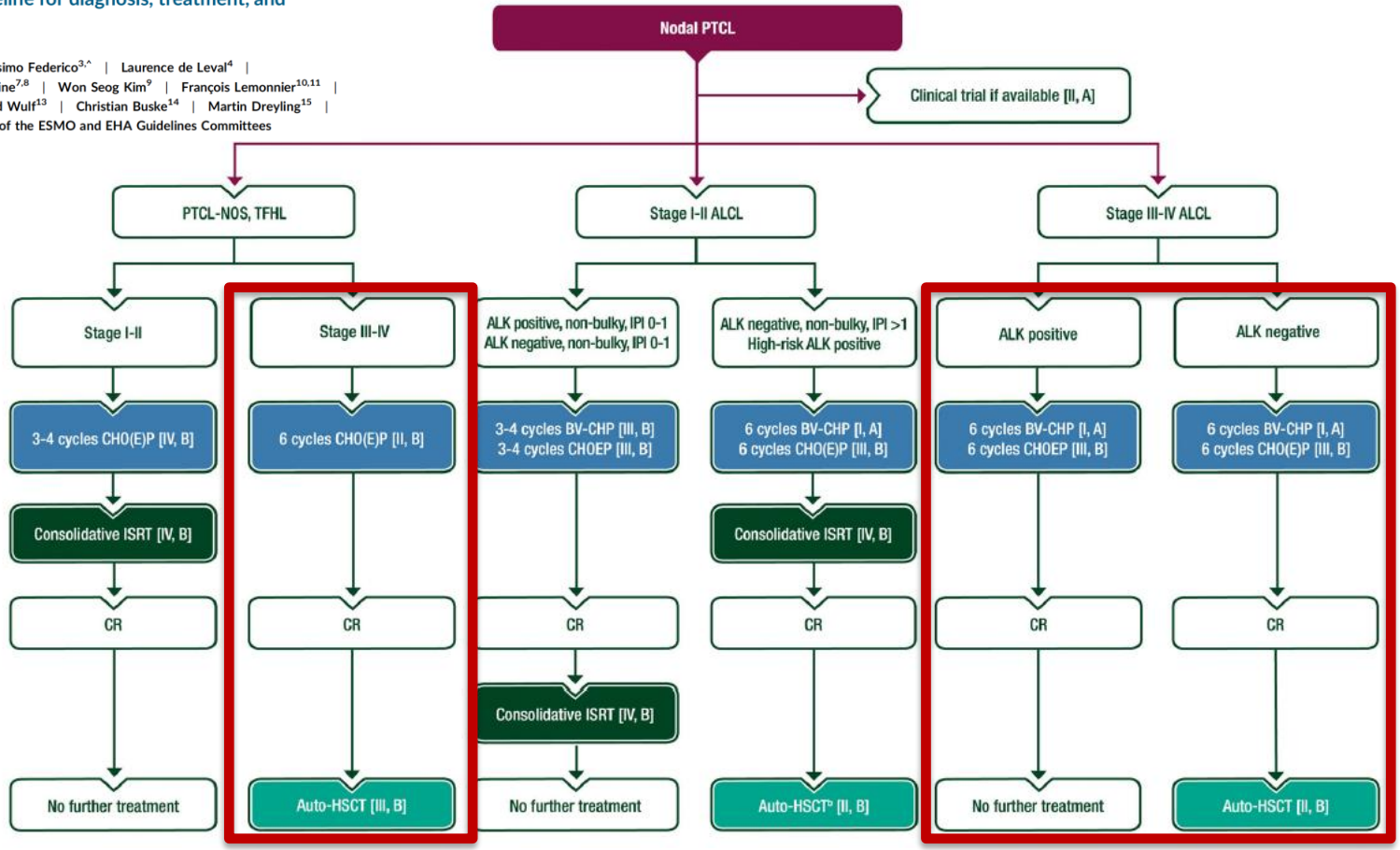
GUIDELINES - CONSENSUS-BASED

HemaSphere eha

Peripheral T- and natural killer-cell lymphomas: ESMO-EHA Clinical Practice Guideline for diagnosis, treatment, and follow-up

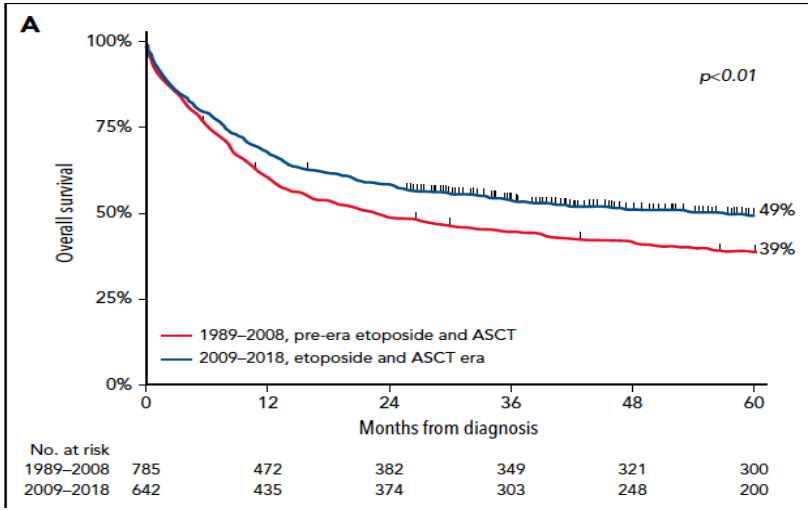
Francesco d'Amore[1,2,^] | Massimo Federico[3,^] | Laurence de Leval[4] | Fredrik Ellin[5,6] | Olivier Hermine[7,8] | Won Seog Kim[9] | François Lemonnier[10,11] | Joost S. P. Vermaat[12] | Gerald Wulf[13] | Christian Buske[14] | Martin Dreyling[15] | Mats Jerkeman[16] | on behalf of the ESMO and EHA Guidelines Committees

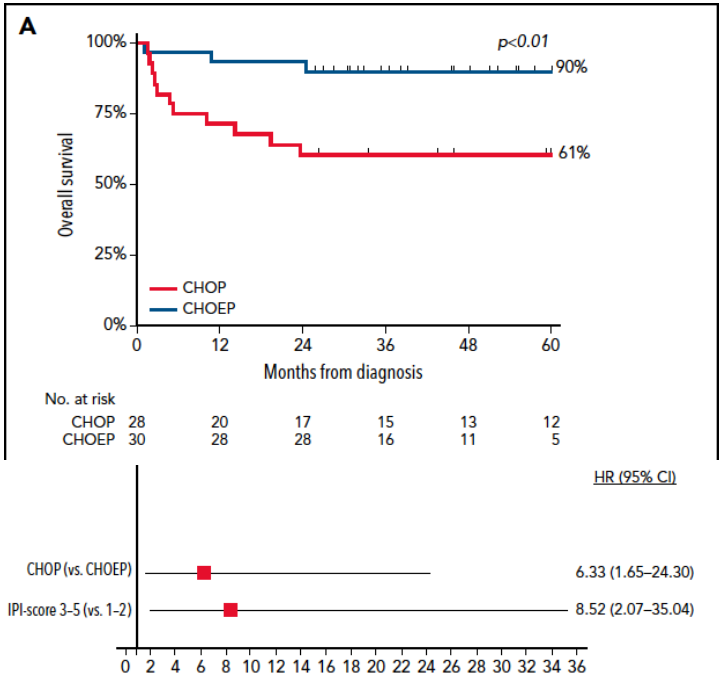


Impact of etoposide and ASCT on survival among patients aged <65 years with stage II to IV PTCL: a population-based cohort study

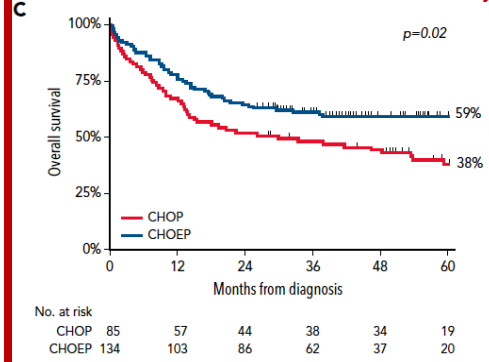
Mirian Brink,[1,*] Frederik O. Meeuwes,[2,3,*] Marjolein W. M. van der Poel,[4] Marie José Kersten,[5] Mariëlle Wondergem,[5] Pim G. N. J. Mutsaers,[6] Lara H. Böhmer,[7] F. J. Sherida H. Woei-A-Jin,[8] Otto Visser,[9] Rimke Oostvogels,[10] Patty M. Jansen,[11] Wouter Plattel,[3] Gerwin A. Huls,[3] Joost S. P. Vermaat,[12] and Marcel Nijland[3]

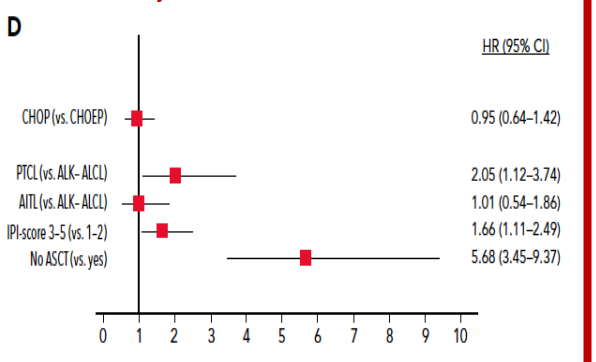
1989-2018: 1427 patients; Netherlands Cancer Registry.





ALK-, PTCL-NOS, AITL





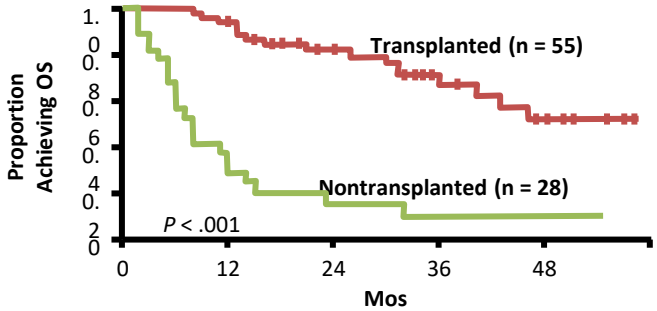
Brink M, et al. Blood 2022

Auto-SCT consolidation in first complete remission

Table 3. Outcomes for autologous stem cell transplant in first remission for PTCL

Study	N (enrolled)	N by PTCL subtype	N (TXP)	Median age (years; range)	EFS/PFS (years)	OS (years)
d'Amore et al[25]	160	PTCL-NOS—62 AITL—30 ALCL—31	115 (72%)	57 (22-67)	44% (5)	51% (5)
Reimer et al[15]	83	PTCL-NOS—32 AITL—27 ALCL—12	55 (66%)	47 (30-65)	36% (3)	48% (3)
Corradini et al[56]	62	PTCL-NOS—28* AITL—10 ALCL—19†	46 (74%)	43 (20-60)	30 (12)	34 (12)
Mehta et al[13]	65‡	PTCL-NOS—32 AITL—21 ALCL—12	39 (60%)	58 (22-75)	38% (4)	52% (4)

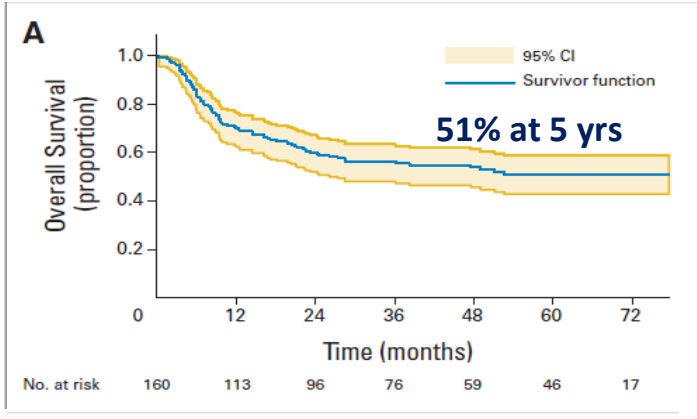
TXP, transplanted.
*Listed as unspecified.
†All were ALK positive.
‡Retrospective, intent-to-transplant.

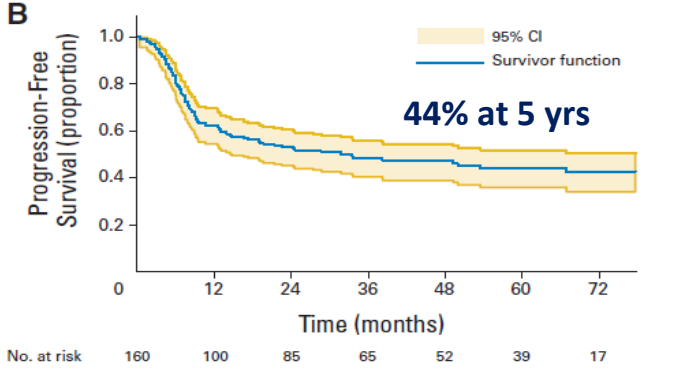


Moskowitz AJ et al, Blood 2014

Phase II study NLG-T-01, CHOEP plus auto-SCT

Characteristic	Patients No.	Patients %
Age, years		
Median	57	
Range	22-67	
Sex		
Male	107	67
Female	53	33
B symptoms	94	59
Elevated sLDH	99	62
PS ≥ 2*	46	29
Bulk	26	17
Clinical stage III to IV	129	81
BM involvement	41	26
IPI ≥ 2	115	72
Histologic subtype		
PTCL-NOS	62	39
ALK-negative ALCL	31	19
AILT	30	19
EATL	21	13
Panniculitis like	6	4
T/NK nasal type	5	3
Hepatosplenic	5	3





D'Amore F et al, J Clin Oncol 2012

LYMPHOID NEOPLASIA

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

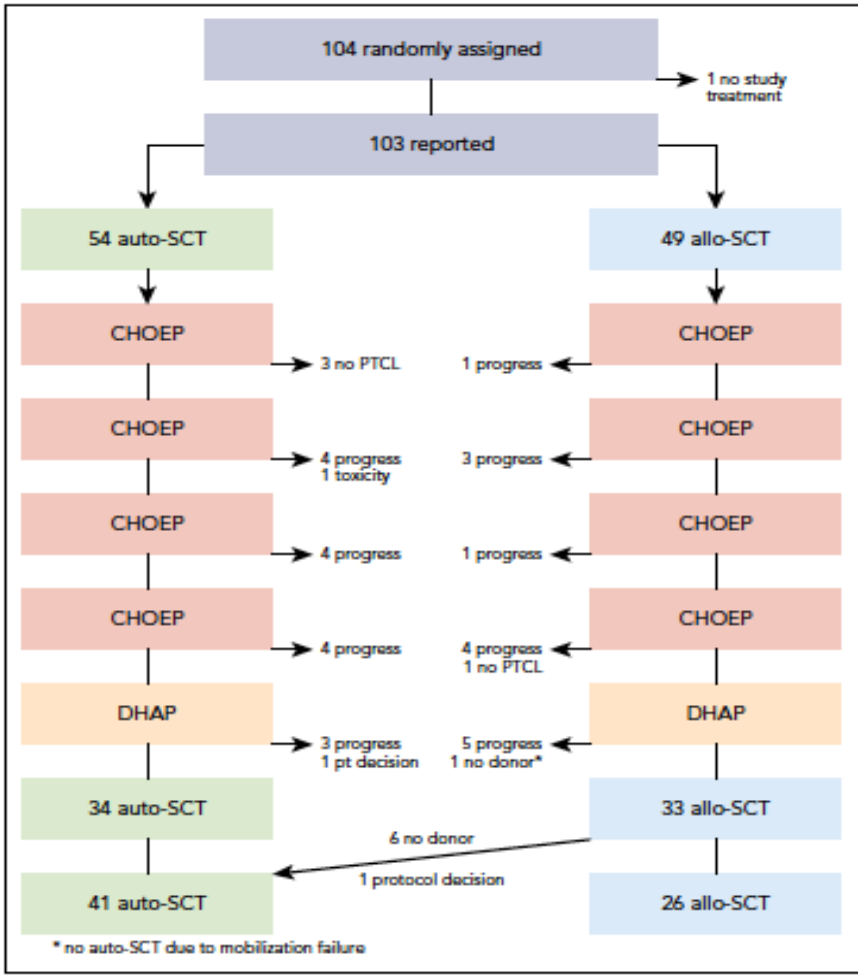
Norbert Schmitz,[1] Lorenz Truemper,[2] Krimo Bouabdallah,[3] Marita Ziepert,[4] Mathieu Leclerc,[5] Guillaume Cartron,[6] Arnaud Jaccard,[7] Peter Reimer,[8] Eva Wagner,[9] Martin Wilhelm,[10] Laurence Sanhes,[11] Thierry Lamy,[12] Laurence de Leval,[13] Andreas Rosenwald,[14,15] Muriel Roussel,[16] Frank Kroschinsky,[17] Walter Lindemann,[18] Peter Dreger,[19] Andreas Viardot,[20] Noël Milpied,[3] Christian Gisselbrecht,[21] Gerald Wulf,[2] Emmanuel Gyan,[22] Philippe Gaulard,[23] Jacques Olivier Bay,[24] Bertram Glass,[25] Viola Poeschel,[26] Gandhi Damaj,[27] David Sibon,[28] Alain Delmer,[29] Karin Bilger,[30] Anne Banos,[31] Mathias Haenel,[32] Martin Dreyling,[33] Bernd Metzner,[34] Ulrich Keller,[35] Friederike Braulke,[2] Birte Friedrichs,[1] Maike Nickelsen,[36] Bettina Altmann,[4,*] and Olivier Tournilhac,[37,*] for the French Lymphoma Study Association (LYSA) and the German Lymphoma Alliance (GLA)

104 patients with PTCLs, except ALK+,

18 to 60 years

Random:

4 cycles of CHOEP and 1 DHAP followed by high-dose therapy + auto-SCT vs. myeloablative conditioning + allo-SCT.



Schmitz N et al, Blood 2021

Auto-SCT vs allo-SCT consolidation in first complete remission

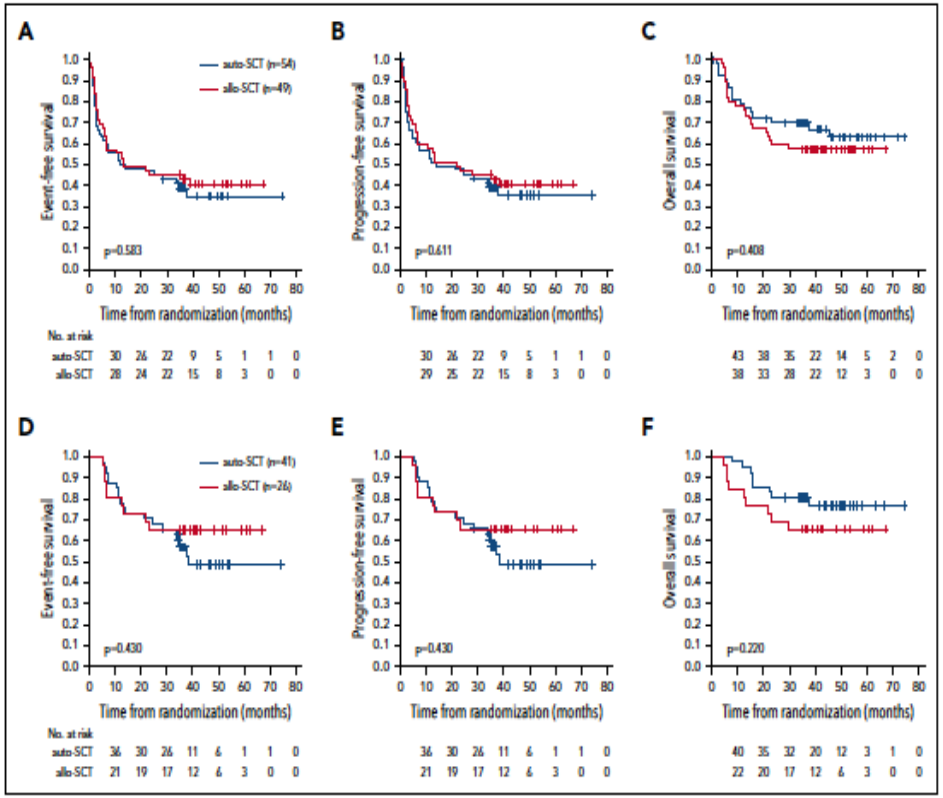


Figure 2. Outcome according to treatment arm. Event-free (A,D), progression-free (B,E), and overall survival (C,F) for all randomized patients (intent-to-treat population) (A-C) and for transplant recipients only (D-F).

LYMPHOID NEOPLASIA

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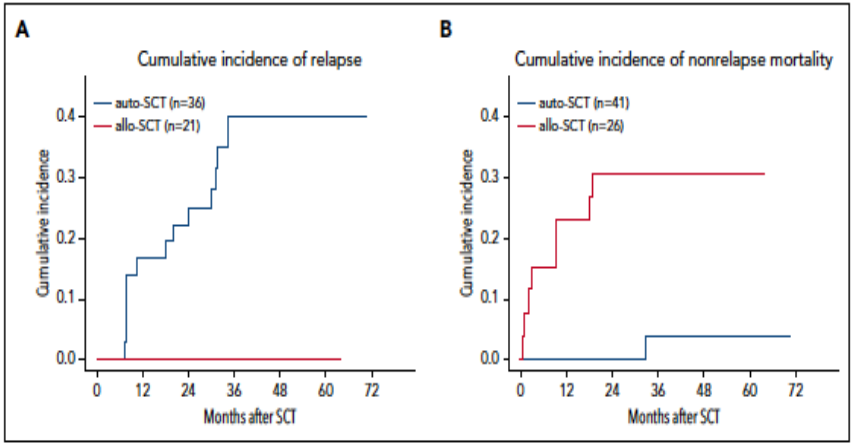

Schmitz N et al, Blood 2021

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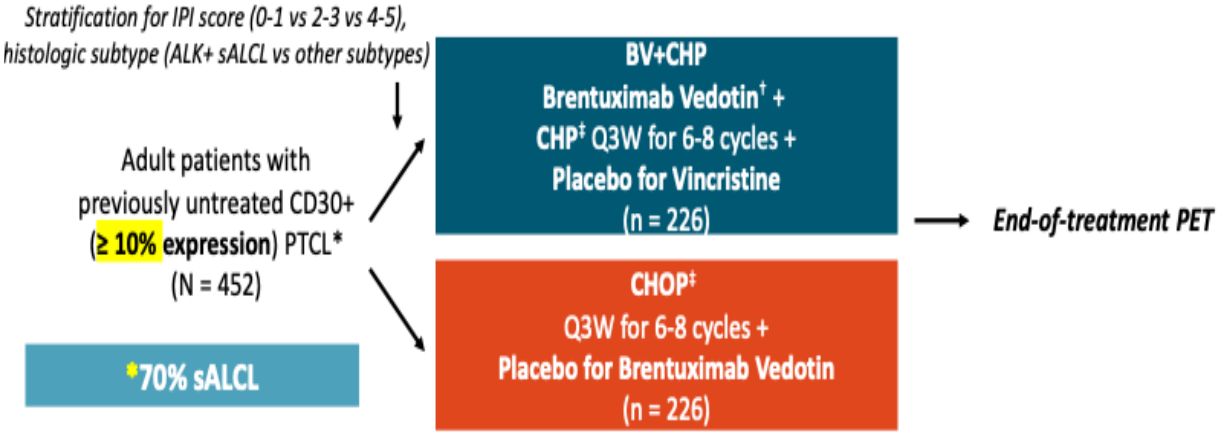
Targeted Therapy in PTCL-CD30

THE LANCET Articles

Brentuximab vedotin with chemotherapy for CD30-positive peripheral T-cell lymphoma (ECHELON-2): a global, double-blind, randomised, phase 3 trial

- Multicenter, randomized, double-blind, double dummy, active-controlled phase III trial

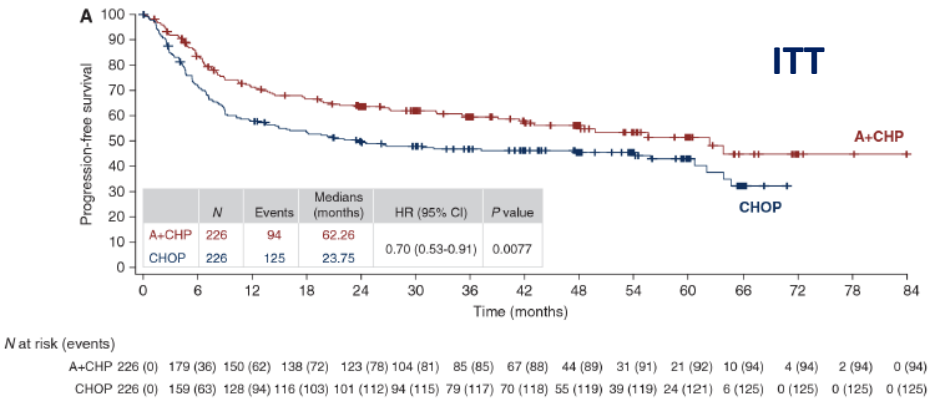


	A+CHP (n=226)	CHOP (n=226)
Stage III/IV disease, n (%)	184 (81)	180 (80)
Disease diagnosis, n (%)		
sALCL	162 (72)	154 (68)
ALK+	49 (22)	49 (22)
ALK–	113 (50)	105 (46)
PTCL-NOS	29 (13)	43 (19)
AITL	30 (13)	24 (11)
ATLL	4 (2)	3 (1)
EATL	1 (0)	2 (1)

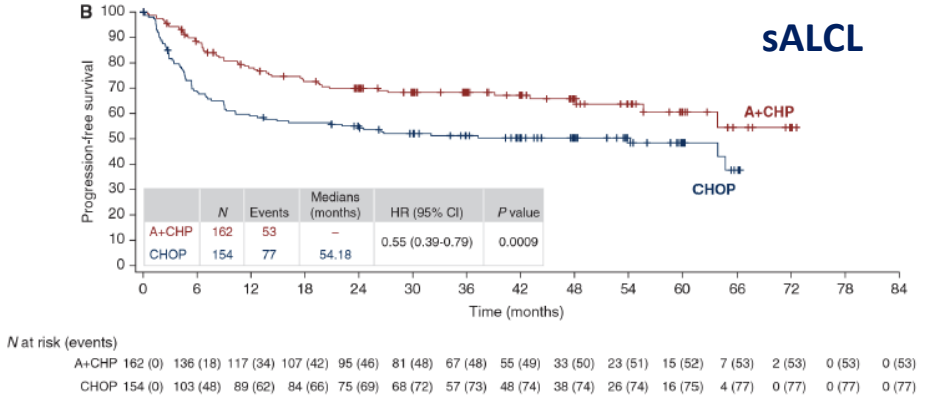
Horwitz S et al, Lancet 2019

Targeted Therapy in PTCL-CD30

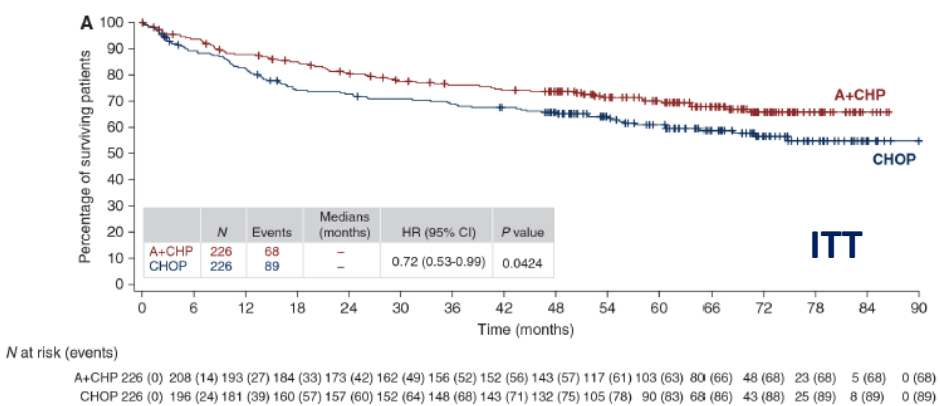
The ECHELON-2 Trial: 5-year results of a randomized, phase III study of brentuximab vedotin with chemotherapy for CD30-positive peripheral T-cell lymphoma☆



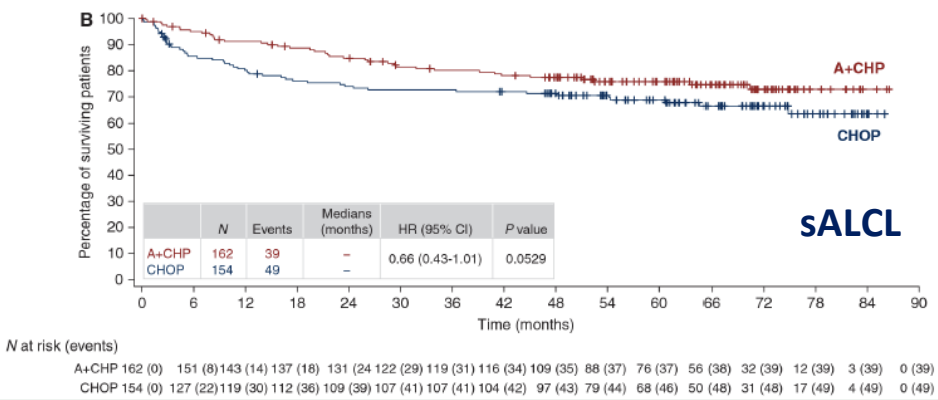
	N	Events	Medians (months)	HR (95% CI)	P value
A+CHP	226	94	62.26	0.70 (0.53-0.91)	0.0077
CHOP	226	125	23.75		



	N	Events	Medians (months)	HR (95% CI)	P value
A+CHP	162	53	–	0.55 (0.39-0.79)	0.0009
CHOP	154	77	54.18		



	N	Events	Medians (months)	HR (95% CI)	P value
A+CHP	226	68	–	0.72 (0.53-0.99)	0.0424
CHOP	226	89	–		



	N	Events	Medians (months)	HR (95% CI)	P value
A+CHP	162	39	–	0.66 (0.43-1.01)	0.0529
CHOP	154	49	–		

Horwitz S et al, Ann Oncol 2022.

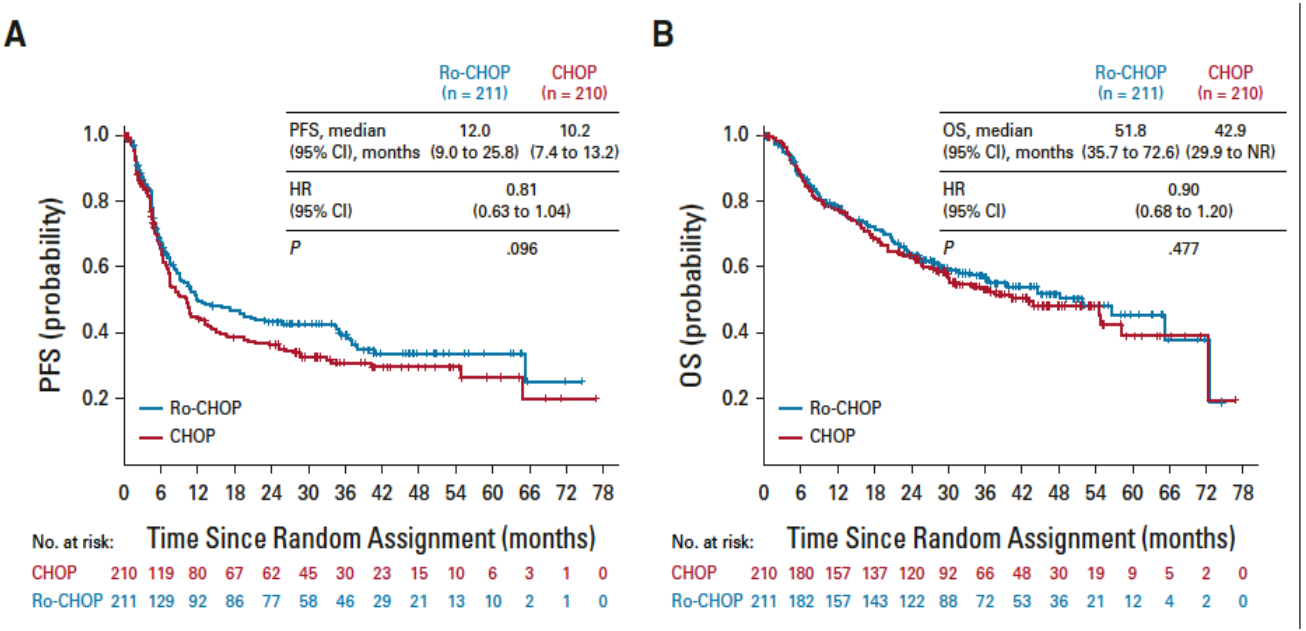
Targeted Therapy in PTCL

original reports

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)

Emmanuel Bachy, MD, PhD[1,2]; Vincent Camus, MD[3]; Catherine Thieblemont, MD, PhD[4]; David Sibon, MD, PhD[5]; René-Olivier Casasnovas, MD[6]; Loïc Ysebaert, MD, PhD[7]; Gandhi Damaj, MD, PhD[8]; Stéphanie Guidez, MD[9]; Gian Matteo Pica, MD[10]; Won Seog Kim, MD, PhD[11]; Soon Thye Lim, MBBS[12]; Marc André, MD[13]; Alejandro Martín García-Sancho, MD, PhD[14]; Maria Jesus Penarrubia, MD, PhD[15]; Philipp B. Staber, MD, PhD[16]; Judith Trotman, MBChB[17]; Andreas Hüttmann, MD[18]; Vittorio Stefoni, MD, PhD[19]; Alessandro Re, MD[20]; Philippe Gaulard, MD[21]; Marie-Helene Delfau-Larue, MD, PhD[22]; Laurence de Leval, MD, PhD[23]; Michel Meignan, MD, PhD[24]; Ju Li, PhD[25]; Franck Morschhauser, MD, PhD[26]; and Richard Delarue, MD[5,27]

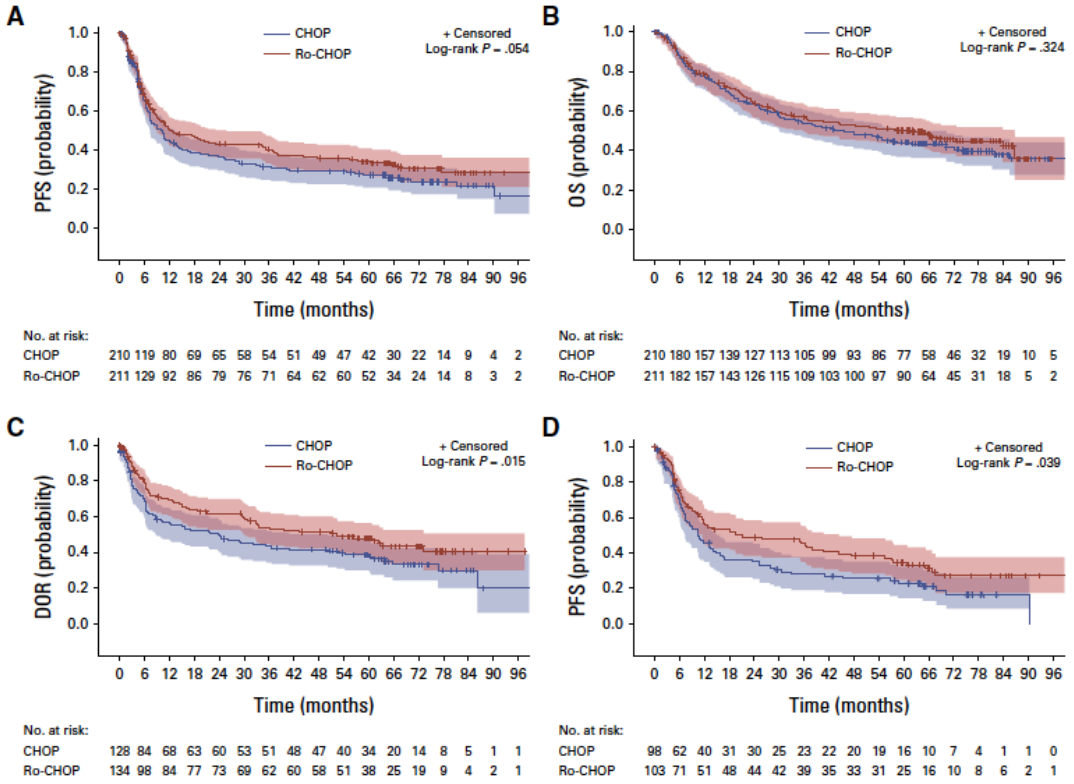
Parameter	Ro-CHOP (n = 211)	CHOP (n = 210)	Total (N = 421)
Median age, years (range)	65 (26-80)	65 (25-81)	65 (25-81)
Age group, years			
≤ 60	73 (34.6)	72 (34.3)	145 (34.4)
> 60	138 (65.4)	138 (65.7)	276 (65.6)
Sex			
Male	125 (59.2)	136 (64.8)	261 (62.0)
Female	86 (40.8)	74 (35.2)	160 (38.0)
Histologic 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.

Romidepsin Plus Cyclophosphamide, Doxorubicin, Vincristine, and Prednisone Versus Cyclophosphamide, Doxorubicin, Vincristine, and Prednisone in Patients With Previously Untreated Peripheral T-Cell Lymphoma: Final Analysis of the Ro-CHOP Trial

An exploratory analysis suggested a benefit in patients with TFH lymphomas.



Regimen	No.	PFS	PFS by Subtype
Ro-CHOP[7,12]	421		
Ro-CHOP	211	Median PFS—12.0 months	Median PFS TFH—19.5 months Non-TFH—8.7 months Median OS TFH—65 months PTCL-NOS—25.8 months
CHOP	210	Median PFS—10.2 months	Median PFS TFH—10.6 months Non-TFH—9 months

Camus V et al, J Clin Oncol 2024.

Romidepsin-CHOEP followed by high-dose chemotherapy and stem-cell transplantation in untreated Peripheral T-Cell Lymphoma: results of the PTCL13 phase Ib/II study

Annalisa Chiappella[1✉], Anna Dodero[1], Andrea Evangelista[2], Alessandro Re[3], Lorella Orsucci[4], Sara Veronica Usai[5], Claudia Castellino[6], Vittorio Stefoni[7], Antonio Pinto[8], Manuela Zanni[9], Rosanna Ciancia[10], Chiara Ghiggi[11], Francesca Gaia Rossi[12], Annalisa Arcari[13], Fiorella Ilariucci[14], Vittorio Ruggero Zilioli[15], Leonardo Flenghi[16], Melania Celli[17], Stefano Volpetti[18], Fabio Benedetti[19], Filippo Ballerini[20], Gerardo Musuraca[21], Riccardo Bruna[22], Caterina Patti[23], Francesco Leonardi[24], Luca Arcaini[25], Massimo Magagnoli[26], Federica Cavallo[27], Anisa Bermema[1], Alessandra Tucci[3], Carola Boccomini[4], Giovannino Ciccone[2], Cristiana Carniti[28], Stefano Aldo Pileri[29] and Paolo Corradini[1,30]

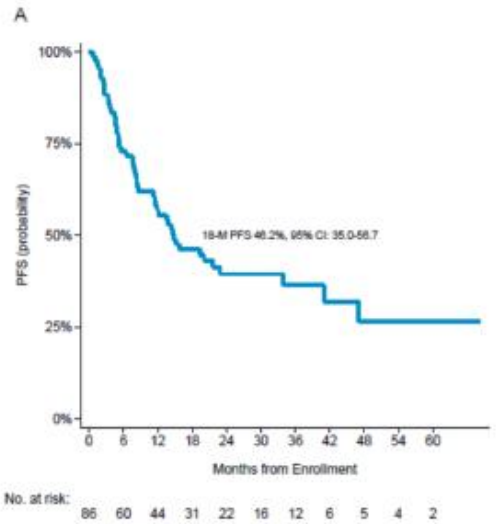
FONDAZIONE ITALIANA LINFOMI

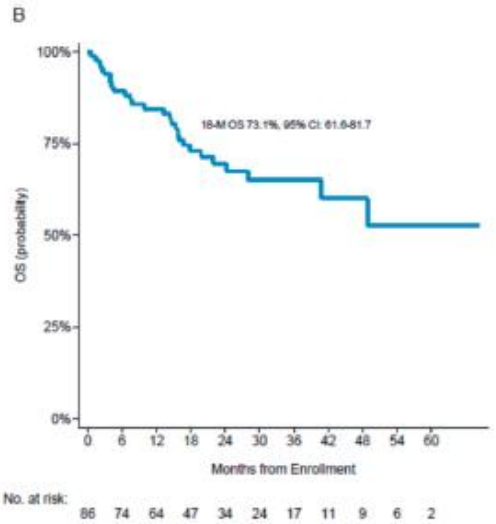
Overall Response Rate at the end of treatment,

n = 86 patients

ORR 57%, CR 56%

86 patients			
Median age	**55 (IQR 49;60)**	**Stage III/IV**	**78 (91%)**
Male	**58 (67%)**	**PS ≥ 2**	**12 (14%)**
IPI III/IV	**29 (34%)**	**BM +**	**31 (36%)**
PIT score ≥2	**34 (43%)**	**LDH > normal**	**43 (50%)**
Histotypes, central pathology review (n=85, 1 case not classified due to inadequate material)		**PTCL-nos 33 (39%) Anaplastic ALK neg 21 (25%) AITL/TFH 31 (36%)**	





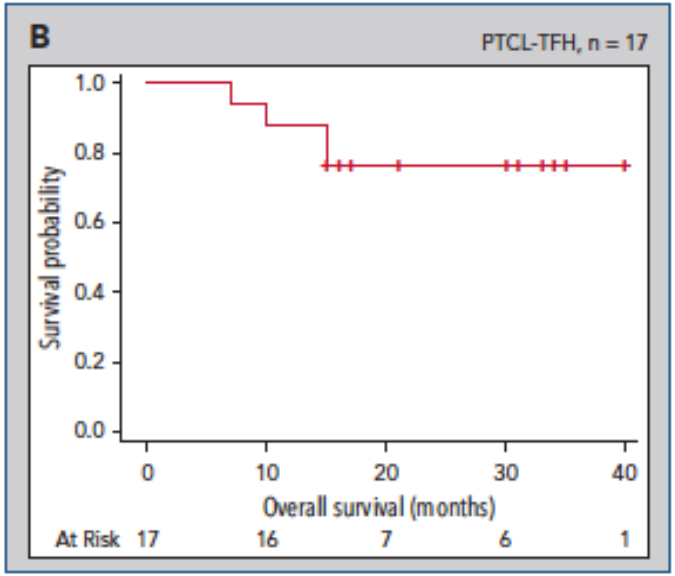
Chiappella A et al, Leukemia 2023.

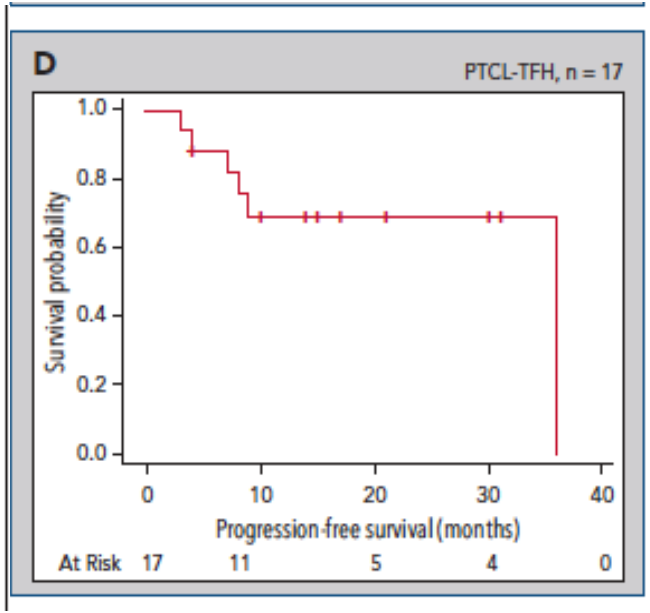
Multicenter phase 2 study of oral azacitidine (CC-486) plus CHOP as initial treatment for PTCL

Jia Ruan,[1] Alison Moskowitz,[2] Neha Mehta-Shah,[3] Lubomir Sokol,[4] Zhengming Chen,[1] Nikita Kotlov,[5] Grigorii Nos,[5] Maria Sorokina,[5] Vladislav Maksimov,[5] Andrea Sboner,[1] Michael Sigouros,[1] Koen van Besien,[1] Steven Horwitz,[2] Sarah C. Rutherford,[1] Erin Mulvey,[1] Maria V. Revuelta,[1] Jenny Xiang,[1] Alicia Alonso,[1] Ari Melnick,[1] Olivier Elemento,[1] Giorgio Inghirami,[1] John P. Leonard,[1] Leandro Cerchietti,[1] and Peter Martin[1]

Characteristic	Number of patients	Percent
No. of patients	21	100
Sex		
Male	13	62
Female	8	38
Age, y		
Median (range)	66	
Range	22-77	
ECOG performance status		
0-1	13	62
>1	8	38
Ann Arbor stage		
III-IV	19	90
LDH		
Normal	11	52
Elevated	10	48
Bone marrow involvement		
Yes	7	33
No	13	62
Unknown	1	5
PTCL subtypes		
PTCL-TFH	17	81
PTCL-NOS	3	14
ATLL	1	5
IPI risk category		
0-1	5	24
2	7	33
3	3	14
4-5	6	29
CD30 expression		
Positive (≥10%)	4	19
Negative (<10%)	17	81

Response	All evaluable* (N = 20)		PTCL-TFH (N = 17)	
	Number	Percentage	Number	Percentage
Overall response	15	75.0	15	88.2
CR	15	75.0	15	88.2
PR	0	0	0	0
SD	1	5.0	0	0
PD	2	10.0	1	5.8
Discontinuation†	2	10.0	1	5.8
Survival				
2-y PFS	65.8% (95% CI, 43.4-88.1)		69.2% (95% CI, 46.7-91.7)	
2-y OS	68.4% (95% CI, 47.3-89.4)		76.1% (95% CI, 55.6-96.5)	
Median follow-up	21.0 mo (range 17.0-33.0)			





Ruan J et al, Blood 2023.

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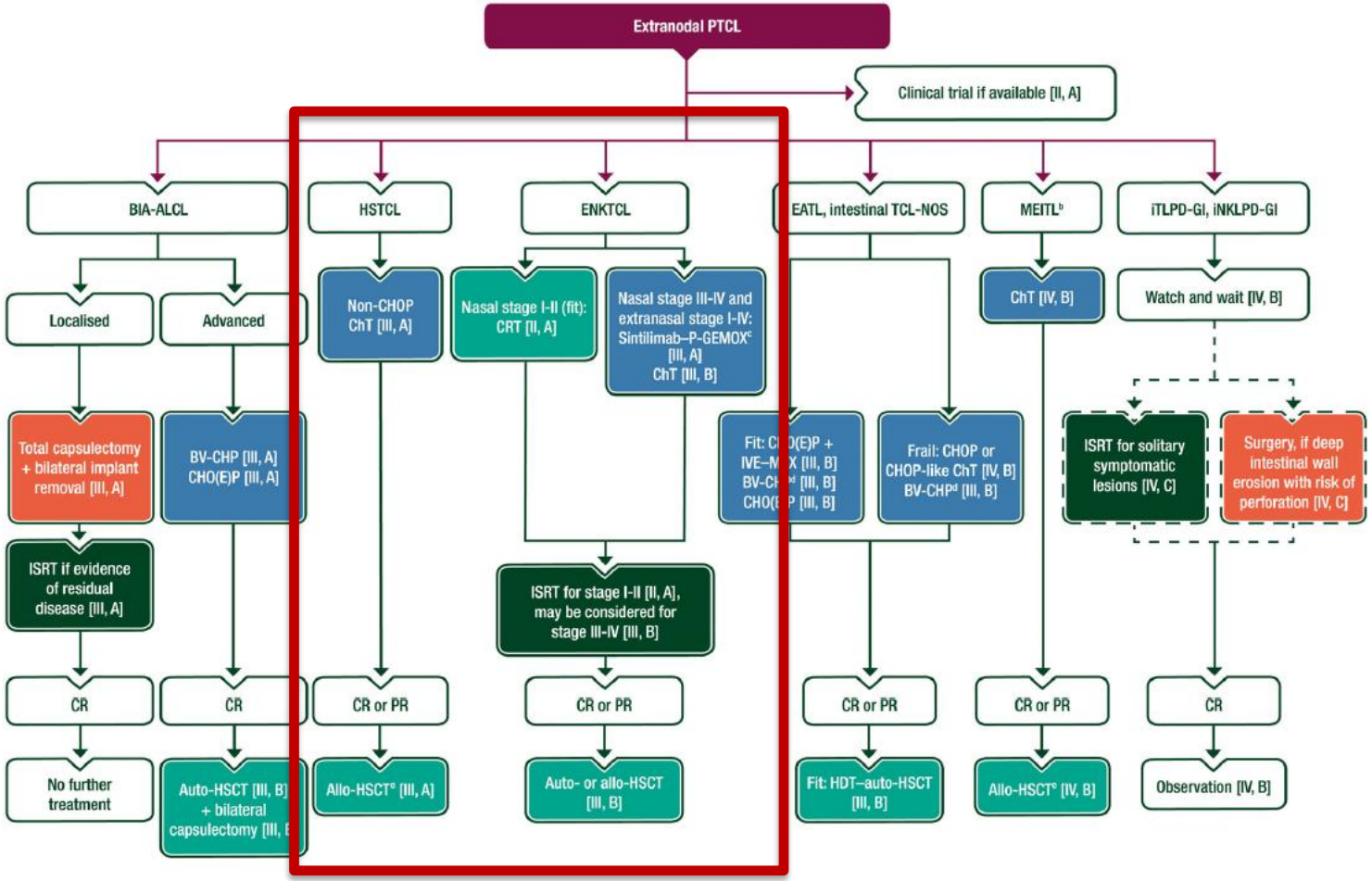
GUIDELINES - CONSENSUS-BASED

HemaSphere eha

Peripheral T- and natural killer-cell lymphomas: ESMO-EHA Clinical Practice Guideline fo follow-up

Francesco d'Amore[1,2,^] | Massimo Fede
Fredrik Ellin[5,6] | Olivier Hermine[7,8] |
Joost S. P. Vermaat[12] | Gerald Wulf[13]
Mats Jerkeman[16] | on behalf of the ESM

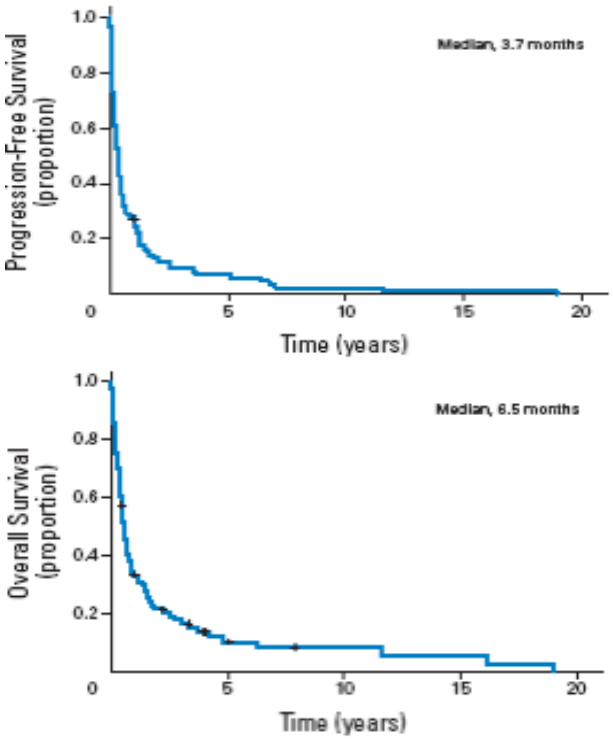


Outline of the discussion

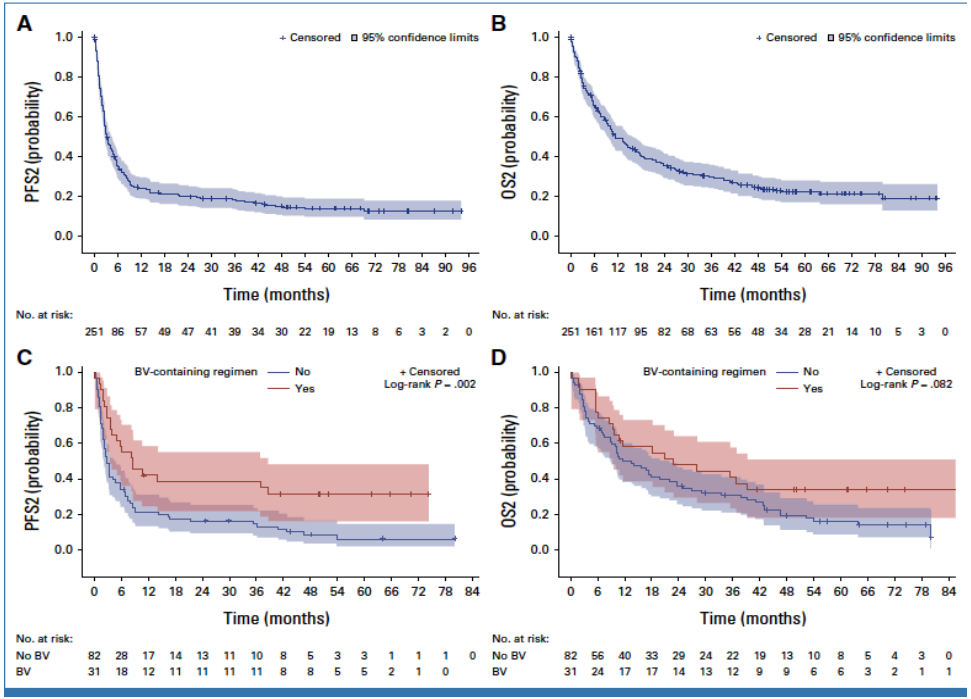
- ✓ First line treatment
  - Common subtypes of PTCL (PTCL, NOS; ALCL; TFHs)
    - The role of etoposide and consolidation with stem cell transplantation
    - The role of novel pathway-directed and subtype-specific therapies
  - Uncommon subtypes of PTCL (EATL, HSTCL) and Extranodal NK-T cell lymphoma
- ✓ **Relapsed/refractory**

Outcome of patients with relapsed/refractory PTCL

Not eligible to transplant



Second-line treatments after CHOP/Ro-CHOP led to poor results, except for a potential benefit for BV-combination strategies in this BV-naive population.



Mak V et al, JCO 2013; Camus V, et al. J Clin Oncol 2024.

REGULAR ARTICLE

blood advances

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Outcome of patients with relapsed/refractory PTCL eligible to transplant

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

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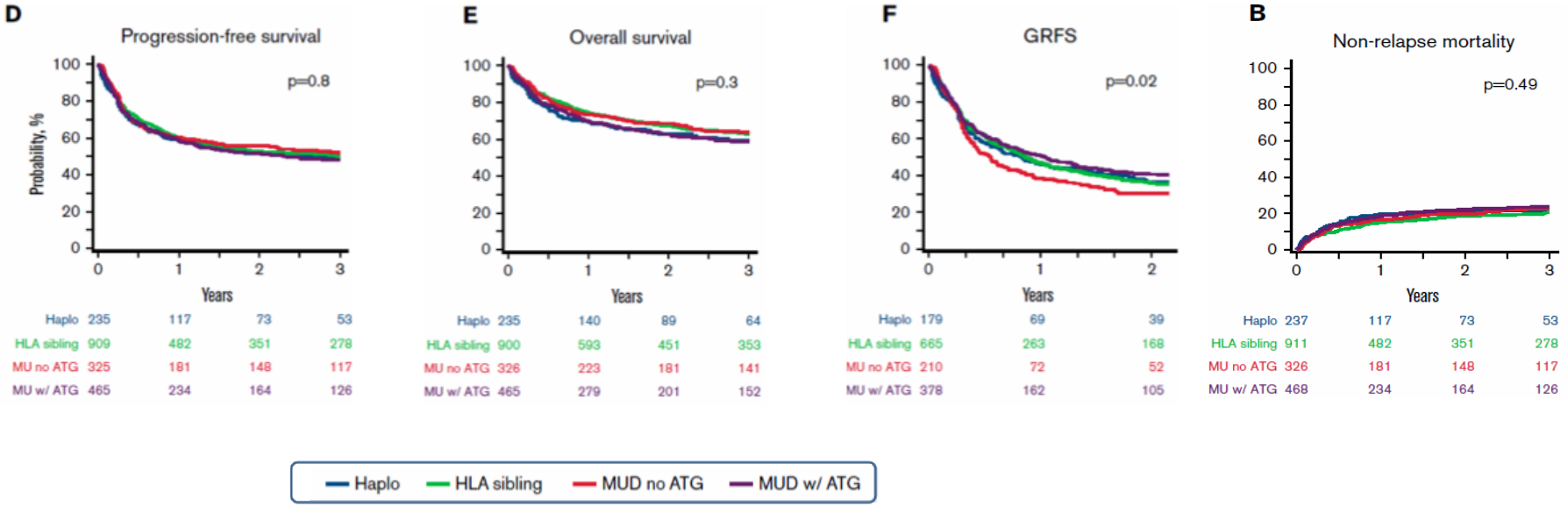
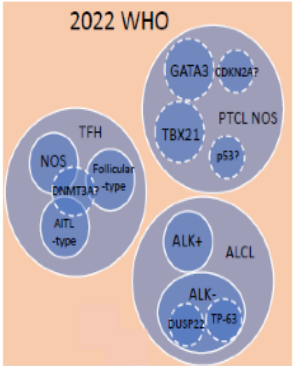


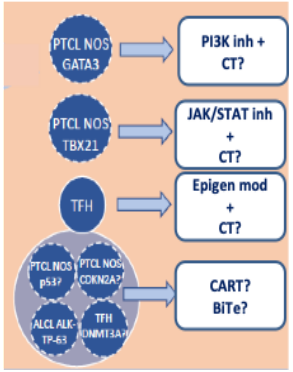
Hamadani M, et al, Blood Adv 2022.

Relapsed/refractory setting: novel agents

Agent	No.	ORR	ORR by Subtype
Romidepsin[16,17]	130	25%	PTCL-NOS–29% AITL–33% ALK-ALCL–24%
Belinostat[19]	120	26%	PTCL-NOS–23% AITL–45% ALK-ALCL–15%
Brentuximab vedotin[26,33]	92	69%	PTCL-NOS–33% AITL–54% sALCL–86%
Cerdulatinib[36]	58	36%	PTCL-NOS–0% AITL/TFH–52% Other–32%
Duvelisib[27]	101	48.5%	PTCL-NOS–48.1% AITL–66.7% ALCL–13.3%
Golidocitinib[28]	88	44%	PTCL-NOS –46% AITL/TFH–56.3% ALCL–10%
Ruxolitinib[29]	25	25%	By histology PTCL-NOS–18% AITL/TFH–33% ALCL–25% JAK/STAT status Activating mutations–20% Functional evidence with pSTAT3–44% None–0%
Valemetostat[30]	119	43.7%	PTCL-NOS–31.7% PTCL TFH–50% AITL–54.8% ALCL–33.3%



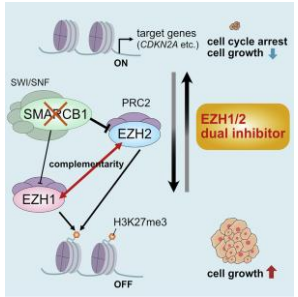
Targeted Agents	Epigenetic Modifying Agents	Pathway Inhibitor
CD30 ALK PD-1 CD94 Bispecific CD30/CD16 PD-1/CD3	HDACi Belinostat Romidepsin Chidamide Azacytidine Valemetostat Enasidinib	PI3K-kinase JAK/STAT



Agent	No.	ORR	ORR by Subtype
Romidepsin + azacitidine[20]	25	61%	TFH–80% Non-TFH–25%
Romidepsin + duvelisib[34]	55	58%	PTCL-NOS–50% AITL/TFH–70% ALCL–100%
Romidepsin + gemcitabine/oxaliplatin[21]	17	58%	PTCL-NOS–40% AITL–100%
Romidepsin + lenalidomide[22,23]	2	65%	PTCL-NOS–50% AITL–79%

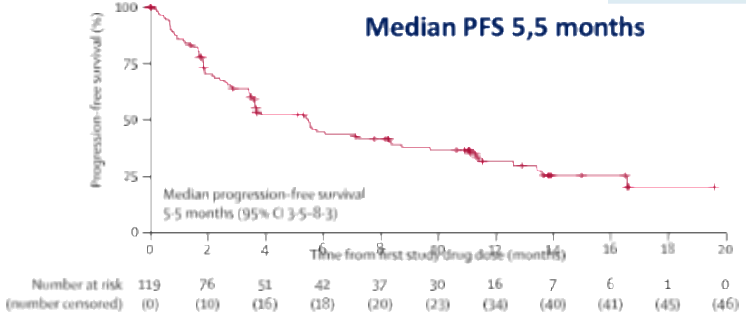
Mehta-Shah N and Horwitz S, J Clin Oncol 2024; Moskowitz A, Blood 2024.

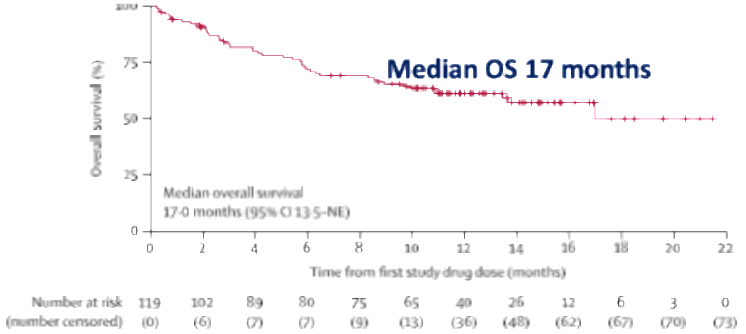
VALENTINE-PTCL01
VALEMETOSTAT: EZH1 andEZH2 Inhibitor phase II study



Variable	ORR/CR	DOR
Entire population	52%/27 % (PET/CT)	11,9 months
TFH	54%	
PTCL-NOS	32%	
ALCL	33%	

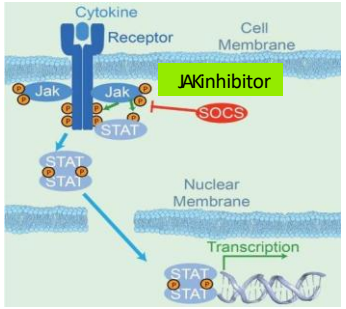
Median time to first response 8 weeks
Median DOR 11,9 months
Low incidence of treatment discontinuation 10% (!!! Thrombocytopenia).
8% proceed to Allo-TMO
Median FUP 12,3 months





Zinzani PL et al, Lancet Oncology 2024.

Golidocitinib, a selective JAK1 Inhibitor in R/R TCL

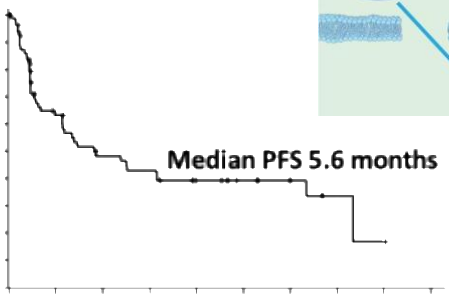


ORR and ORR by Subtype	%
All pts ORR/CR rate	44%/24%
PTCL-NOS (23/50)	46% (23/50)
AITL	56% (9/16)
ALCL	10% (1/10)

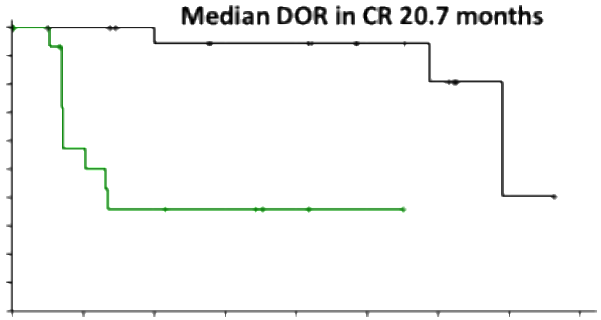
Prior HDAC Inhibitor	
Yes	24/44 (55%)
No	15/44 (34%)

Median DoR (months) 20·7 months
Median follow-up time (months) (IQR) 12· 5 months
Discontinuation drug 9%

PFS



DOR



Song Y et. al. Lancet Oncology 2024.

Take home messages

- PTCLs are an heterogeneous group of lymphomas
- Outcome is poor in the majority of PTCL with current standard treatment
- The knowledge of the biological features of the disease should drive the choice of target therapies
- Except for CD30+ ALCL, there is no standard of care for relapsed/refractory nodal PTCL
- Allogeneic transplant is an effective treatment in chemosensitive relapsed PTCL
- Consider clinical trials for PTCLs patients

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