Should ASCT in 1st remission be the standard of care for patients with PTCL?

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2nd Postgraduate Lymphoma Conference

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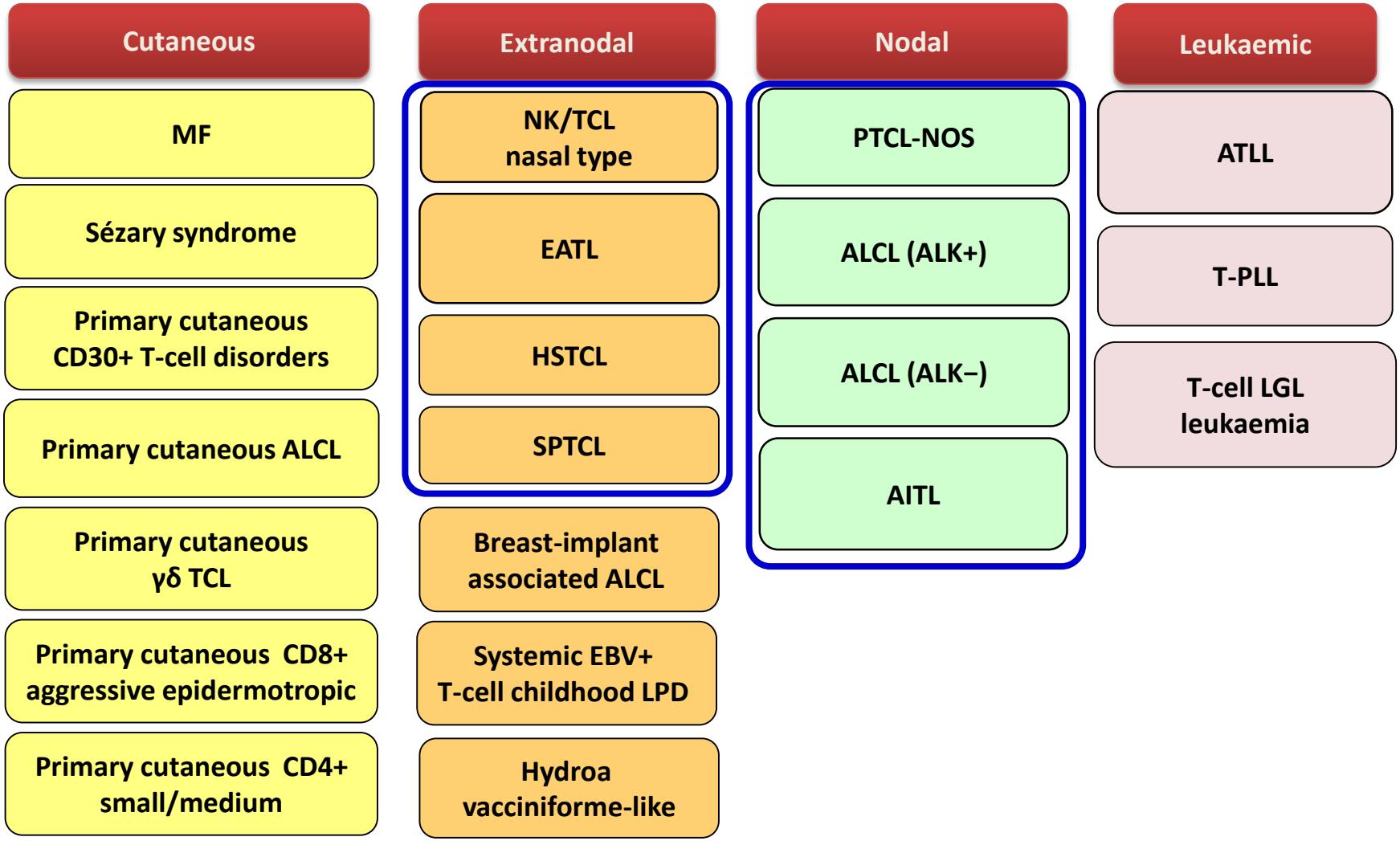
Rome, Italy

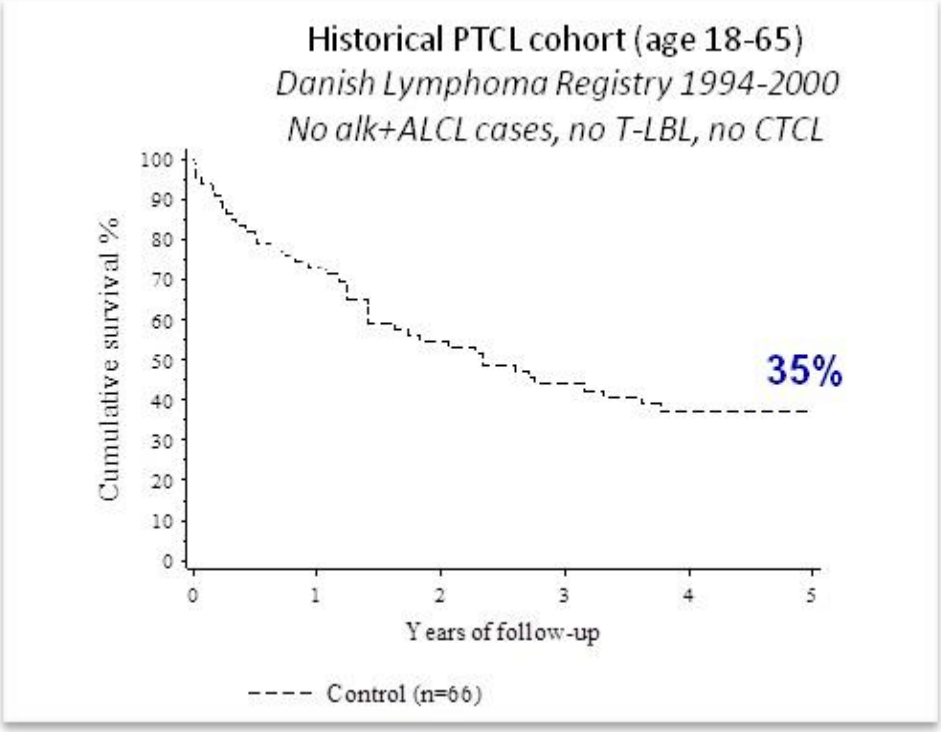
2008 WHO classification of PTCL: 20 distinctive subtypes



Adapted from Swerdlow SH, et al. WHO Classification of Tumours of Haematopoietic and Lymphoid Tissues. 2008.

Outcome with conventional chemotherapy <u>without</u> consolidating stem cell transplant

Nordic registry data



Meta-analysis of conventional chemotherapy <u>without</u> ASCT

(Emory University, Atlanta, US)

31 clinical trials: tot 2815 pts (period:1990-2010)

*Overall (all subtypes): **5 yr OS*** **38.5%**

Subtype	5-Year OS
Nasal-type NK/T-cell	48%
AITL	36.5%
PTCL, NOS	34%
Enteropathy-type	21%
Panniculitis-like	~50%
Hepatosplenic	0–10%
ALCL (alk pos+neg)	**56.5%**

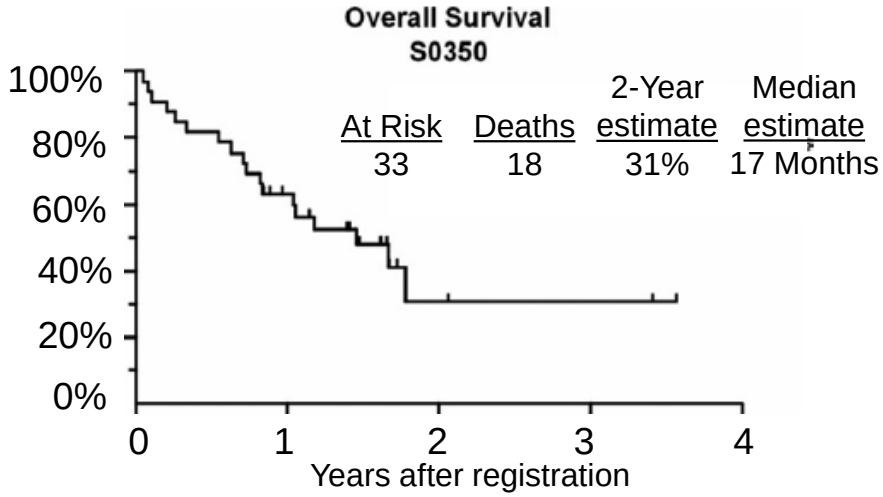
Abouyabi s et al, ISNR Hematology 2011

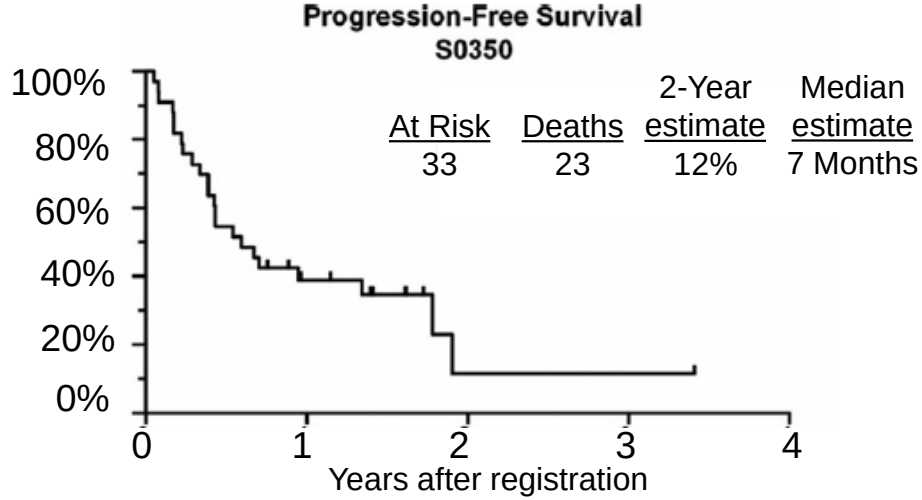
The backbone regimen issue

Does Gemcitabine+platin improve on CHOP?
The SWOG experience

Phase 2 Trial of Combined Cisplatin, Etoposide, Gemcitabine, and Methylprednisolone (PEGS) in Peripheral T-Cell Non-Hodgkin Lymphoma

Southwest Oncology Group Study S0350





Disappointing outcomes:

- ORR 39%; CR 24%, PR 15%
- med PFS: 9 mo, med OS: 17 mo
- 2-yr PFS: 12%, 2-yr OS: 31% (designed target: 67%)

Mahadevan et al Cancer 2013

CEOP-Pralatrexate

bjh research paper

A phase II study of cyclophosphamide, etoposide, vincristine and prednisone (CEOP) Alternating with Pralatrexate (P) as front line therapy for patients with peripheral T-cell lymphoma (PTCL): final results from the T- cell consortium trial

Trial cohort	
N pts	33
PTCL-NOS	21
AITL	8
ALCL	4
CS IV	61%
IPI I-H/H	46%

Toxicity gr 3-4	
Anæmia	27%
Febrile n.penia	18%
Mucositis	18%
Sepsis	15%
Thr.penia	12%
> creat	12%
> liver trans.	12%

Efficacy	
2y PFS	39%
2y OS	60%
SCT	45% (all in cCR)

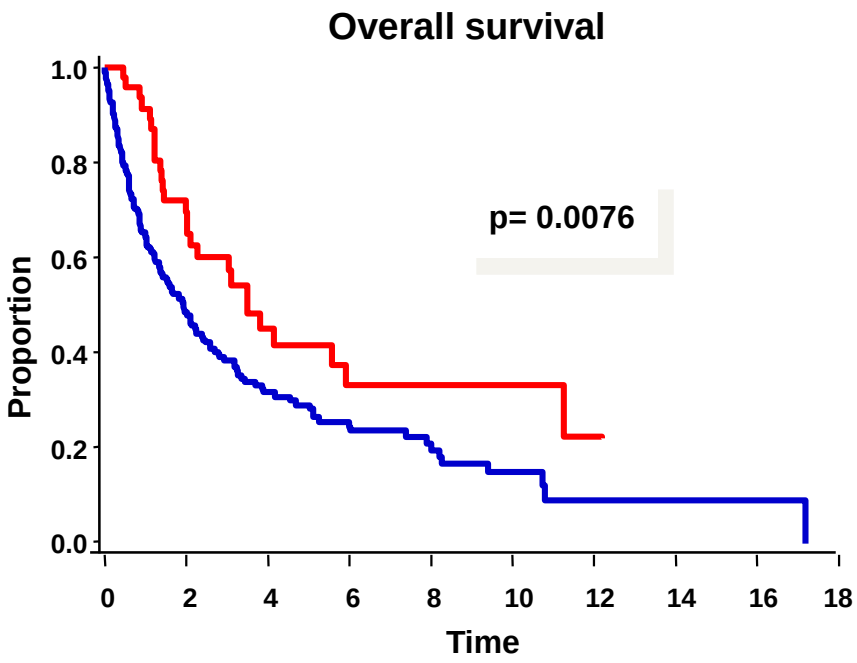
Authors' statement → CEOP-P did not improve outcomes compared to historical CHOP data

Advani R et al. Br J Haematol 2015

Upfront ASCT – Some retrospective analyses

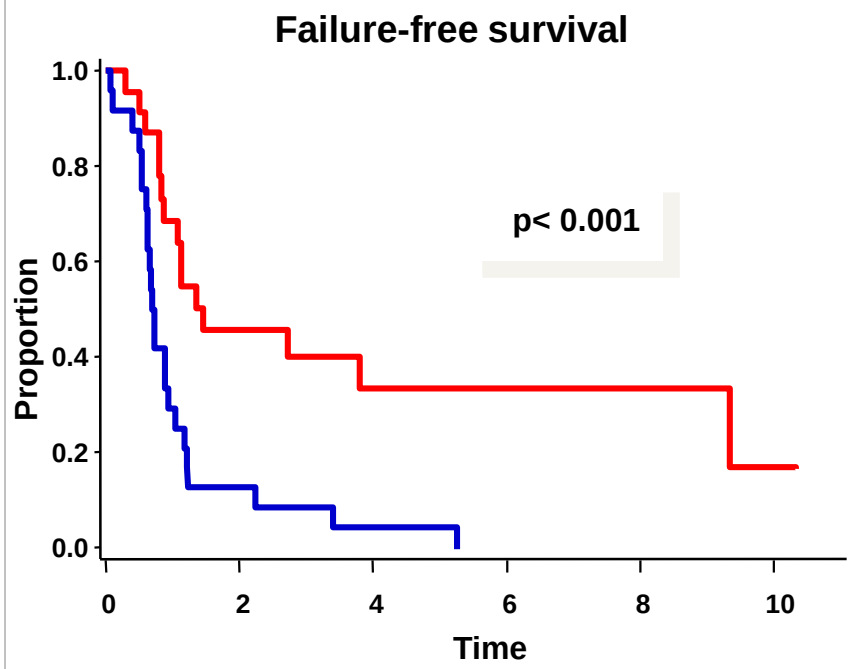
HDT in PTCL-NOS

possibly an advantage



HD Therapy	CENSOR	FAIL	TOTAL	MEDIAN
yes	21	27	48	3.5
no	63	148	211	1.95

if so, rather upfront



Transplantation	CENSOR	FAIL	TOTAL	MEDIAN
1. line	8	15	23	1.4
2. line	0	24	24	0.71

Armitage, Vose, et al. J Clin Oncol (2008)

Intensified induction + upfront ASCT in EATL

Retrospective analysis of prospectively collected data

Evaluation of enteropathy-associated T-cell lymphoma comparing standard therapies with a novel regimen including autologous stem cell transplantation

Michal Sieniawski,[1] Nithia Angamuthu,[1] Kathryn Boyd,[2] Richard Chasty,[3] John Davies,[4] Peter Forsyth,[5] Fergus Jack,[6] Simon Lyons,[7] Philip Mounter,[8] Paul Revell,[9] Stephen J. Proctor,[1] and Anne L. Lennard[1]

BLOOD, 6 MAY 2010 • VOLUME 115, NUMBER 18

No subtype distinction

Parameter	Comment	Values
N pts	CHOP-like IfosfVepEpi + MTX+ASCT	N_{tot}= 54 N_{tot}= 26
Data period	CHOP-like IfosfVepEpi + MTX+ASCT	1994-1998 1998-2009
Outcome (historical comparison)	5 yr OS	22 vs 52%

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

Tot N=755 sPTCL pts

Key Points

- Population-based data show a favorable outcome with upfront autologous stem cell transplantation in PTCL.

In 252 nodal PTCL and EATL (excl. alk+ ALCL), upfront auto-SCT was associated with a superior OS (HR, 0.58; p5 .004) and PFS (HR, 0.56; p5 .002) compared with matched patients treated without auto-SCT.

Upfront ASCT – Prospective studies

Largest prospective trials in systemic PTCL with SCT in 1st line

Studyb	Design	N pts	Med FU	Efficacy (5 y OS/PFS)	Ref
Nordic/German[1] +/-ALZ & auto (y)	phase 3	217	30 mo	---	Final analysis 2016
Nordic auto[2]	phase 2	160	54 mo	51%/44%	JCO 2012
German auto[3]	phase 2	83	33 mo	40%/36%	JCO 2009
German allo[4]	phase 3	104	12 mo	1y 69%/41% (EFS) No diff auto/allo >STOP	ICML 2015 (Interim analysis)

[1] d'Amore et al, ASH 2012
[2] d'Amore et al, JCO 2012
[3] Reimer at al, JCO 2009
[4] Schmitz et al, ICML 2015

Backbone differences between the Nordic and German auto trials

Comparison of treatment schedules	Induction	Conditioning regimen
Nordic trial	**CHOEP-14 x6**	BEAM
German trial	**CHOP-21 x 4-6** + DexaBEAM/ESHAP (mobilizing)	HdCy+TBI

OS	Nordic trial	German trial
3-yrs	57%	48%
5-yrs	51%	40%

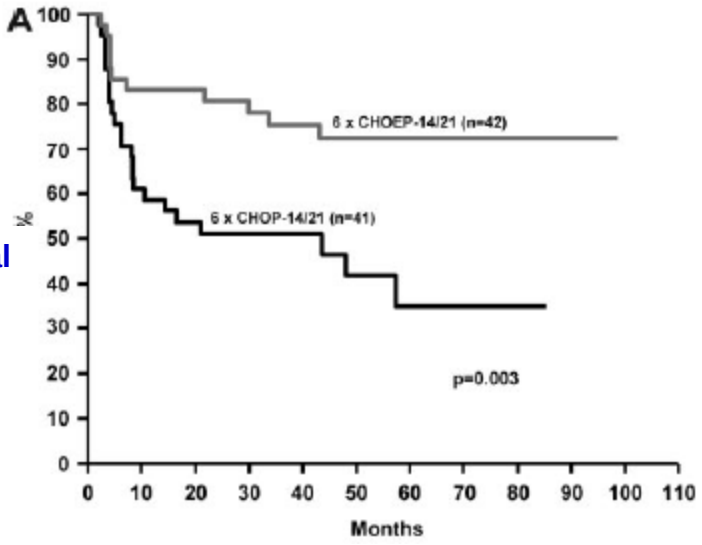
PFS	Nordic trial	German trial
3-yrs	49%	36%
5-yrs	44%	n.d.

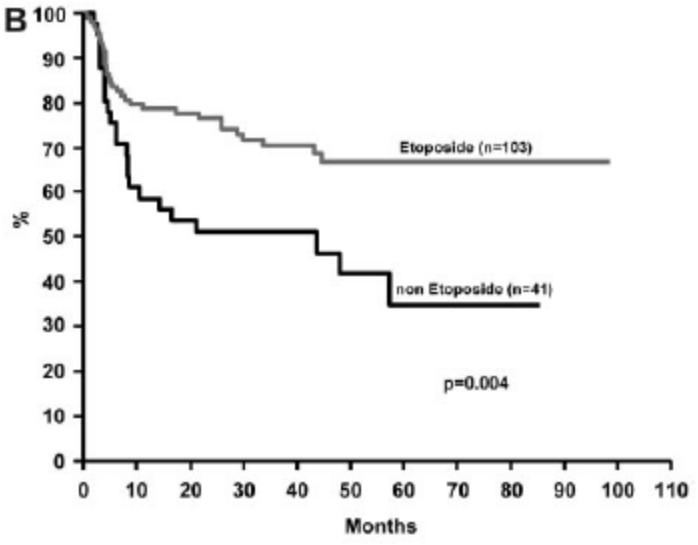
The addition of etoposide to CHOP

The DSHNHL experience in aggressive lymphomas: retrospective PTCL subset analysis

Event-free survival

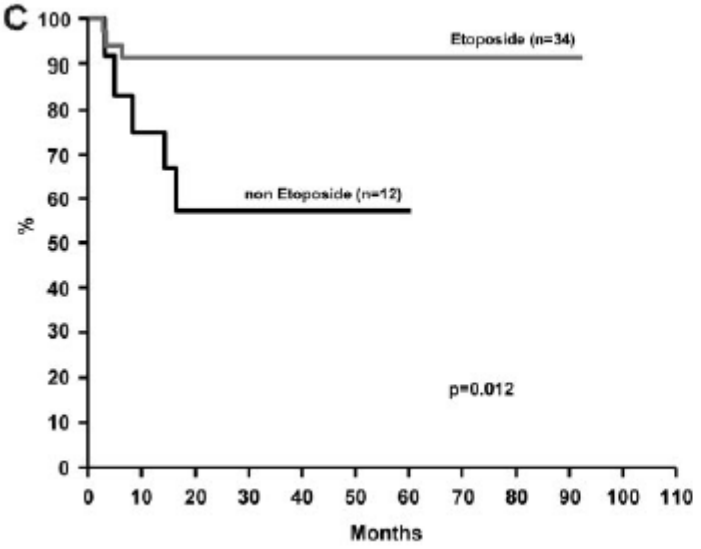
NHL B1 trial

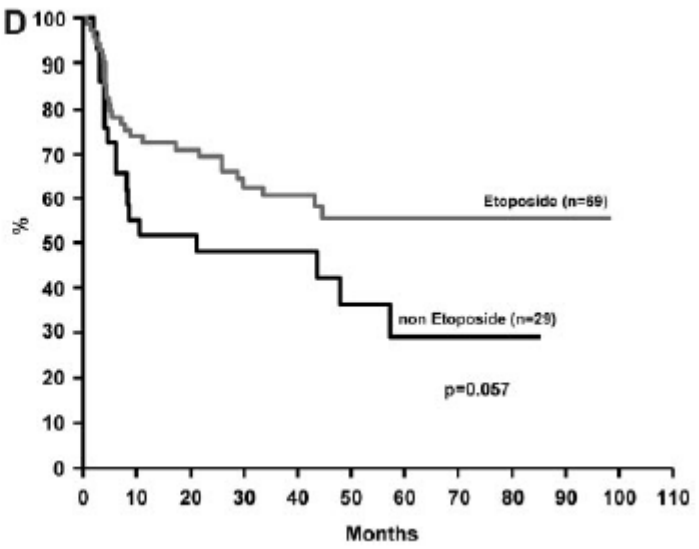




NHL B1 and Hi-CHOEP trials

alk+ ALCL





No alk+ ALCL

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

Update Nordic data – auto SCT

- Registry
- NLG-T-01
- ACT

Should SCT in 1st remission be recommended for pts with PTCL?

Hematological Oncology
Hematol Oncol 2015; **33**: 120–128
Published online 23 July 2014 in Wiley Online Library
(wileyonlinelibrary.com) **DOI**: 10.1002/hon.2153

Original Research Article

Evaluation of clinical trial eligibility and prognostic indices in a population-based cohort of systemic peripheral T-cell lymphomas from the Danish Lymphoma Registry

Martin Bjerregaard Pedersen[1]*, Stephen Jacques Hamilton-Dutoit[2], Knud Bendix[2], Michael Boe Møller[3], Peter Nørgaard[4], Preben Johansen[5], Elisabeth Ralfkiaer[6], Peter De Nully Brown[7], Per Boye Hansen[8], Bo Amdi Jensen[9], Jakob Madsen[10], Claudia Schöllkopf[11] and Francesco d'Amore[1]

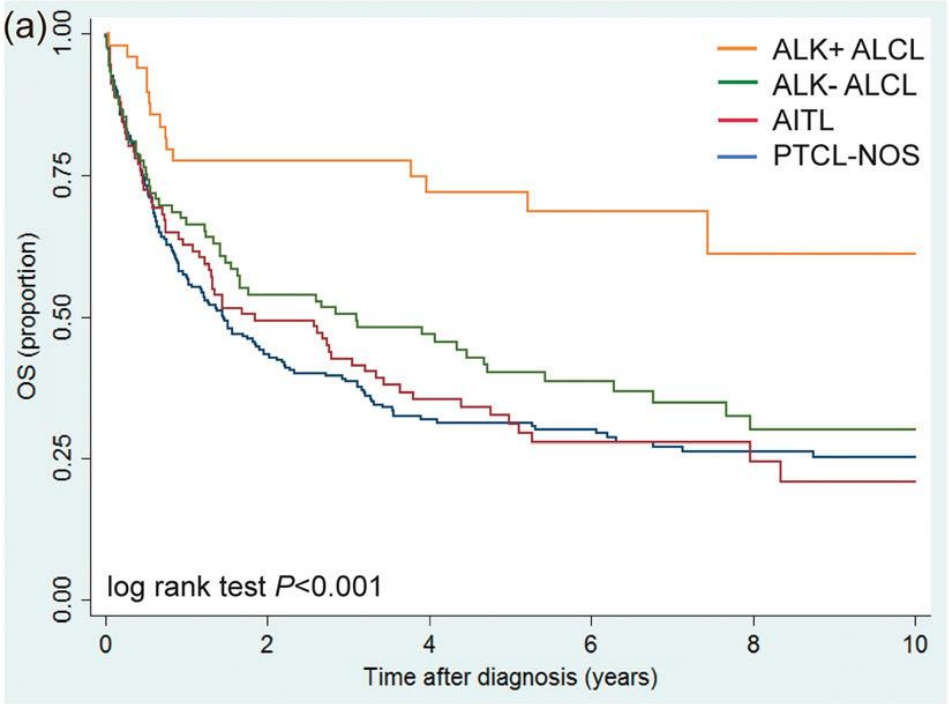
- age >65yrs (47%)
- alk+ALCL (no pediatric cases) (3%)
- stage I low-risk non-bulk disease (2%)
- severe co-morbidity (4%)

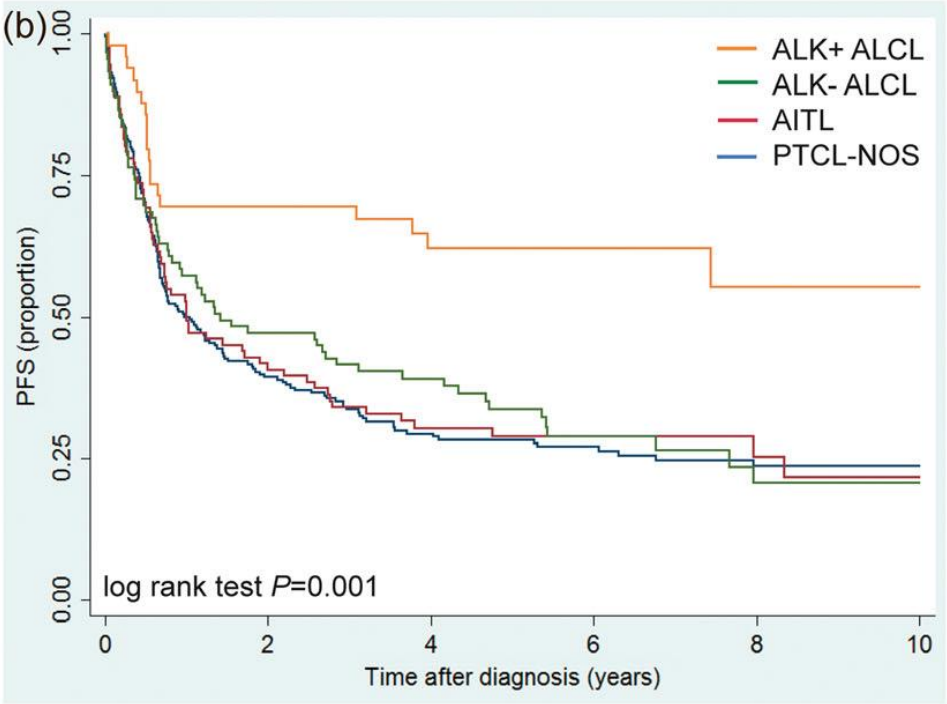
- Even if so, approximately 50% would not be eligible

OS (a) and PFS (b)

Nodal PTCL subtypes

Cohort of the Danish lymphoma registry



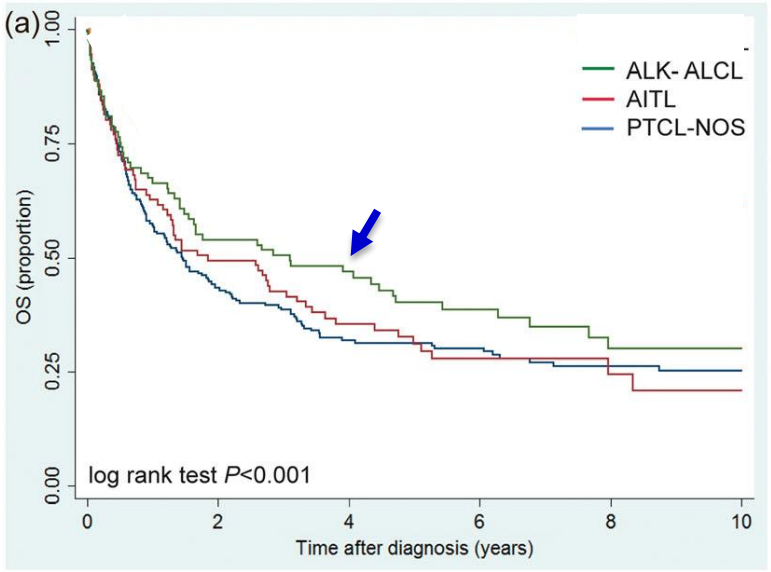


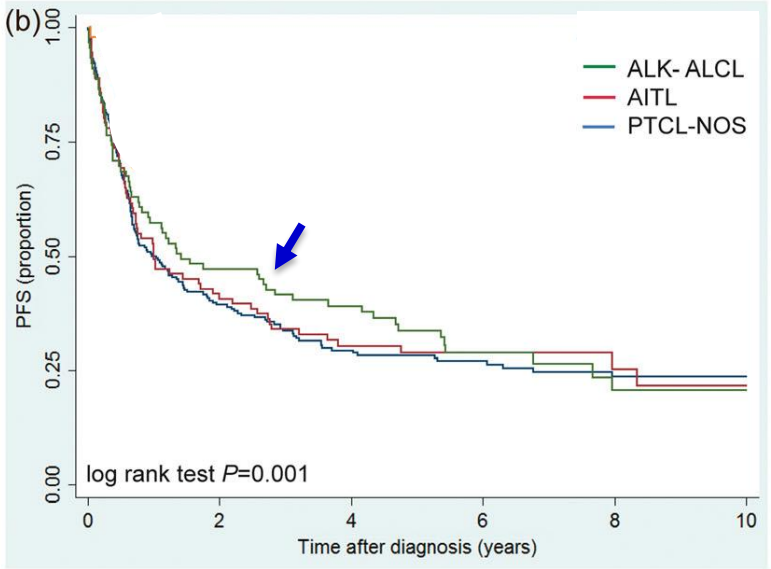
Pedersen MB et al, Hematol Oncol 2015, 33:120-128

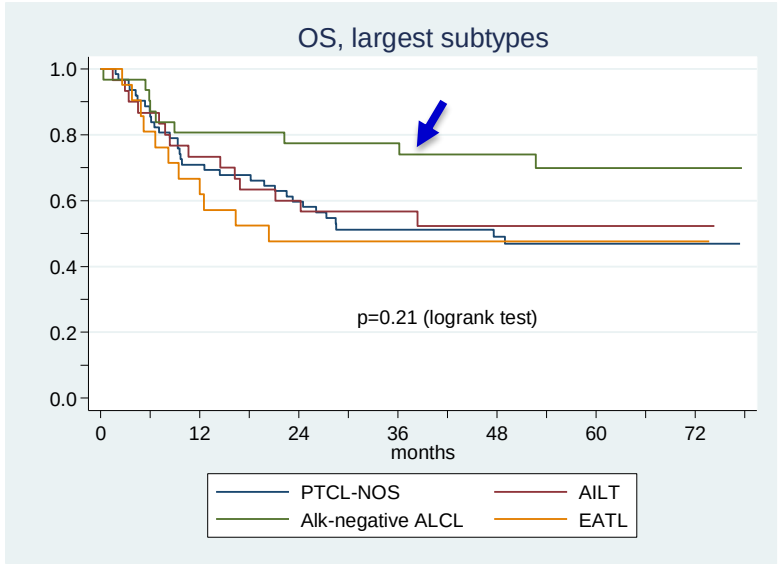
Outcome in DLR (registry) and NLG-T-01 (trial) cohorts

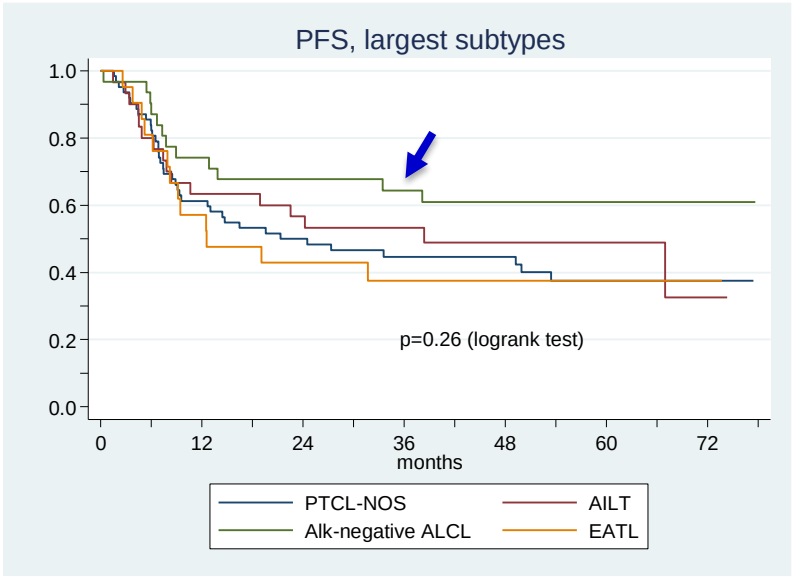
(NB: no ALK+ ALCL included in NLG-T-01)

OS (a) and PFS (b) for nodal PTCL subtypes







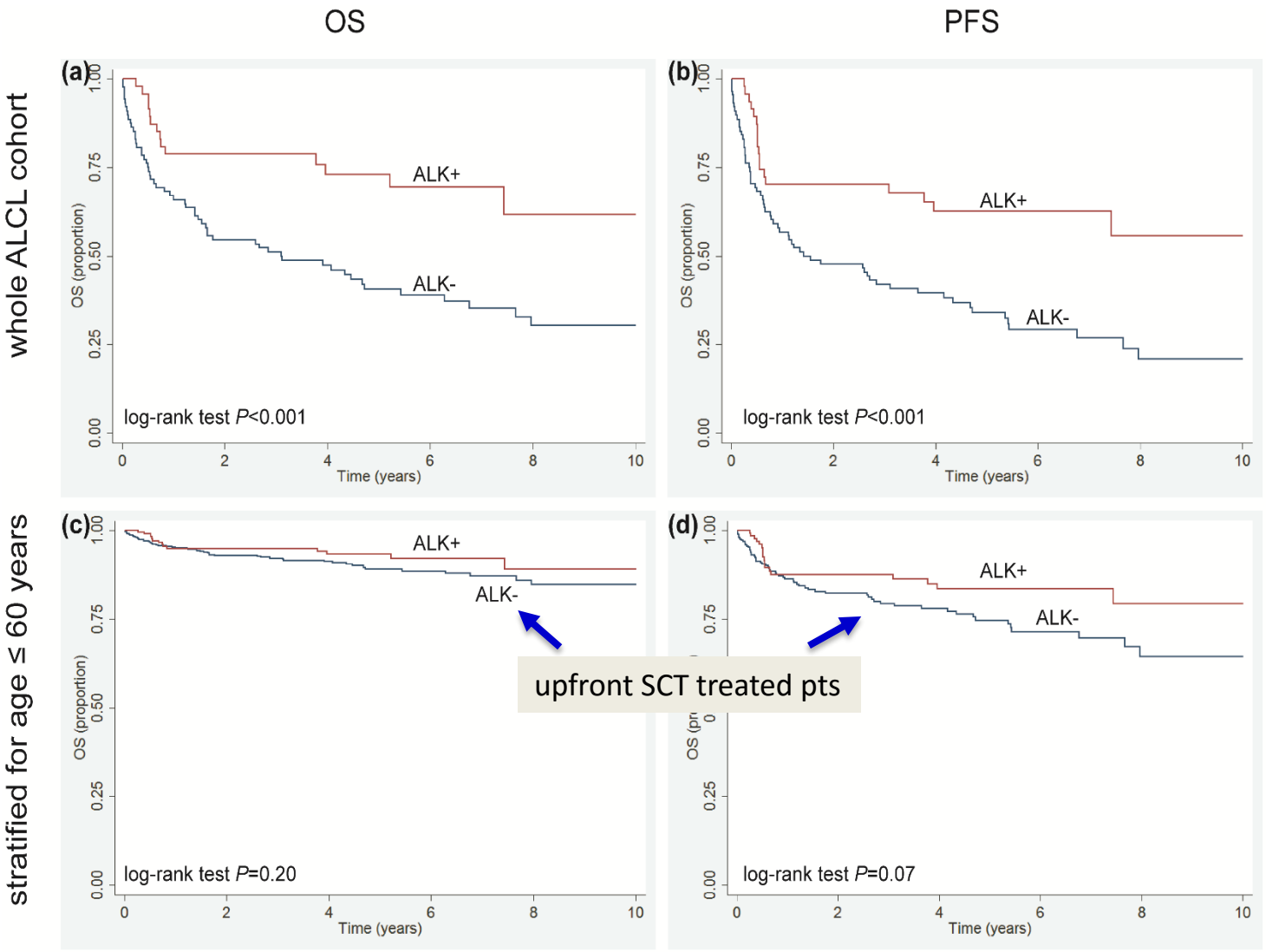


Pedersen MB et al, Hematol Oncol 2015, 33:120-128

d'Amore F et al, J Clin Oncol 2012, 3093-3099

ALCL subtype: prognosis, ALK status and age

Cohort of the Danish lymphoma registry 2000-2010



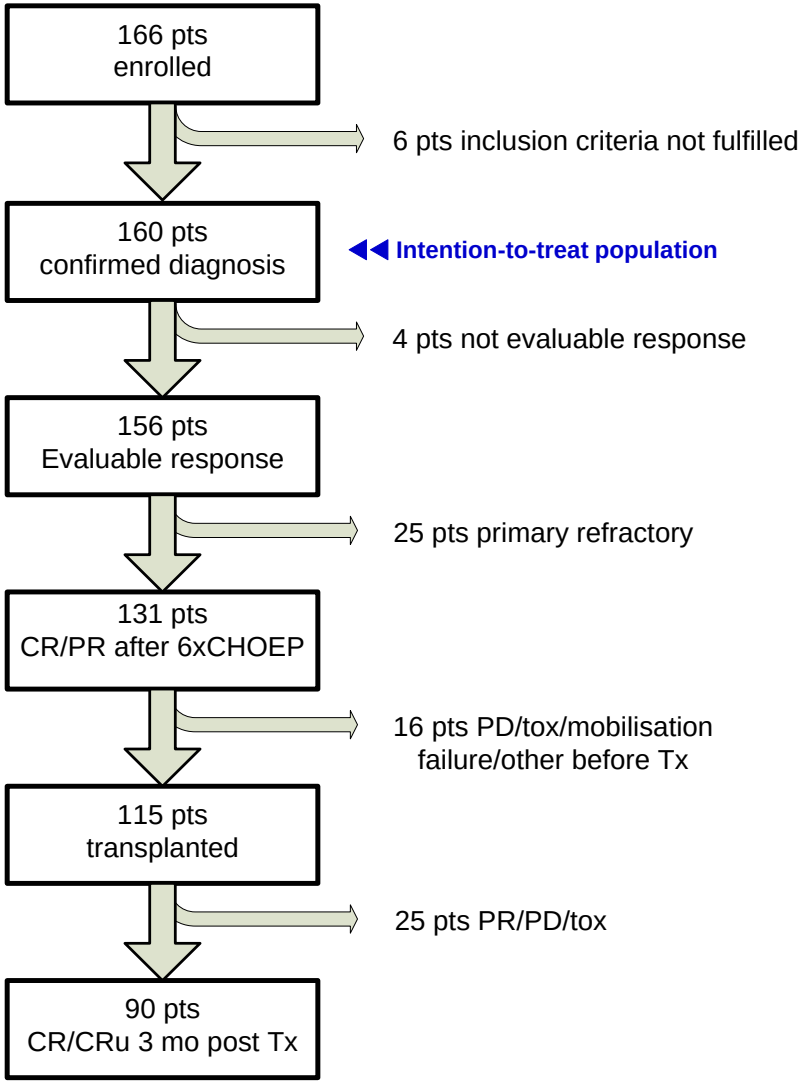
Pedersen MB et al, unpublished

NORDIC LYMPHOMA GROUP

NLG-T-01: Flow chart

Flow chart of the NLG-T-01 study cohort showing the number and types of treatment failures and the responding patients throughout the different stages of the treatment algorithm.

ORR pre-Tx	131 (82%)
CR/CRu	82 (51%)
PR	49 (31%)
% Tx	115 (72%)
CR/CRu 100d post-Tx	90 (56%)



Conclusions

NORDIC LYMPHOMA GROUP

Should autoSCT in 1st remission be rcommended for (the 50% transplant eligible) patients with PTCL?

- No randomized clinical trials are presently available to answer the question in a definitive way
- HDT with ASCT 'per se' does probably not make a major difference in PTCL
- However, on the basis of presently available retro- and prospective data and limited to pts that are

  ① transplant-eligible

  ② chemosensitive (CR, PR)

  ③ 'risk-eligible' (i.e. excluding 'stage I non-bulk IPI 0-1')

=> yes, as it probably provides the possibility to improve the quality of remission in chemosensitive pts and thereby the duration of response

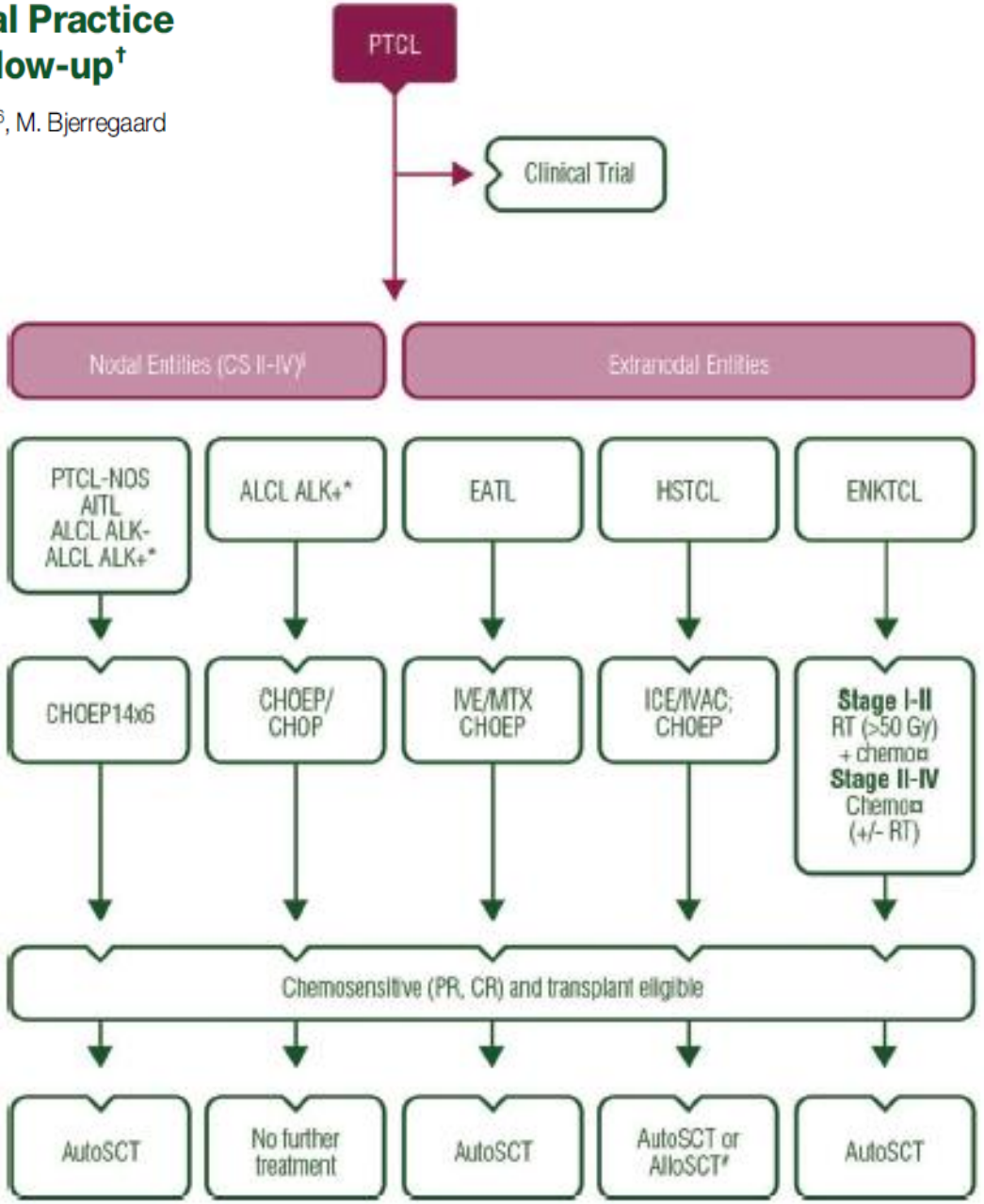
Annals of Oncology 26 (Supplement 5): v108–v115, 2015
doi:10.1093/annonc/mdv201

Peripheral T-cell lymphomas: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up†

F. d'Amore[1], P. Gaulard[2], L. Trümper[3], P. Corradini[4], W.-S. Kim[5], L. Specht[6], M. Bjerregaard Pedersen[1] & M. Ladetto[7], on behalf of the ESMO Guidelines Committee*

New ESMO guidelines 2015

1st line



Present scenario and unmet needs in PTCL

Targeted

- A uniform treatment for the different PTCL entities is not a likely future scenario. The marked PTCL heterogeneity makes a direct comparison with DLBCL not meaningful

Backbone

- While testing potentially game-changing new drugs with high activity and low toxicity, backbone regimens superior to CHOP should be explored. So far, anthracyclines should still be a component of upfront backbone regimens

SCT

- Based on existing data, BOTH autologous AND allogeneic transplant should be regarded as useful tools in the management of PTCL. While autologous SCT may serve as upfront consolidation in chemosensitive disease, allogeneic SCT represents a valuable tool in those patients that relapse after ASCT

Unmet need

- Approximately 50% of all new PTCL patients are not transplant eligible due to age and/or frailty and represent, along with relapsed disease, a considerable unmet clinical need

Thank you for your attention ☺