

CHOP vs. Ro-CHOP

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Equipe

« Pathologie des Cellules Lymphoïdes »
UMR 5239 CNRS – UCB – ENS - HCL



The Lymphoma
Study Association

First line chemotherapy regimens

- CHOP
- CHOEP: no comparative study
- DA-EPOCH: no published study
- ESHAP: studies in relapse
- GDP: studies in relapse
- HyperCVAD/MA
- Others

Anthracyclines are associated with an improved PFS and OS in AITL and PTCLnos

All pts

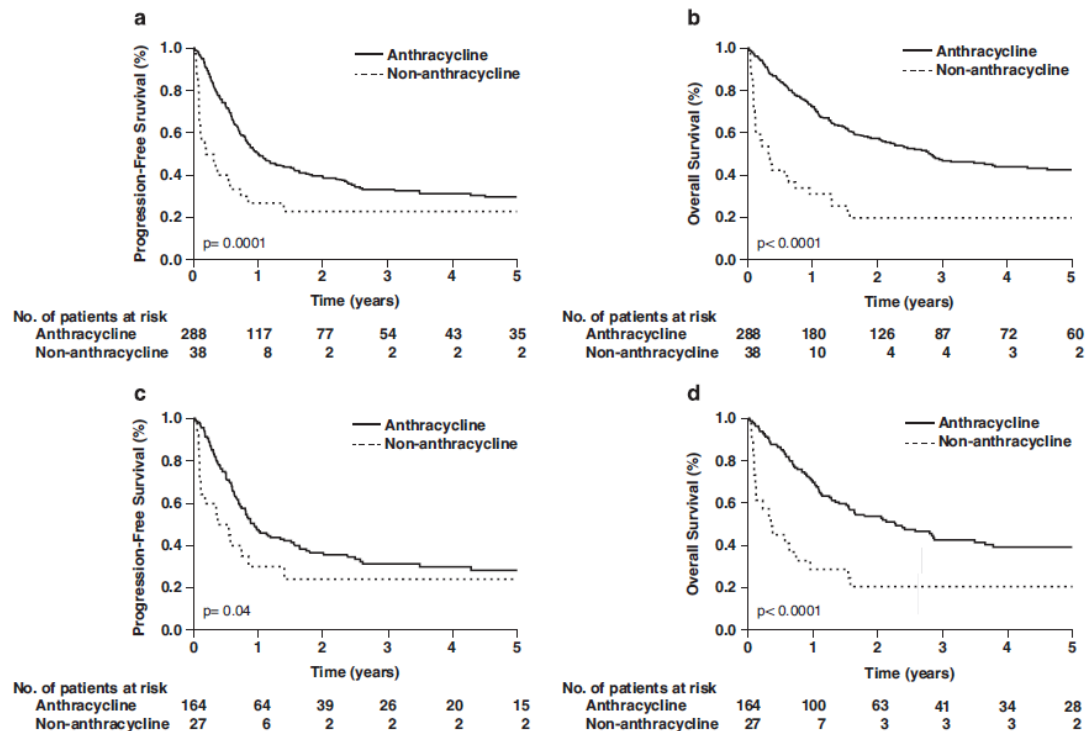


Table 4. Multivariate analysis for progression-free and overall survival

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

Abbreviations: AITL, angioimmunoblastic T-cell lymphoma; CI, confidence interval; HR, hazard ratio; IPI, International Prognostic Index; PTCL-NOS, peripheral T-cell lymphoma-not otherwise specified.

PTCL/AITL

Retrospective analysis of 442 patients, 65% of them with anthracycline regimen

Peripheral T-cell lymphomas in a large US multicenter cohort: prognostication in the modern era including impact of frontline therapy

J. S. Abramson¹, T. Feldman², A. R. Kroll-Desrosiers³, L. S. Muffly⁴, E. Winer⁵, C. R. Flowers⁶, F. Lansigan⁷, C. Nabhan⁴, L. J. Nastoupil⁶, R. Nath³, A. Goy², J. J. Castillo⁸, D. Jagadeesh³, B. Woda³, S. T. Rosen⁹, S. M. Smith⁴ & A. M. Evens^{10*}

Multicenter retrospective analysis

341 newly diagnosed PTCL

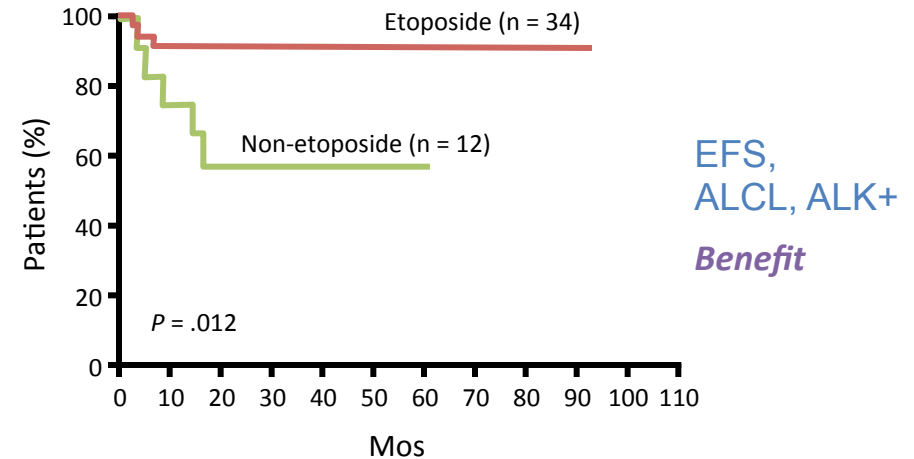
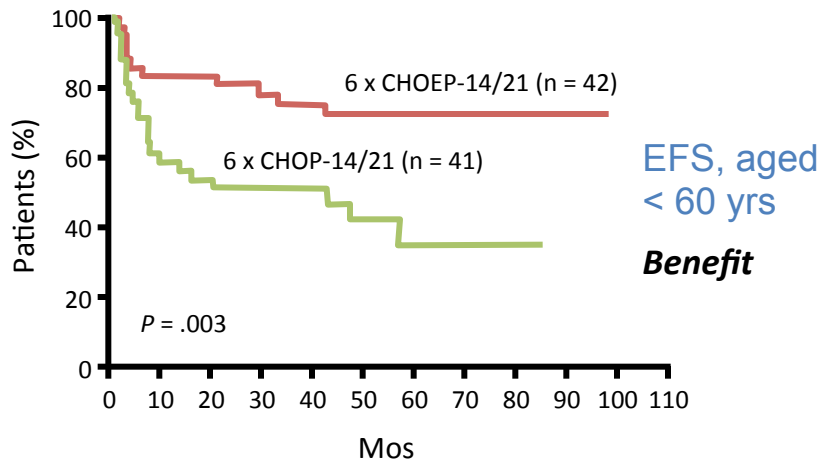
318 treated with chemotherapy: CHOP-like (70%) & HyperCVAD/MA (6%)

3-y PFS and OS= 32% and 52%

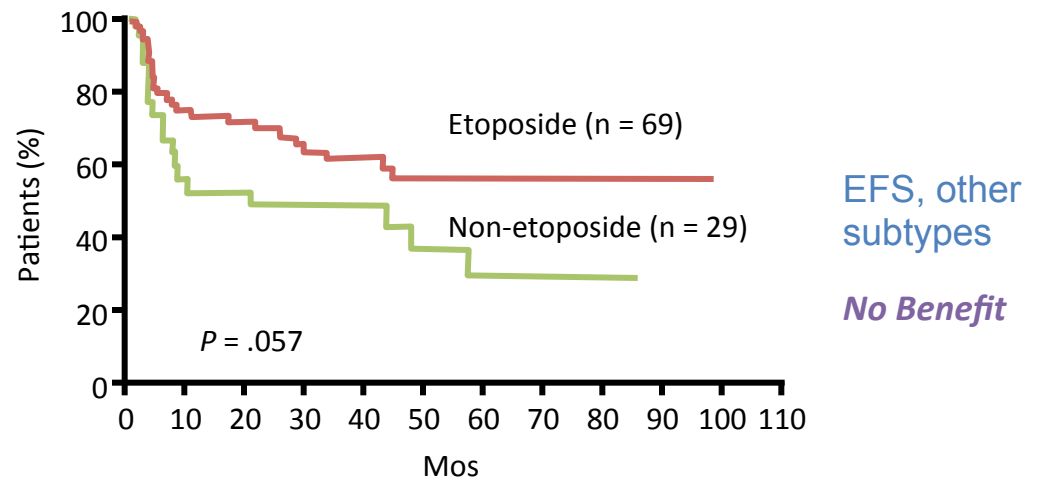
The most dominant prognostic factor was response to initial therapy

No overall survival difference was observed based on choice of upfront regimen or SCT in first remission.

In the real world we have to decide whether CHOEP is better than CHOP



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

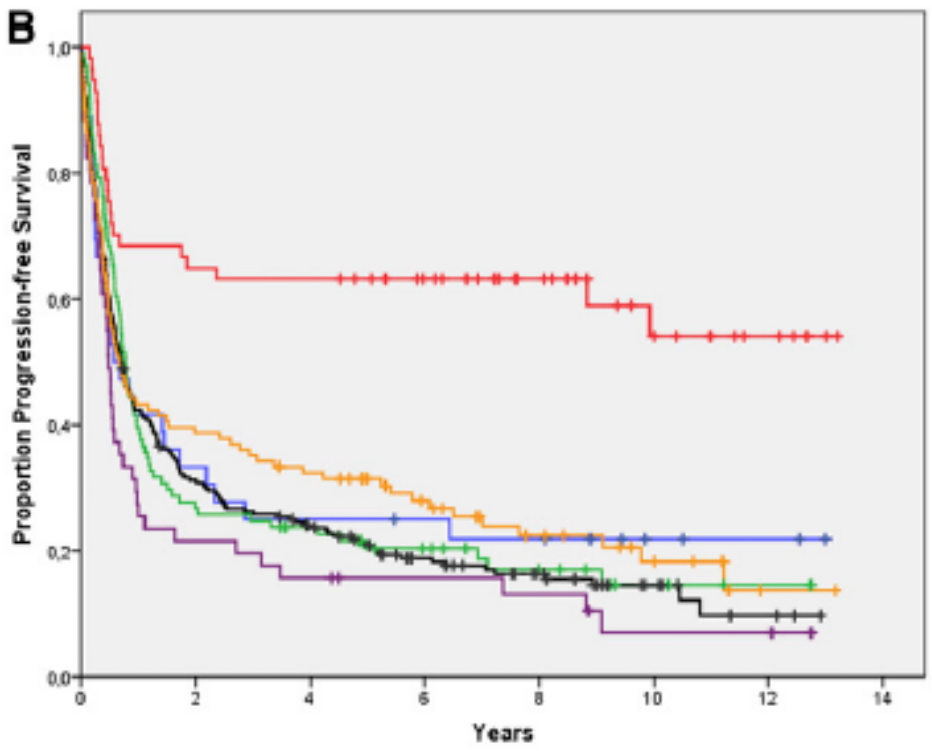
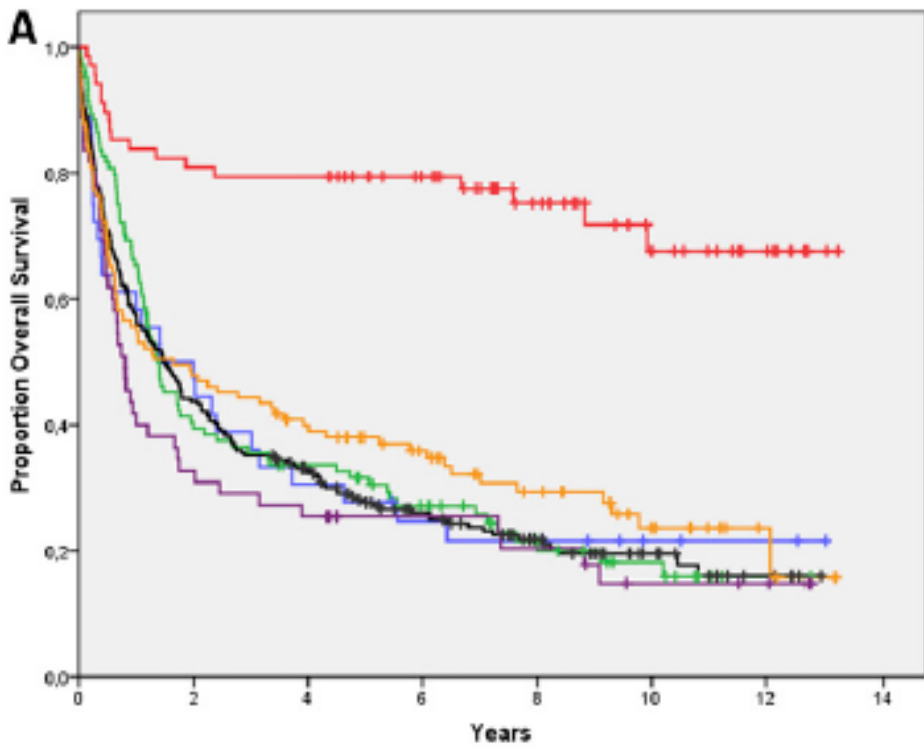


Real-world data on prognostic factors and treatment in peripheral T-cell lymphomas: a study from the Swedish Lymphoma Registry

Fredrik Ellin,^{1,2} Jenny Landström,² Mats Jerkeman,³ and Thomas Relander³

Blood. 2014;124(10):1570-1577

Swedish Lymphoma Registry: 755 PTCL



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

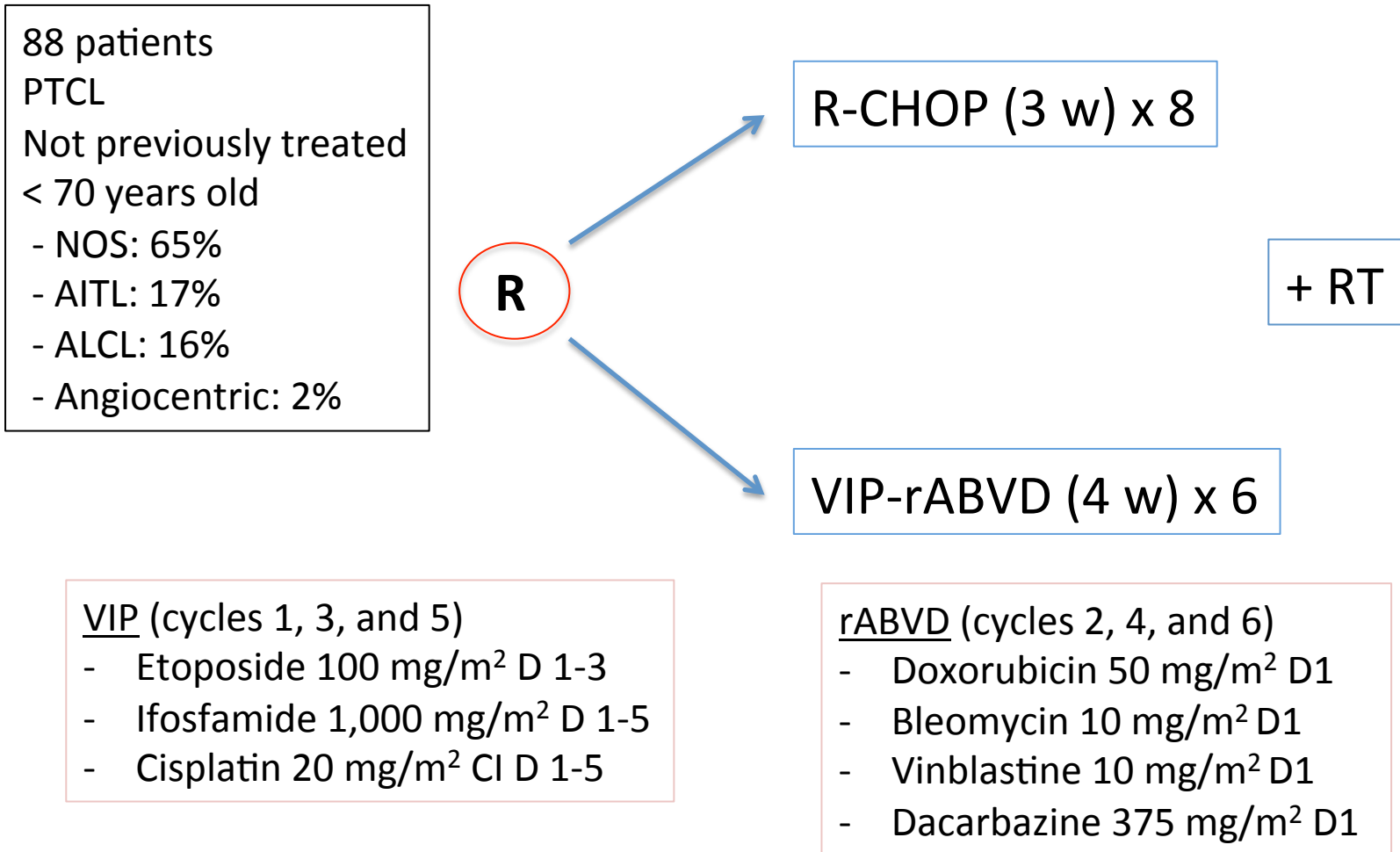
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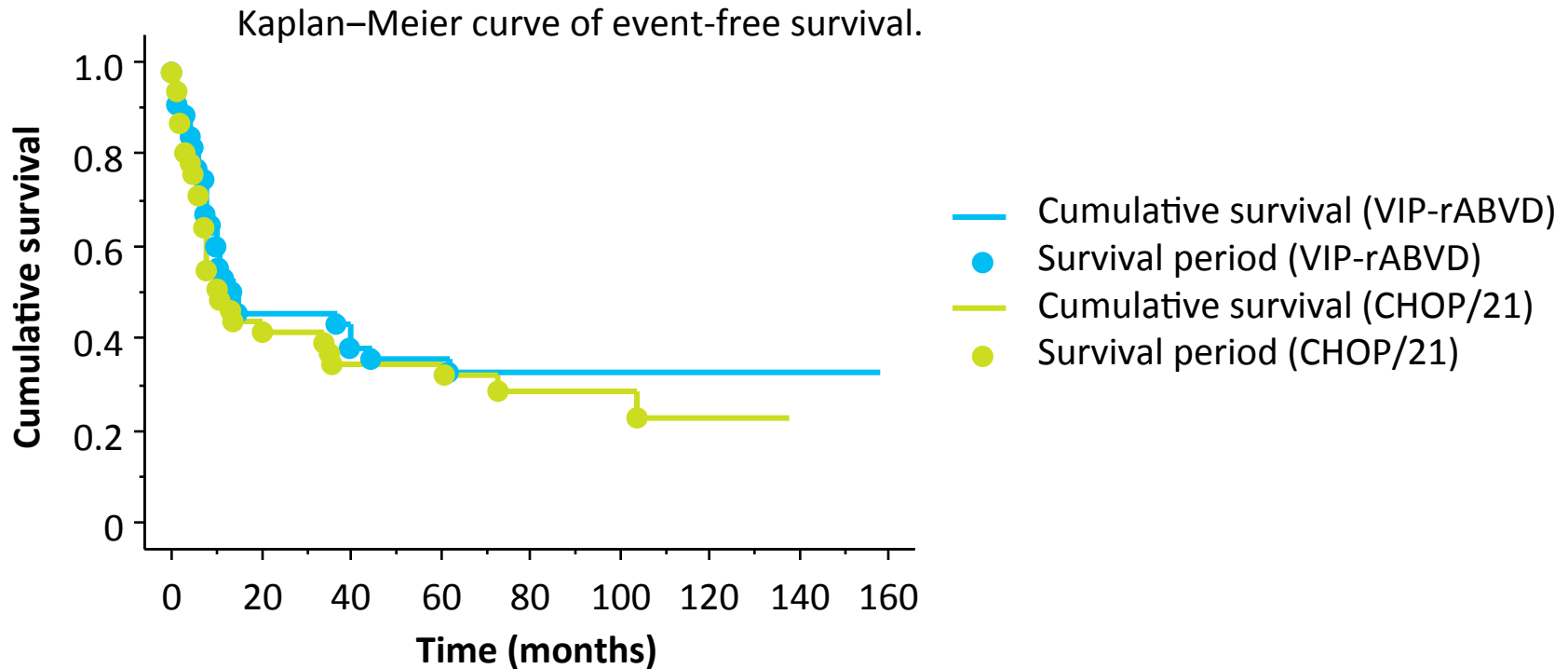
Table 4. Multivariable analysis of factors for OS and PFS in ALKneg ALCL, AITL, TCL U, and EATL patients up to age 70 treated with CHOP/CHOEP

	OS (n = 248)		PFS (n = 243)	
	HR (95% CI)	P	HR (95% CI)	P
Age	1.003 (0.984-1.023)	.730	1.000 (0.982-1.018)	.998
Male gender	1.60 (1.12-2.29)	.010	1.66 (1.16-2.35)	.005
Ann Arbor III-IV	1.56 (1.03-2.31)	.028	1.54 (1.05-2.25)	.028
Extranodal involvement >1	1.55 (1.03-2.35)	.037	1.57 (1.04-2.35)	.030
WHO PS >0	1.78 (1.23-2.57)	.002	1.81 (1.26-2.60)	.001
PTCL NOS	1.00	—	1.00	—
ALKneg ALCL	0.81 (0.50-1.25)	.307	0.78 (0.50-1.21)	.261
AITL	0.90 (0.59-1.39)	.643	0.90 (0.59-1.38)	.628
EATL	1.92 (1.18-3.14)	.009	1.52 (0.95-2.45)	.083
TCL U	1.98 (0.96-4.09)	.066	2.05 (0.99-4.24)	.052
Etoposide	0.81 (0.53-1.25)	.341	0.87 (0.57-1.32)	.507
Auto-SCT ITT	0.58 (0.40-0.84)	.004	0.56 (0.39-0.81)	.002

The Only Randomized Study



Event-Free Survival in the 88 Patients



SIE-SIES-GITMO Guidelines

- CHOP remains the standard chemotherapy for nodal DLBCL. In the setting of the standard of care, CHOP is the standard therapy for lymphoma. Exception could be etoposide-containing CHOP in young patients and those with ALK+ lymphomas (evidence: low; recommendation: low).

CHOP is the standard

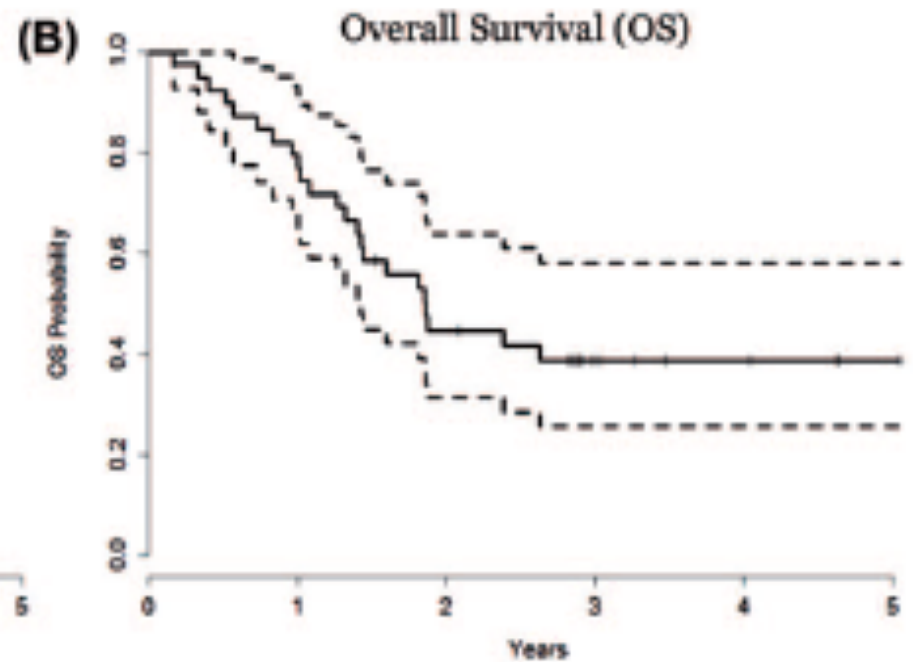
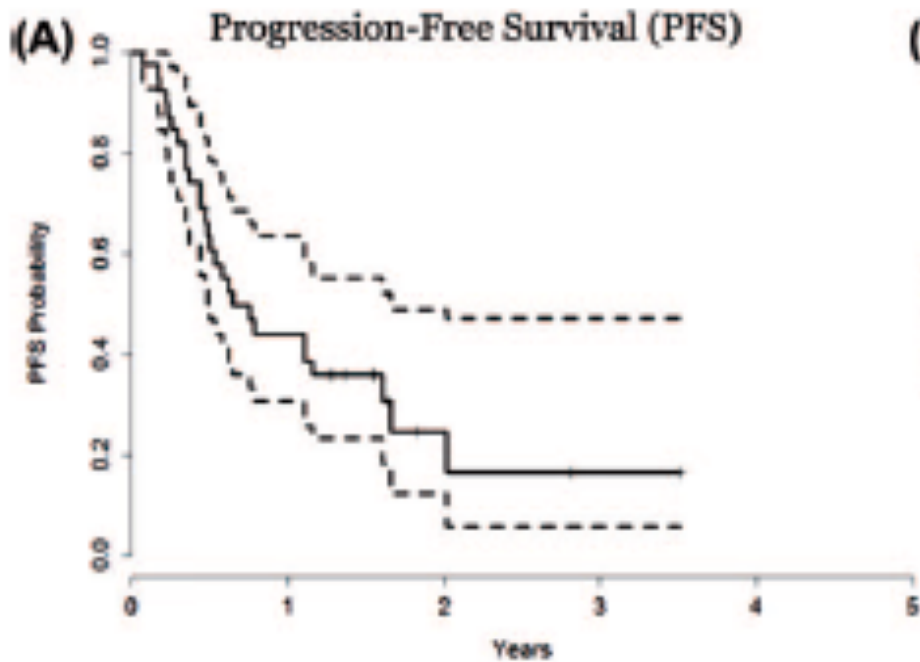
- To be replaced?
- To combine with something?

Candidates to be added to CHOP

- Alemtuzumab: waiting for results
- Lenalidomide
- Pralatrexate: sequential combination
- Belinostat: ongoing
- Brentuximab vedotin: ongoing
- Bevacizumab
- bortezomib
- **Romidepsin: ongoing**

-CHOP

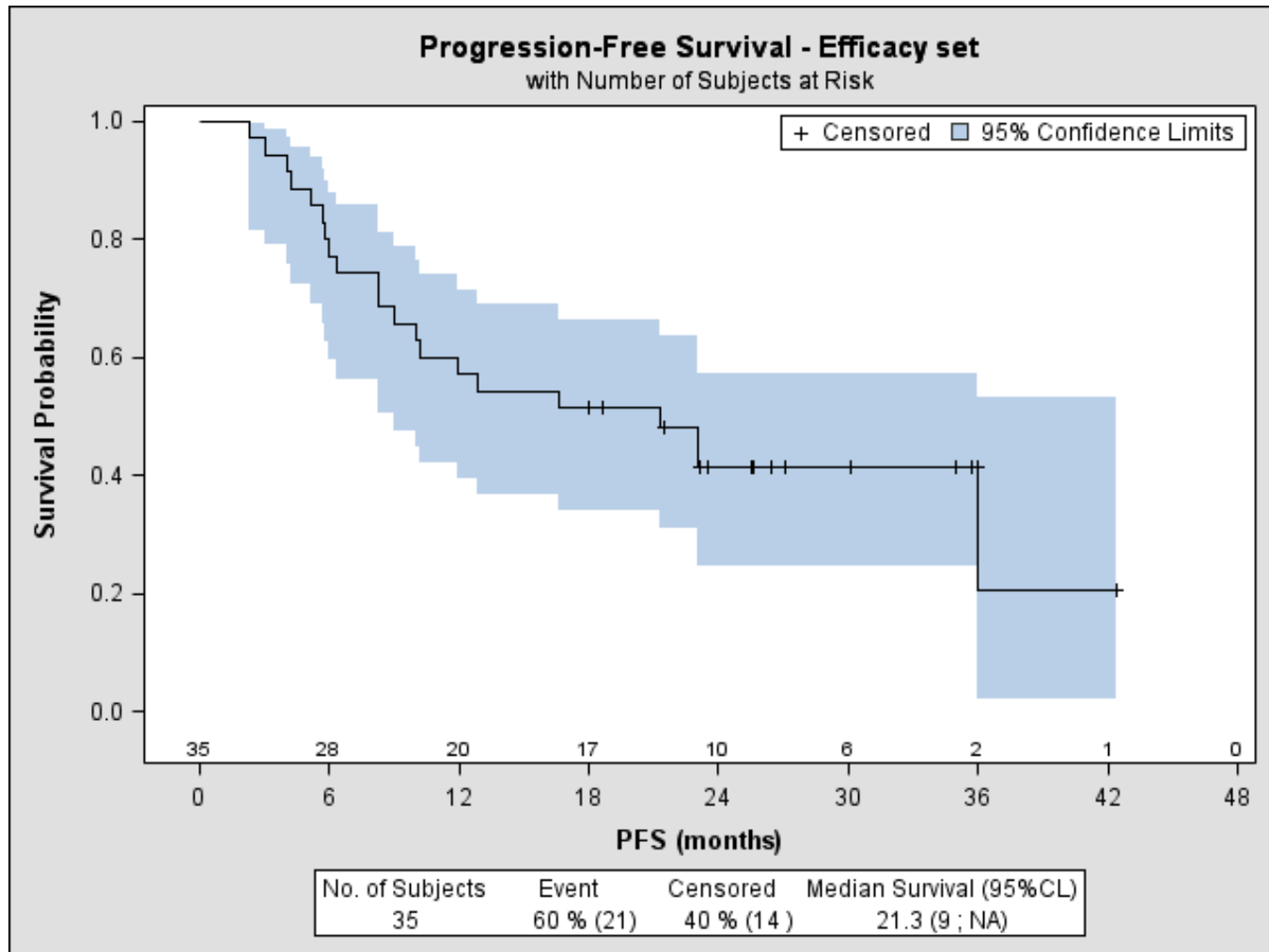
CR: 49%, PR 41% - Median PFS 7.7 months



Ro-CHOP – Phase Ib/II

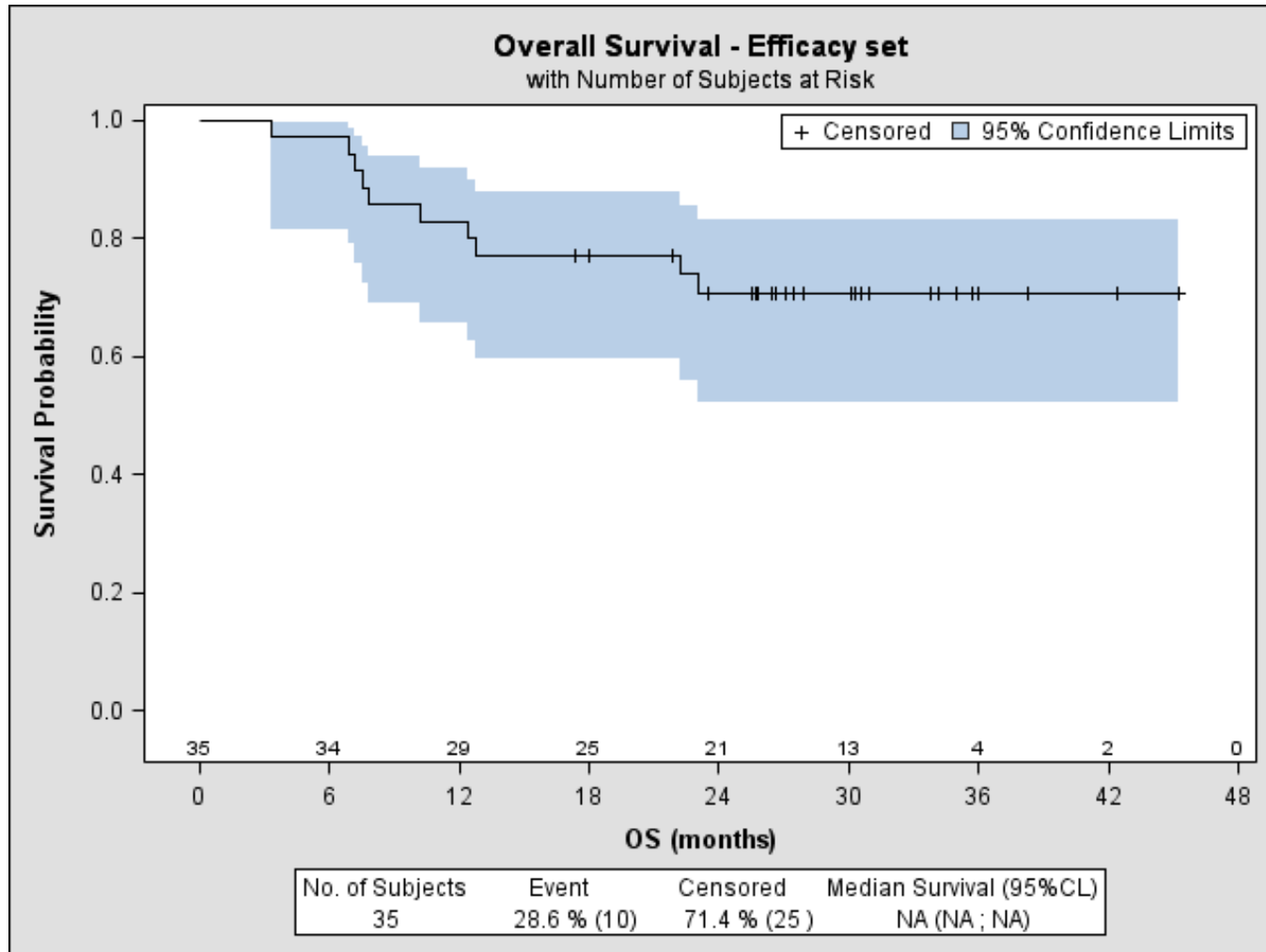
- Dose of romidepsin: 12 mg/m²
- Responses (35 patients evaluable)
 - CR 18 = 51%
 - PR 5 = 17%
 - PD 9 = 26%

Follow-Up 30 Months)



1-year estimated PFS 57% (95%CI 39 – 71)

OS (median PFS 30 months)



1-year estimated OS 82% (95%CI 65 – 91)

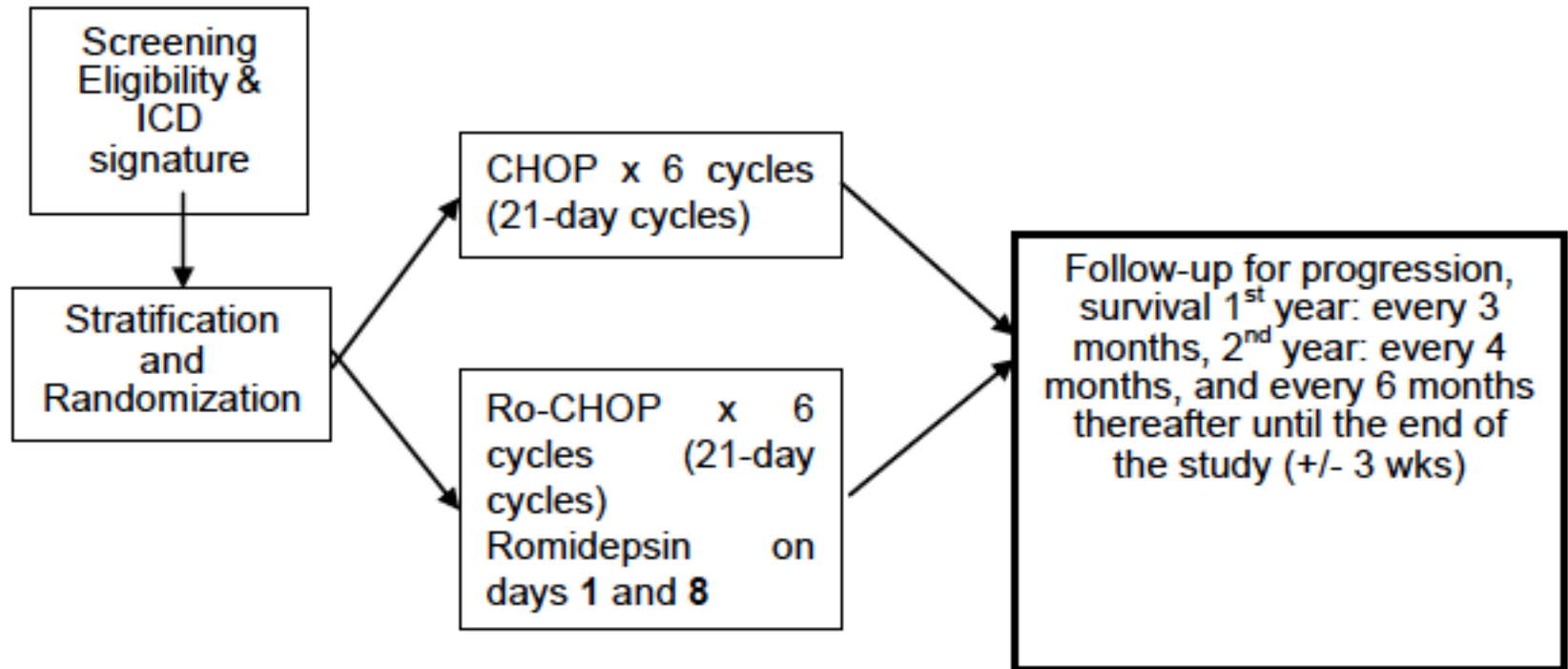
Ro-CHOP Phase III Study



Screening Phase

Treatment Phase

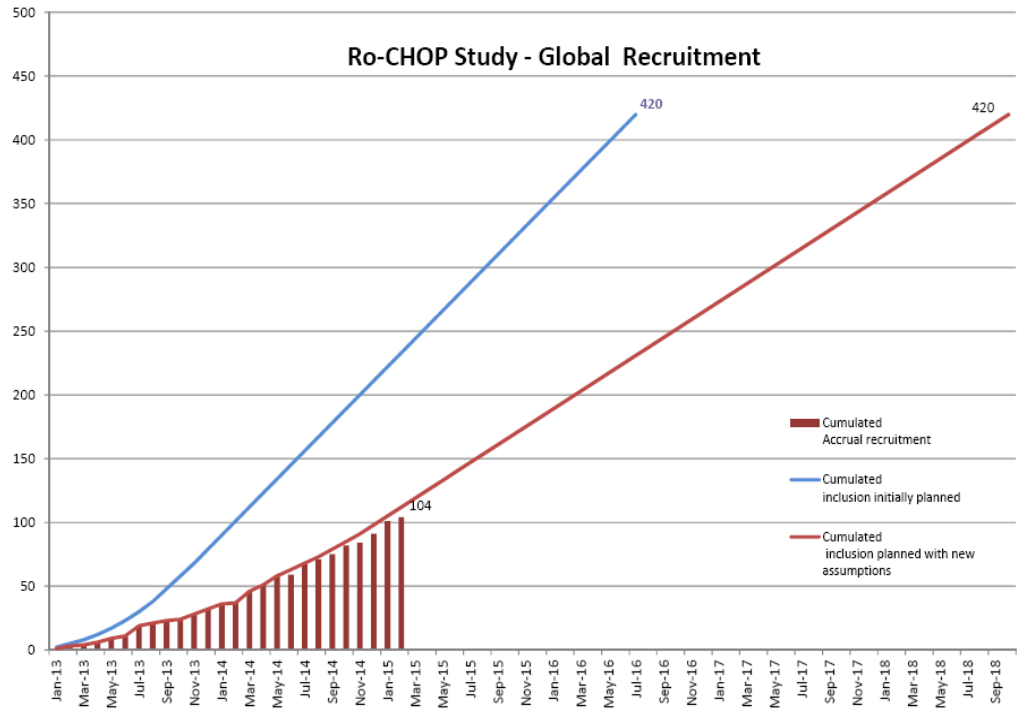
Follow Up Phase



Approximately 420 patients have to be enrolled in the study. Patients will be recruited over 3, 5 years.

Ro-CHOP study

- All PTCL except Alk +ALCL, 18-80y
- Phase III
- CHOP21 x 6 versus CHOP21 x 6 + romidepsin 12 mg/m² D1&D8
- Primary objective: PFS



- 100th patient included in January 2015
- DSMC n°1 (first 50 patients): no issue in toxicity, continuation of the study
- DSMC n°2 planned in July 2015
- First patient in Singapore planned in March 2015