ESMO–EHA Clinical Practice Guideline for Peripheral T-cell Lymphoma

Francesco d'Amore, MD, DMSc
Department of Haematology, Aarhus University Hospital
Department of Clinical Medicne, Aarhus University

Singapore Lymphoma Scientific Symposium 2025

ANNALS OF ONCOLOGY DRIVING INNOVATION IN ONCOLOGY
e-pub May25

SPECIAL ARTICLE

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

F. d'Amore[1,2†], M. Federico[3‡], L. de Leval[4], F. Ellin[5,6], O. Hermine[7,8], W. S. Kim[9], F. Lemonnier[10,11], J. S. P. Vermaat[12], G. Wulf[13], C. Buske[14], M. Dreyling[15] & M. Jerkeman[16], on behalf of the ESMO* and EHA Guidelines Committees*

Departments of [1]Haematology and [2]Clinical Medicine, Aarhus University Hospital, Aarhus University, Aarhus, Denmark; [3]CHIMOMO Department, University of Modena and Reggio Emilia, Emilia-Romagna, Italy; [4]Institute of Pathology, Department of Laboratory Medicine and Pathology, Lausanne University Hospital and Lausanne University, Lausanne, Switzerland; [5]Department of Clinical Sciences, Lund University, Lund; [6]Department of Internal Medicine, Kalmar County Hospital, Kalmar, Sweden; [7]Department of Hematology, Université de Paris, Assistance Publique-Hôpitaux de Paris (AP-HP), Paris; [8]Imagine Institute, Hôpital Necker, INSERM U1163, Paris, France; [9]School of Medicine, Sungkyunkwan University, Samsung Medical Center, Seoul, Korea; [10]Lymphoid Malignancies Unit, Hôpital Henri-Mondor, Assistance Publique-Hôpitaux de Paris (AP-HP), Créteil; [11]Institut Mondor de Recherche Biomédicale, Université Paris Est Créteil, INSERM, Créteil, France; [12]Department of Hematology, Leiden University Medical Centre, Leiden, The Netherlands; [13]Department of Hematology and Medical Oncology, University Medical Center Göttingen, Göttingen; [14]Institute of Experimental Cancer Research, Ulm Medical University, Ulm; [15]Department of Medicine III, Ludwig Maximilian University, Munich, Germany; [16]Department of Oncology, Skåne University Hospital, Lund, Sweden

DOI: 10.1002/hem3.70128

GUIDELINES - CONSENSUS-BASED

HemaSphere eha
e-pub May25

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

Disclosures

- Institutional fees for the implementation of a First-in-Human clinical trial from **Genmab**
- Institutional fees from **Servier** for the implementation, as coordinating international PI, of a Nordic clinical trial on PTCL
- Institutional fees as advisory board member for **Frost AB**
- Non-remunerated member of the Scientific Committee of the **European School of Haematology**

ESMO-EHA CPG PTCL >> Overview

Nodal | Extranodal | Leukemic

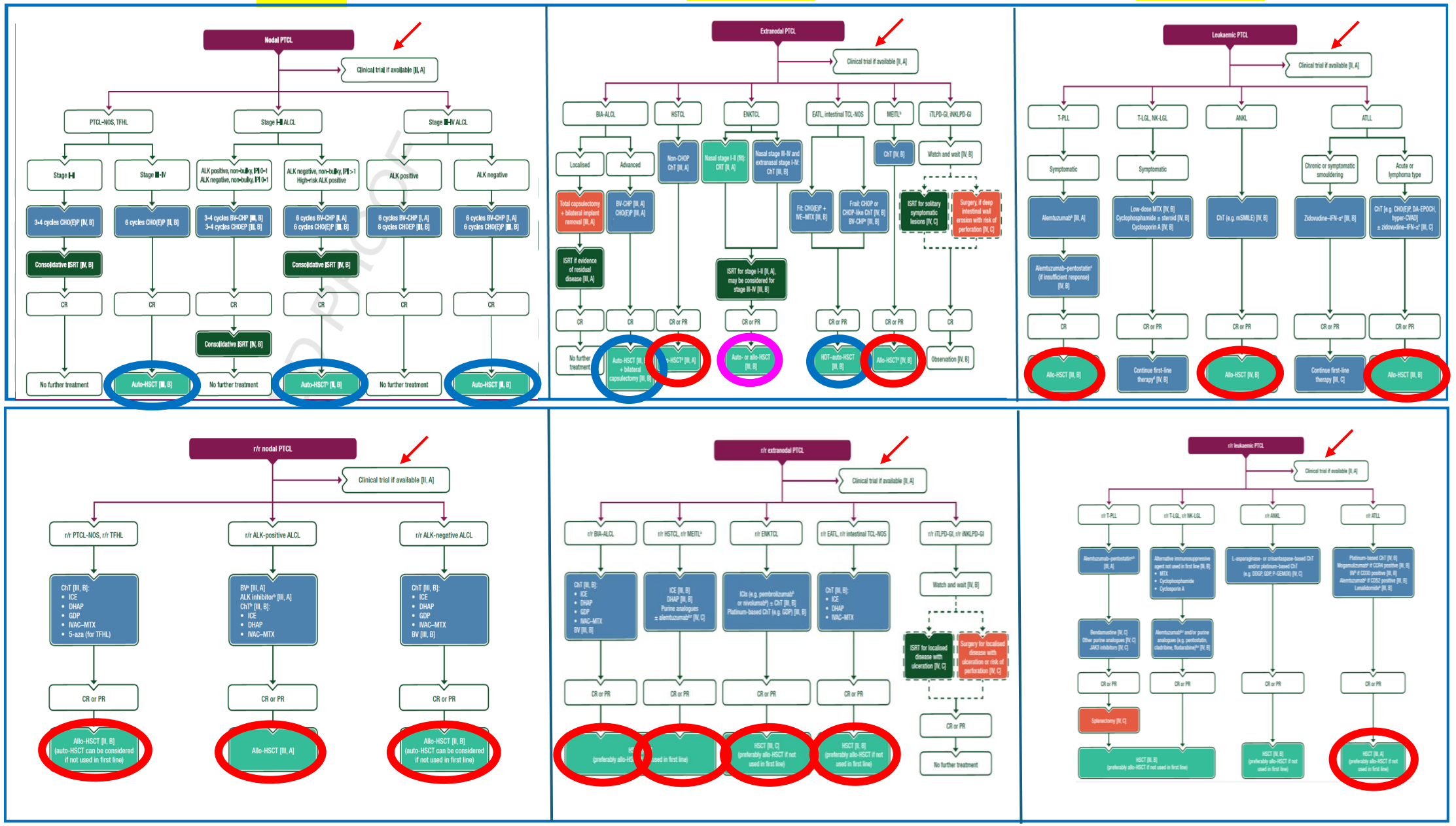
1st line

Rel/ref

auto

allo

'case-by-case'



d'Amore F et al. Ann Oncol. 2025;36(6):626-644.& Hemasphere. 2025;9(5):e70128.

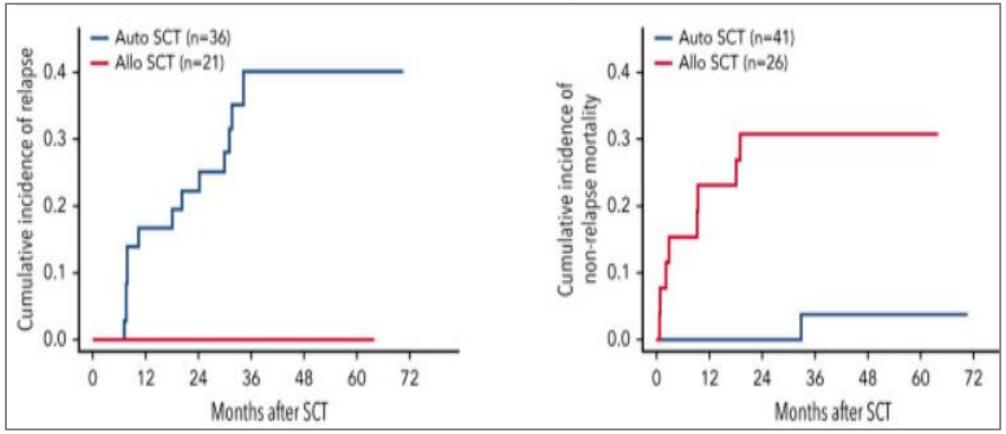
. 2024 Nov 10;42(32):3788-3794.

Upfront Auto or Allo HSCT in PTCL? The German-French AATT trial

Primary analysis

Schmitz N et al. Blood 2021; 137(19):2646–2656

	Auto	Allo	
3y EFS	38%	43%	ns
OS	70%	57%	ns
TRM	0%	31%	--
REL	36%	0%	--



AUTO: Lower TRM → Higher RR

ALLO: Lower RR → Higher TRM

Long-term follow up

Tournilhac O et al. JCO 2024; 42(32):3788-3794

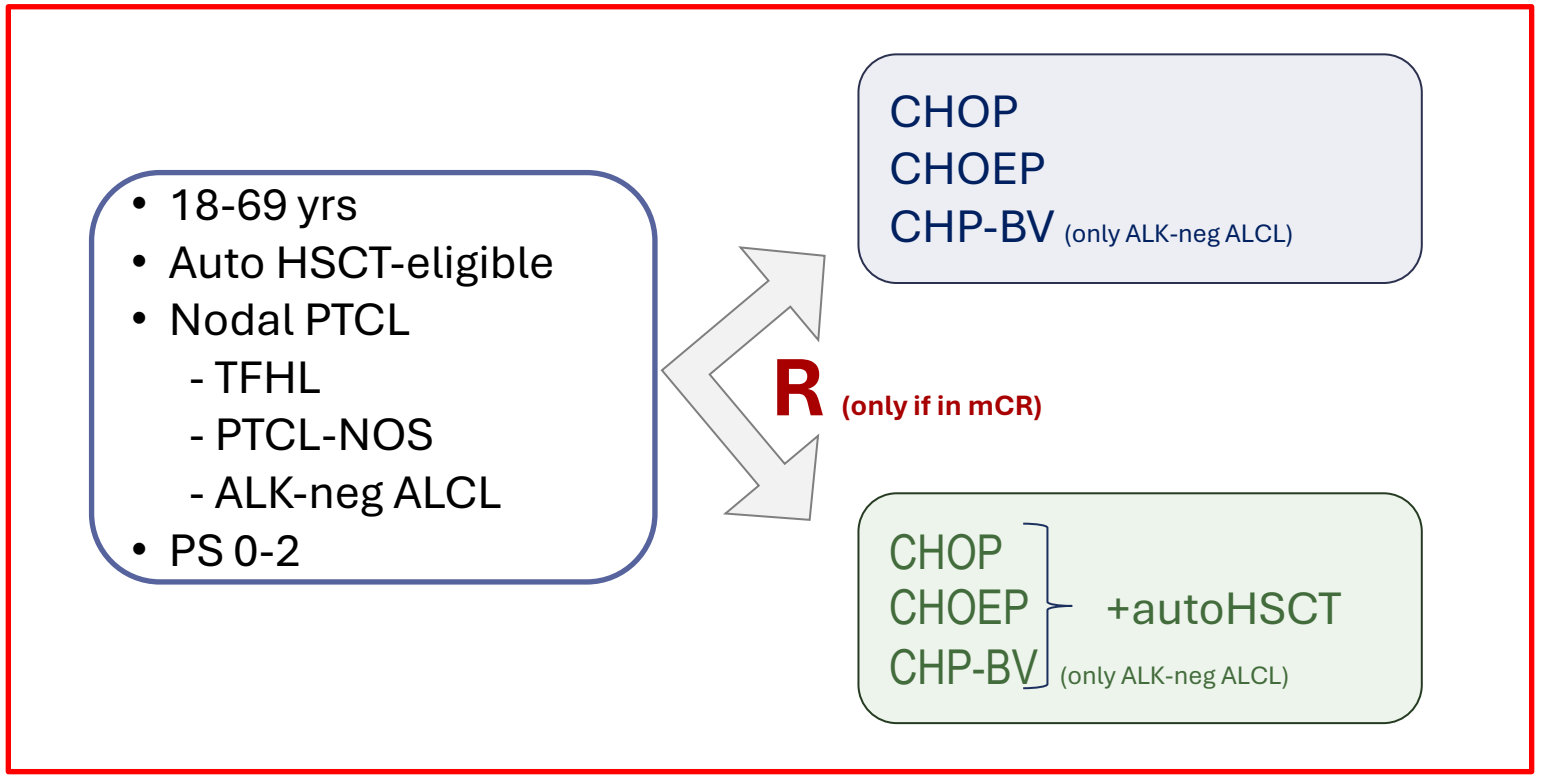
	Auto	Allo	
7y EFS	34%	38%	ns
OS	61%	55%	ns
TRM	3%	31%	--
REL	55%	8%	--

Authors' conclusions:

- If a Tx consolidation is chosen upfront, auto Tx should be the modality of choice in chemosensitive Tx eligible (CPG25: …in nodal PTCL and some extranodal entities)
- AlloSCT is the treatment of choice for younger, Tx-eligible pts with r/r PTCL
- AlloSCT is generally not recommended as part of first-line consolidation (CPG25:…except for HSTCL and MEITL, where alloTx consolidation is recommended in chemosensitive pts)

Upfront auto-HSCT or ‘No further treatment’ after mCR in nodal PTCL?

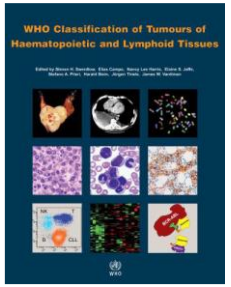
The TRANSCRIPT trial



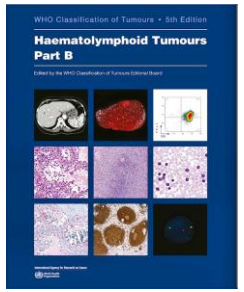
- Clinicaltrials.gov: NCT05444712
- Started inclusion: 8/22
- PI: dr. Bachy (France)
- Primary end-point: PFS
- Enrollment goal: 204 pts
- Expected completion: 4/28

Compared to ESMO PTCL CPG 2015 >> Increased complexity

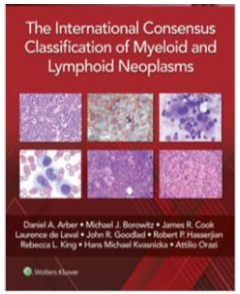
2008
WHO 4th ed.



2022/-24
WHO 5th ed.

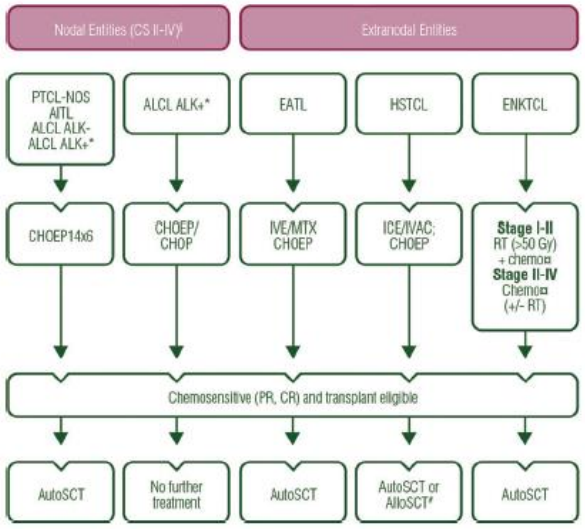


2022/-25
ICC



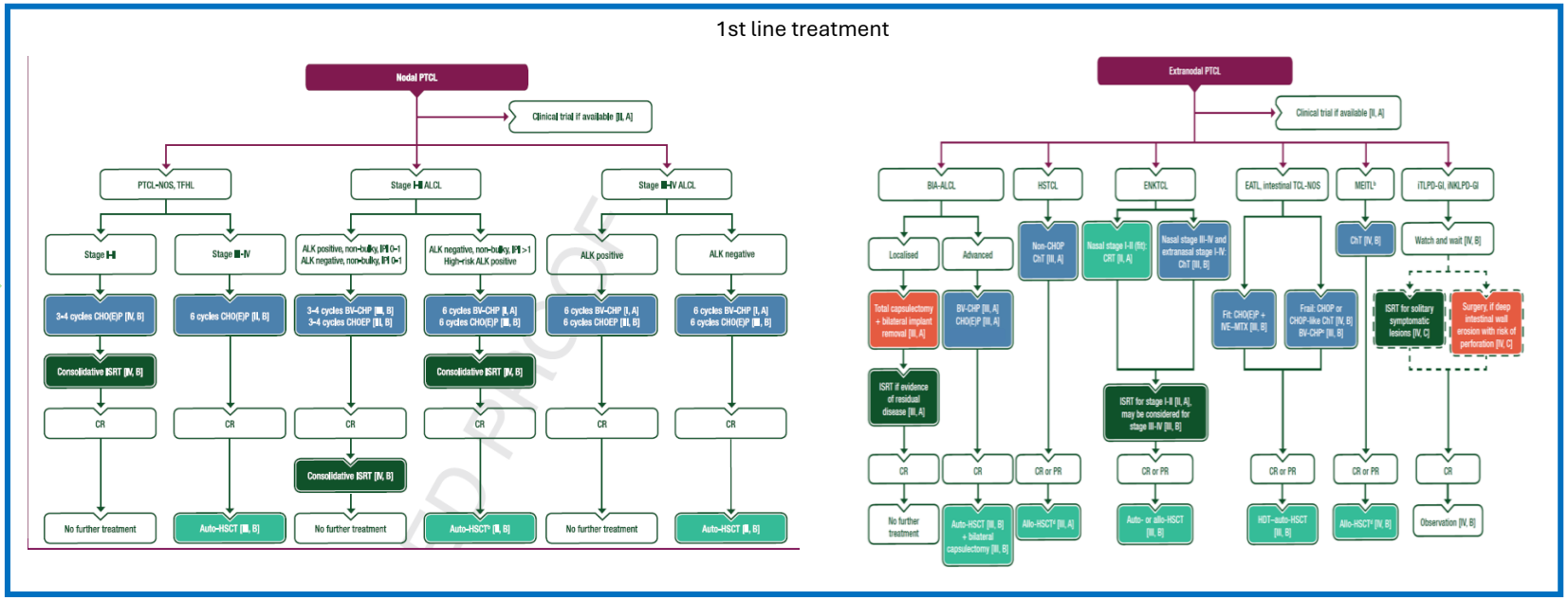
2015

1st line treatment



2025

1st line treatment



d'Amore F et al. Ann Oncol 2015

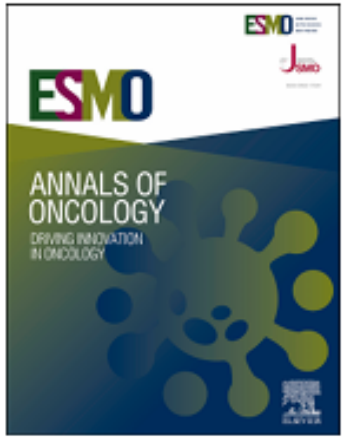
d'Amore F et al. Ann Oncol 2025 & HemaSphere 2025

ESMO CPG 2025 for *all* lymphomas, incl PTCL (only nodal)

Do NOT confuse the ESMO-EHA PTCL CPG 2025 (May) with the ESMO 'all lymphomas" CPG 2025 (Aug):

1) **Text for PTCL recommendations originating the ESMO-EHA CPG for PTCL**
2) **Only nodal PTCL included**
3) **Includes less background information on PTCL than the PTCL-specific guideline.**

Journal Pre-proof **epub August 2025**



Lymphomas: ESMO Clinical Practice Guideline for diagnosis, treatment and follow-up†

T.A. Eyre, K. Cwynarski, F. d'Amore, L. de Leval, M. Dreyling, D.A. Eichenauer, A.J.M. Ferreri, E. Giné, M.J. Kersten, M. Ladetto, L. Specht, C. Thieblemont, J. Walewski, E. Zucca, M. Jerkeman, on behalf of the ESMO Guidelines Committee

PII: S0923-7534(25)00911-1

DOI: https://doi.org/10.1016/j.annonc.2025.07.014

Reference: ANNONC 1872

ESMO-EHA CPG PTCL >> Staging and Risk Assessment - General

Selected recommendation points

- At diagnosis, a PET-CT is the preferred imaging modality for all nodal and extranodal (non-leukaemic) PTCLs [I, B].
- In all cases, a BM biopsy is recommended for accurate staging [V, A].
- Rebiopsy is recommended at relapse or progression [V, A].
- For nodal PTCL, the International Prognostic Factor Index is still the preferred prognostic tool [IV, B].

d'Amore F et al. Ann Oncol. 2025;36(6):626-644.& Hemasphere. 2025;9(5):e70128.

Prognostic indices in PTCL

BJHaem
BRITISH JOURNAL OF HAEMATOLOGY
British Society for Haematology

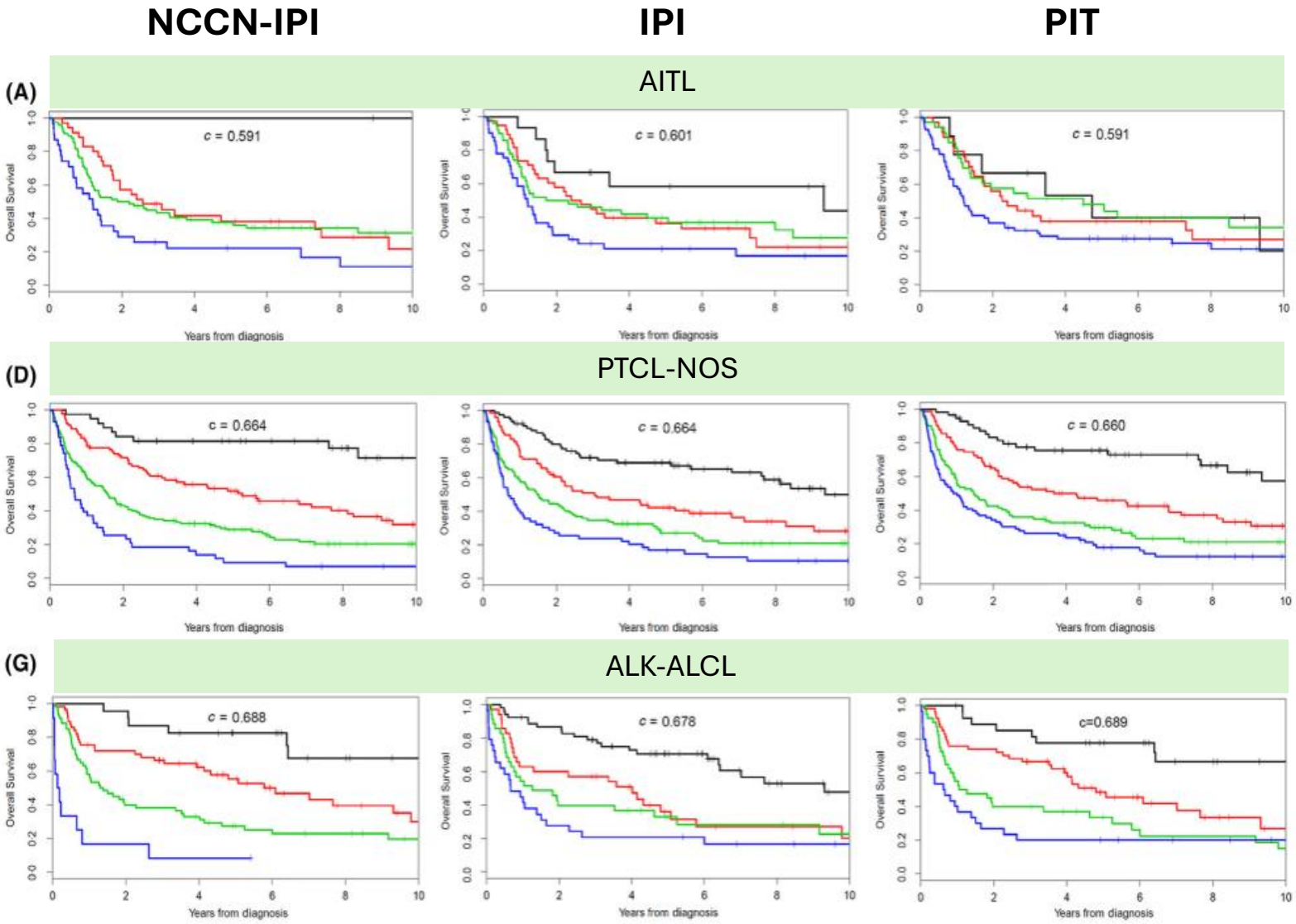
Correspondence | Free Access

Comparison of the NCCN-IPI, the IPI and PIT scores as prognostic tools in peripheral T-cell lymphomas

Fredrik Ellin, Matthew J. Maurer, Line Srour, Umar Farooq, Mats Jerkeman, Joseph M. Connors, Karin E. Smedby, N. Nora Bennani, Stephen M. Ansell, Graham W. Slack ... See all authors

First published: 11 March 2019 | https://doi.org/10.1111/bjh.15859 | Citations: 15

"Based on our results it seems reasonable to recommend continued use of the IPI for stratification and adjustments in clinical studies of ALK-neg ALCL and PTCL NOS until more specific prognostic biomarkers are available."



ESMO-EHA CPG PTCL >> RESPONSE AND FOLLOW-UP

- A diagnostic imaging **interim evaluation** can be carried out to assess chemosensitivity (optional) [II, B].
- Interim **PET/CT** response **has outcome-predictive value in nodal PTCL** [II, B].
- Diagnostic imaging (preferably PET-CT) **can be repeated at EOT** along with a **BM biopsy, if initially involved** [II, B].
- For pts in ongoing CR, **follow-up** can be **discontinued after 3 years** in non-transplanted asymptomatic patients [III, B] and after **5 years in** asymptomatic **patients who have received auto-HSCT** (e.g. emerging signs of myelodysplasia) [III, B].
- **Routine** surveillance with **PET-CT or** diagnostic **CT cannot** be recommended for patients with CR [III, D].
- **EBV DNA monitoring** is **recommended** for patients with **ENKTCL** [II, A] and can be considered in patients with nodal PTCL and circulating EBV DNA at diagnosis [IV, C].

d'Amore F et al. Ann Oncol. 2025;36(6):626-644.& Hemasphere. 2025;9(5):e70128.

Interim PET in PTCL

Key Points

- As reported previously, outcome remained unaf-fected by iPET-based treatment changes
- On multivariable analy-sis, only TMTV and iPET response independently predicted survival. Due to small numbers and events, PET did not predict survival in ALK-pos lymphoma.

REGULAR ARTICLE

blood advances

Baseline and interim functional imaging with PET effectively risk stratifies patients with peripheral T-cell lymphoma

Neha Mehta-Shah,[1,2,*] Kimiteru Ito,[3,*] Kurt Bantilan,[1] Alison J. Moskowitz,[1] Craig Sauter,[4] Steven M. Horwitz,[1] and Heik[illegible]höder[3]

[1]Lymphoma Service, Department of Medicine, Memorial Sloan Kettering Cancer Center, New York, NY; [2]Division of Oncology, Department of Medicine, Washi[illegible] University in St. Louis, St. Louis, MO; and [3]Molecular Imaging and Therapy Service, Department of Radiology, and [4]Bone Marrow Transplant Service, Department of Me[illegible] Memorial Sloan Kettering Cancer Center, New York, NY

22 JANUARY 2019 x VOLUME 3, NR 2

Key Points

- In peripheral T-cell lymphomas treated upfront, baseline total metabolic tumor volume and interim 5-point score are prognostic.
- Interim PET response (assessed by 5-point score) further risk stratifies patients with low and high baseline clinical risk scores.

Hematological ONCOLOGY

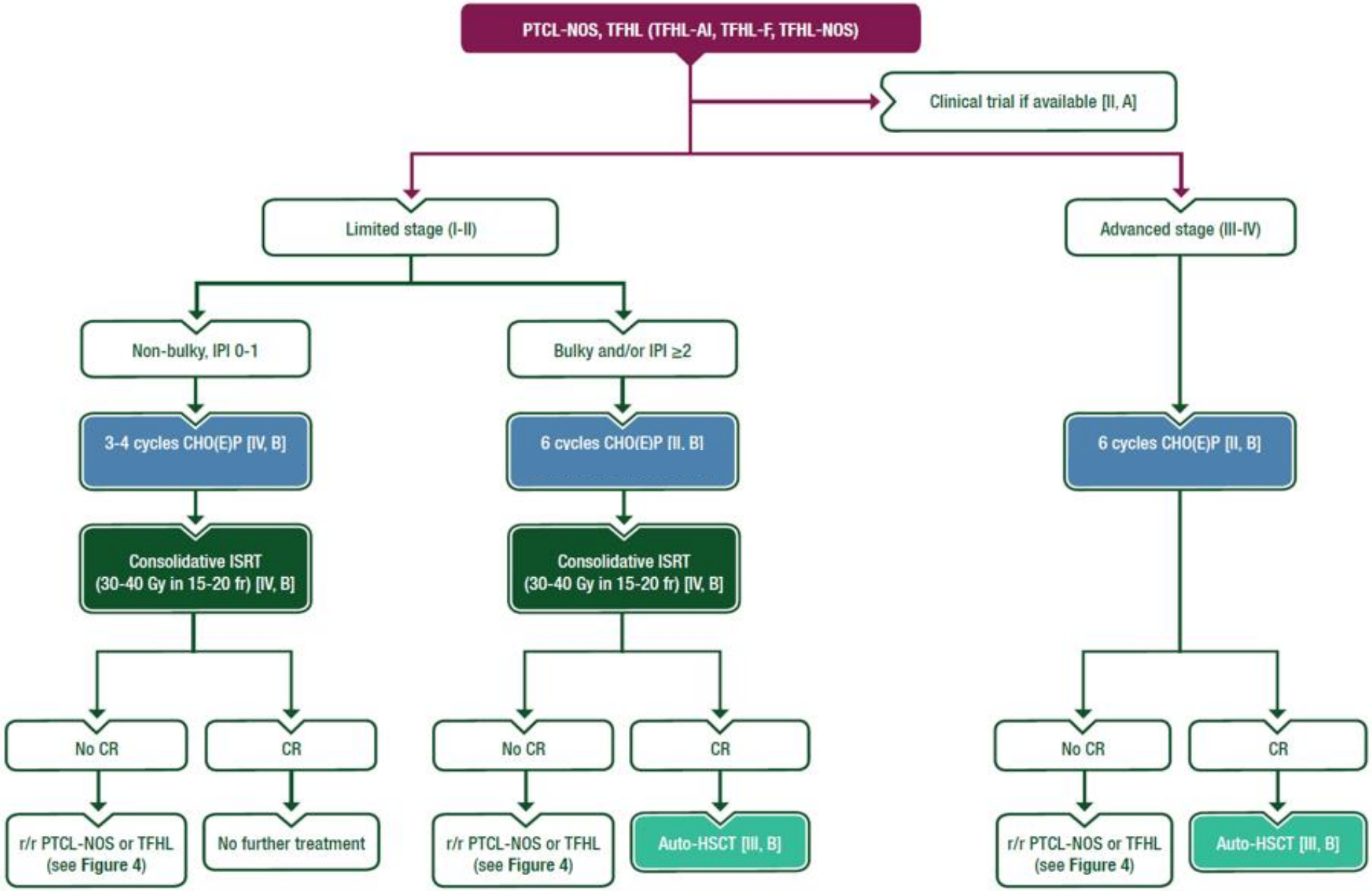
ORIGINAL RESEARCH ARTICLE | Open Access

Baseline and interim PET-based outcome prediction in peripheral T-cell lymphoma: A subgroup analysis of the PETAL trial

Christine Schmitz, Jan Rekowski, Stefan P. Müller, Bernd Hertenstein, Christiane Franzius, Arnold Ganser, Frank M. Bengel, Frank Kroschinsky, Jörg Kotzerke, Paul La Rosée, Martin Freesmeyer, Heinz-Gert Hoeffkes, Andreas Hertel, Dirk Behringer, Rolf Mesters, Matthias Weckesser, Stefan Mahlmann, Uwe Haberkorn, Uwe Martens, Gabriele Prange-Krex, Winfried Brenner, Aristoteles Giagounidis, Regina Moeller, Volker Runde, Matthias Sandmann, Hubertus Hautzel, Stefan Wilop, Thomas Krohn, Heinz Dürk, Michael Heike, Ferras Alashkar, Marcus Brinkmann, Guido Trenn, Dietmar Wacker, Christiane Kreisel-Büstgens, Helga Bernhard, Gerhard Heil, Rolf Larisch, Lars Kurch, Karl-Heinz Jöckel, Dieter Hoelzer, Wolfram Klapper, Ronald Boellaard, Ulrich Dührsen, Andreas Hüttmann ... See fewer authors

First published: 18 February 2020 | https://doi.org/10.1002/hon.2697 | Citations: 17

1st line treatment of PTCL-NOS and TFHL



d'Amore F et al. Ann Oncol. 2025;36(6):626-644.& Hemasphere. 2025;9(5):e70128.

Limited-stage nodal PTCL

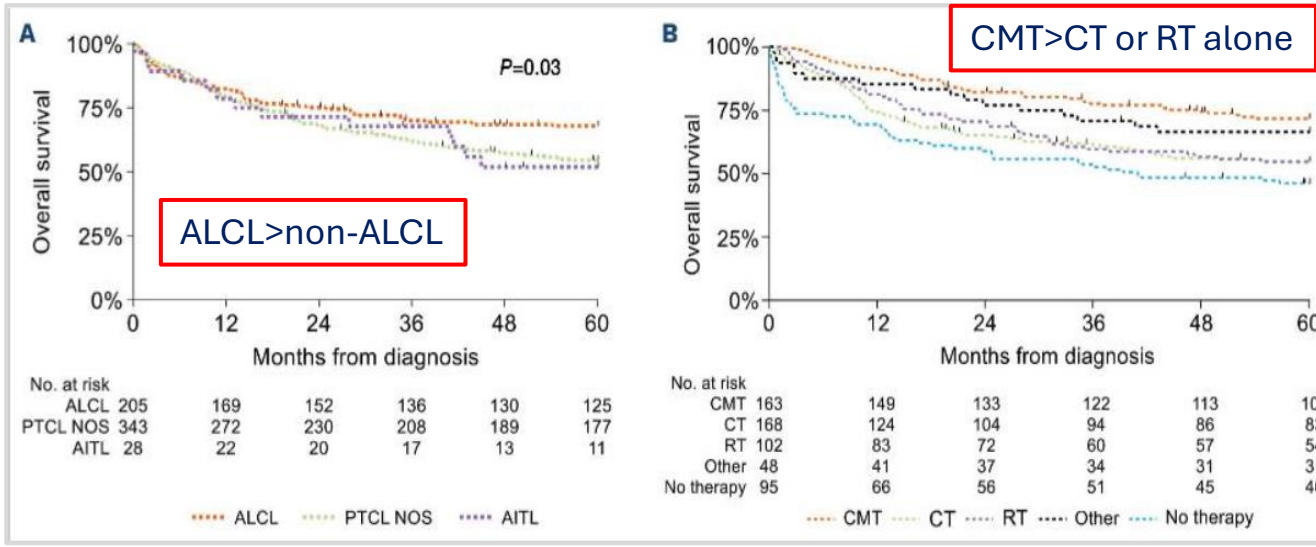
haematologica
Journal of the Ferrata Storti Foundation

Haematologica. 2023 Oct 5;109(4):1163–1170. doi: 10.3324/haematol.2023.283174

only st I

Outcome of combined modality treatment in first-line for stage I(E) peripheral T-cell lymphoma; a nationwide population-based cohort study from the Netherlands

Frederik O Meeuwes [1,2], Mirian Brink [3], Wouter Plattel [2], Marjolein WM van der Poel [4], Marie José Kersten [5], Mariëlle Wondergem [5], Lara Böhmer [6], FJ Sherida H Woei-A-Jin [7], Otto Visser [8], Rimke Oostvogels [9], Patty M Jansen [10], Karen J Neelis [11], Anne PG Crijns [12], Laurien A Daniëls [13], Tjeerd JF Snijders [14], Joost SP Vermaat [15],



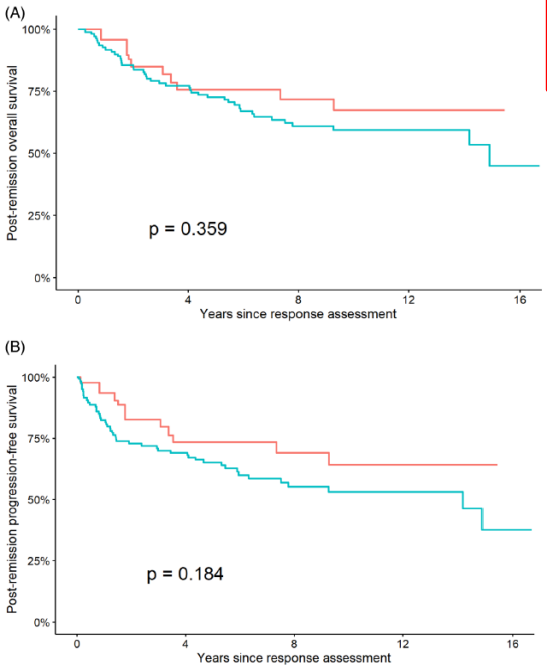
RESEARCH ARTICLE

Am J Hematol. 2023;98:388–397

AJH WILEY

Outcome of limited-stage peripheral T-Cell lymphoma after CHOP(–like) therapy: A population based study of 239 patients from the Nordic lymphoma epidemiology group

Ahmed Ludvigsen Al-Mashhadi [1,2,3] | Henrik Cederleuf [4] | Rasmus Kuhr Jensen [1,2] | Torsten Holm Nielsen [5,6] | Martin Bjerregård Pedersen [1,2,3] | Thomas Bech Mortensen [7] | Thomas Relander [4] | Mats Jerkeman [4] | Anne Ortved Gang [5,8] | Anne Louise Kristensen [9] | Michael Roost Clausen [10] | Peter de Nully Brown [5] | Marianne Tang Severinsen [1] | Lasse Hjort Jakobsen [1] | Fredrik Ellin [4] | Tarec Christoffer El-Galaly [1,2,7]



In non-ALK+ALCL pts , those with >2 IPI factors had a 5yOS of 20%

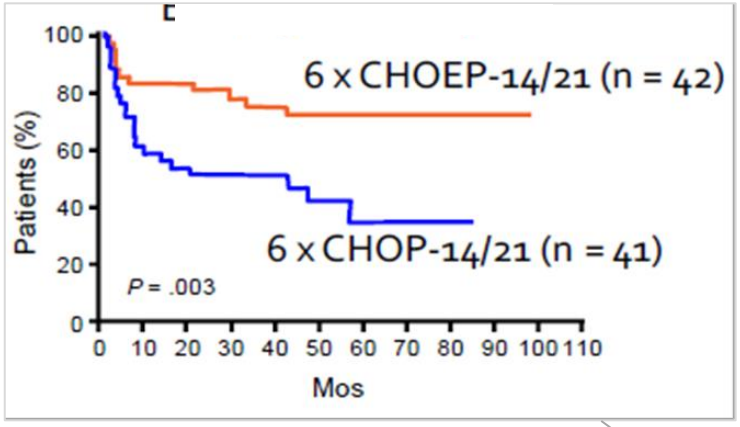
There was no difference in treatment-specific outcome after 3–4 cycles vs. 6–8 cycles of CHOP(like) ±RT

The addition of etoposide to CHOP - The German experience in aggressive lymphomas

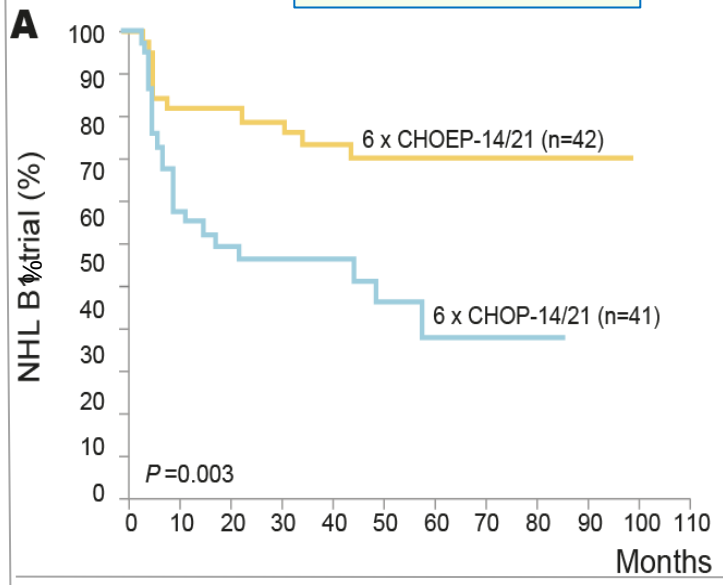
'Post-hoc' PTCL subset analysis from prospective randomized trials performed by the German Study Group on Aggressive Lymphomas

Event-free survival

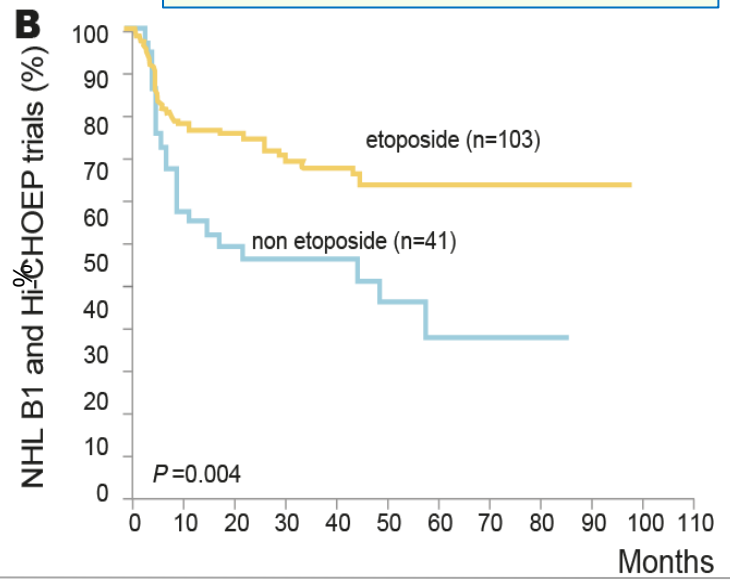
All PTCL aged ≤60 and with normal s-LDH



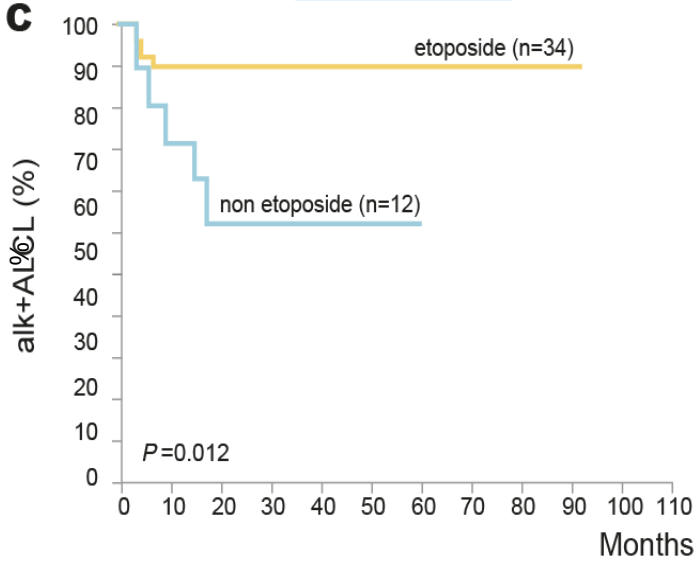
All PTCL in NHL B1 trial



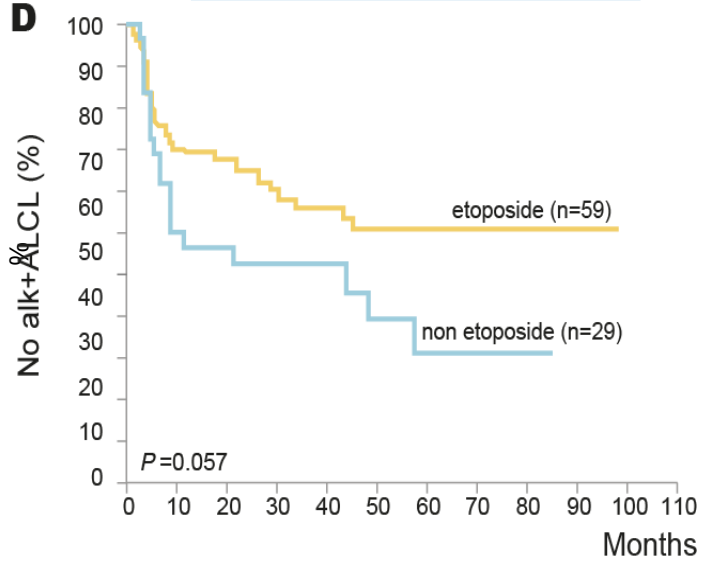
All PTCL in NHL B1 and Hi-CHOEP trial



alk-pos ALCL



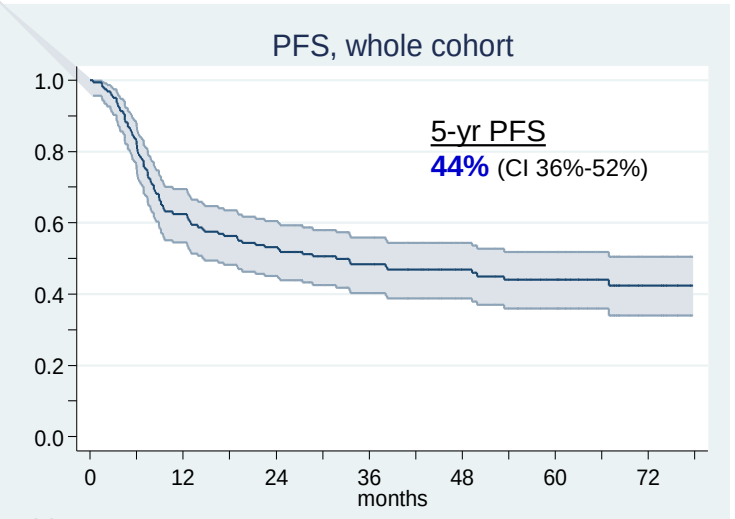
alk-neg ALCL, AITL, PTCL-NOS

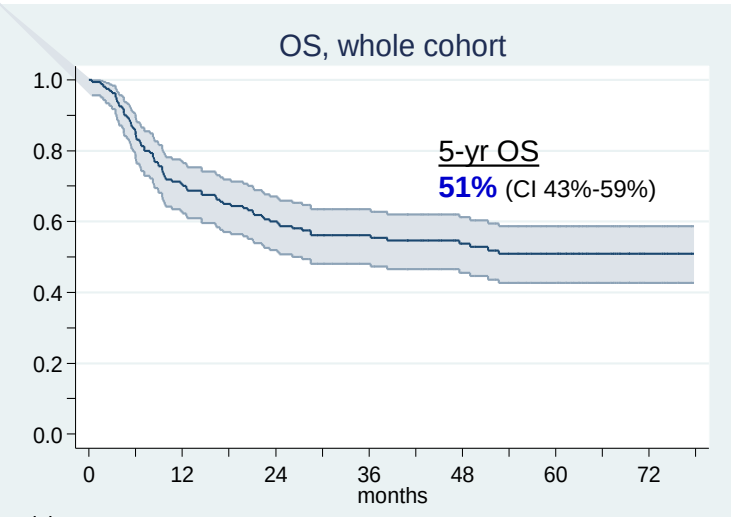


Schmitz et al.Blood 2010 Nov 4;116(18):3418-25

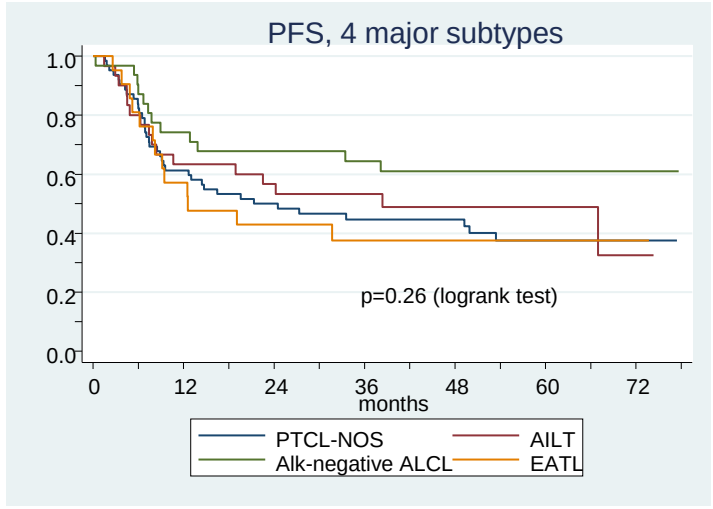
NLG-T-01: Etoposide and auto HSCT – whole cohort and subtypes (no ALK+ ALCL)

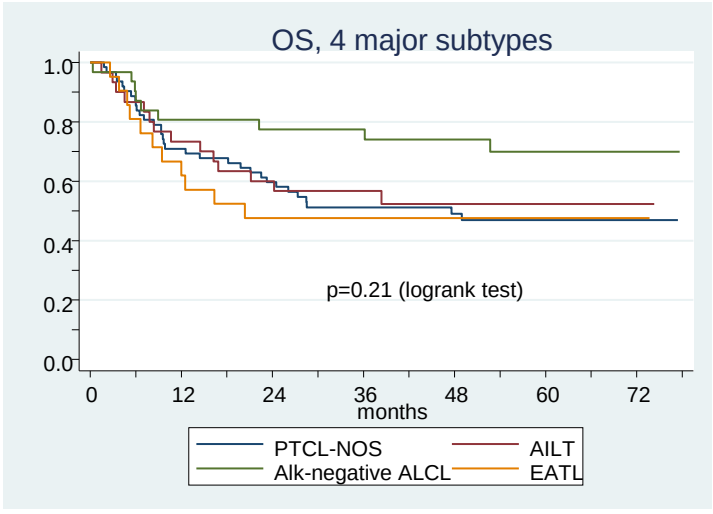
Whole cohort





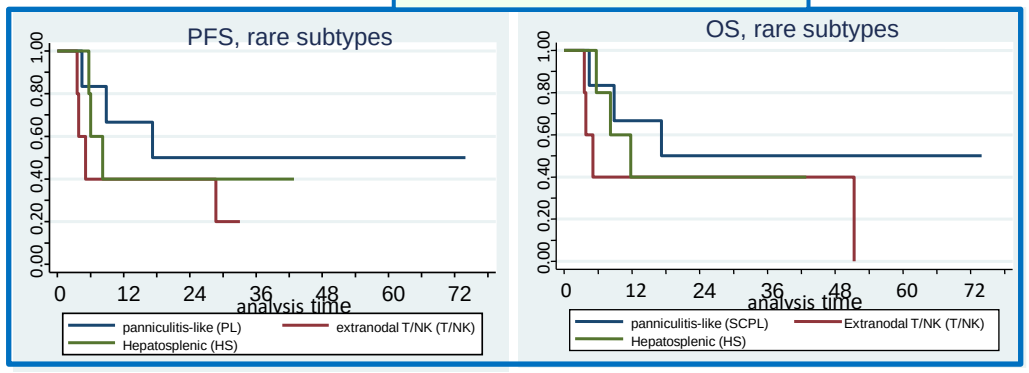
Major subtypes





Histology	5-yr OS	95% CI	5-yr PFS	95% CI
ALCL	**70%**	50%-83%	**61%**	42%-76%
AILT	**52%**	33%-69%	**49 %**	30%-65%
EATL	**48%**	26%-67%	**38 %**	18%-57%
PTCL-NOS	**47%**	34%-59%	**38 %**	25%-50%

Rare ex.nod. subtypes



d'Amore F et al. JCO 2012

Etoposide and autoHSCT: Population-based data from the Swedish lymphoma registry

CLINICAL TRIALS AND OBSERVATIONS

Real-world data on prognostic factors and treatment in peripheral T-cell lymphomas: a study from the Swedish Lymphoma Registry

Fredrik Ellin,[1,2] Jenny Landström,[2] Mats Jerkeman,[3] and Thomas Relander[3]

BLOOD, 4 SEPTEMBER 2014 • VOLUME 124, NUMBER 10

Key Points

- Population-based data show a favorable outcome with upfront autologous stem cell transplantation in PTCL.
- The addition of etoposide to CHOP was associated with favorable PFS in patients ≤60 years with PTCL.

N=755 pts with non-leukemic, non-cutaneous PTCL

In an intention-to-treat analysis in 252 nodal PTCL and EATL pts (excluding alk–positive ALCL), upfront auto SCT was associated with a superior OS (HR 0.58; P5 .004) and PFS (HR 0.56; P5 .002) compared with pts treated without auto-SCT.

The addition of etoposide to CHOP resulted in superior PFS, but only borderline for OS, in pts <60 years (HR 0.49; P 5 .008 and HR 0,58; P5 .052, respectively) .

BJHaem
BRITISH JOURNAL OF HAEMATOLOGY
British Society for Haematology

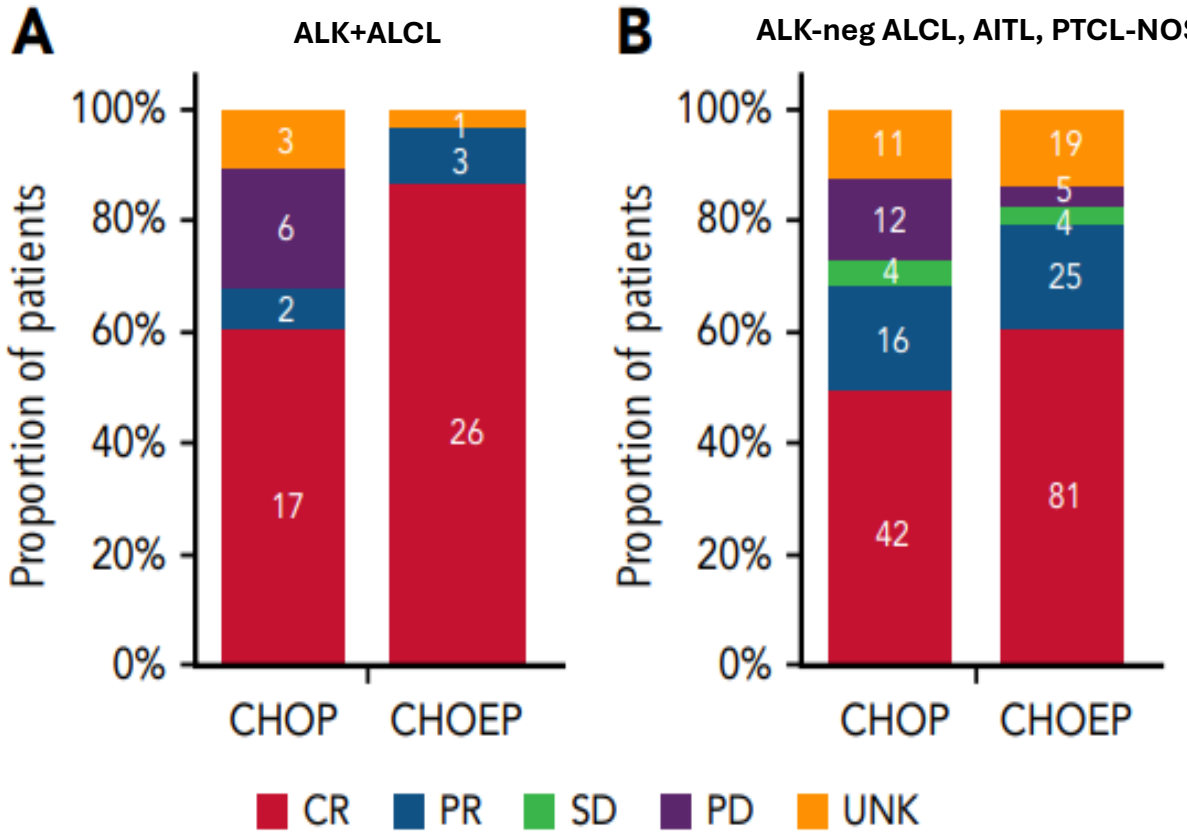
Research Paper

The addition of etoposide to CHOP is associated with improved outcome in ALK+ adult anaplastic large cell lymphoma: A Nordic Lymphoma Group study

Henrik Cederleuf, Martin Bjerregård Pedersen, Mats Jerkeman, Thomas Relander, Francesco d'Amore, Fredrik Ellin

- The median age of the cohort was 40 y (range 18–85). The 5-y OS and PFS was 78% and 64%, respectively.
- Age stratification of the patients demonstrated, efter adjustment for risk factors, an association between treatment with CHOEP and improved OS for patients aged 41–65 y, (HR = 0·38, *P* = 0·047).

Etoposide and autoHSCT: Population-based data from the Dutch Cancer registry

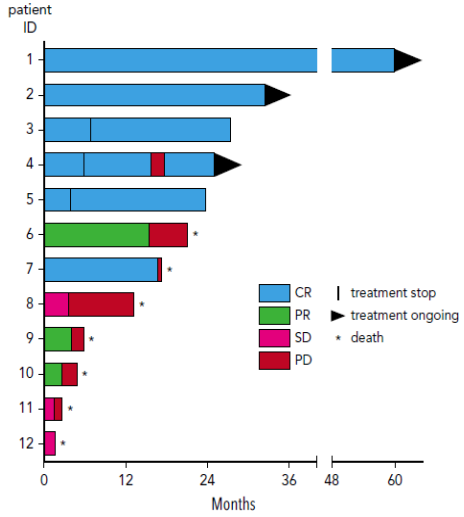


KEY POINTS

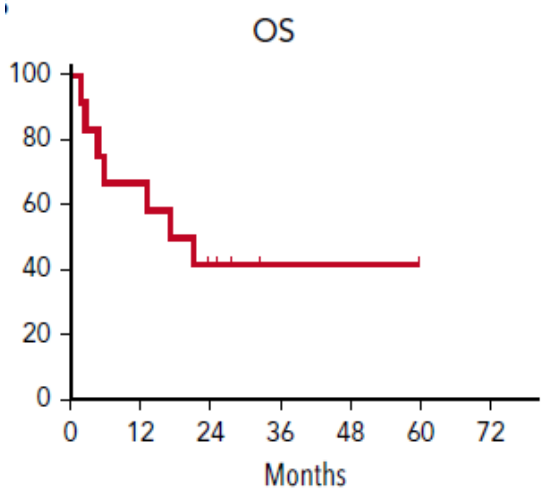
- In advanced-stage T-cell lymphoma, the addition of etoposide to CHOP improved OS in ALK$^+$ ALCL but not in ALK$^-$ ALCL, AITL, or PTCL NOS.
- Consolidation with ASCT in the first-line setting significantly increased OS in ALK$^-$ ALCL, AITL, and PTCL NOS.

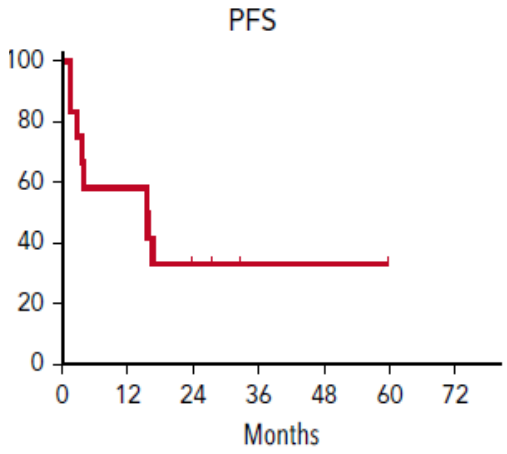
Brink M, et al. Blood. 2022 Sep 1;140(9):1009-1019.

New drugs: 5-aza in r/r TFHL



- N = 12 patients with stage III/IV AITL
- **5-azacytidine** (median of 5.5 cycles)
- ORR 75%: CR 6/12 ; PR 3/12; SD 3/12
- Median PFS 15mo
- 5 out of 12 pts associated myeloid disorder
- (MDS/CMML)



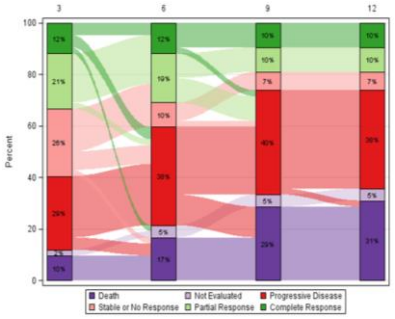


Lemonnier F et al. Blood 2018

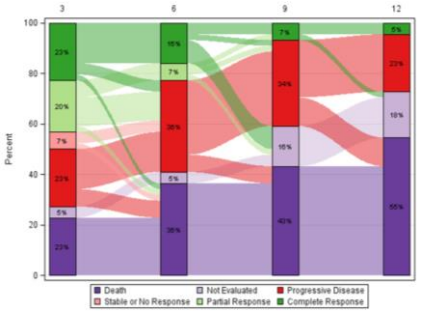
ORACLE study: oral 5-aza vs ICT (Bendamustine, Gemcitabine or Romidepsin)

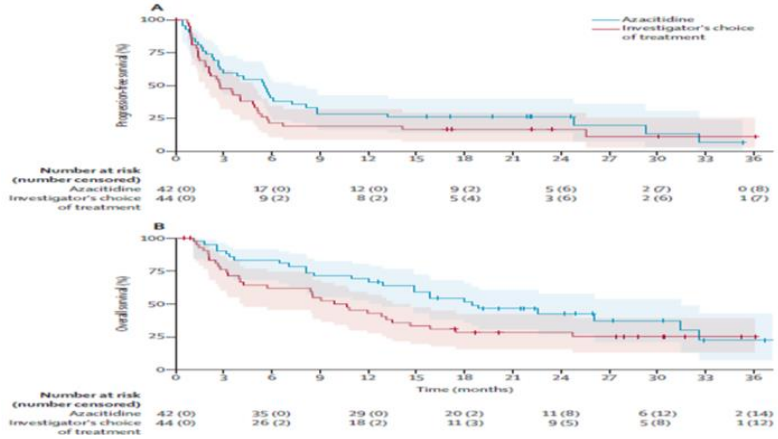
	CC-486 N=42	Investigator's choice N=44	
3 months (or PTD cycle 1-3)			
Overall response rate	**14 (33%)** [19.6%-49.5%]	**19 (43.2%)** [28.3%-59%]	p =0.33
Complete response rate	**5 (11.9%)** [4%-25.6%]	**10 (22.7%)** [11.5%-37.8%]	p =0.18
6 months (or PTD cycle 4-6)			
Overall response rate	**13 (31%)** [17.6-47.1%]	**10 (22.7%)** [11.5%-37.8%]	p =0.40
Complete response rate	**5 (11.9%)** [4%-25.6%]	**7 (15.9%)** [6.6%-30.1%]	p =0.56

5-aza



ICT



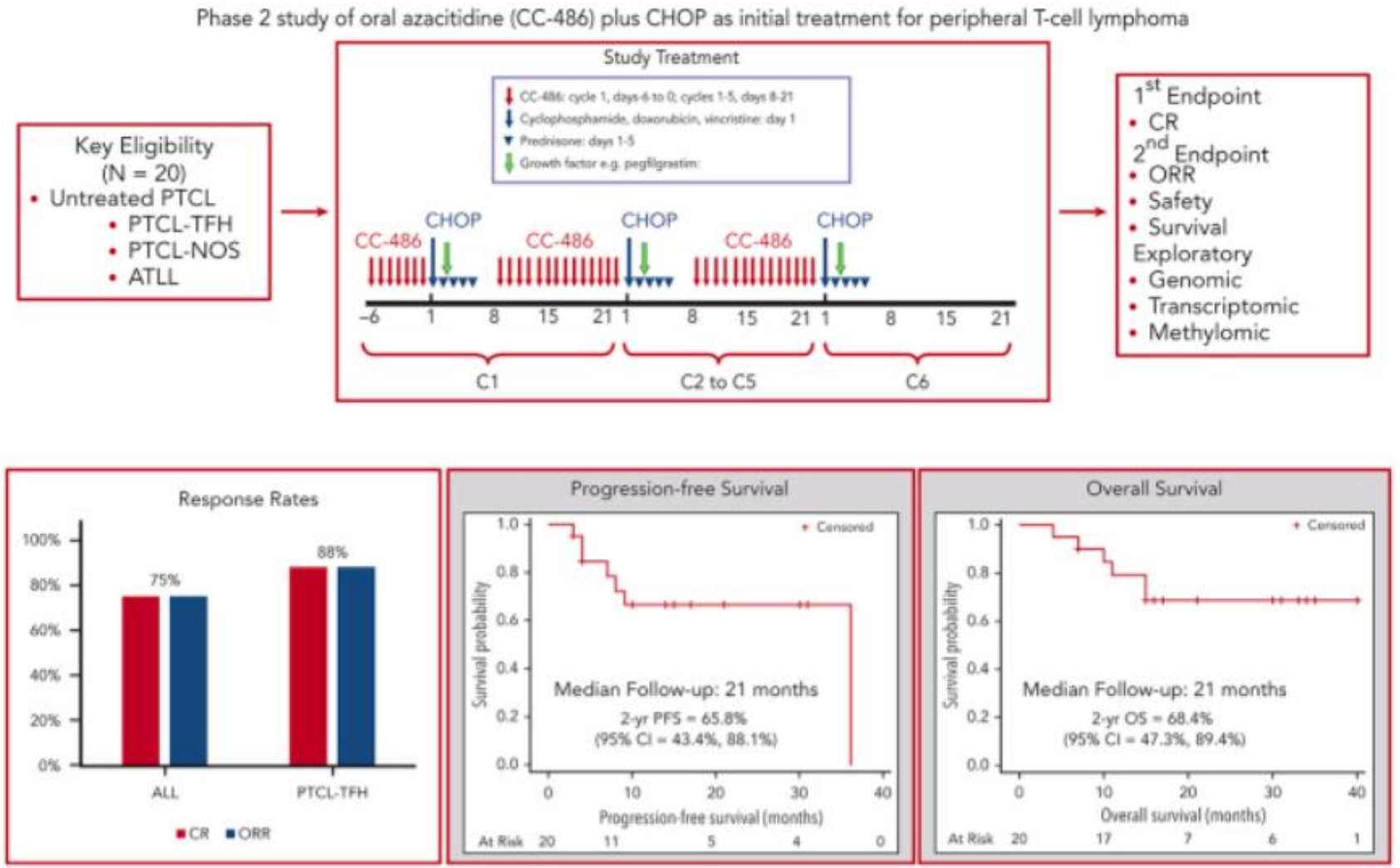


Primary EP: PFS

- 5-aza >>5.6 mo (95%CI, 2.66-8.11)
- ICT >> 2.8 mo (95%CI, 1.87-4.83) mo
- strat. log-rank test p=0.0421), HR 0.634 (95%CI, 0.38; 1.07),
- Optimistic hypothesis of PFS improvement (p<0.025) not met

Depuis J. Lancet Haematol 2024 Jun;11(6):e406-e414.

Upfront CHOP + oral 5-Aza (C486) in nodal PTCL (non-ALCL)



This regimen is being further evaluated in the ALLIANCE randomized ph 2 study, stratifying chemotherapy based on age (CHOP for >60y, CHOEP for ≤60y), to compare: ① oral azacitidine plus CHOP/or CHOEP vs ② PI3K inhibitor duvelisib plus CHOP/or CHOEP vs ③ CHOP/orCHOEP in CD30⁻ PTCL (NCT04803201).

Ruan J, et al. Blood 2023; 141(18):2194-2205

Chidamide + s.c. 5-aza + CHOP in newly diagnosed PTCL

45 pts with 'de novo' PTCL (mostly AITL) included over a 3y period (3/21 – 12/23)

The Chi+5-Aza-CHOP regimen

- CHOP .....D 1-5
- 5-Aza100mg SC..... D 1-5
- Chidamide 20mg x 2 q week of each cycle (cycle length: 3 w)

Pts in PR/CR after 4-6 cycles proceed to auto HSCT followed by oral chidamide 20mgx2 q week as maintenance

Primary end-point: ORR
Secondary end-points: CR rate, safety parameters, OS, PFS

41 pts received the Chi+AZ-CHOP regimen for at least 2 cycles (median 5)

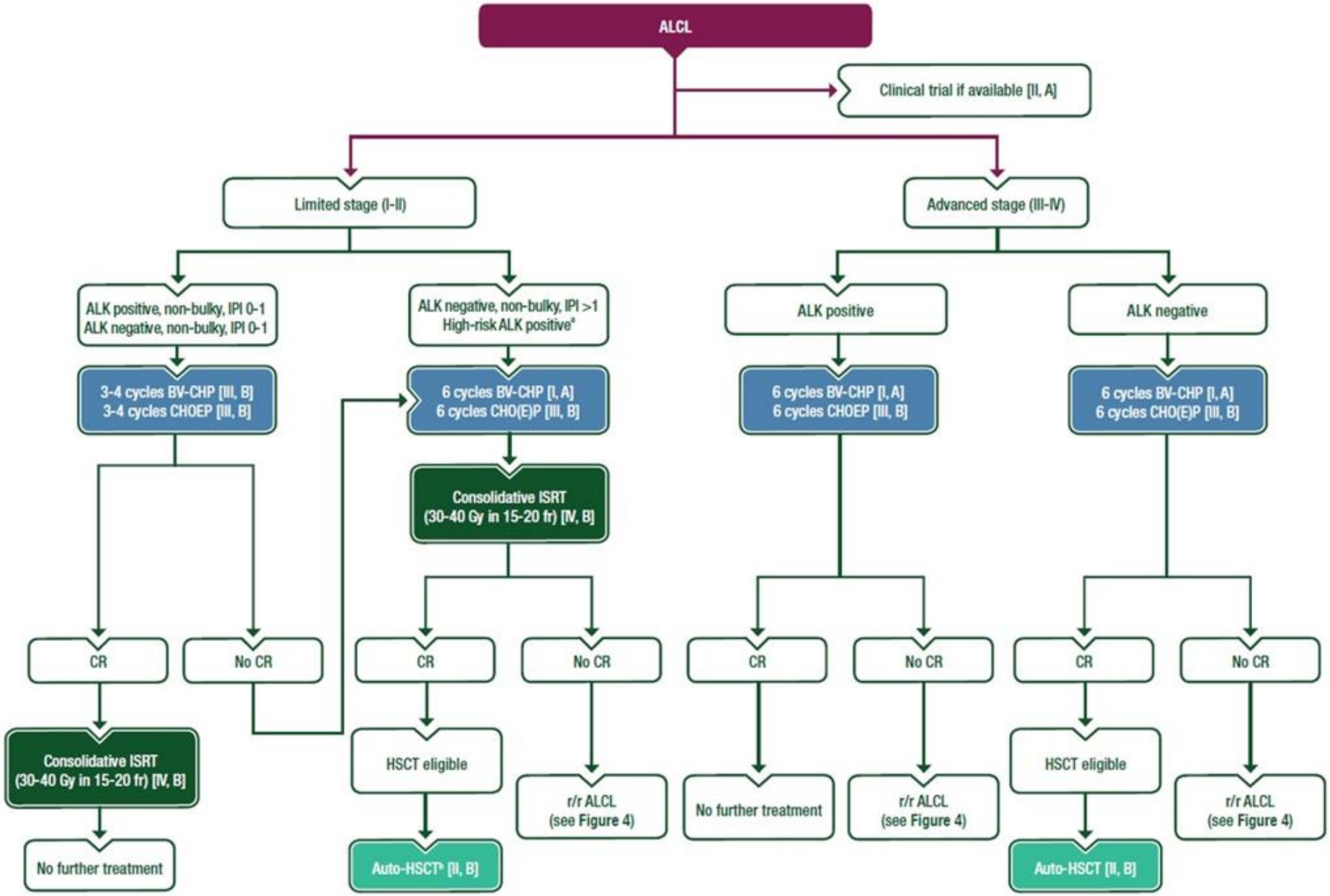
- ORR 85.3% with CR 48.7%
- 5 PD while on treatment,
- 17 pts received ASCT; post ASCT ORR was 100% and CR rate 88.2%

In patients with AITL (n=23), post-induction ORR was 86.9% and CR 60.8%

Characteristics	No. of patients, %
Median age, y (range)	45 (25-73)
> 60	16 (35.6)
≤60	29 (64.4)
Gender	
Male	25 (55.6)
Female	20 (44.4)
PTCL-subtypes	
PTCL-NOS	7 (15.6%)
AITL	27 (60%)
MEITL	4 (8.9%)
MF	2 (4.4%)
ALK-neg ALCL	5 (11.1%)
Ann Arbor stages Ⅲ-Ⅳ	40 (88.9)
Bone Marrow Involvement	6 (13.3)
IPI	
3-5	17 (62.2)

Xiao C et al, e-poster P2106; EHA 2024

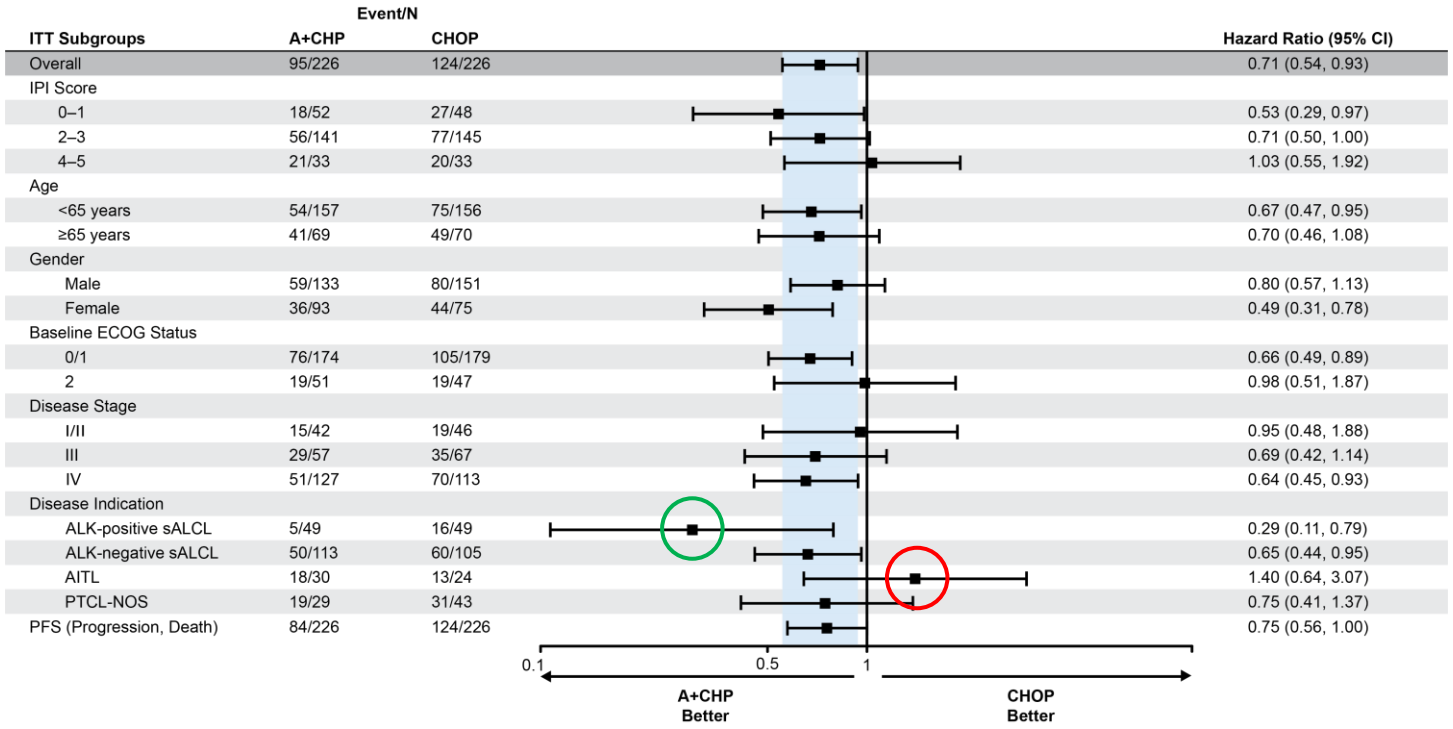
1st line treatment of ALK-pos and ALK-neg ALCL



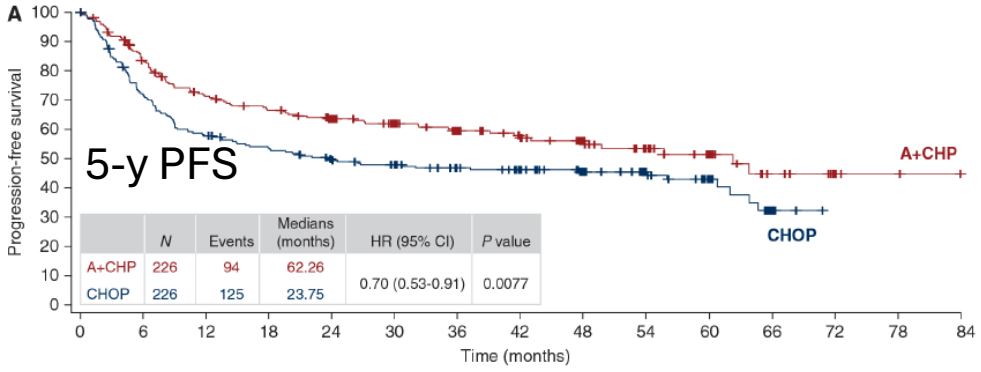
d'Amore F et al. Ann Oncol. 2025;36(6):626-644.& Hemasphere. 2025;9(5):e70128.

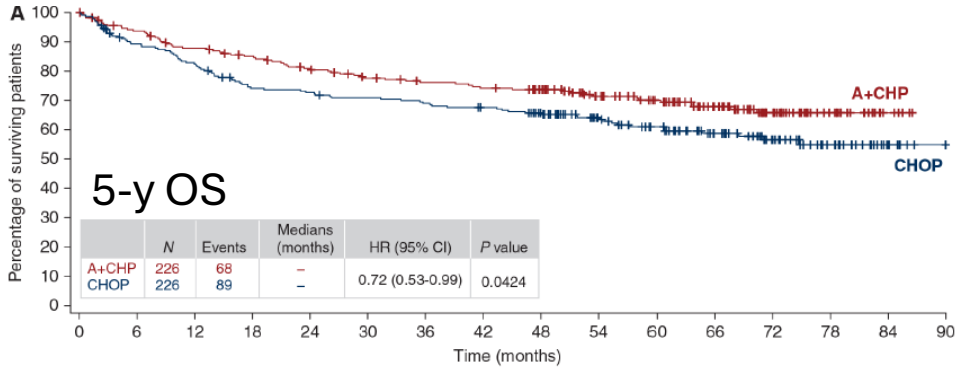
ECHELON-2

	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)



ALCL-driven





Sustained outcome advantage

Horwitz Set al. Lancet Oncol 2018
Horwitz S et al. Ann Oncol 2022

Etoposide and ALK+ ALCL: Pooled analysis of 263 pts enrolled in 6 clinical trials

LETTERS TO THE EDITOR

David Sibon et al.

haematologica 2019; 104:e562

ALK-positive anaplastic large-cell lymphoma in adults: an individual patient data pooled analysis of 263 patients

Table 1. Demographics and clinical characteristics of adults with systemic ALK-positive ALCL.

Characteristic	All patients	No etoposide during induction, n (%)	Etoposide during induction, n (%)	P
No. of patients	263	171	92	
Study				<0.0001
LYSA-1	48 (18.3)	48 (28.1)	0	
LYSA-2	10 (3.8)	3 (1.8)	7 (7.6)	
DSHNHL	78 (29.7)	21 (12.3)	57 (62)	
Japan	44 (16.7)	37 (21.6)	7 (7.6)	
IPTCLP	74 (28.1)	54 (31.6)	20 (21.7)	
Mayo Clinic	9 (3.4)	8 (4.7)	1 (1.1)	
Cohort				<0.0001
LYSA	58 (22.1)	51 (29.8)	7 (7.6)	
DSHNHL	78 (29.7)	21 (12.3)	57 (62)	
Japan	44 (16.7)	37 (21.6)	7 (7.6)	
IPTCLP-Mayo Clinic	83 (31.6)	62 (36.3)	21 (22.8)	
Age				
Median (years)	34	34	35	0.978
Range (years)	18-76	18-76	19-71	
≤ 60 years	232 (88.2)	146 (85.4)	86 (93.5)	0.082

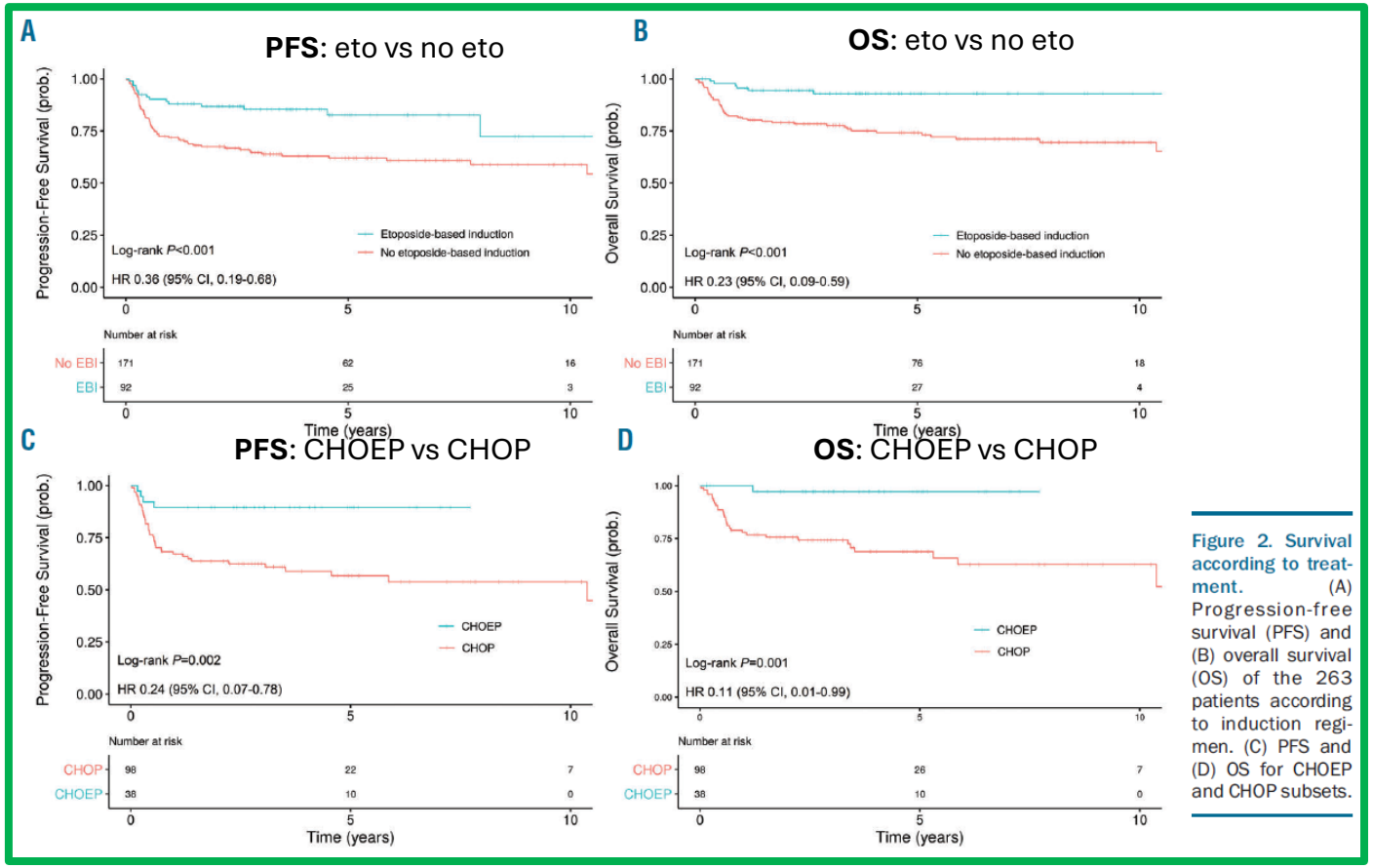


Figure 2. Survival according to treatment. (A) Progression-free survival (PFS) and (B) overall survival (OS) of the 263 patients according to induction regimen. (C) PFS and (D) OS for CHOEP and CHOP subsets.

AutoHSCT after BV-CHP – added efficacy?

Etoposide added to BV-CHP (CHEP-BV) – added efficacy?

Key Points

Consolidative SCT should be considered in patients with CD30$^+$PTCL in a CR following frontline treatment with A+CHP.

STIMULUS REPORT

blood advances 11 OCTOBER 2022 • VOLUME 6, NUMBER 19

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

Kerry J. Savage,[1] Steven M. Horwitz,[2] Ranjana Advani,[3] Jacob Haaber Christensen,[4] Eva Domingo-Domenech,[5] Giu
Franck Morschhauser,[7] Onder Alpdogan,[8] Cheolwon Suh,[9] Kensei Tobinai,[10] Andrei Shustov,[11] Marek Trneny,[12] Sa
Pier Luigi Zinzani,[14] Lorenz Trümper,[15] Tim Illidge,[16,17] Owen A. O'Connor,[18] Barbara Pro,[19] Harry Miao,[20] Veronica

- Exploratory subgroup's analysis of ECHELON-2 pts on the impact of auto SCT on PFS in pts from the ECHELON-2 trial.
- PTCL pts with ALCL and non-ALCL, who were in CR after frontline treatment with BV-CHP or CHOP were included.
- The median PFS follow-up was 47.57 months. The PFS HR was 0.36, reflecting a 64% reduction in the risk of a PFS event in patients who underwent SCT compared to those who did not.
- The median PFS in patients who underwent SCT was not reached, vs 55.66 months in patients who did not undergo SCT.
- PFS results favored the use of SCT in both ALK− ALCL and non-ALCL subgroups.
- These data support the consideration of consolidative SCT in patients with CD30+PTCL who achieve CR following treatment with A+CHP.

Brentuximab vedotin plus cyclophosphamide, doxorubicin, etoposide, and prednisone followed by brentuximab vedotin consolidation in CD30-positive peripheral T-cell lymphomas: a multicentre, single-arm, phase 2 study

Herrera A et al. Lancet Haematol 2024;11:e671-81

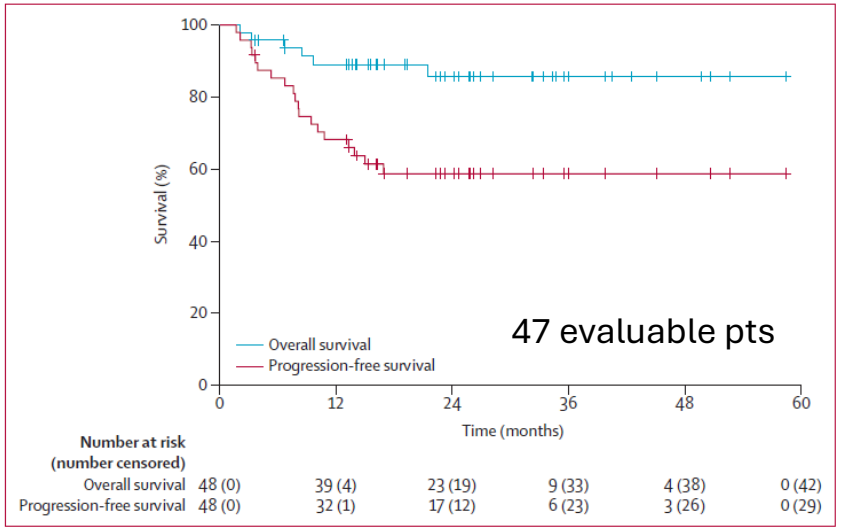
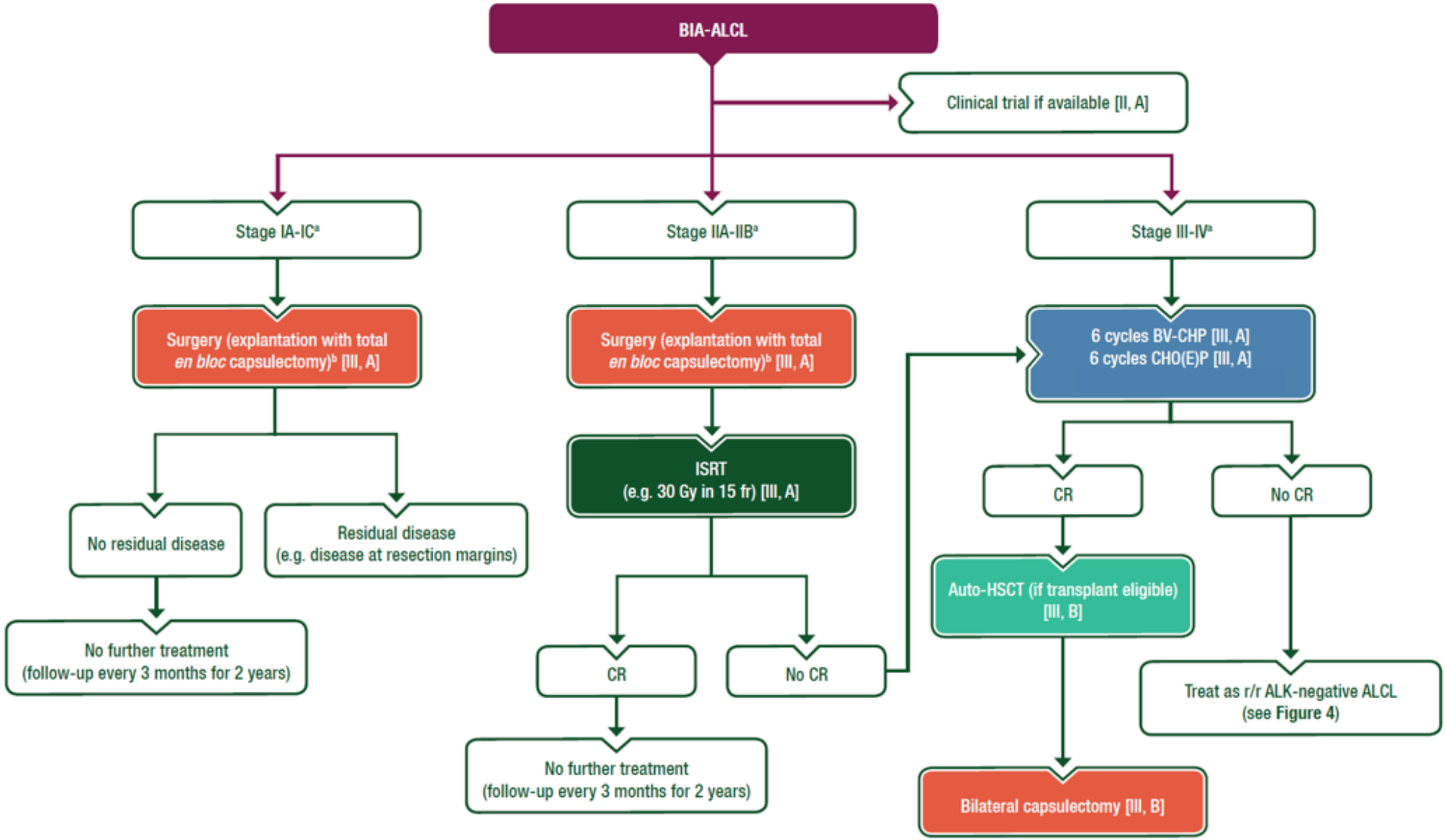


Figure 2: Progression-free and overall survival in all treated participants

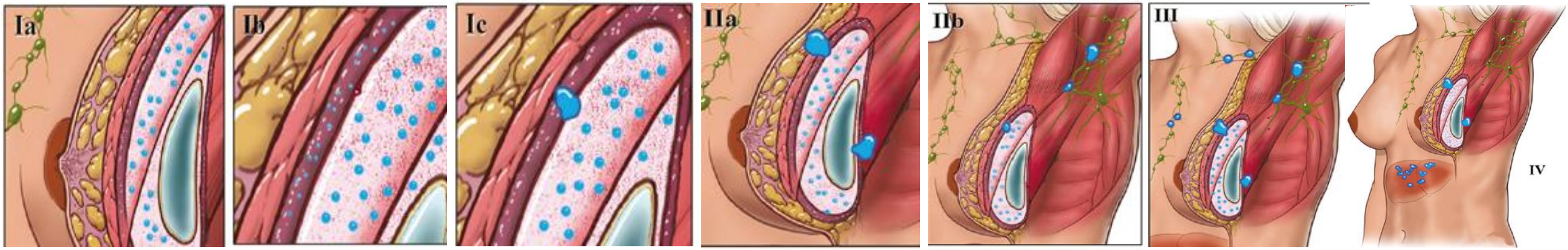
- Median foll-up: 25 mo
- P-EP: >>CR rate 79%, (87% in ALCL and 75% in non-ALCL pts)
- Overall 2-y PFS and OS: 59% (CI95% 43-71) and 86% (CI95% 71-93), respectively
- Best outcomes in BV-CHEP + autoHSCT (+ postTx BV consolidation)

1st line treatment of BIA-ALCL



d'Amore F et al. Ann Oncol. 2025;36(6):626-644.& Hemasphere. 2025;9(5):e70128.

BIA-ALCL – TNM staging



Clemens M et al, JCO 2016 – [Am Assoc Plast Surg]

Table 1. Proposed TNM Staging for Breast Implant–Associated Anaplastic Large-Cell Lymphoma

TNM or Stage Designation		Description
T: tumor extent		
	T1	Confined to effusion or a layer on luminal side of capsule
	T2	Early capsule infiltration
	T3	Cell aggregates or sheets infiltrating the capsule
	T4	Lymphoma infiltrates beyond the capsule
N: lymph node		
	N0	No lymph node involvement
	N1	One regional lymph node (+)
	N2	Multiple regional lymph nodes (+)
M: metastasis		
	M0	No distant spread
	M1	Spread to other organs/distant sites
Stage		
	IA	T1N0M0
	IB	T2N0M0
	IC	T3N0M0
	IIA	T4N0M0
	IIB	T1-3N1M0
	III	T4N1-2M0
	IV	TanyNanyM1

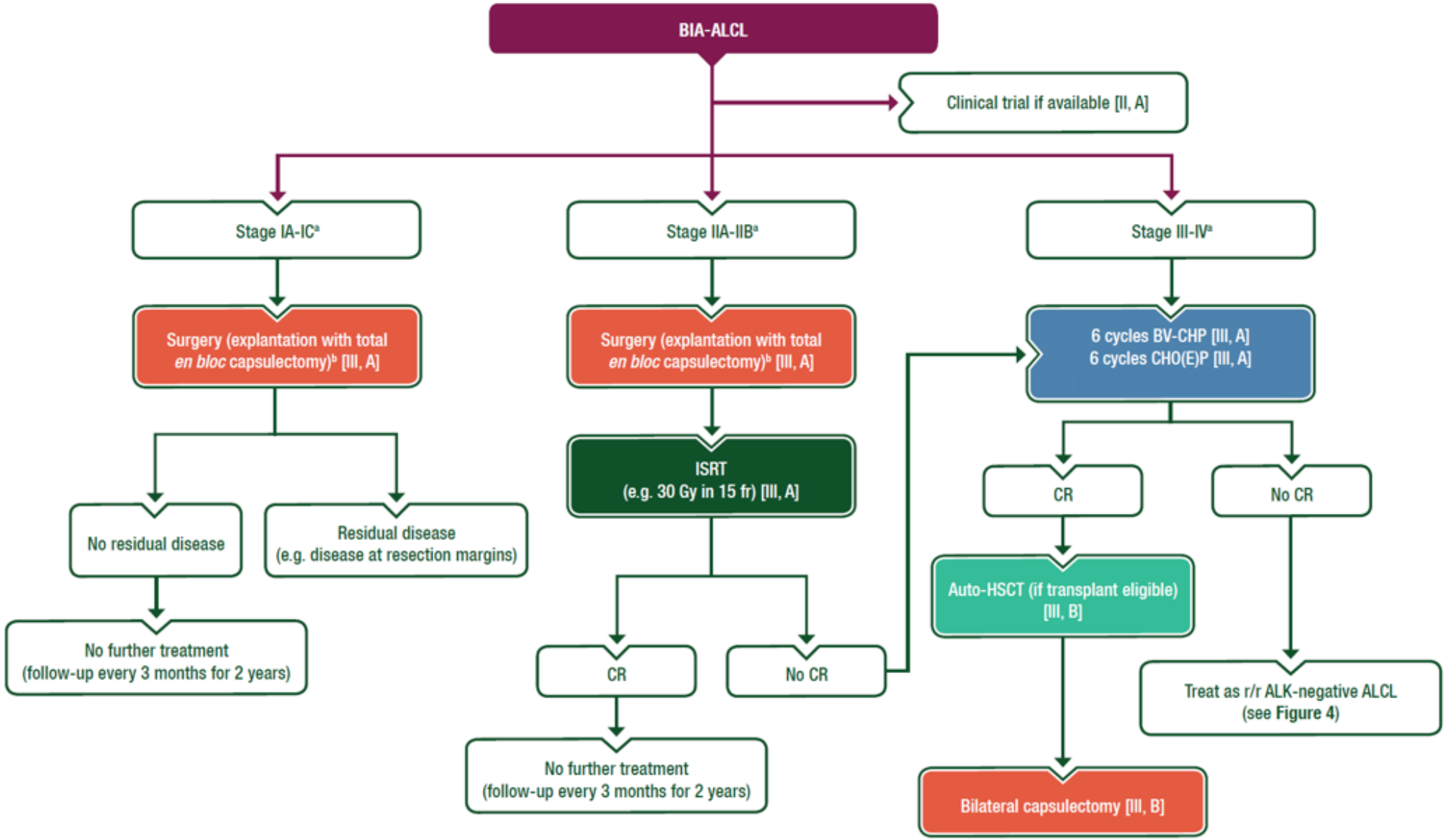
Turton P et al, BJH 2021 (ad. from Clemens M) - UK

	Description of lymphoma cells	Stage	
T = Tumour extent (penetration of capsule)			
T1	Only in the effusion or on luminal side of the capsule	1A	T1N0M0
T2	Superficial infiltration of the luminal side of the capsule	1B	T2N0M0
T3	Cell aggregates/sheets penetrate the capsule	1C	T3N0M0
T4	Cells infiltrate beyond the capsule	2A	T4N0M0
N = Node extent			
N0	No lymph node involvement		
N1	One local/regional node involved	2B	T1-3N1M0
N2	More than one local/regional node involved	3	T4N1-2M0
M = Metastatic disease			
M0	No involvement of distant sites		
M1	Disease present at distant sites	4	T1-4N0-2M1

ESMO-EHA CPG PTCL 2025 (ad. from Clemens M & Turton P)

TNM	Description of lymphoma extent	BIA-ALCL stage	TNM stage counterpart
T [tumour extent (penetration of capsule)]			
T1	Only in the effusion or on luminal side of the capsule	IA	T1 N0 M0
T2	Superficial infiltration of the luminal side of the capsule	IB	T2 N0 M0
T3	Cell aggregates or sheets penetrate the capsule	IC	T3 N0 M0
T4	Cells infiltrate beyond the capsule	IIA	T4 N0 M0
N (node extent)			
N0	No lymph node involvement		
N1	One local or regional node involved	IIB	T1-3 N1 M0
N2	More than one local or regional node involved	III	T4 N1-2 M0
M (metastatic disease)			
M0	No involvement of distant sites		
M1	Disease present at distant sites	IV	T1-4 N0-2 M1

1st line treatment of BIA-ALCL



d'Amore F et al. Ann Oncol. 2025;36(6):626-644.& Hemasphere. 2025;9(5):e70128.

1st line treatment of BIA-ALCL

- A multidisciplinary approach is recommended for diagnostic assessment, staging and treatment planning [III, A].
- Total capsulectomy with removal of the breast implant and excision of any associated mass is recommended for patients with no signs of further disease dissemination [III, A]
- A representative biopsy (excision preferred) should be obtained if suspicious regional lymph nodes are found [III, A].
- Removal of the contralateral implant is recommended, particularly if textured [III, A].
- Mastectomy is not recommended [IV, D].
- ISRT (e.g. 30 Gy in 15 fractions) is recommended following surgery in adapted TNM stage IIA-IIB and in stage IA-IC if there is evidence of residual disease [III, A].
- Six cycles of BV-CHP, CHOP or CHOEP are recommended for patients with residual disease following ISRT and those with advanced stage (stage III-IV) [III, A].
- Auto-HSCT can be considered in patients with advanced stage responding to ChT (as in systemic ALK- ALCL) [III, B].

d'Amore F et al. Ann Oncol. 2025;36(6):626-644.& Hemasphere. 2025;9(5):e70128.

Association of *BRCA*1/2 and/or *P53* gene mutations and BIA-ALCL

Letter to *Blood*
10 SEPTEMBER 2020 | VOLUME 136, NUMBER 11

TO THE EDITOR:

Increased prevalence of *BRCA1/2* mutations in women with macrotextured breast implants and anaplastic large cell lymphoma of the breast

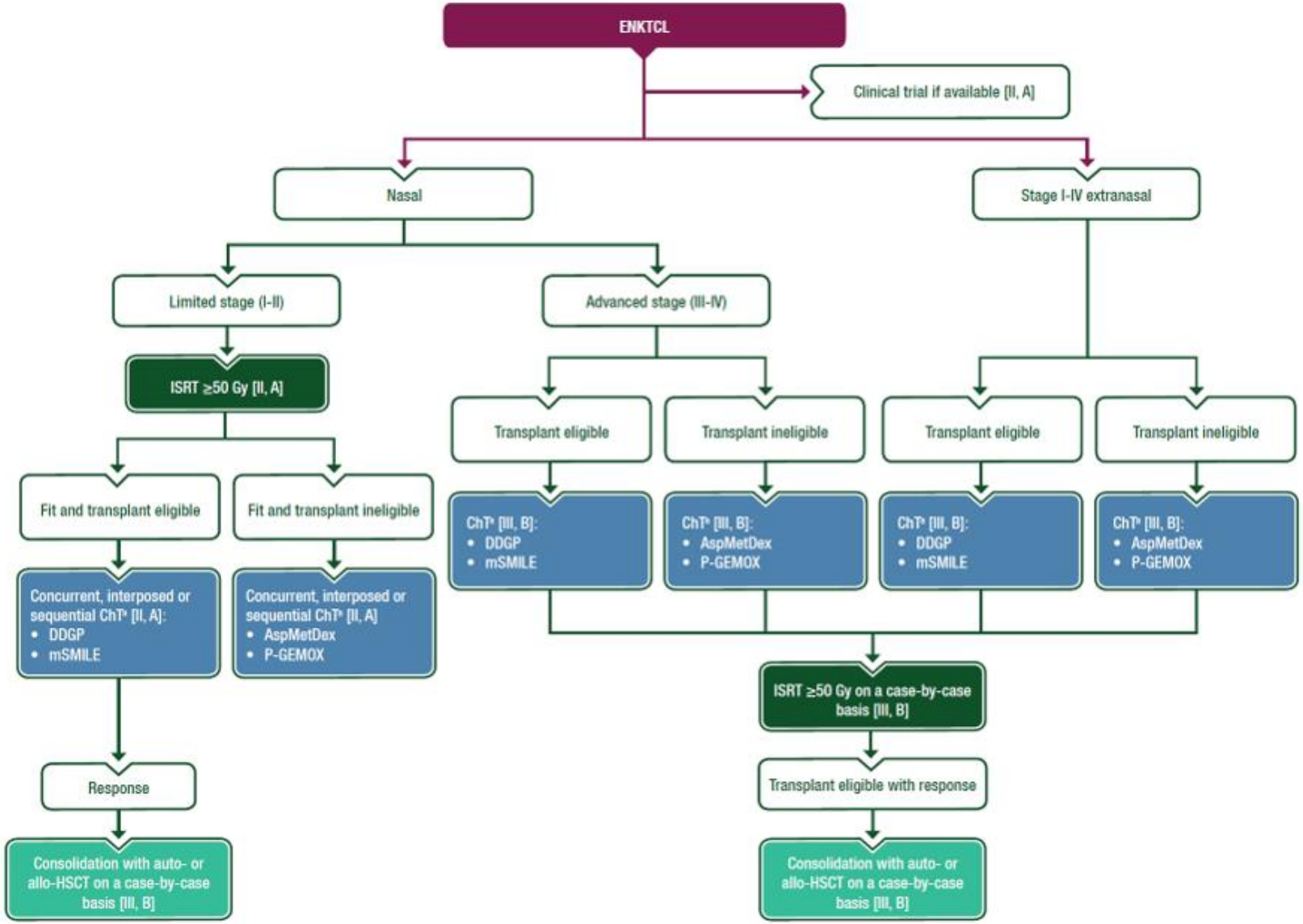
Mintsje de Boer,[1] Michael Hauptmann,[2,3] Nathalie J. Hijmering,[4] Carel J. M. van Noesel,[5] Hinne A. Rakhorst,[6] Hanne E. J. Meijers-Heijboe
Jan Paul de Boer,[8] René R. W. J. van der Hulst,[1] Daphne de Jong,[4,*] and Flora E. van Leeuwen[2,*]

Adlard J, Burton C, Turton P. Increasing evidence for the association of breast implant-associated anaplastic large cell lymphoma and Li Fraumeni syndrome. *Case Rep Genet*. 2019;2019:5647940.

Statement from the American Association of Plastic Surgeons Consensus on BIA-ALCL (Plast Reconstr Surg; 154: 473, 2024.)

- Genomic studies have shown that patients with BIA-ALCL, in general, demonstrate an above average accumulation of chromosomal and genetic abnormalities.
- Therefore, physicians should be aware of associations with concomitant neoplasia, as in the case of patients with Li Fraumeni syndrome (germline *TP53* mutations) and patients who are *BRCA1/2* carriers.
- Therefore, predisposing genetic factors, such as *BRCA* and *p53 abnormalities*, may be additional contraindications to the use of textured implants.
- Further clinical research is required for more detailed risk stratification with additional outcomes analyses before a broad genetic testing of BIA-ALCL patients can be recommended.

1st line treatment of ENKTCL



d'Amore F et al. Ann Oncol. 2025;36(6):626-644.& Hemasphere. 2025;9(5):e70128.

Check-point protein inhibition in ENKTL

THE LANCET
Haematology

ARTICLES · Volume 11, Issue 5, E336-E344, May 2024

First-line sintilimab with pegaspargase, gemcitabine, and oxaliplatin in advanced extranodal natural killer/T cell lymphoma (SPIRIT): a multicentre, single-arm, phase 2 trial

Prof Xiao-Peng Tian, MD [a,*] · Jun Cai, MD [a,*] · Prof Yi Xia, MD [a,*] · Yu-Chen Zhang, MD [a,*] · Prof Liang Wang, MD [g,*] · Pan-Pan Liu, MD [a]

- Phase 2 trial to assess the safety and activity of sintilimab plus P-GEMOX in the first-line setting for advanced ENKTL.
- Primary end-point: CR rate in ITT-population
- 34 pts enrolled and at a median follow-up of 21 months, the CR rate was 85% (29 of 34 pts), 5 pts had PR attaining a ORR of 100%
- No severe AEs occurred
- Sintilimab + GEMOX seems to be a safe and active first-line treatment for advanced stage ENKTL.

1st line treatment of ENKTCL

- EBV DNA in peripheral blood should be monitored by quantitative PCR at baseline and during therapy as a biomarker of response, in addition to imaging-based response assessment [II, A].
- Fit patients with limited-stage disease should receive ISRT (≥50 Gy) with concurrent, interposed or sequential anthracycline-free, L-asparaginase-containing ChT [e.g. DDGP or modified SMILE (mSMILE) for transplant-eligible and AspMetDex or P-GEMOX for transplant-ineligible patients] [II, A].
- A multiagent, anthracycline-free, L-asparaginase-containing regimen can be recommended for patients with stage III and IV nasal disease or stage I-IV extranasal disease (e.g. DDGP or mSMILE for transplant-eligible and AspMetDex or P-GEMOX for transplant-ineligible patients) [III, B]. Addition of ISRT can be decided on a case-by-case basis [III, B].
- If available, Crisantaspase (Erwinia Chrysanthemi-derived L-asparaginase) should be offered to patients, who have developed hypersensitivity or inactivating antibodies to E.coli-derived L-asparaginase [III, A].
- In transplant-eligible responding high-risk patients, consolidative auto- or allo-HSCT can be considered [III, B]. The choice of HSCT should be made on a case-by-case basis considering factors such as pretherapeutic risk profile, response to first-line therapy, performance status (PS) and donor availability [III, B].
- Based on encouraging recent results, upfront treatment with anti-PD-1 antibodies (e.g. sintilimab) in combination with L-asparaginase containing regimens (e.g P-GEMOX) can also be considered.

d'Amore F et al. Ann Oncol. 2025;36(6):626-644.& Hemasphere. 2025;9(5):e70128.

1st line treatment of EATL

- In fit and transplant-eligible patients, one cycle of CHOP or CHOEP, followed by three cycles of IVE alternated with intermediate-dose MTX can be considered [III, B].
- Alternative regimens are six cycles of BV-CHP [Food and Drug Administration (FDA) approved, not European Medicines Agency (EMA) approved] or CHO(E)P [III, B].
- Consolidative high-dose ChT and auto-HSCT can be considered for transplant-eligible responding patients [III, B].
- Six cycles of CHOP or CHOP-like ChT [IV, B] or six cycles of BV-CHP [III, B; FDA approved, not EMA approved] can be recommended for frail or otherwise transplant-ineligible patients.

- This CPG also includes algorithm/recommendations for RCDII

d'Amore F et al. Ann Oncol. 2025;36(6):626-644.& Hemasphere. 2025;9(5):e70128.

BV-CHP + Etoposide/MTX+ ASCT in EATL

Sibon D et al. **The Eatl-001 Trial: Results of a Phase 2 Study of Brentuximab Vedotin and CHP Followed By Consolidation with High-Dose Therapy - Autologous Stem-Cell Transplantation (HDT-ASCT) in the Frontline Treatment of Patients with Enteropathy-Associated T-Cell Lymphoma.** Blood. 2021;138(suppl 1):136 (ASH 2021)

Fase 2 study of the CELAC (French Network of Centers of Expertise for Lymphomas Associated with Celiac disease)

- First prospective ph 2 study dedicated to EATL
.
- BV-CHP was well tolerated and induced high response rates, allowing the majority of patients to be transplanted
- Novel therapeutic approach with promising efficacy compared to historical controls

Study parameter	
Inclusion criteria	• De novo CD30+ (>10%) EATL (WHO2016) • 18-65 y • PS 0-3
Treatment	4xBV+CHP >> 2xEto (200mg/m2) + MTX (3g/m2) >> autoHSCT (BEAM)
Trial cohort	• 14 pts, (med. age:54y, (34-65), 64% males • CD30+ range 10-100% (9 pts 100%) • 11 bowel obstr. (6) or jejunal perforation (5) • All had CD dx prior or concomitantly with EATL • 9 had RCDII
Toxicity	• 2 toxic deaths during HDT-ASCT • AEs consistent with known safety profile for BV-CHP
Response	• ORR 79% (11/14) with CR 64% - 11 pts went on to auto-HSCT
Outcome	• Med follow-up: 2.1y • No relapse • 2y PFS:63%; 2yOS 68%

Thank you for your attention