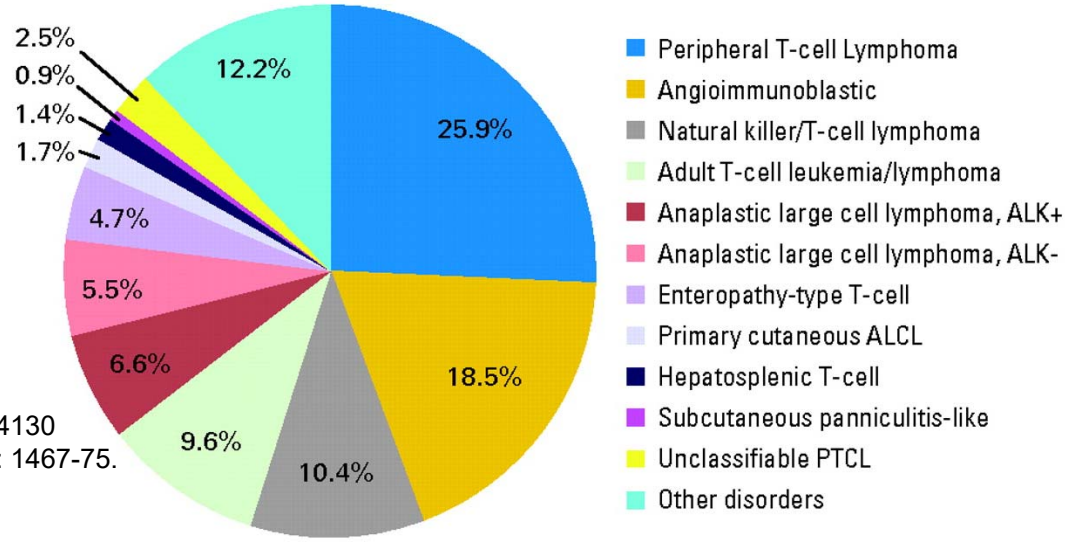
NCCN 11th Annual Congress:
Hematologic Malignancies™

How I Treat Peripheral T-cell Lymphoma

Steven M. Horwitz, MD
Memorial Sloan Kettering Cancer Center

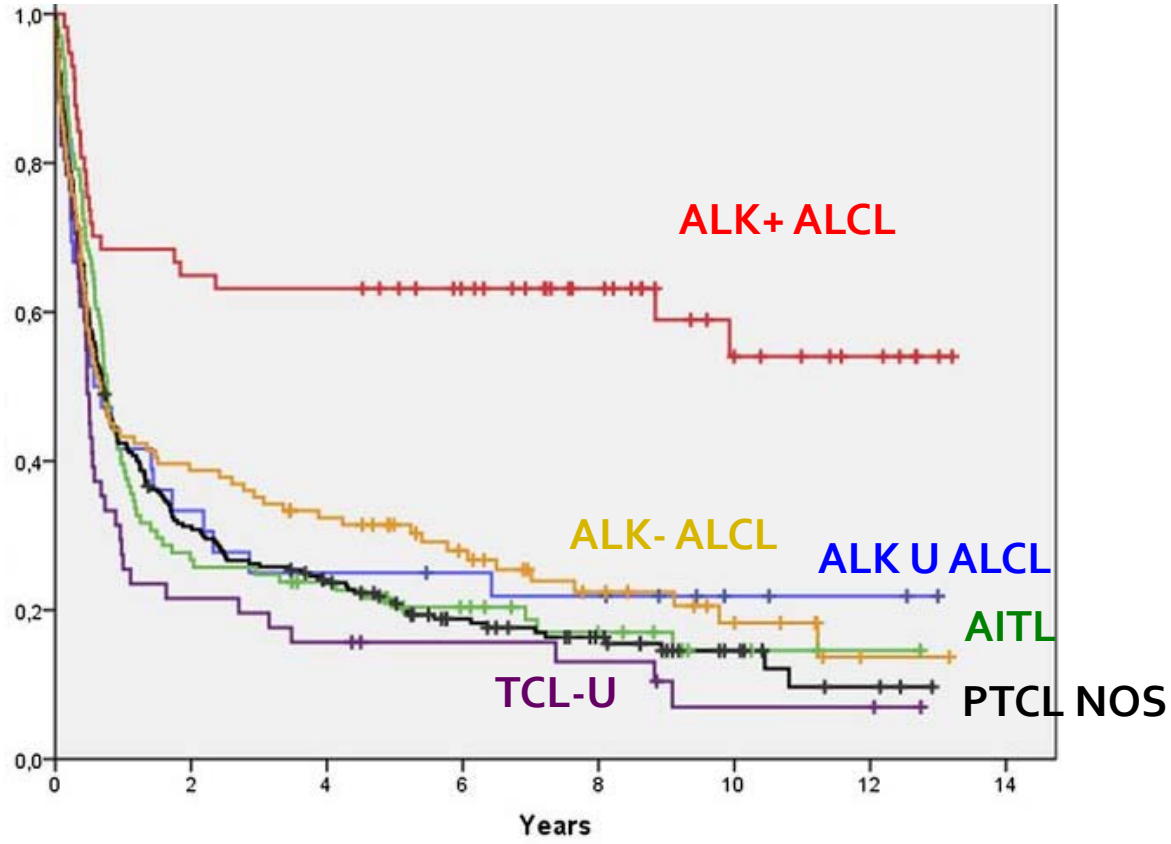
Proportion of Major T-cell Subtypes: North America

Registry	PTCL-NOS	AITL	ALCL, ALK +	ALCL, ALK -	NK/T	ATL	EATL
IPTCL (NA)	34%	16%	16%	8%	5%	2%	6%
BCCA	59%	5%	6%	9%	9%	NA*	5%
COMPLETE	34%	15%	11%	8%	6%	2%	3%



Vose JM, et al. *J Clin Oncol.* 2008;26:4124-4130
Savage, K.J., et al.. Ann Oncol,2004.**15**(10): 1467-75.
Foss, F.M., et al., Blood, 2012. **120**(21).

Swedish National Registry: PFS in 755 patients with PTCL

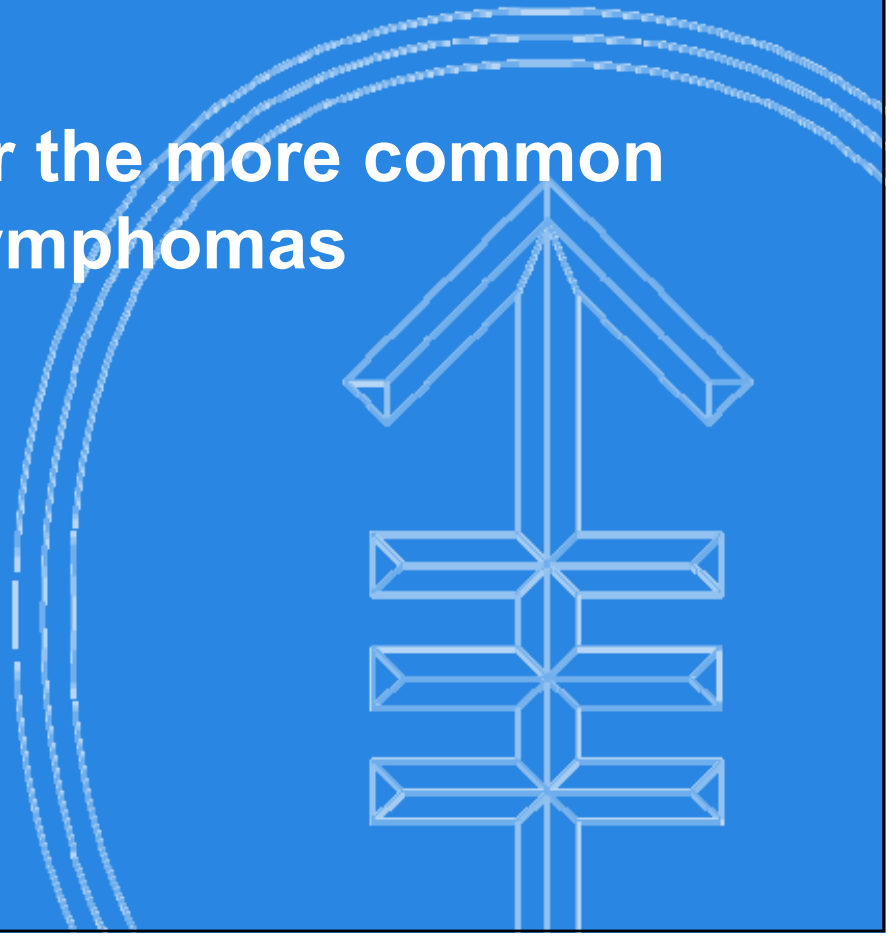


Fredrik Ellin et al. Blood 2014;124:1570-1577

blood

Memorial Sloan Kettering Cancer Center

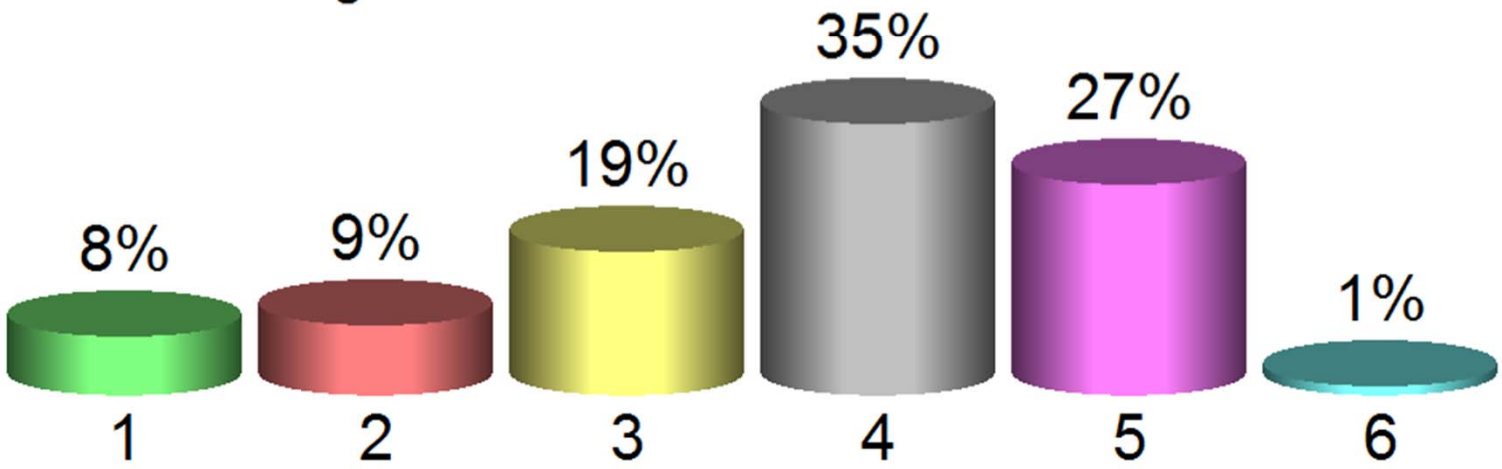
Initial Treatment for the more common Peripheral T-cell Lymphomas



Audience Polling Results

For a fit patient with newly diagnosed PTCL, in the absence of a clinical trial, what is you preferred initial treatment approach?

1. CHOP
2. CHOEP
3. EPOCH
4. CHOEP or EPOCH-HDT-ASCT
5. CHOEP or EPOCH-Allo SCT
6. Something else



CHOP-Based Treatment for Mature T-Cell and NK-Cell Lymphomas

Always

- Anaplastic Large Cell-ALK-1 positive

Sometimes

- Peripheral T-cell lymphoma NOS
- Angioimmunoblastic T-cell lymphoma
- Anaplastic Large Cell-ALK-1 positive
- Enteropathy-type intestinal lymphoma
- Subcutaneous panniculitis-like T-cell

Never

Mycosis fungoides

Sezary syndrome

Primary cutaneous CD30+ disorders

- Anaplastic large cell lymphoma
- Lymphomatoid papulosis

T-cell large granular lymphocytic

Extranodal NK / T-cell lymphoma-nasal

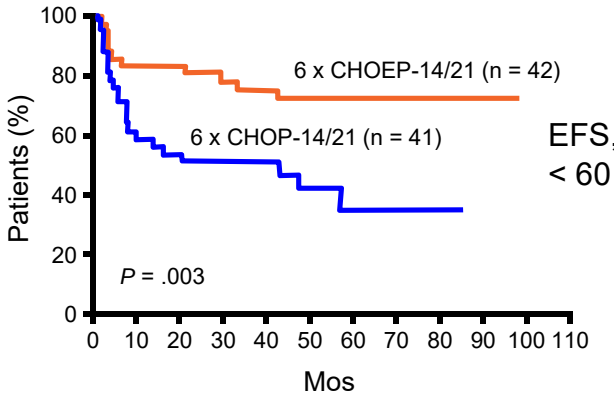
Hepatosplenic T-cell lymphoma

NK / T-cell leukemia / lymphoma

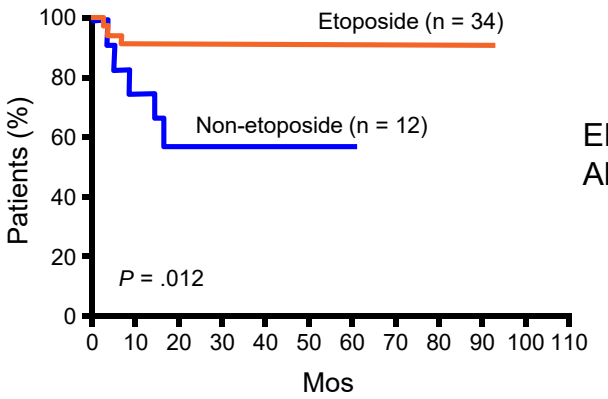
Adult T-cell leukemia / lymphoma

T-cell prolymphocytic leukemia

Adding Etoposide to CHOP: German Prospective High-Grade NHL Studies

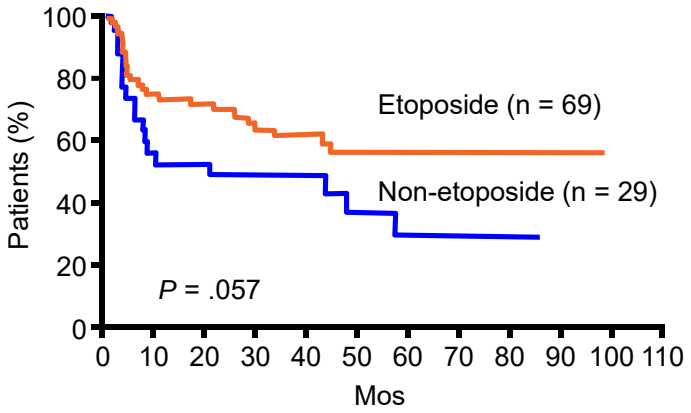


EFS, aged < 60 yrs



EFS, ALCL, ALK+

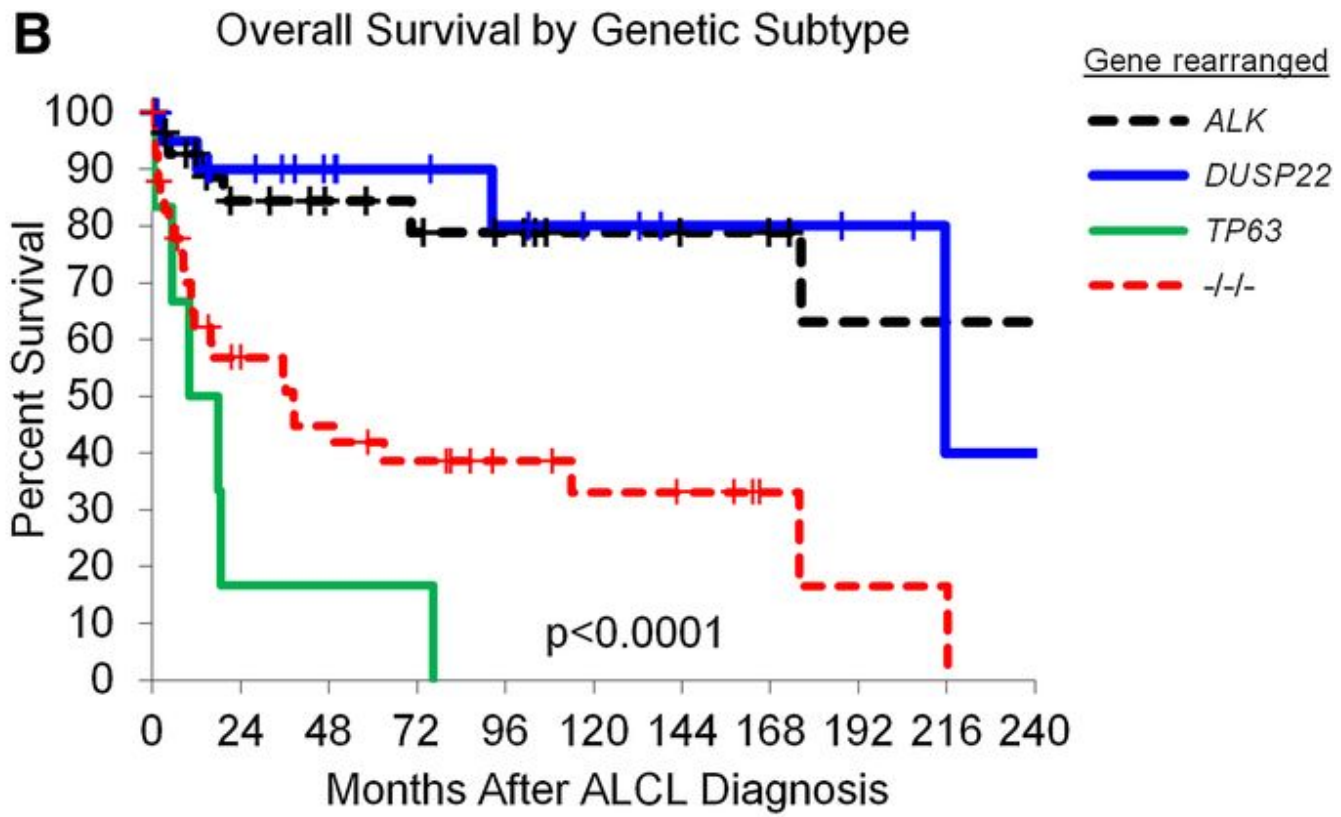
PTCL Subtype	n
ALCL, ALK+	78
ALCL, ALK-	113
PTCL-NOS	70
AITL	28
Other	31
Total	320



EFS, other subtypes

Schmitz N, et al. Blood. 2010;116:3418-3425.

ALCL: OS based on genetic subtype



Parrilla Castellar E R et al. Blood 2014;124:1473-1480

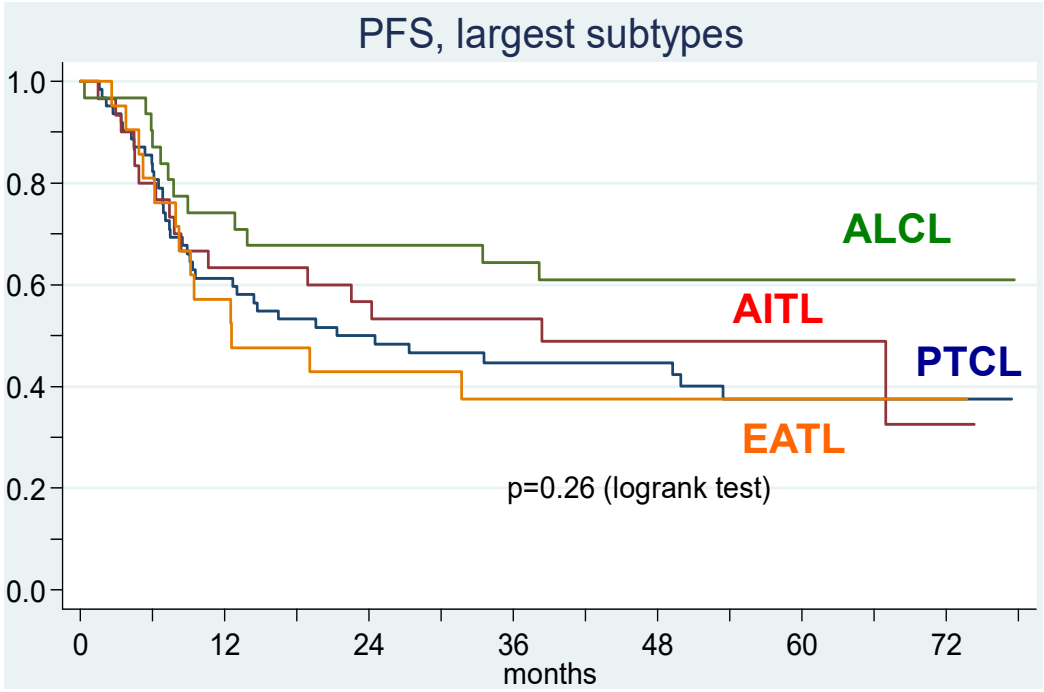
CHOEP-ASCT Nordic Lymphoma Group

ND PTCL, N = 166
Med Age-57 years
ALK+/ALCL excluded

→ **CHOEP x 4-6** →

CR
PR

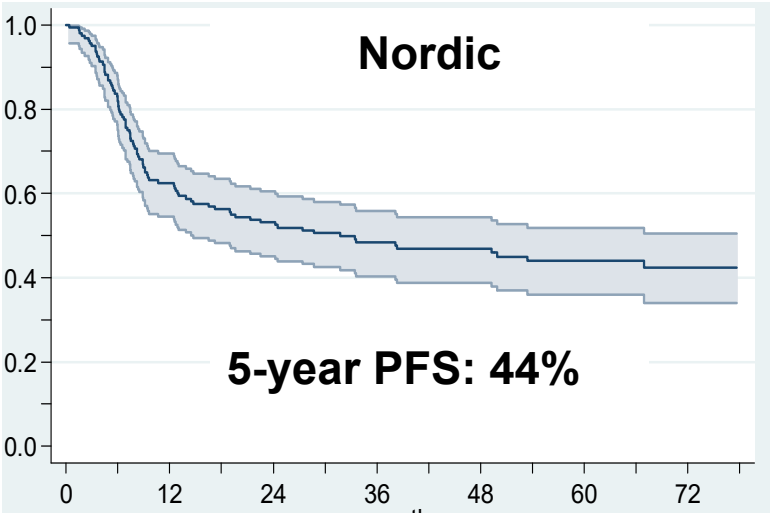
→ **HDT/ASCT**
N = 115
90 CR 3-month post

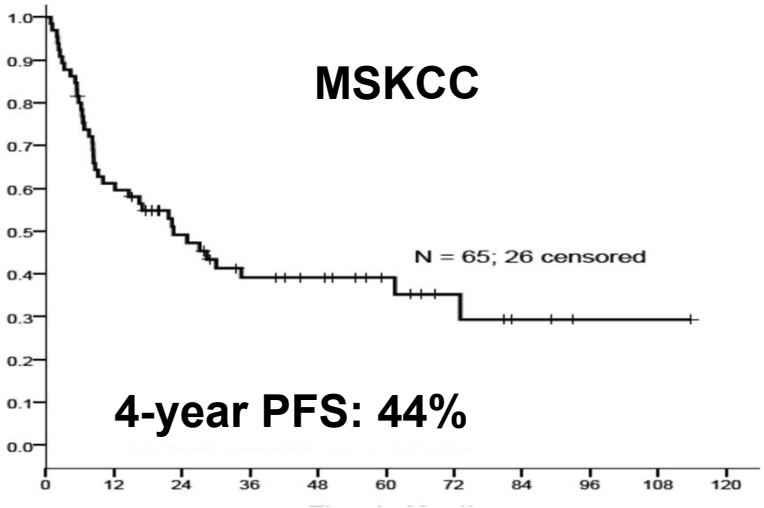


Subtype	5 yr PFS	5 yr OS
ALCL -	61	70
AITL	47	52
PTCL	38	49
EATL	38	48

D'Amore et al. JCO 2012 Sep 1;30(25):3093-9

Autologous stem cell transplantation as first-line therapy in PTCL





Swedish Registry

	Auto-SCT ITT (n = 128)	Non–auto-SCT (n = 124)
5 yr OS	48%	26%
5 yr PFS	41%	20%

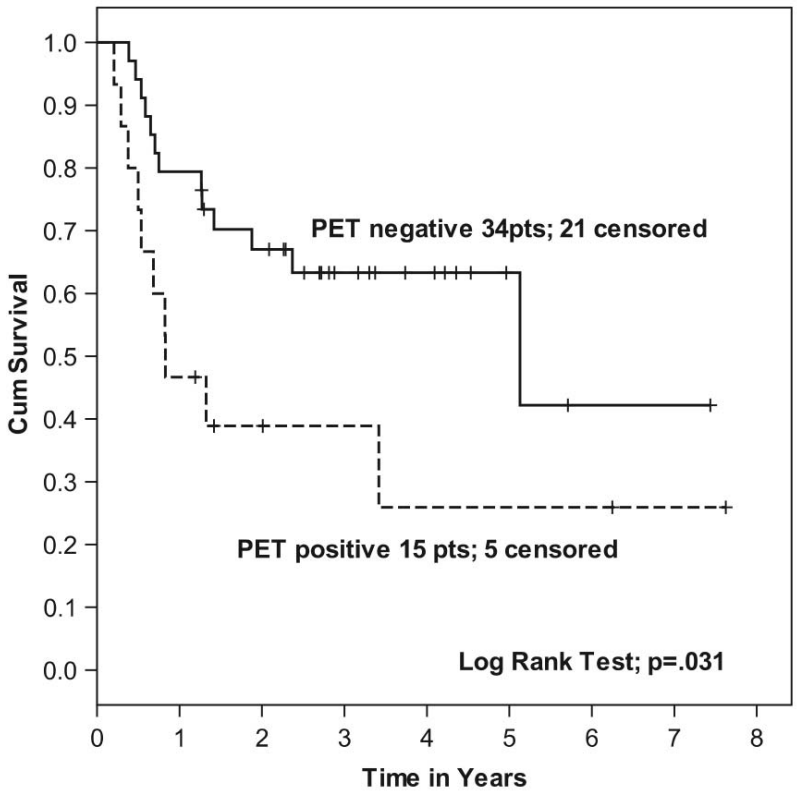
1 D'Amore, et al. *J Clin Oncol.* 2012;30(25):3093-3099

2 Mehta et al. CLLM 2013;13(6):664-70

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

Prognosis by Interim PET

PFS by Interim PET



ASCT-ITT; PFS by Interim PET/IPI

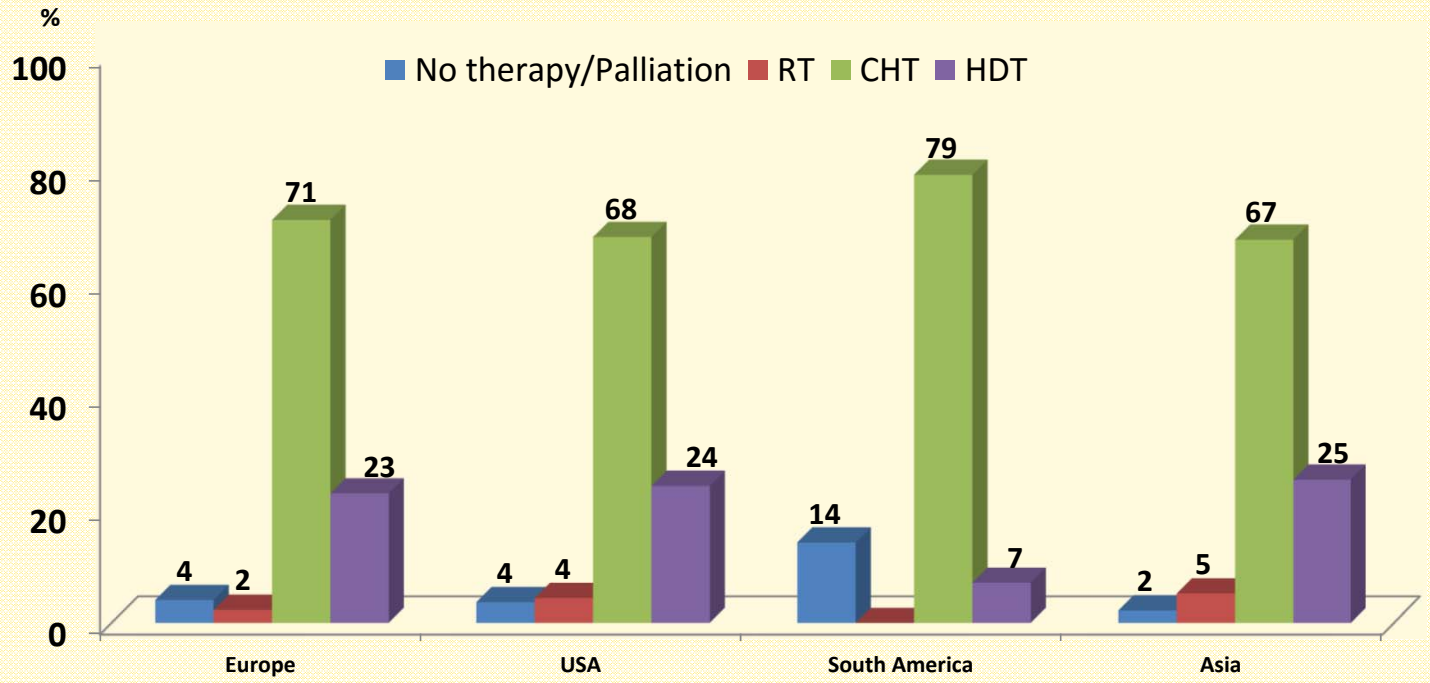
N=61	% EFS		
	2 yrs	3 yrs	5 yrs
CR – IPI 0-2	**78.9**	**66.2**	**66.2**
CR – IPI >2	**52.7**	**52.7**	**52.7**
No CR IPI 0-2	**32.3**	**21.5**	**21.5**
No CR - High IPI >2	**26.7**	**10.0**	**10.0**

Casulo et al., Leukemia & Lymphoma 2013; 54(10): 2163–2167
Mehta et al. Clin Leuk Lym 2013;13(6):664-70

Type of Therapy by Region

	N	%
No Tx/palliation	46	6
RT	21	3
CHT	564	71
HDT	158	20

★ Includes
- ALL subtypes
- Tx in CR1/PR1 + Relapse



Courtesy of Monica Bellei and Massimo Federico

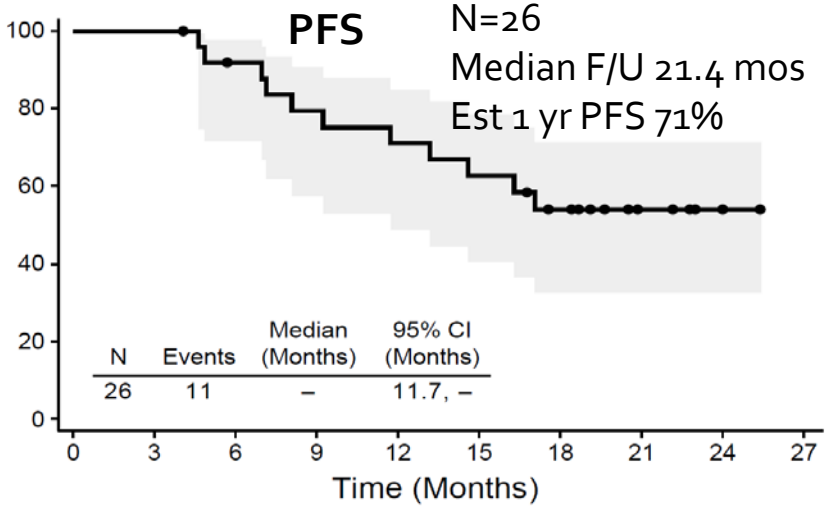
Bellei et al Curr Hematol Malig Rep 2015; 10: 448-455

Brentuximab vedotin (BV) Beyond Relapsed ALCL

PTCL (Relapsed)[1]	Best Clinical Response				Overall Response
	CR n (%)	PR n (%)	SD n(%)	PD n (%)	CR + PR n (%)
Mature T-/NK-cell (n=34)	8 (24)	6 (18)	6 (18)	14 (41)	**14 (41)**
AITL (n=13)	5 (38)	2 (15)	3 (23)	3 (23)	**7 (54)**
PTCL-NOS (n=21)	3 (14)	4 (19)	3 (14)	11 (52)	**7 (33)**

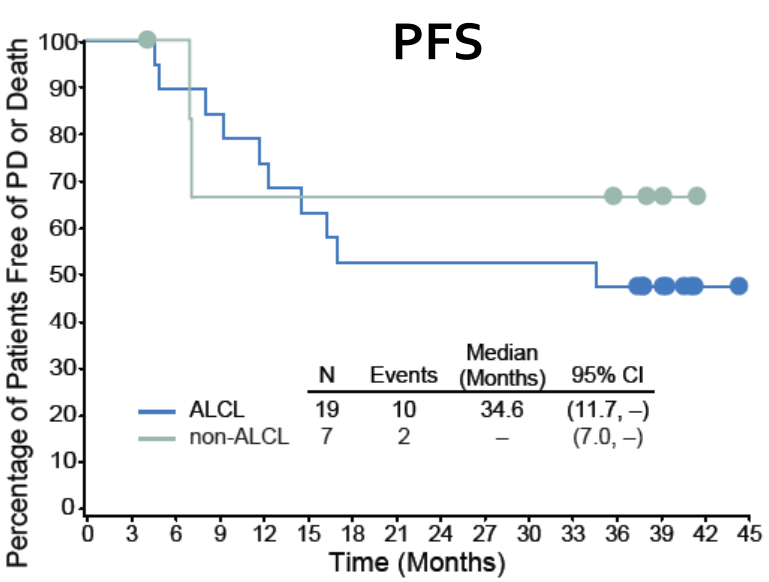
Front-Line: BV + cyclophosphamide, doxorubicin and prednisone (CHP)[2]

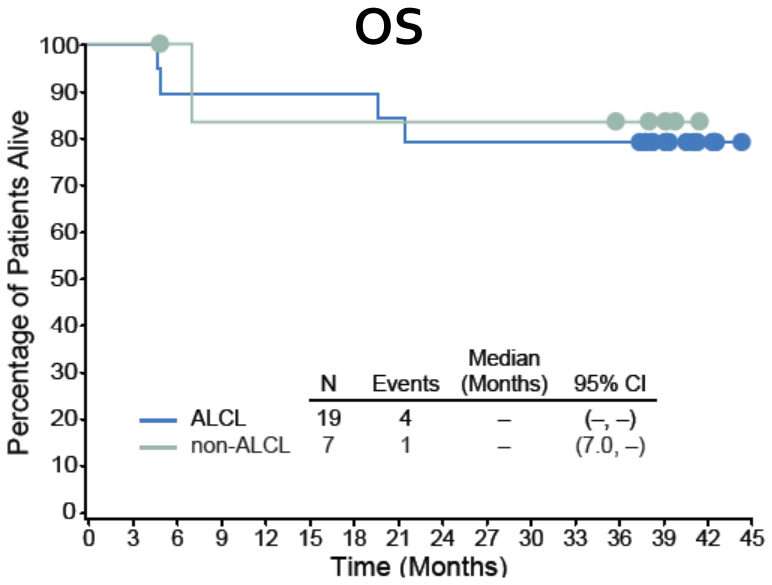
	ALCL N (%)	Other N (%)	Total N (%)
ORR	19 (100)	7 (100)	26 (100)
CR	16 (84)	7 (100)	23 (88)
PR	3 (16)	--	3 (12)



1. Horwitz S M et al. Blood 2014;123:3095-3100
2. Fanale et al JCO 2014:3137-3143;

BV + CHP in PTCL



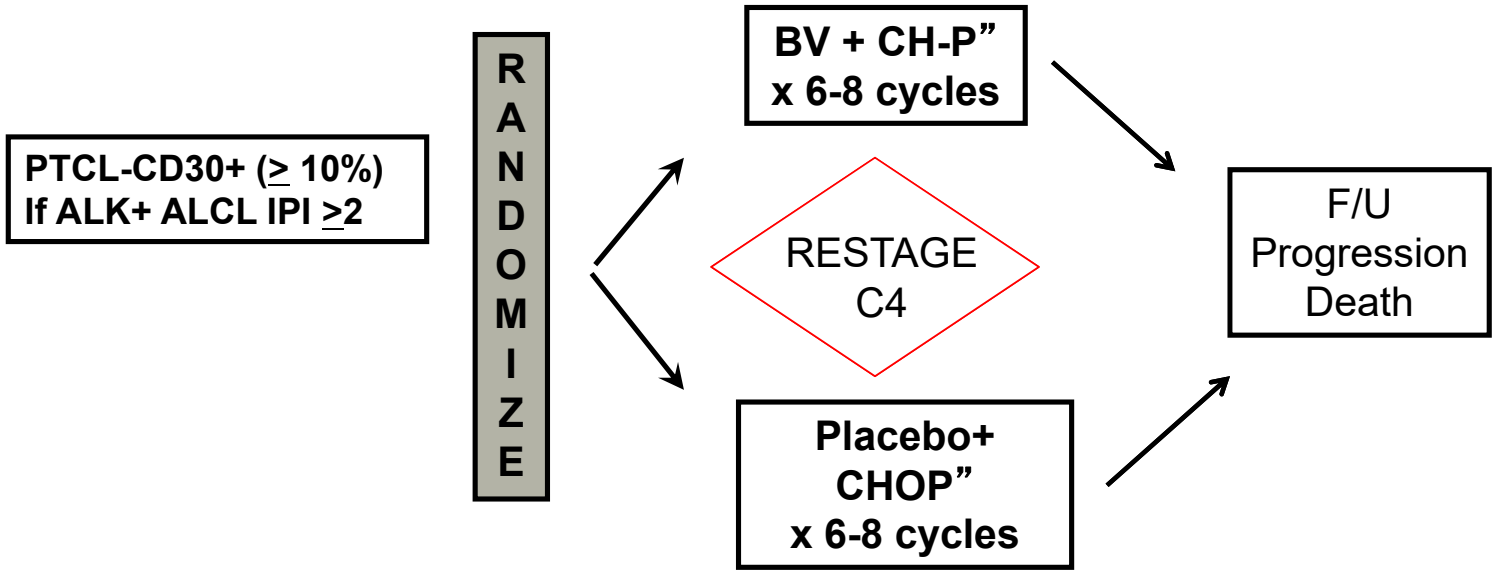


- Median follow-up 38.7 months (range, 4.6 to 44.3),
- Estimated 3-year PFS rate was 52% (95% CI: 31, 69)
  - ALCL (47%)
  - non-ALCL patients (71%)
- Estimated 3-year OS rate was 80% (95% CI: 59, 91)
  - 79% for ALCL patients
  - 86% non-ALCL patients

Horwitz et al, ASH 2015; Abstract 1537

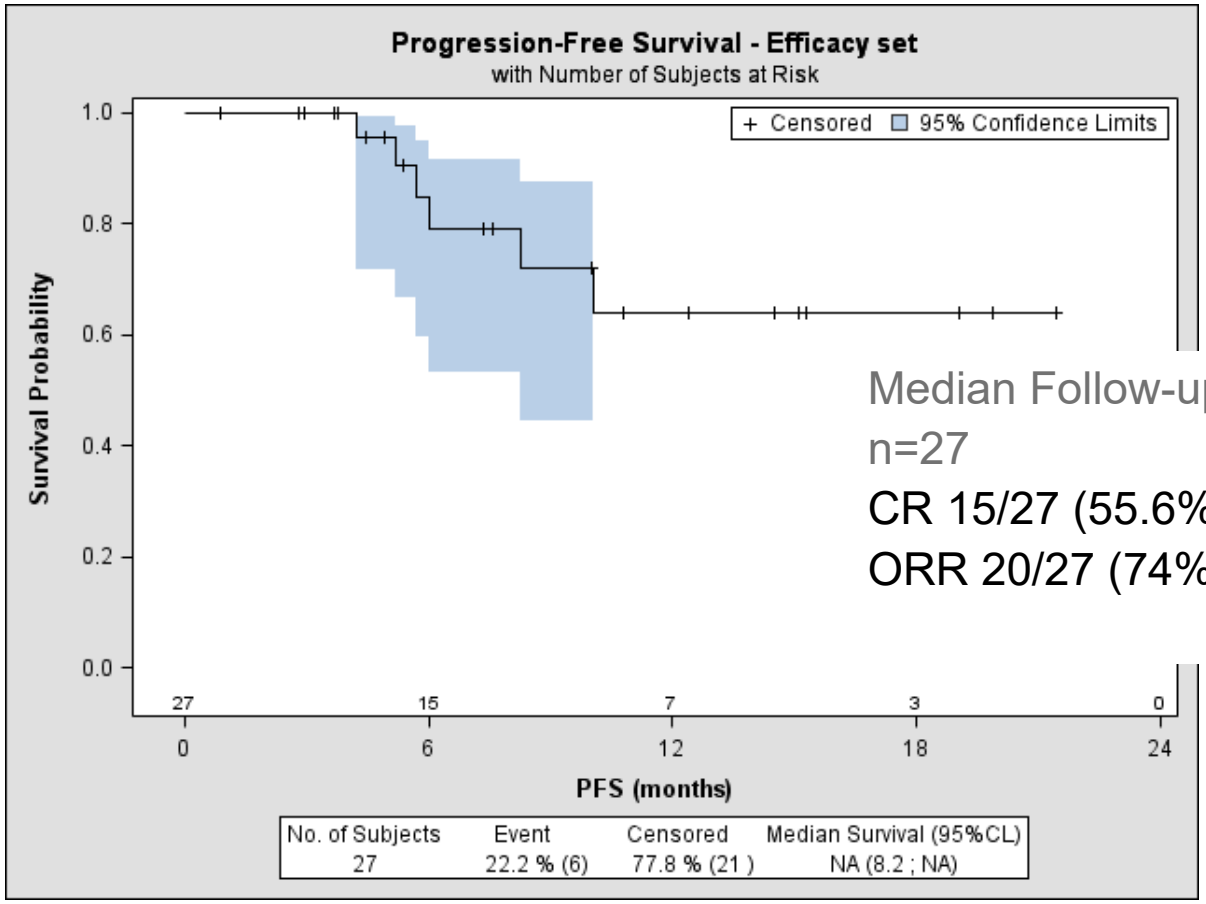
A Randomized, Double-Blind, Placebo-Controlled, Phase 3 Study of Brentuximab Vedotin and CHP (A+CHP) Versus CHOP in the Frontline Treatment of Patients with CD30-positive Mature T-cell Lymphomas

ECHELON-2; NCT01777152



Primary endpoint: improvement in PFS

Romidepsin-CHOP Phase I-II PFS



Median Follow-up 10 months

n=27

CR 15/27 (55.6%)

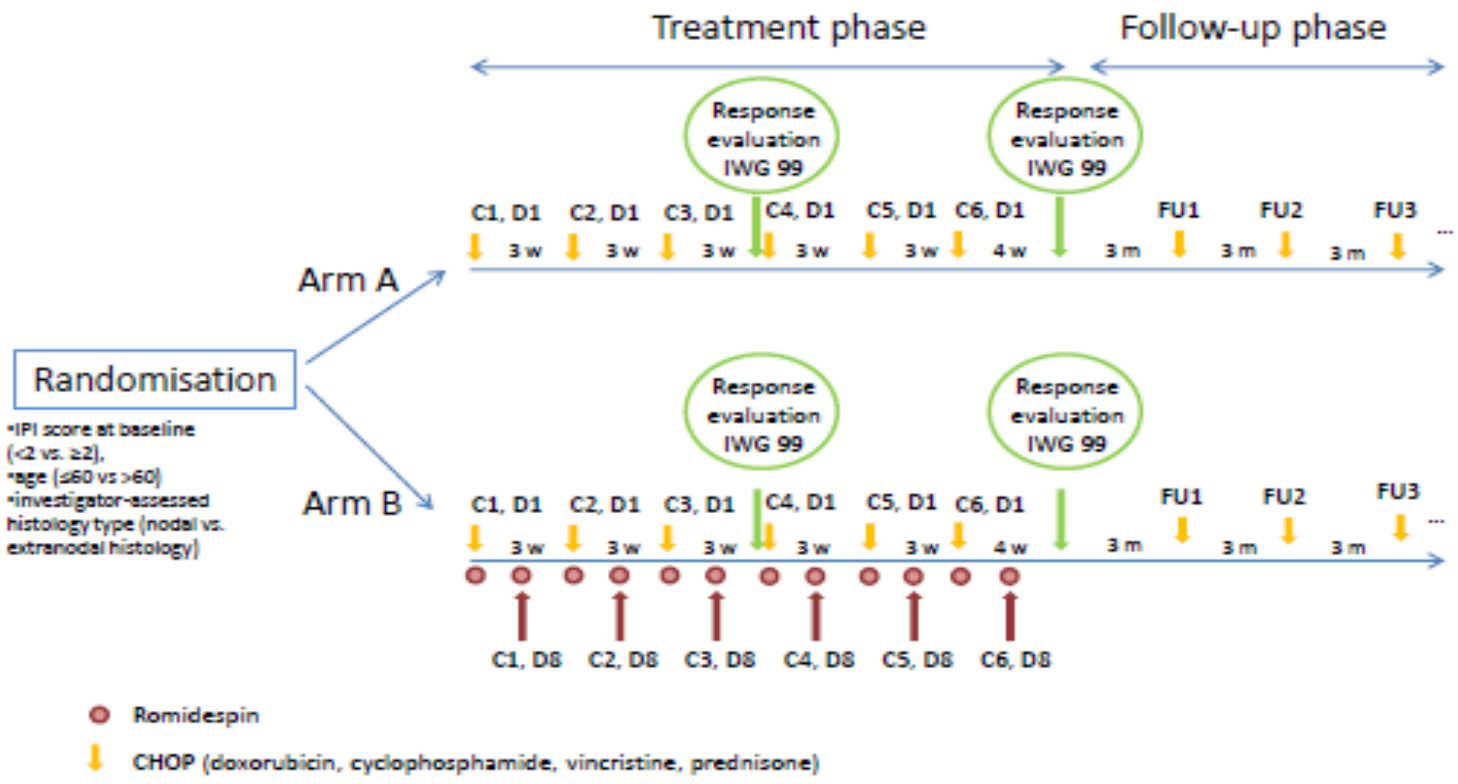
ORR 20/27 (74%)

1 year estimated PFS 63.9% (95%CI 35.4 – 82.5)

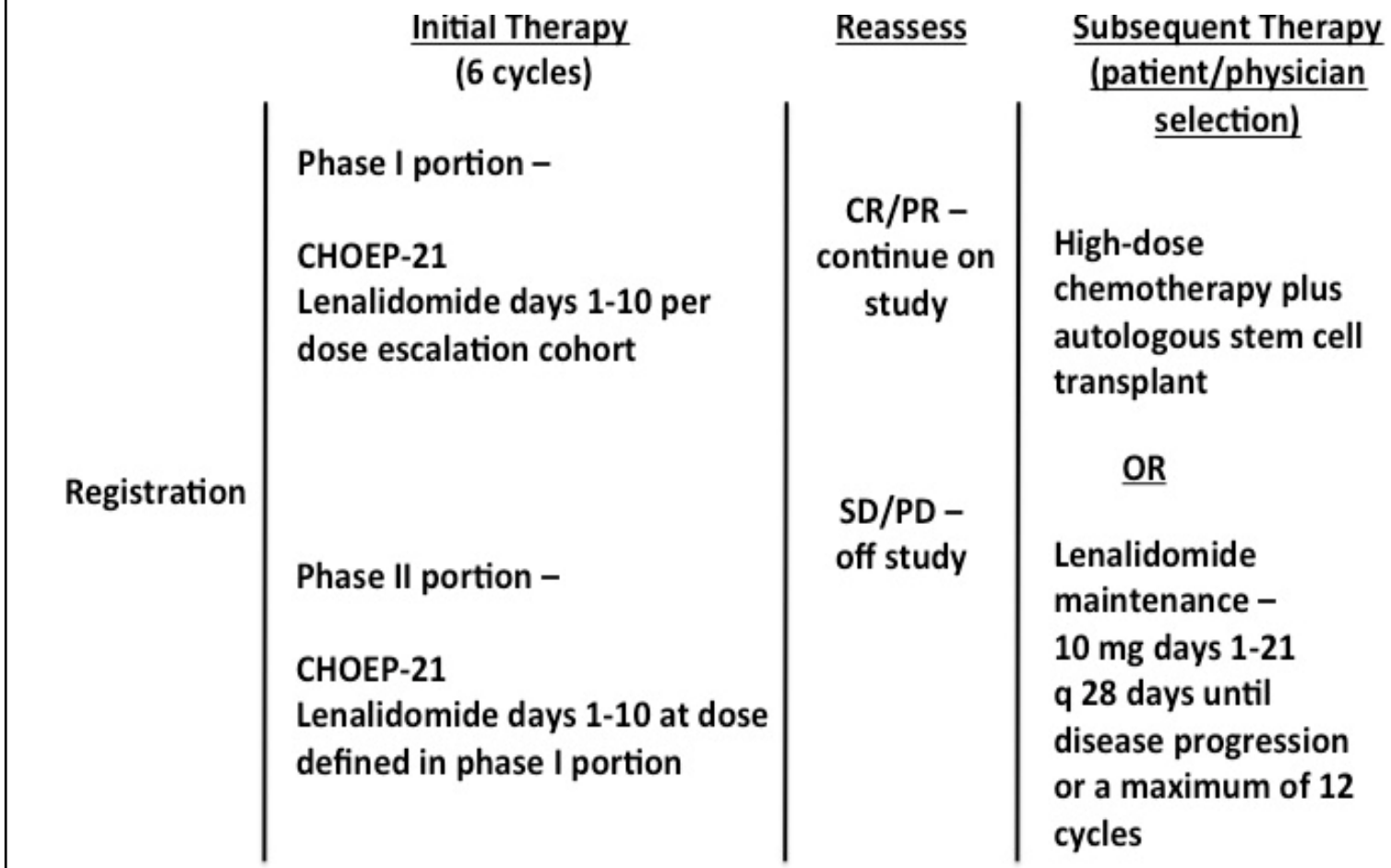
Delarue et al ASH 2014

Romidepsin-CHOP: Phase III Study (NCT01796002)

- International randomized, open-label study
- Principal objective: PFS improvement
- Planned accrual: 420 patients



Phase I/II of CHOEP-Lenalidomide: T-cell Consortium (NCT02561273)



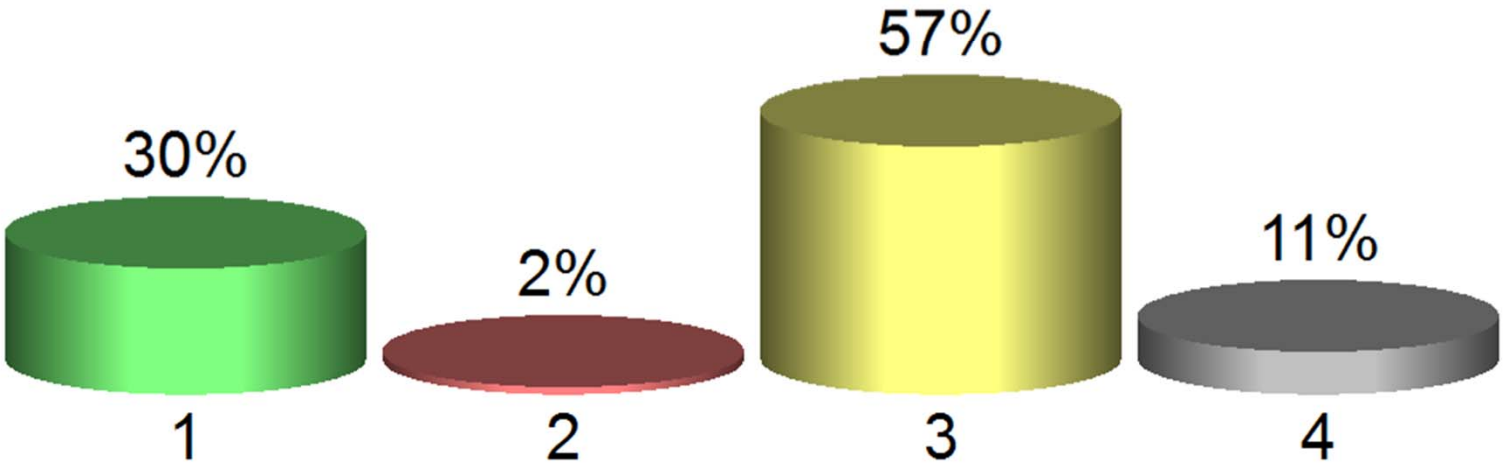
Memorial Sloan Kettering Cancer Center

Relapsed Peripheral T-cell lymphoma (PTCL)

Audience Polling Results

For a fit patient with relapsed PTCL, in the absence of a clinical trial, what is you preferred treatment approach?

1. ICE or DHAP-ASCT
2. "Single agent" until progression
3. ICE or DHAP-Allo SCT
4. "Single agent" followed by Allo



National Comprehensive Cancer Network®

NCCN Guidelines Version 2.2016
Peripheral T-Cell Lymphomas

SUGGESTED TREATMENT REGIMENS FOR PTCL-NOS AND EATL

Second-line Therapy (with intention to proceed to transplant) and Subsequent Therapy:

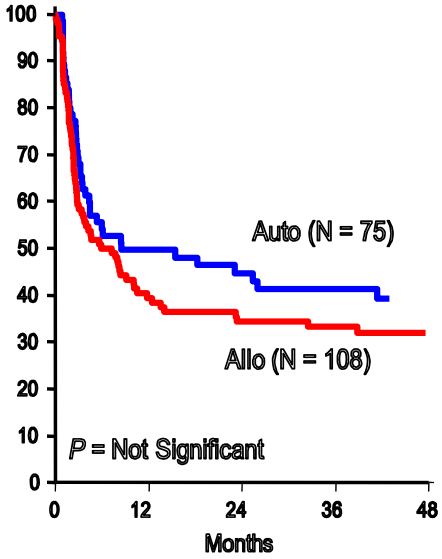
- Clinical trial preferred
- Preferred single agents/combination regimens
  - Single agents (alphabetical order)
    - Belinostat
    - Brentuximab vedotin for CD30+ PTCL
    - Pralatrexate
    - Romidepsin
  - Combination regimens (alphabetical order)
    - DHAP (dexamethasone, cisplatin, cytarabine)
    - ESHAP (etoposide, methylprednisolone, cytarabine, cisplatin)
    - GDP (gemcitabine, dexamethasone, cisplatin)
    - GemOx (gemcitabine, oxaliplatin)
    - ICE (ifosfamide, carboplatin, etoposide)

Alternative Regimens:

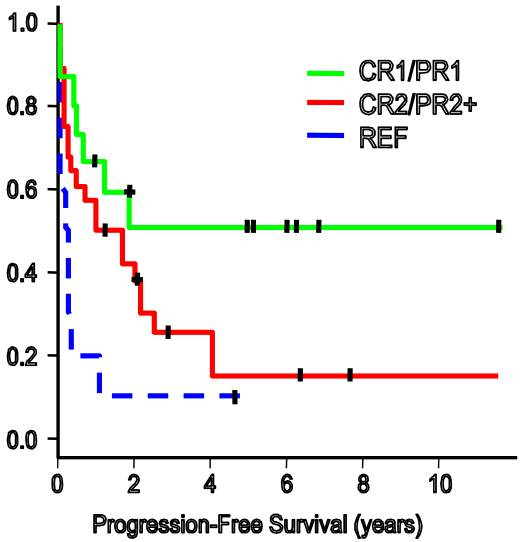
- Single agents (alphabetical order)
  - Bendamustine
  - Gemcitabine
  - Lenalidomide
- Combination regimen
  - GVD (gemcitabine, vinorelbine, liposomal doxorubicin)

Autologous Transplantation in Relapsed PTCL

CIBMTR: PFS excluding pt in CR1 (Most patients ALCL)

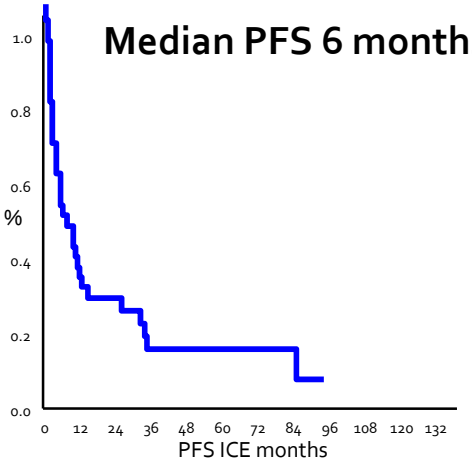


The Stanford Experience Auto



MSKCC

Median PFS 6 months



Response to ICE 70% (28/40)

Received ASCT 68% (27/40)

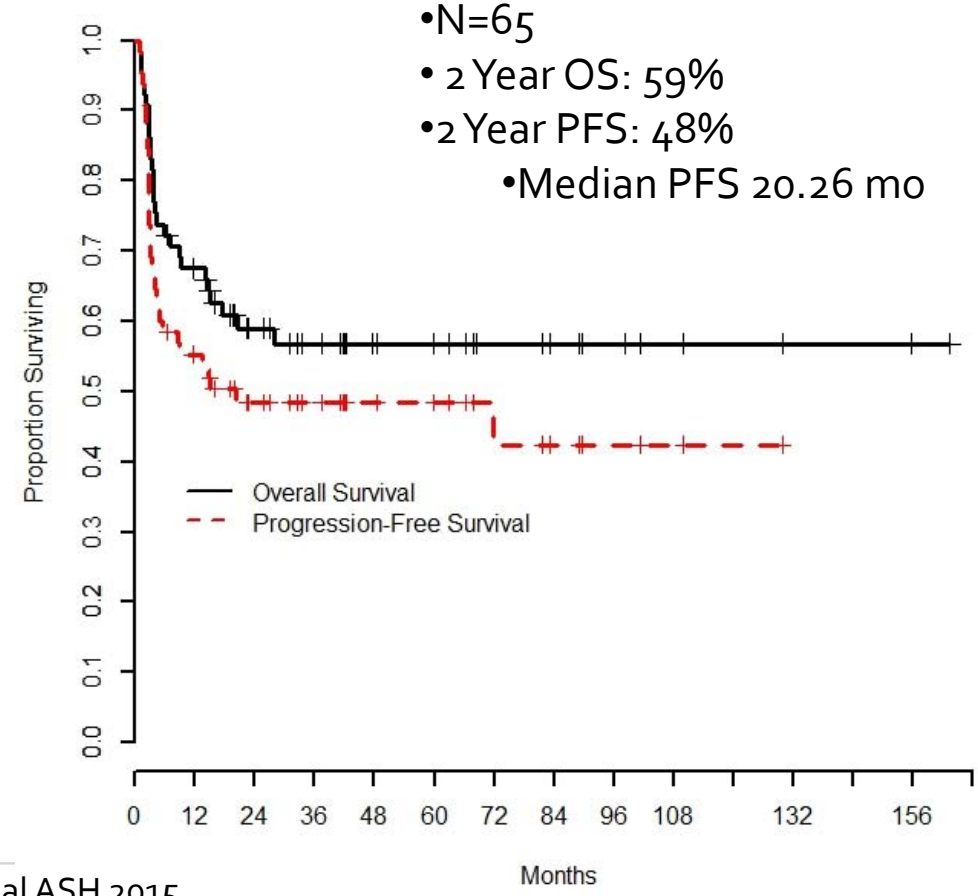
- Benefits are unclear. Most single institution studies show low PFS rates while registry data suggests better outcomes

Smith S, et al. JCO September 1, 2013 vol. 31 no. 25 3100-3109

Chen AI, et al. *Biol Blood Marrow Transplant.* 2008;14(7):741-747.

Horwitz et al, ASH Annual Meeting Abstracts 2005;106:2679.

Allogeneic Transplantation in T-cell Lymphoma: MSKCC



- N=65
- 2 Year OS: 59%
- 2 Year PFS: 48%
  - Median PFS 20.26 mo

N. Mehta-Shah et al ASH 2015

FDA Approved Agents for PTCL
ORR (%) by Lymphoma Subtype

Subtype	Pralatrexate	Romidepsin	Belinostat	Brentuximab vedotin
PTCL, NOS	31	29	23	33
AITL	8	30	46	54
ALCL	29	24	15	86

O' Connor OA, et al. *J Clin Oncol*. 2011;29:1182-1189
Coiffier B, et al. *J Clin Oncol*. 2012;30:631-636
O'Connor OA et al, ASCO 2013; Horwitz, S et al ICML 2013
Pro B, et al. J Clin Oncol. 2012;30:2190-2196
Horwitz S M et al. Blood 2014;123:3095-3100

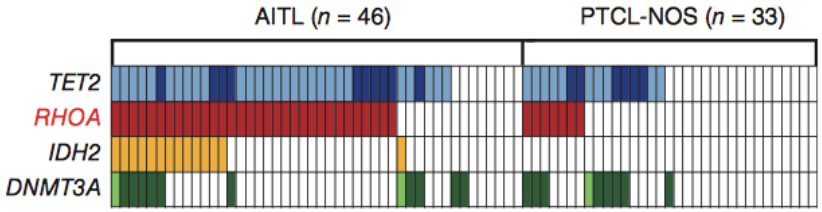
Targets in T Cell Lymphoma

JAK/STAT in TCL

TCL subtype	% with JAK/STAT activating mutations
ALCL	38%
Extranodal NK/TCL	5.9%
T-PLL	36%
γδ-T cell lymphomas	33%
MEITL	36.8%
LGL	28-40%
Sezary Syndrome	11%

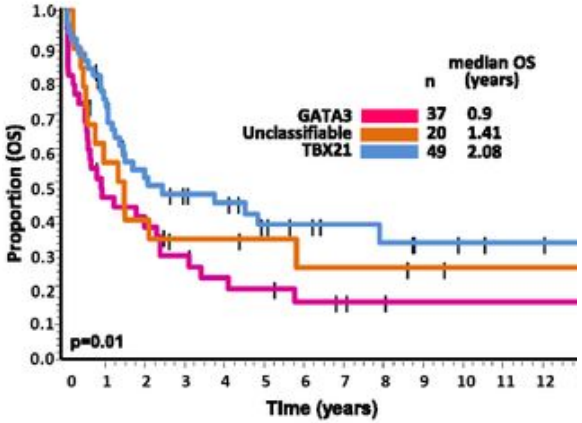
Kucuk C et al. Nature communications 2015;6:6025.
Kiel MJ et al. Nature communications 2015;6:8470.
Kiel MJ et al. Blood 2014;124:1460-72.
Crescenzo R et al Cancer cell 2015;27:516-32.
Koskela HL et al. N Engl J Med 2012;366:1905-13.
Jerez A et al. Blood 2012;120:3048-57.

IDH2 Mutations in TFH-like lymphoma (AITL and some PTCL-NOS)



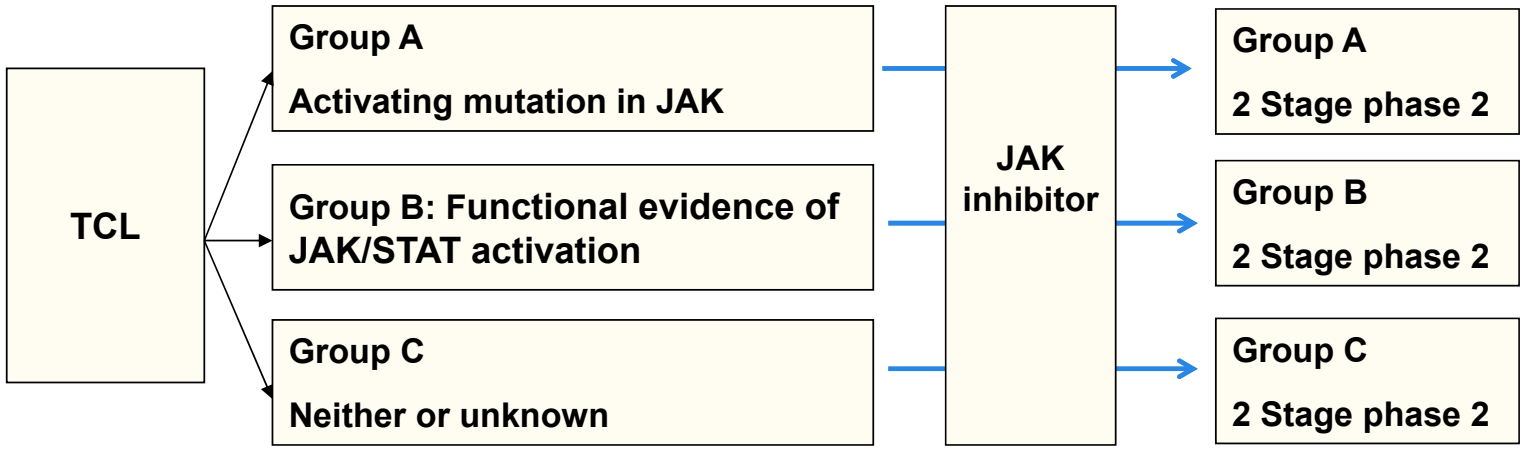
Sakata-Yanagimoto et al, *Nat Gen* 2014

PTCL: Gata3 high tumors show a worse OS enriched for PI3K-induced signatures



Iqbal J et al. Blood 2014;123:2915-2923

Ruxolitninb: Study Design; PI A. Moskowitz



DANA-FARBER CANCER INSTITUTE

Weill Cornell Medical College

LEUKEMIA & LYMPHOMA SOCIETY®
fighting blood cancers

PTCL: Initial Treatment

- Clinical Trial
  - Current: CHOP-like +X
    - BV
    - Romidespin
    - Lenalidomide
  - Future: Novel regimen
- CHOEP-ASCT in CR1 for Most
  - ALCL
    - ALK+; -IPI
    - *DUSP22* rearranged?
    - Low IPI, Early Stage?

PTCL: Relapse

- Clinical Trial
  - Novel agents/Regimens, targeted
  - Checkpoint inhibitors-studies ongoing
  - Standard agents
    - BV-ALCL
    - Others-little data to strongly suggest one over the other
- If Intent for Transplantation
  - Allo>Auto

NCCN Member Institutions