Advances in Malignant lymphomas:
The case of extranodal and T-cell lymphomas

Santiago de Chile
April 5-6, 2016

Auditorio Dr. Lucas Sierra
Hospital del Salvador
Av. Providencia 364

Presidents:
Maria Elena Cabrera
Carlos Sergio Chiattone
Massimo Federico

The T-Cell Project: overall results from the analysis of the first 1,500 registered patients

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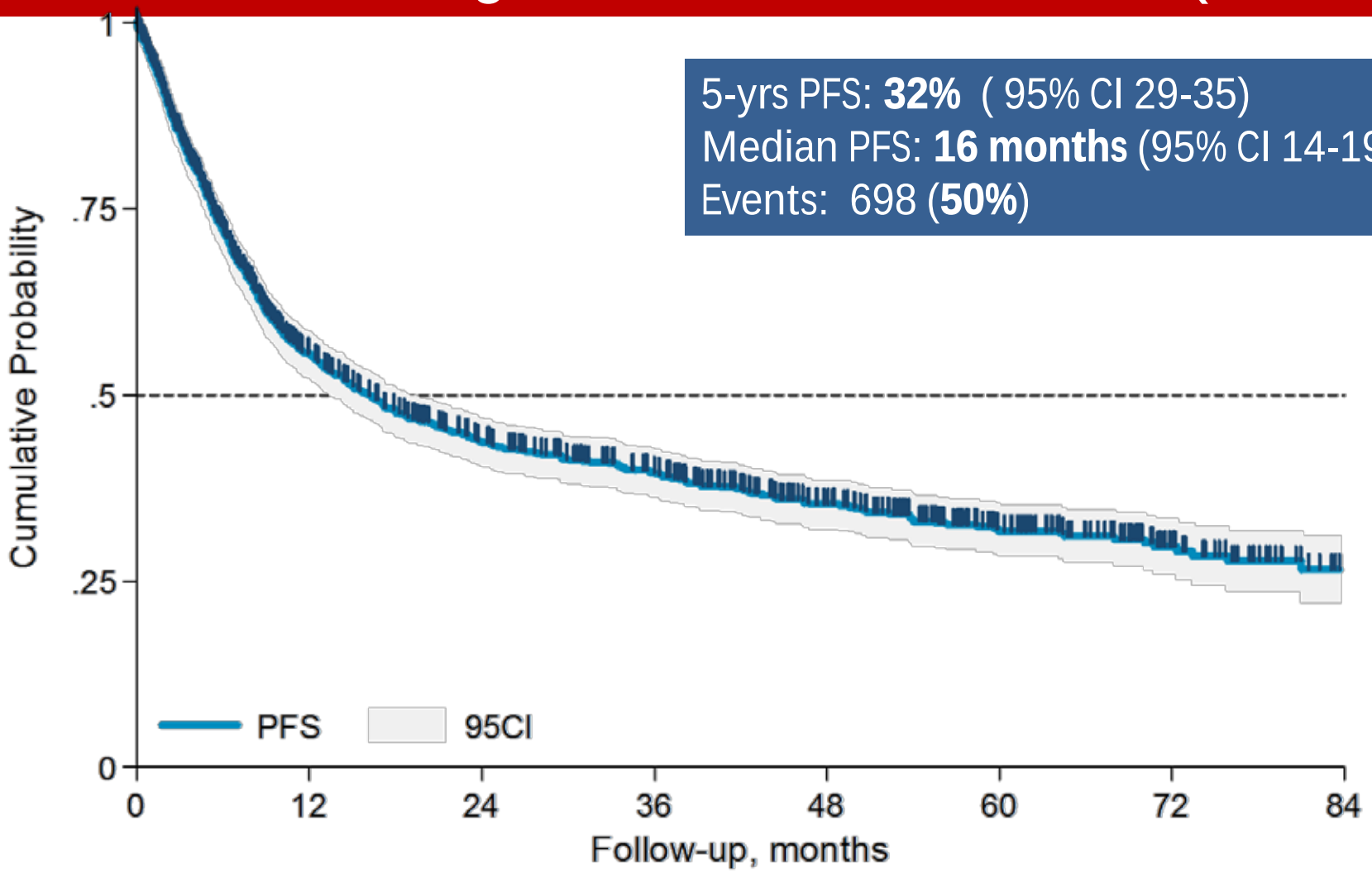
Analysis of data of patients registered up to March 15, 2016 and with available data (N=1,389). Part 2.

Response to Initial treatment (N=1020)

	N	%	%TOT
CR/CRu	474	**53%**	**47%**
PR	164	**18%**	**16%**
NR/PD	249	**28%**	**24%**
	887	100%	87%
Not evaluable	50		**5%**
	937		92%
Best Supportive Care	**83**		**8%**
			100%

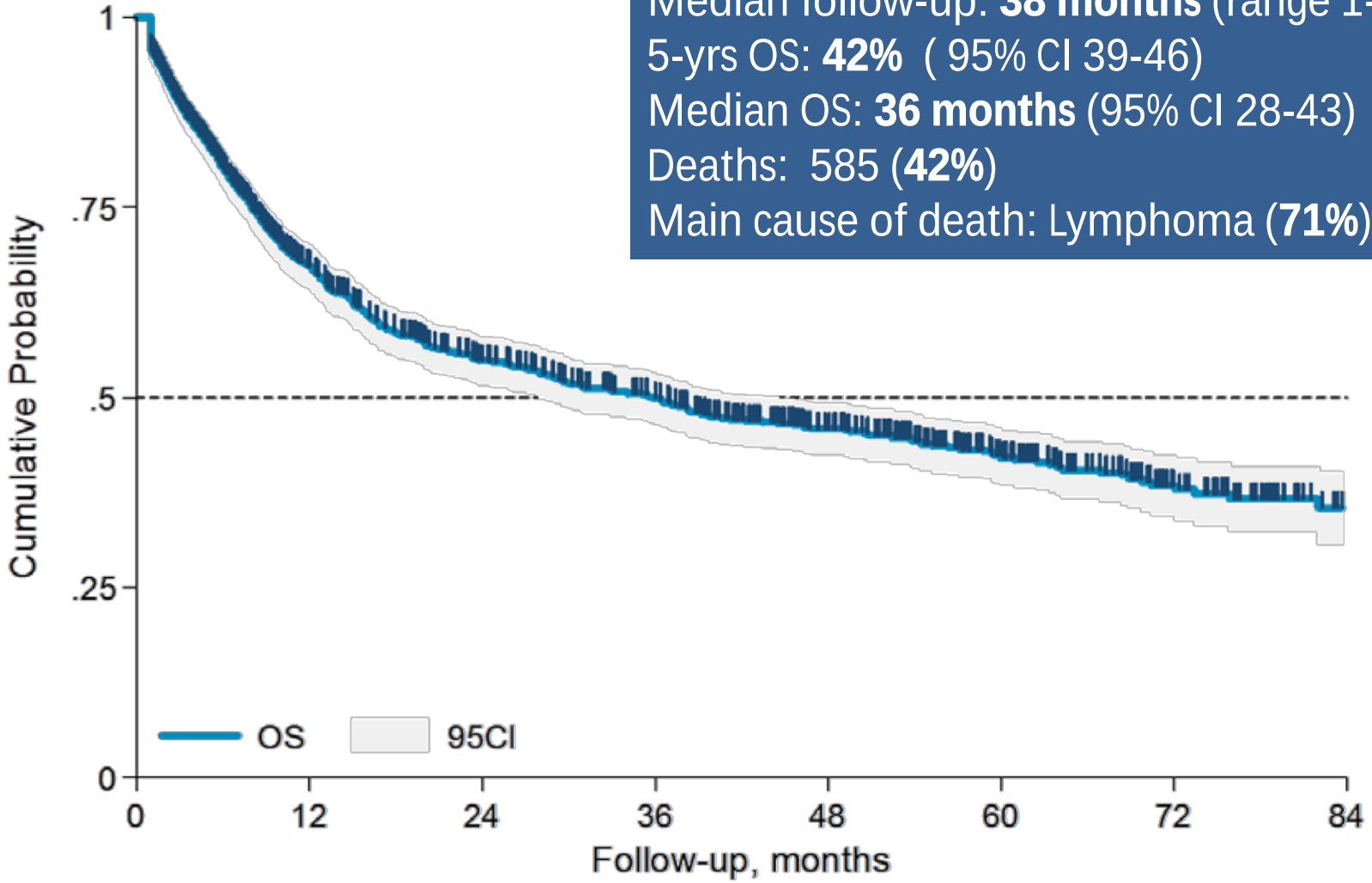
Progression Free Survival (N=1,389)

5-yrs PFS: **32%** (95% CI 29-35)
Median PFS: **16 months** (95% CI 14-19)
Events: 698 (**50%**)



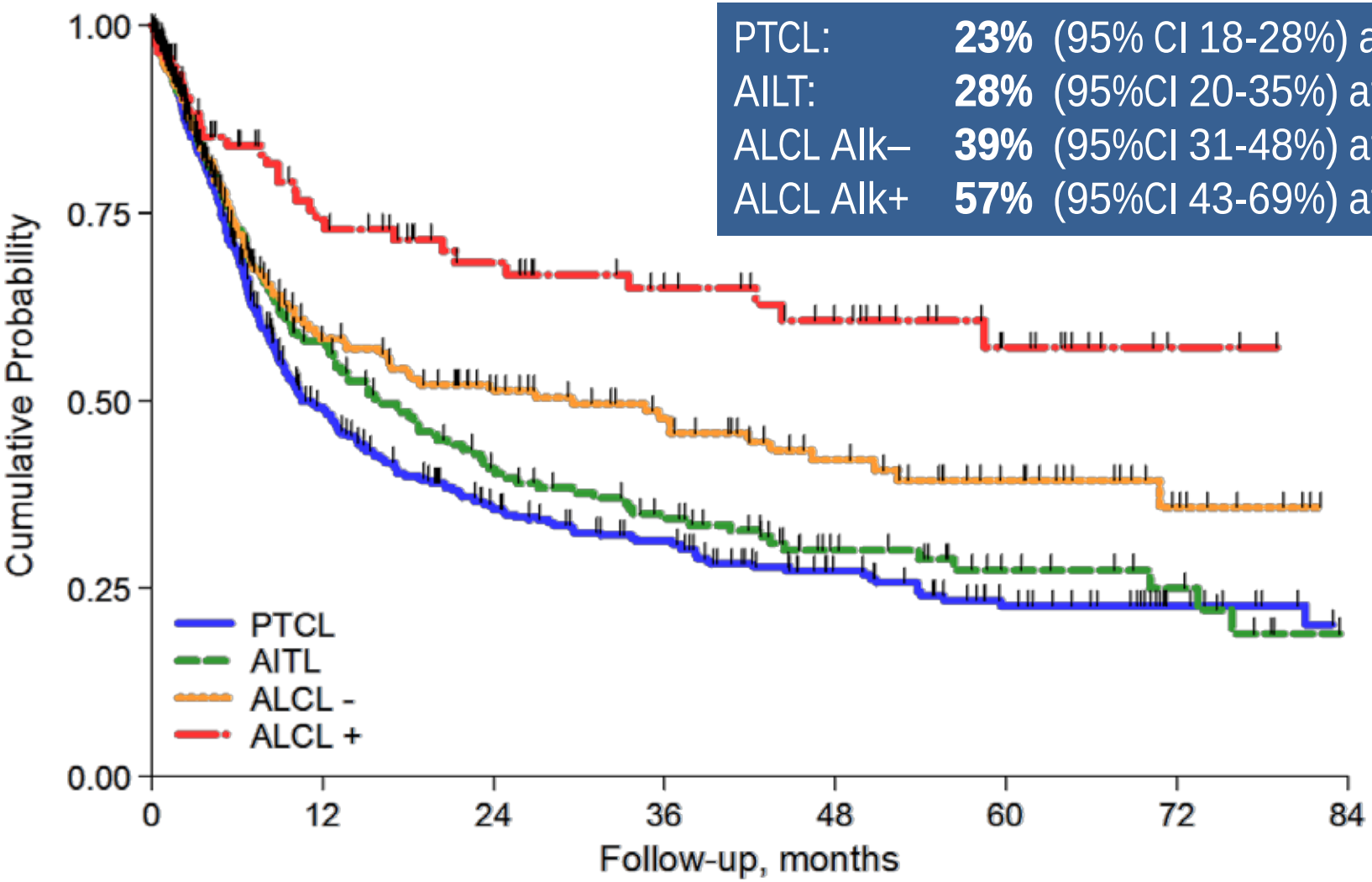
Overall survival (N=1,389)

Median follow-up: **38 months** (range 1-112)
5-yrs OS: **42%** (95% CI 39-46)
Median OS: **36 months** (95% CI 28-43)
Deaths: 585 (**42%**)
Main cause of death: Lymphoma (**71%**)



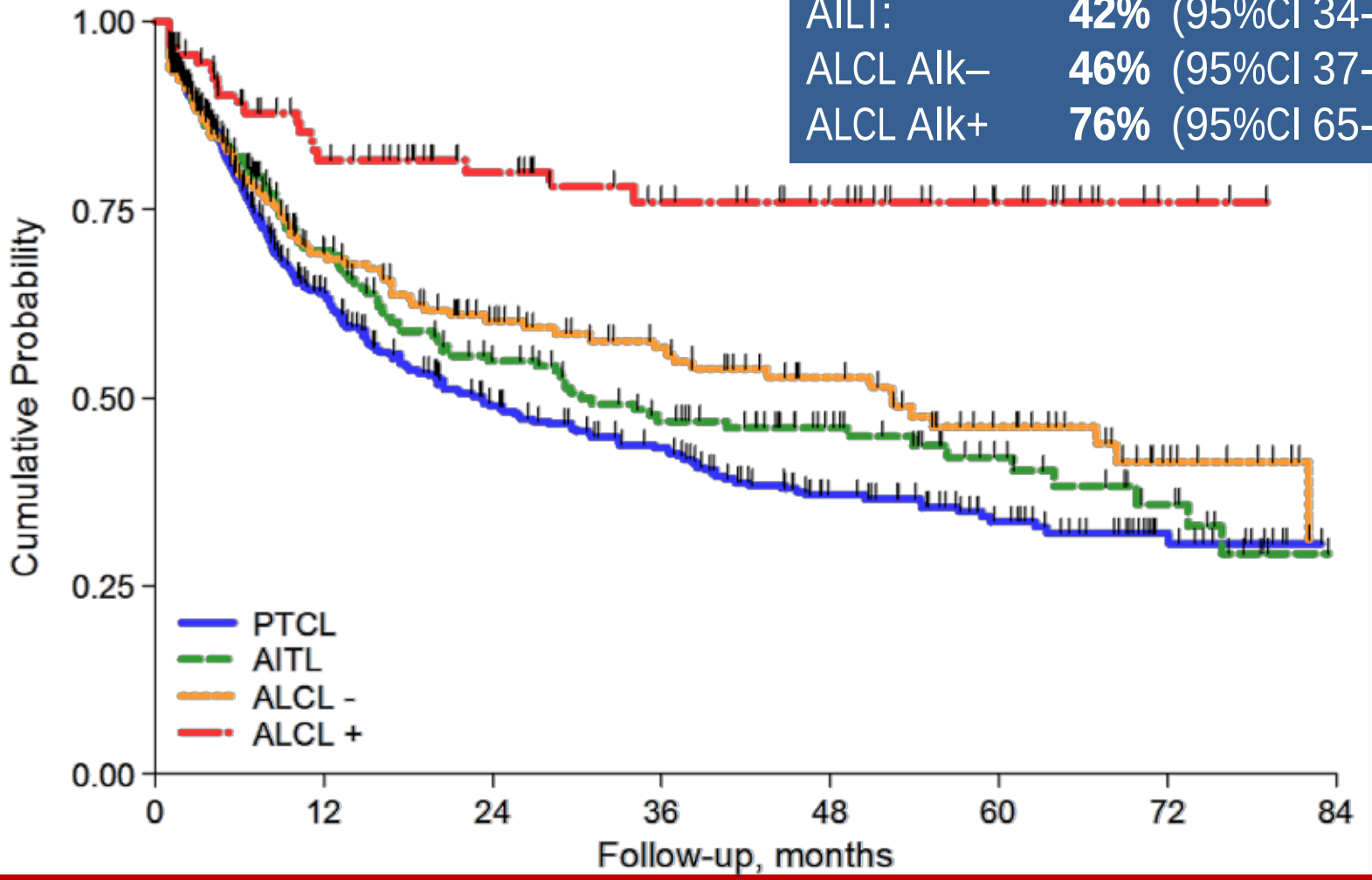
Progression free survival (N=1077)

PTCL:	**23%**	(95% CI 18-28%) at 5 yr
AILT:	**28%**	(95%CI 20-35%) at 5-yr
ALCL Alk–	**39%**	(95%CI 31-48%) at 5-yr
ALCL Alk+	**57%**	(95%CI 43-69%) at 5-yr



Overall survival (N=1077)

PTCL:	**34%**	(95% CI 28-39%) at 5 yr
AILT:	**42%**	(95%CI 34-50%) at 5-yr
ALCL Alk–	**46%**	(95%CI 37-55%) at 5-yr
ALCL Alk+	**76%**	(95%CI 65-84%) at 5-yr



Outcomes by PTCL Subtypes by IPI

	PTCL-NOS		AITL		ALK+ ALCL		ALK– ALCL		NKTCL		ATLL	
	ITCLP	TCP	ITCLP	TCP	ITCLP	TCP	ITCLP	TCP	ITCLP	TCP	ITCLP	TCP
N	340	504	243	249	87	116	72	208	136	154	126	-
5-year OS, %												
ALL	32	37	32	46	70	79	49	49	32	51	14	-
IPI 0/1	50	64	56	72	90	85	74	73	57	55	28	-
IPI 4/5	11	19	25	23	33	67	13	39	0	17	7	-
5-year PFS, %												
ALL	20	23	18	27	60	57	36	39	29	43	12	-
IPI 0/1	33	46	34	45	80	73	62	59	53	48	26	-
IPI 4/5	6	11	16	15	25	50	13	24	0	0	0	-

#247: The role of transplant in the treatment of Peripheral T-cell Lymphomas (PTCLs): an analysis from the T-Cell project database.

S.M.Horwitz[1] , M.Bellei[2], L.Marcheselli[2], J.M.Vose[3], S.Montoto[4], Y.H.Ko[5], M.E.Cabrera[6], C.S. Chiattone[7], A.J.Ferreri[8], W.S.Kim[9], D.Laszlo[10], A.Nagler[11], G.Rossi[12], A.Shustov[13], U.Vitolo[14], M.Federico[2]

13-ICML
13th International Conference on Malignant Lymphoma
Palazzo dei Congressi, Lugano, Switzerland, June 17-20, 2015

1338 pts by 73 sites from14 countries world-wide

- Treatment data available on 959 Pts.
- A total of 194 Pts (20%) underwent HDT
- 56 (6%) and 15 (1%) Pts were consolidated with HDT after achieving a CR (HDT-CR1) or a PR (HDT-PR1) with induction therapy
- 123 (13%) received HDT as salvage (HDT-S)
- HDT given as consolidation or salvage was autologous in 63 (89%) or in 94 (76%) and allogeneic in 8 (11%) or 29 (24%) respectively

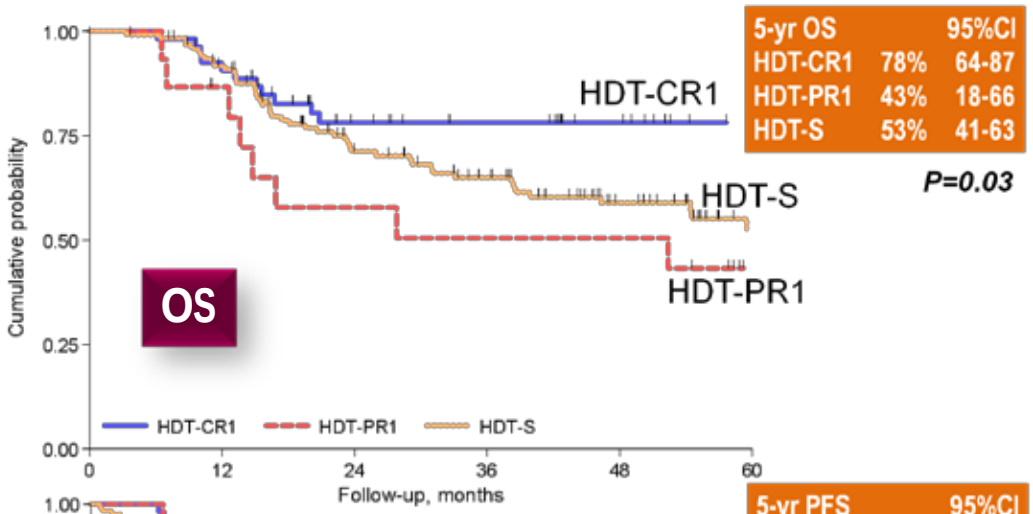
Baseline characteristics of transplanted Pts and HDT use by subtype

13-ICML
13th International Conference on Malignant Lymphoma
Palazzo dei Congressi, Lugano, Switzerland, June 17-20, 2015

Baseline Characteristics of transplanted patients [194]	N	%
Age, y; Mean (range)	48 (18-72)	
Male gender	129	66
Clinical data [194]		
ECOG performance status > 1	34	17
B symptoms (yes)	109	56
Disease-related symptoms (yes)	136	70
Disease extent [155]		
Stage III-IV	123	79
Number of extranodal sites > 1	53	34
Bulky disease (>5 cm)	30	19
Transplant use by subtype [959]	**N**	**%**
PTCL, NOS (N=352)	62	18
AITL (N=161)	37	23
ALCL, ALK- (N=142)	30	15
ALCL, ALK+ (N=77)	15	19
NKTCL (N=110)	22	20
Extranodal PTCLs, other (N=84)	21	25
Unclassifiable PTCLs (N=33)	7	21

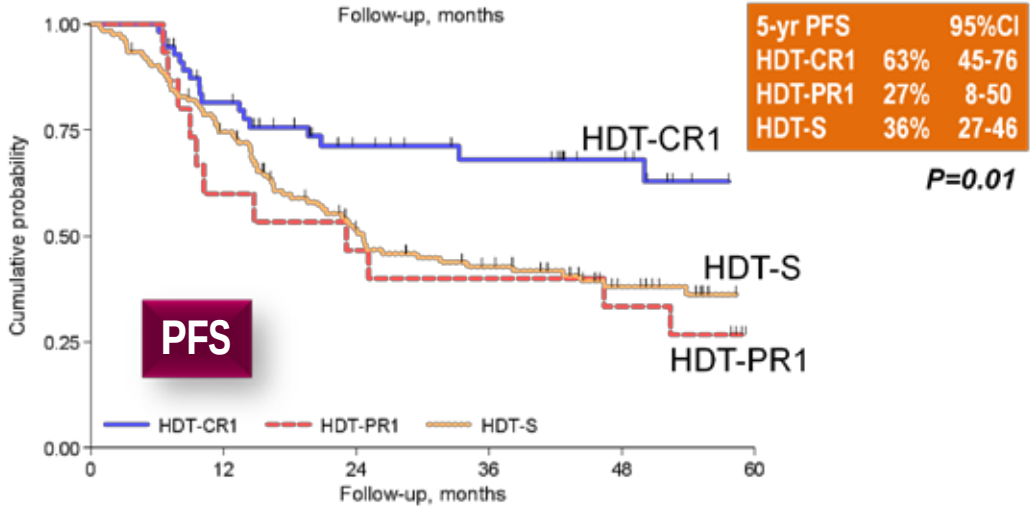
OS, PFS & Survival After Relapse

- Median follow-up: 37 mos



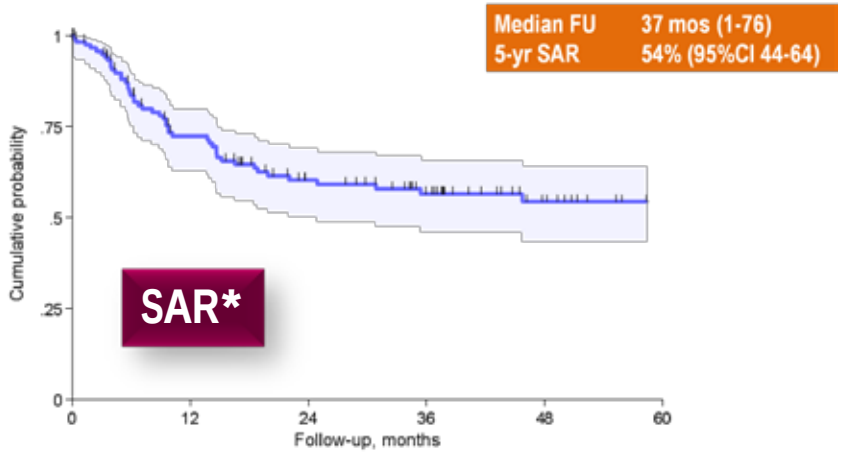
5-yr OS		95%CI
HDT-CR1	78%	64-87
HDT-PR1	43%	18-66
HDT-S	53%	41-63

P=0.03



5-yr PFS		95%CI
HDT-CR1	63%	45-76
HDT-PR1	27%	8-50
HDT-S	36%	27-46

P=0.01



Pts who received HDT @ relapse

8552 - CD30 expression in Peripheral T-cell lymphomas (PTCLs): a subset analysis from the international, prospective T-Cell Project

Federico M[1], Bellei M[1], Luminari S[1], Horwitz SM[2], Montoto S[3], Zucca E[4], Pileri SA[5], Ko YH[6] , Zinzani PL[5], Connors JM[7], Foss FM[8], Polliack A[9], Cabrera ME[10], Kim WS[6], Spina M[11], De Souza CA[12], Bobillo Varela S[13], Dlouhy I[14], Advani RH[15], and Vose JM[16] on behalf of the T-Cell Project

- 792 pathology forms filled out by site staff and available at time of analysis
- CD30 expression tested in 490 pts (62%) and reported as CD30+ in 349 (71%) and CD30- in 141 (29%).
- Vast majority of Pts treated with CHOP/CHOP like regimens irrespective of CD30 status (63% in both groups, P=1.0).
- Brentuximab vedotin as first line therapy was reported in only 5 Pts (all enrolled in clinical trials).

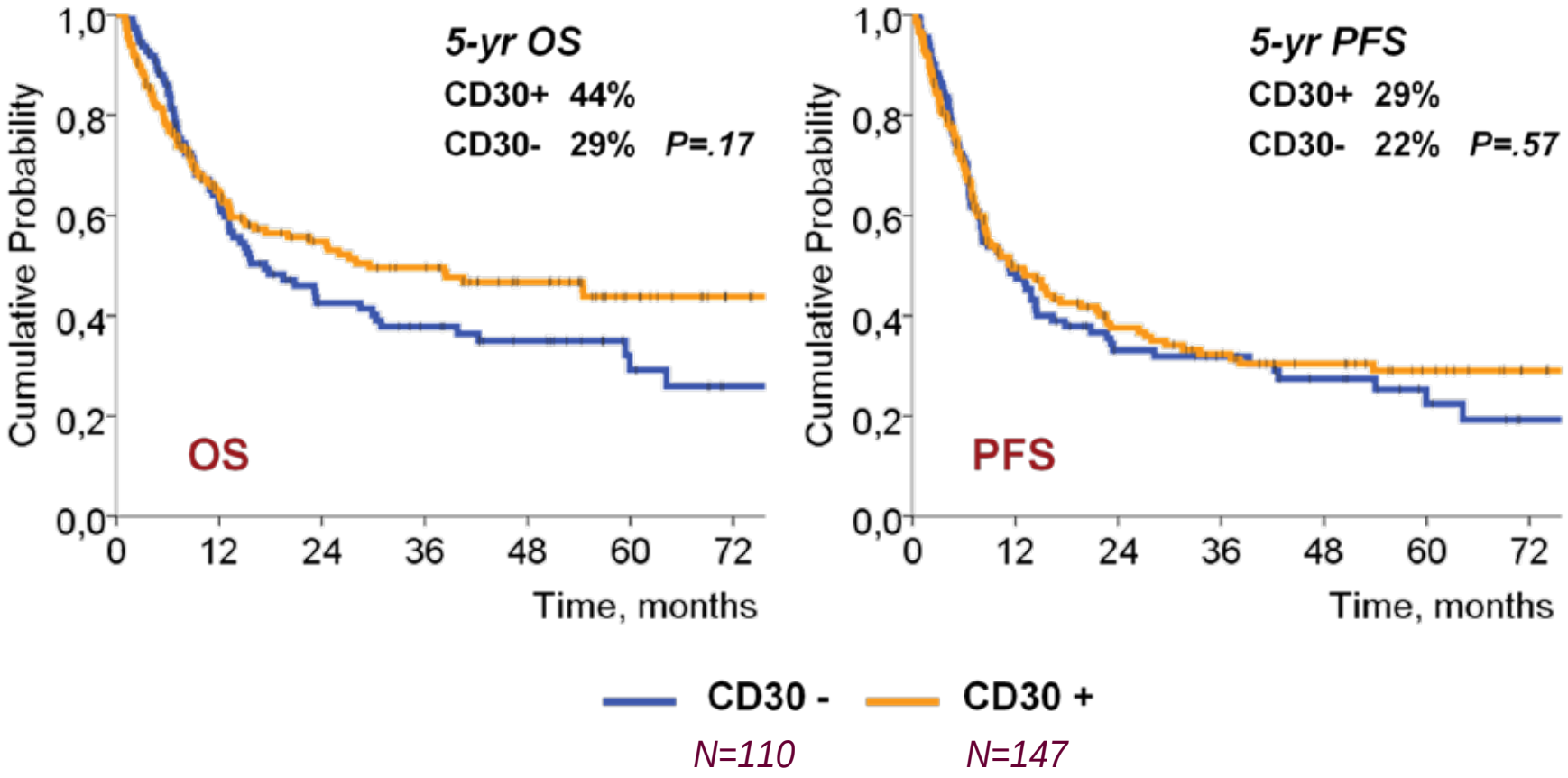
CD30 expression by subtypes (N=490)

PTCL subtype	CD30 negative		CD30 positive	
	N	%	N	%
PTCL-NOS, 205 (42%)	85	41	120	59
AITL, 66 (13%)	16	24	50	76
ALCL, 145 (30%)	-	-	145	100
NKTCL, 27 (5%)	13	48	14	52
EATL, 24 (5%)	11	46	13	54
Other, 23 (5%)	16	70	7	30

***PTCL-NOS**, Peripheral T-Cell Lymphoma not otherwise specified; **AITL**, Angioimmunoblastic; **ALCL**, Anaplastic Large Cell Lymphoma; **NKTCL**, NK/T-Cell Lymphoma; **EATL**, Enteropathy-type Lymphoma*

OS and PFS by CD30 status: Pts with any subtype but ALCL (N=257)

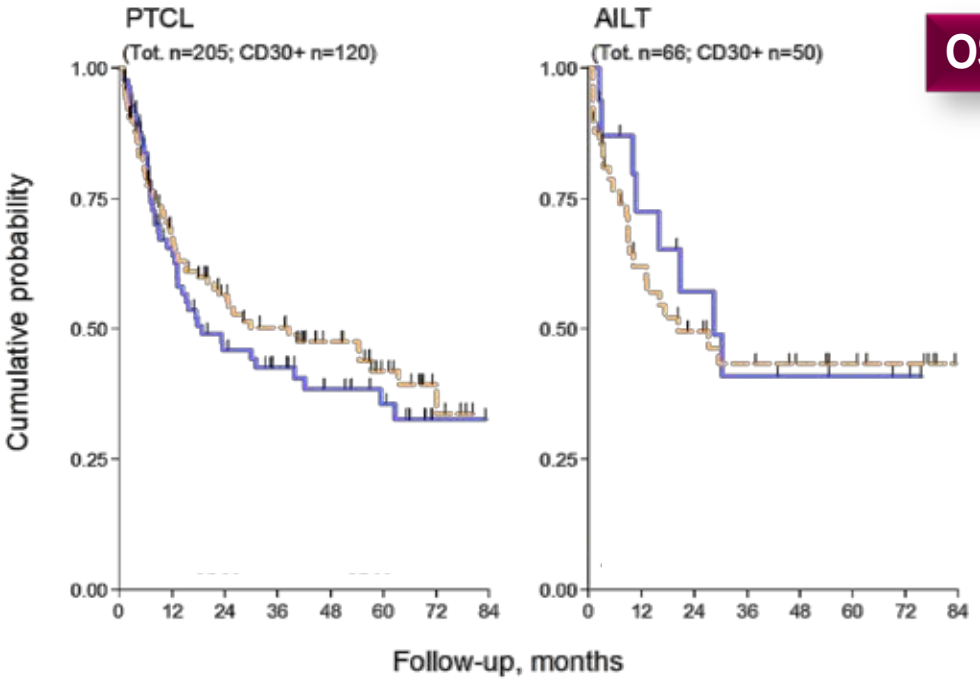
- No difference in CR rate (44% vs 51%, P=.26), 5-yr PFS and 5-yr OS depending on CD30 status



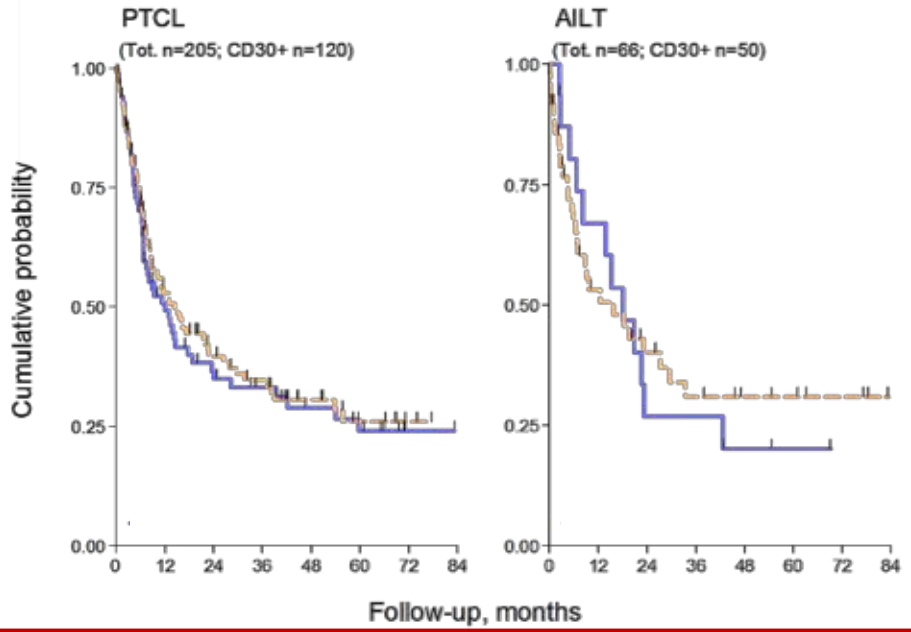
OS & PFS – PTCL-NOS and AILT: CD30- vs CD30+

2015 ASCO Annual Meeting
Illumination&Innovation
transforming data into learning
May 29-June 2, 2015 | McCormick Place | Chicago, Illinois

OS



PFS



CD30 - CD30 +

Conclusions

Data from the T-cell project confirm that CD30 is expressed in many PTCLs other than ALCL, thus suggesting a routine assessment for all PTCLs. Again, this analysis suggests that CD30 expression has no prognostic significance. The very limited use of anti CD30 targeted therapy in this sample doesn't allow to establish the predictive value of CD30 expression in PTCLs.

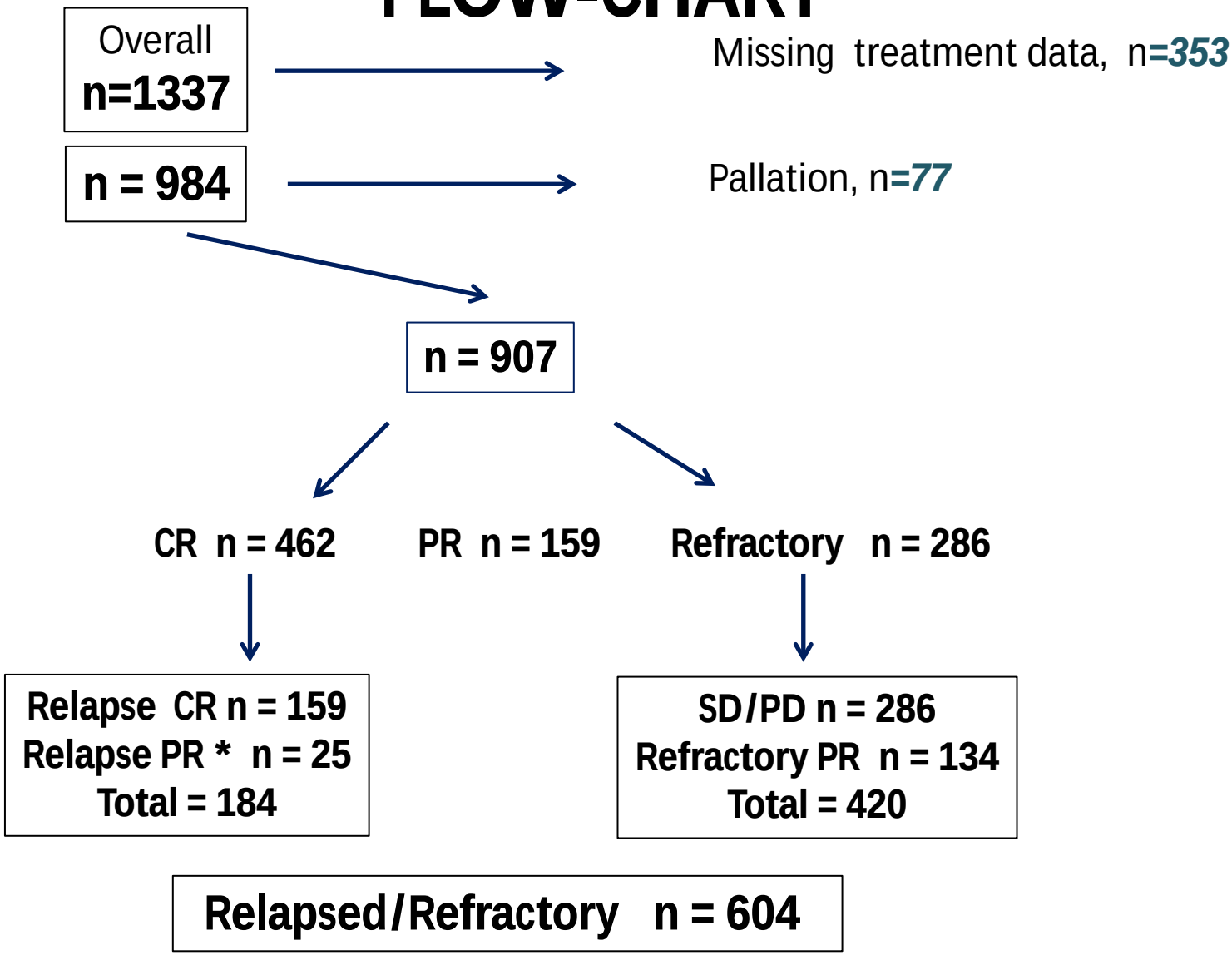
T-Cell Project

Survival analyses on patients with refractory/relapsed disease

TCP Trial Office, February 2, 2016

By Luigi Marcheselli, Monica Bellei, and Massimo Federico

FLOW-CHART



* Relapse in PR if date of progression > 6 months from date of end of first treatment

Patients characteristics (n=604)

Variable	Status	N (%)
Age at diagnosis	Median	58 (range 17-89)
Age at refr/relap.	Median	60 (range 18-93)
Age at refr./relap.	>60	293 (49)
Gender	Male	394 (65)
1 st line therapy	CHT	506 (84)
	RT	3 (0.5)
	CHT/RT	64 (11)
	HDT cons.	31 (5)
Response	CR	159 (26)
	PR	159 (26)
	<PR	286 (47)
Status	Relapse after CR	159 (26)
	Relapse after PR	25 (4)
	PR refractory	134 (22)
	Refractory (<PR)	286 (47)

Patients characteristics (n=604)

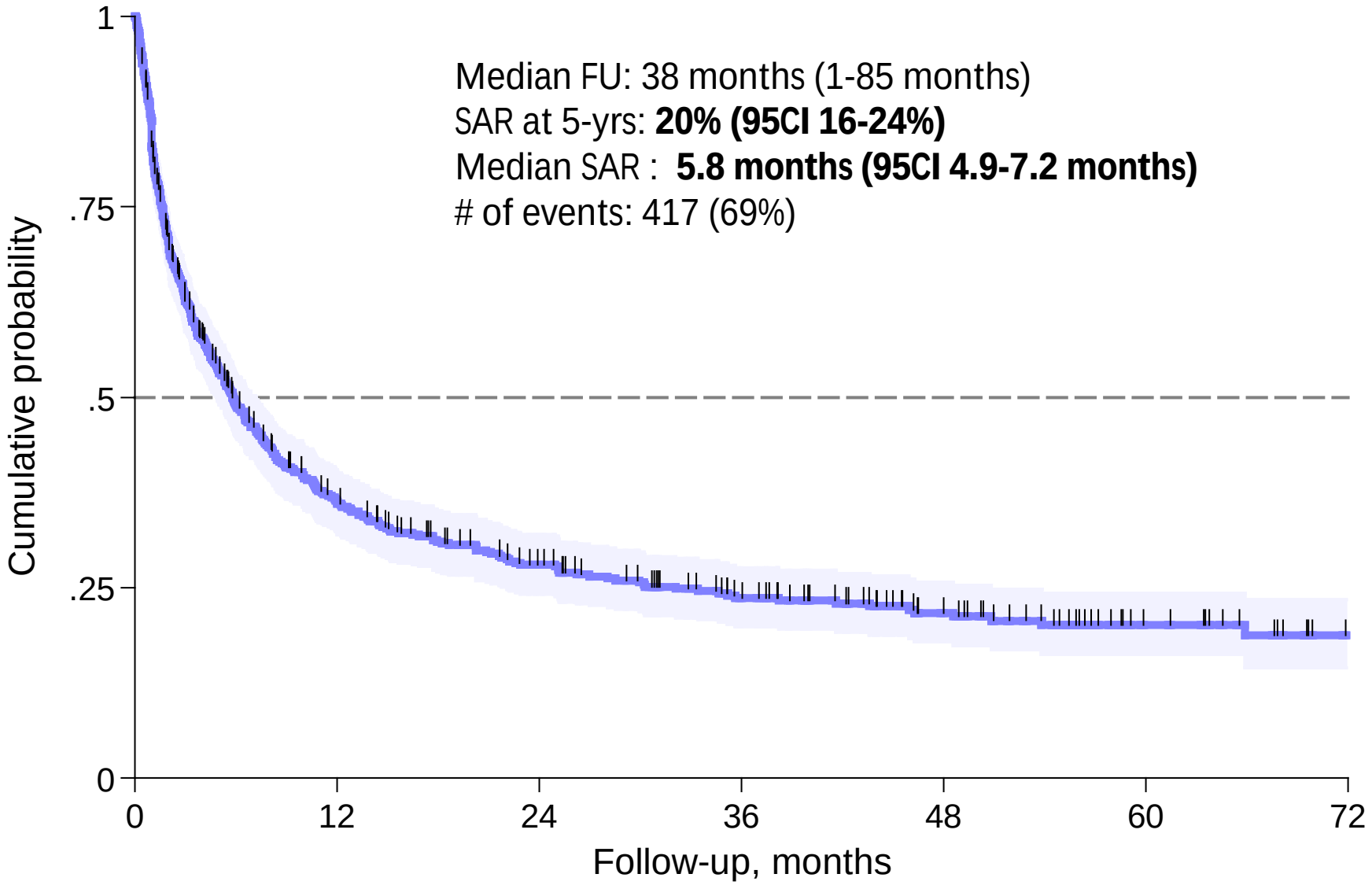
Variable	Status	N (%)
Time to relapse [n=184]	Median	8 mo (1-73)
Time to rel/ref.	Refractory	420 (69)
	Early (<12 mo)	119 (20)
	Late (>12 mo)	65 (11)
Salvage	HDT	96 (16)
	Potential HDT	120 (20)
	CR/PR not eligible	129 (21)
	Not eligible <PR	259 (43)
CHT 1st line [n=570]	Anthracycline	408 (72)
	With etoposide	112 (20)
	Other	50 (9)
Histology	PTCL	255 (42)
	AITL	107 (18)
	ALCL	115 (19)
	Other	127 (21)

* Age at ref/rel. ≤65 , response CR/PR, HCV and HBV negative, not treat with HDT in first line

Characteristics at diagnosis (n=604)

Variable [n]	Status	N (%)
Age	>60	276 (46)
PS [601]	>1	172 (29)
LDH [568]	>ULN	312 (55)
Stage [572]	III-IV	437 (76)
ENS [527]	>1	174 (33)
IPI [498]	0-1	119 (24)
	2	155 (31)
	3-5	224 (45)
Albumin [536]	<3.5 g/dL	242 (45)
NLR [569]	>6.5	169 (30)
PIT [485]	0-1	273 (56)
	2-4	212 (44)

Survival After R/R (SAR) (n=604)



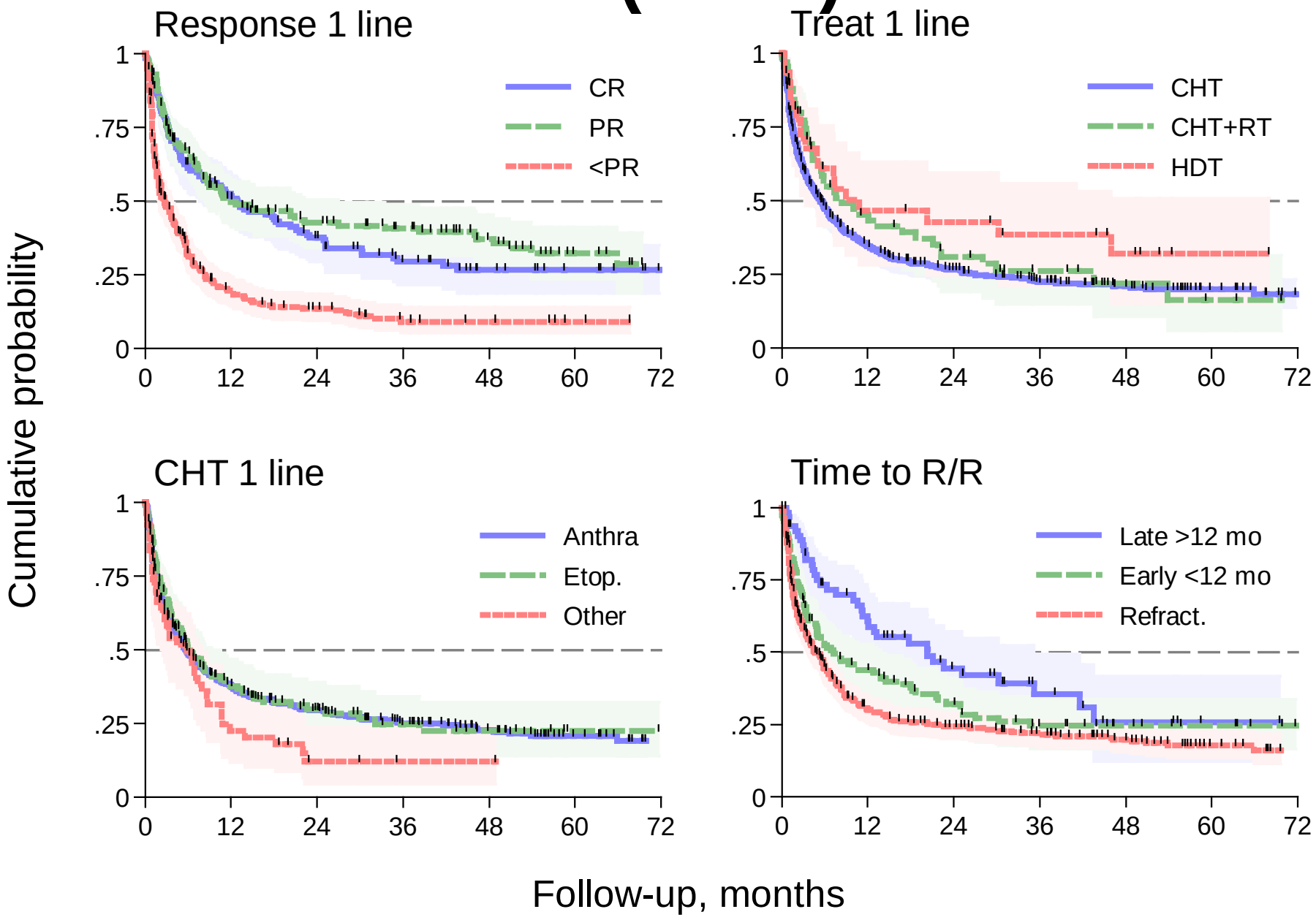
Univariate analysis (n=604)

Variable [n]	Status	5-yr OS% (95CI)	HR (95CI)	P-value
Age at ref/rel.	**≤ 60**	24 (18-30)	1.00	
	>60	15 (10-21)	1.32 (1.09-1.60)	0.005
Status	Relapse CR	27 (19-35)	1.00	
	Relapse PR	24 (9-42)	1.33 (0.81-2.20)	0.263
	Refractory PR	34 (25-44)	0.80 (0.59-1.08)	0.150
	Refractory	9 (5-14)	2.26 (1.78-2.88)	<0.001
Response 1st line	CR	27 (19-35)	1.00	
	PR	32 (23-41)	0.86 (0.65-1.15)	0.332
	<PR	9 (5-14)	3.99 (1.78-2.87)	<0.001
Treatment 1 line	CHT	20 (16-24)	1.00	
	CHT+RT	16 (6-31)	0.81 (0.59-1.11)	0.190
	HDT	32 (15-51)	0.66 (0.42-1.05)	0.078
Time to rel/ref [184]	**≤ 12 mo**	25 (17-34)	1.00	
FU <30 mo	> 12 mo	26 (12-41)	*0.61 (0.40-0.92)*	*0.018*
FU >30 mo		No PH	*3.59 (0.66-19.7)*	*0.141*

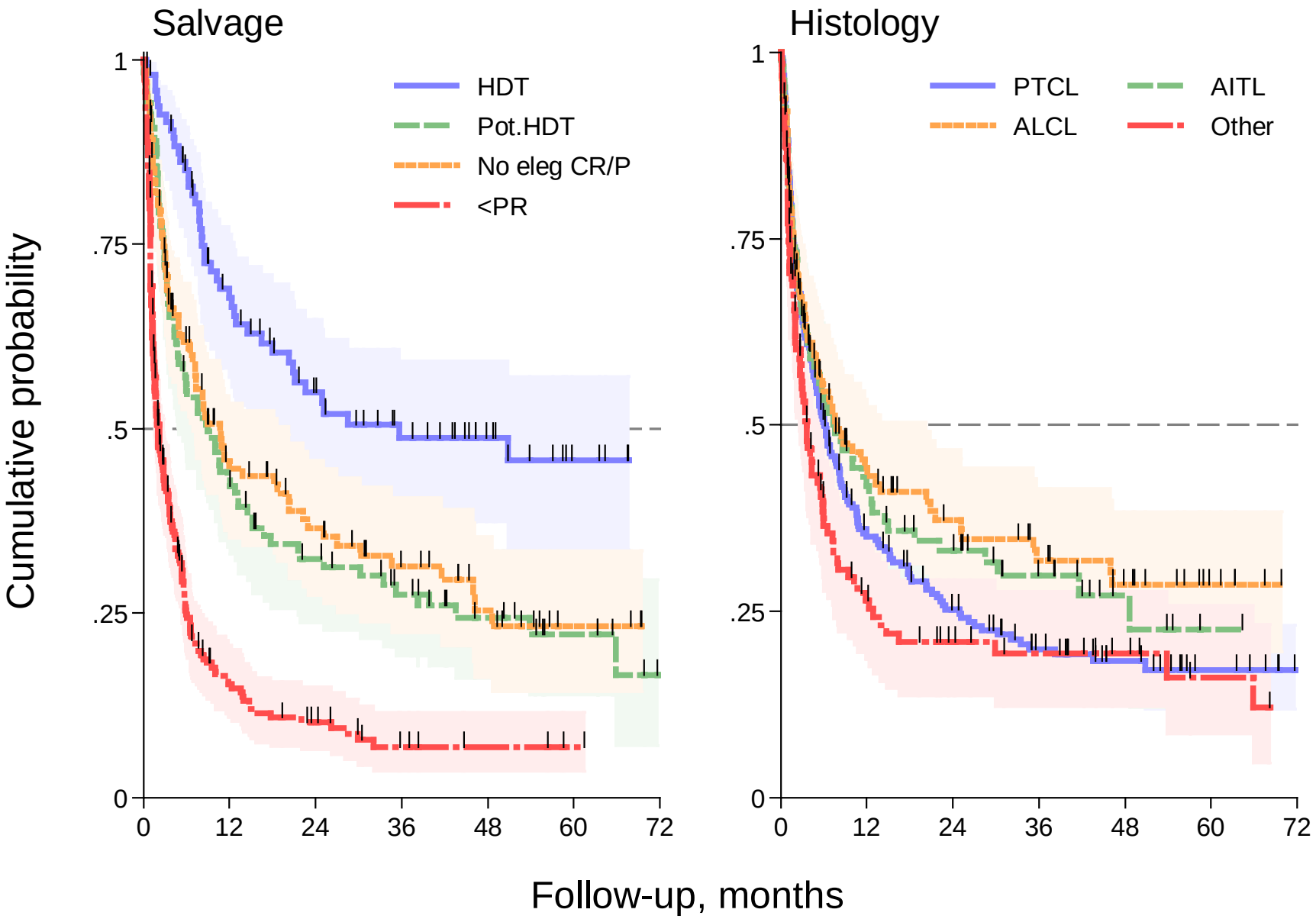
Univariate analysis (n=604)

Variable [n]	Status	5-yr OS% (95CI)	HR (95CI)	P-value
Salvage	No eleg. HDT, <PR	7 (4-12)	1.00	
	No eleg HDT, CR/PR	23 (14-33)	0.39 (0.30-0.51)	<0.001
	Eleg. HDT, CR/PR	22 (14-32)	0.42 (0.33-0.55)	<0.001
	HDT	46 (34-57)	0.21 (0.15-0.29)	<0.001
CHT [n=570]	Anthracycline	21 (16-26)	1.00	
	Etoposide	23 (14-32)	0.95 (0.74-1.22)	0.708
	Other	12 (4-24) [at 4 yrs]	1.35 (0.98-1.87)	0.067
Histology	PTCL	17 (12-23)	1.00	
	AITL	23 (12-35)	0.86 (0.65-1.13)	0.275
	ALCL	29 (20-38)	0.78 (0.60-1.03)	0.082
	Other	16 (9-26)	1.24 (0.97-1.60)	0.087
Area	South EU	20 (14-27)	1.00	
	EU	29 (17-43)	0.85 (0.59-1.23)	0.393
	USA	9 (1-29)	1.01 (0.74-1.38)	0.950
	South America	14 (8-21)	1.59 (1.25-2.02)	<0.001
	Far East	27 (16-39)	0.96 (0.70-1.33)	0.821

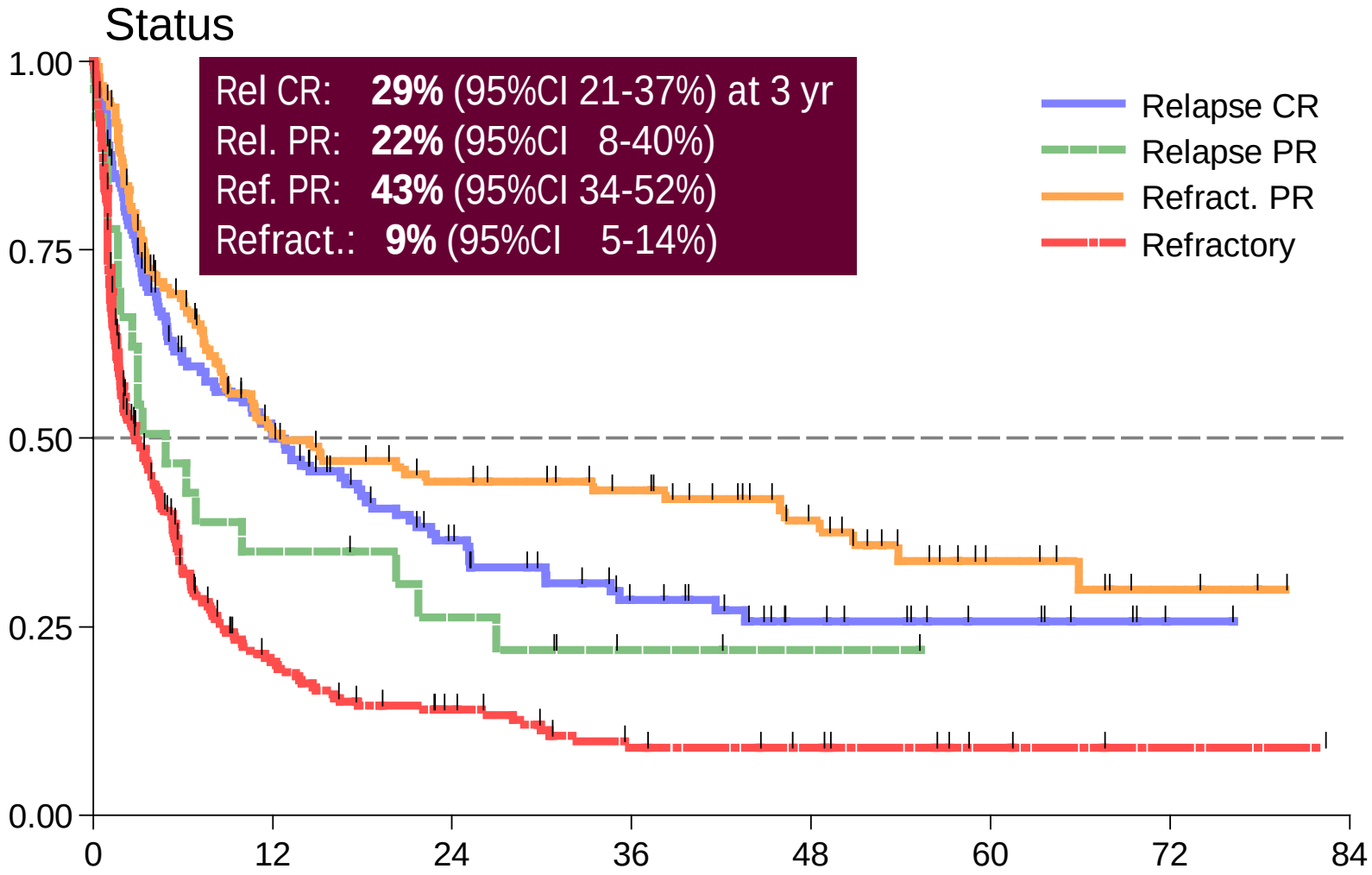
SAR (n=604)


Response 1 line
CR
PR
<PR
Treat 1 line
CHT
CHT+RT
HDT
CHT 1 line
Anthra
Etop.
Other
Time to R/R
Late >12 mo
Early <12 mo
Refract.
Cumulative probability
0
.25
.5
.75
1
0
12
24
36
48
60
72
Follow-up, months

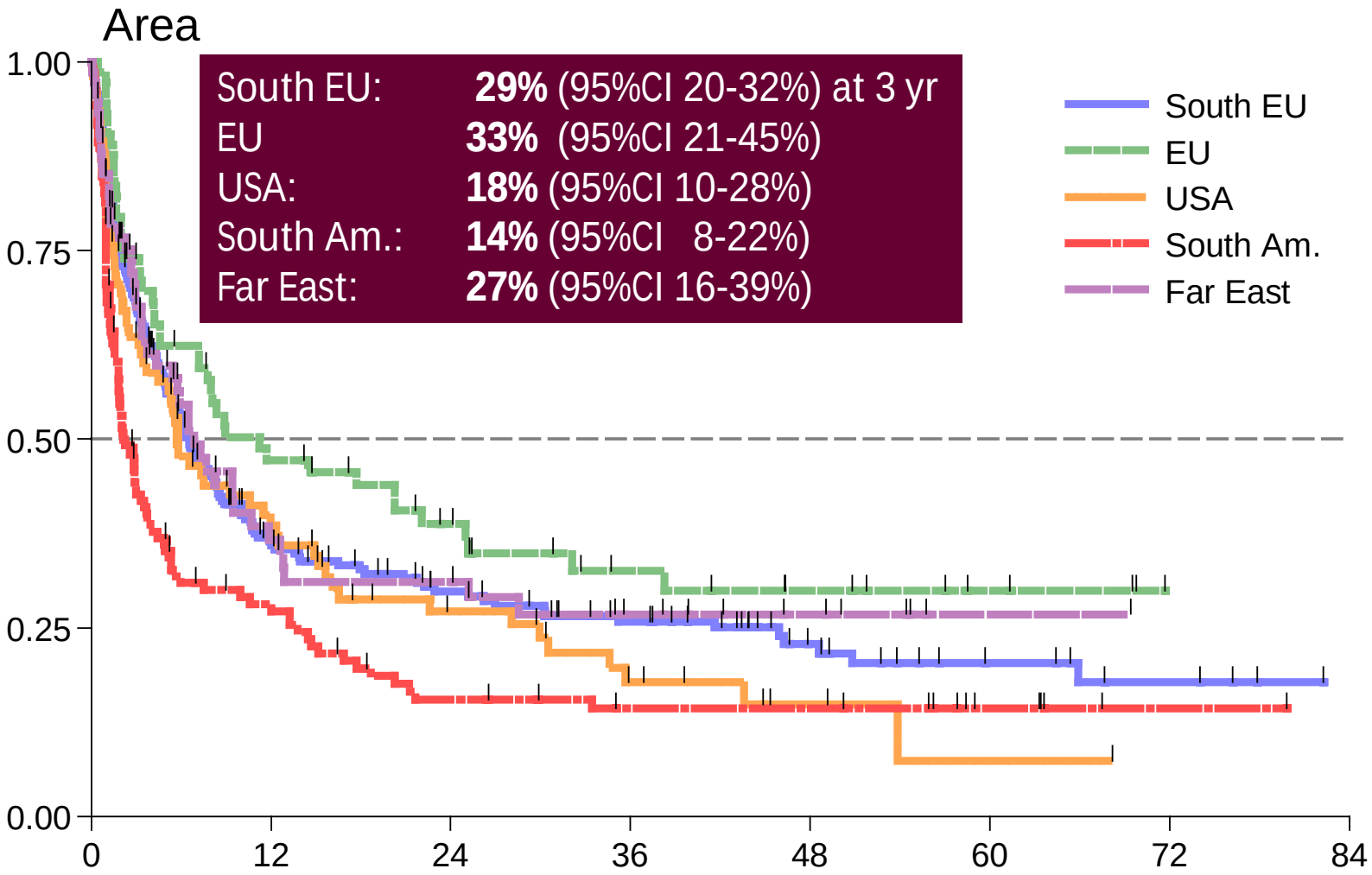
SAR (n=604)


Salvage
Histology
HDT
Pot.HDT
No eleg CR/P
<PR
PTCL
AITL
ALCL
Other
Cumulative probability
1
.75
.5
.25
0
0
12
24
36
48
60
72
Follow-up, months

SAR by status (N=631)



SAR by geographic area (N=631)



Histology by area (n=604)

N (%)	South EU	EU	USA	South Am.	Far East	Total
PTCL	112 (42)	18 (36)	38 (48)	66 (50)	21 (28)	*255 (42)*
AITL	52 (19)	12 (24)	20 (25)	5 (6)	15 (20)	*107 (18)*
ALCL	55 (20)	10 (20)	8 (10)	38 (29)	4 (5)	*115 (19)*
Other	50 (16)	10 (20)	13 (16)	20 (15)	34 (46)	*127 (21)*
Total	269	50	79	132	74	604

Potential salvage by area (n=604)

N (%)	South EU	EU	USA	South Am.	Far East	Total
HDT	58 (22)	8 (16)	9 (11)	11 (8)	10 (13)	*96 (16)*
Pot. HDT	42 (16)	9 (18)	17 (22)	32 (24)	20 (27)	*120 (20)*
CR/PR not eleg.	73 (27)	14 (28)	20 (25)	10 (8)	12 (16)	*129 (21)*
Not eleg <PR	96 (36)	19 (38)	33 (42)	79 (60)	32 (43)	*259 (43)*
Total	269	50	79	132	74	604

Advances in Malignant lymphomas:
The case of extranodal and T-cell lymphomas

Santiago de Chile
April 5-6, 2016

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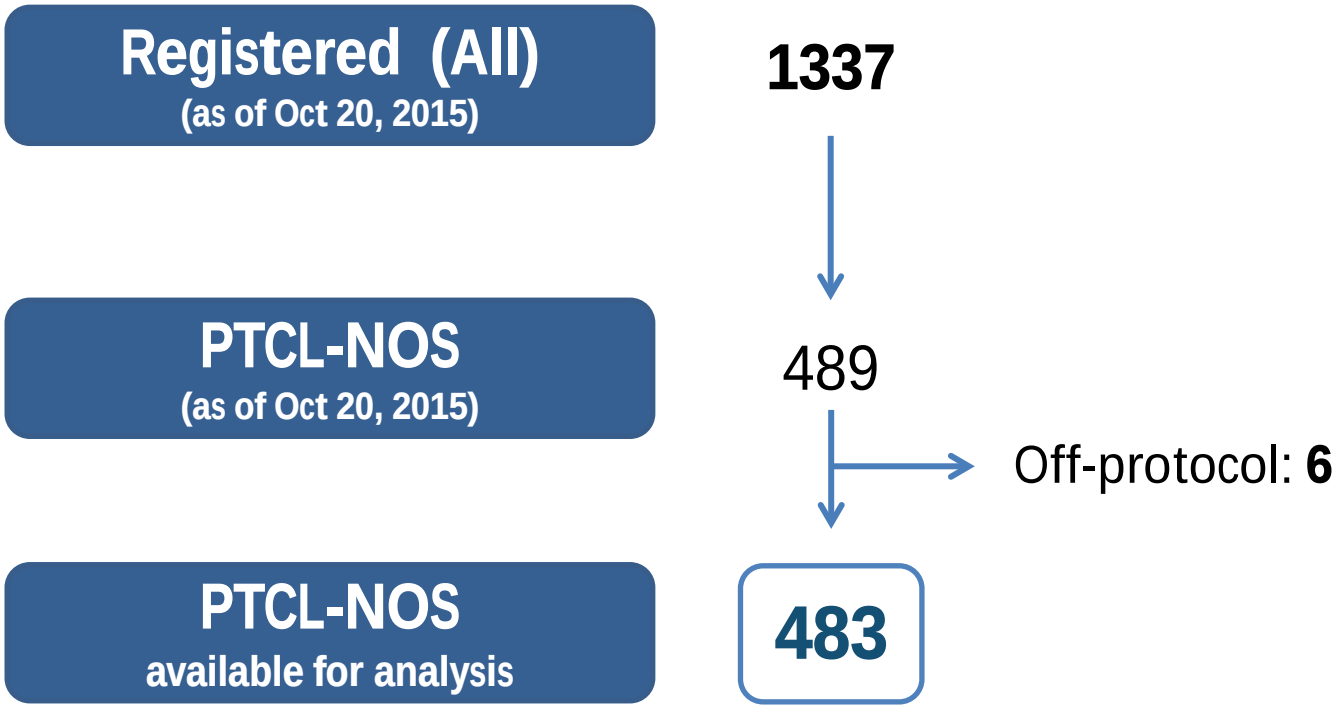
Massimo Federico

T-Cell Project

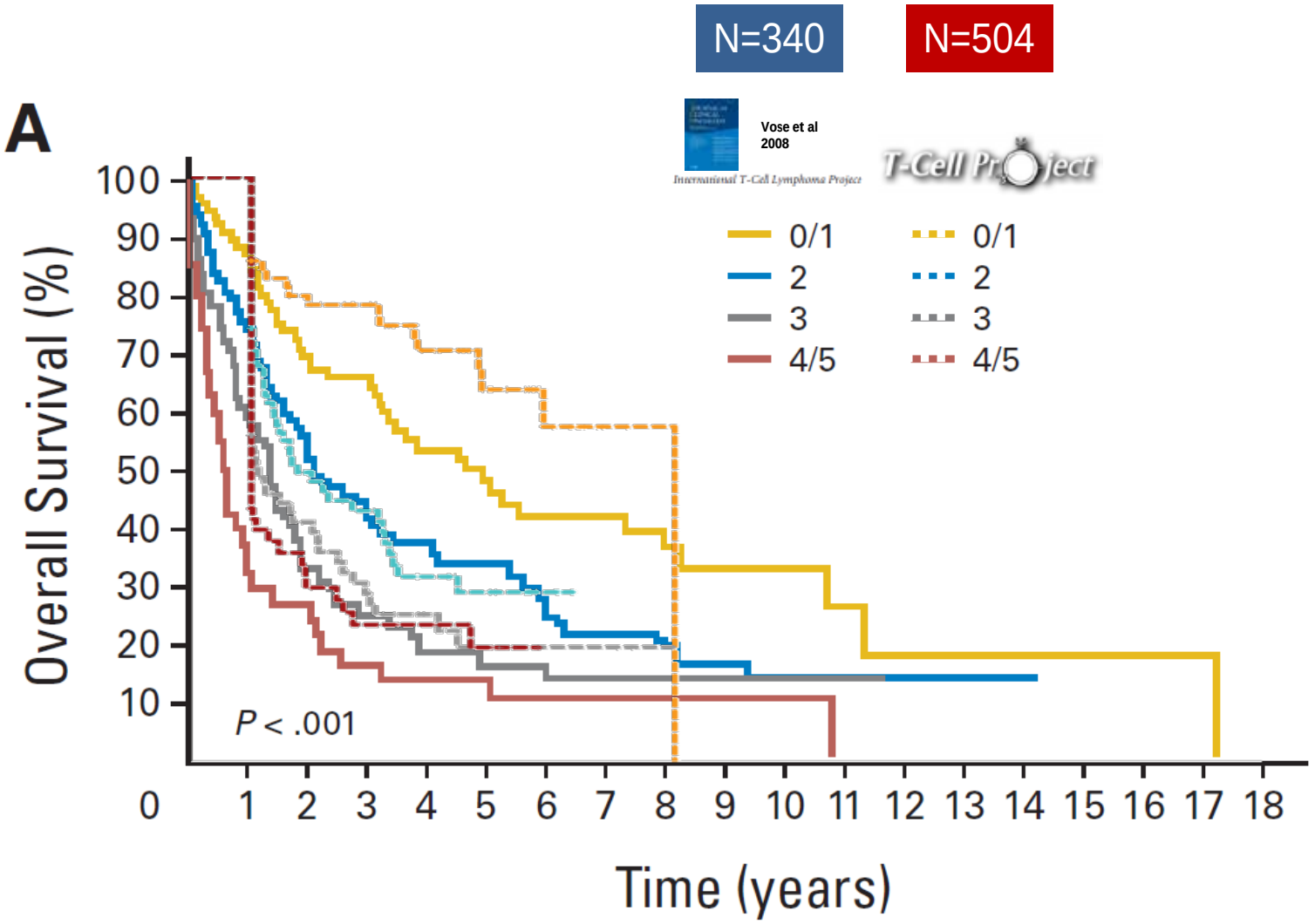
Proposed Prognostic model for PTCL-NOS developed on TCP data

Patients registered as of October 20, 2015.
Data updated as of November 2, 2015.
Report date: November 27, 2015
Analyses by: Luigi Marcheselli, Monica Bellei

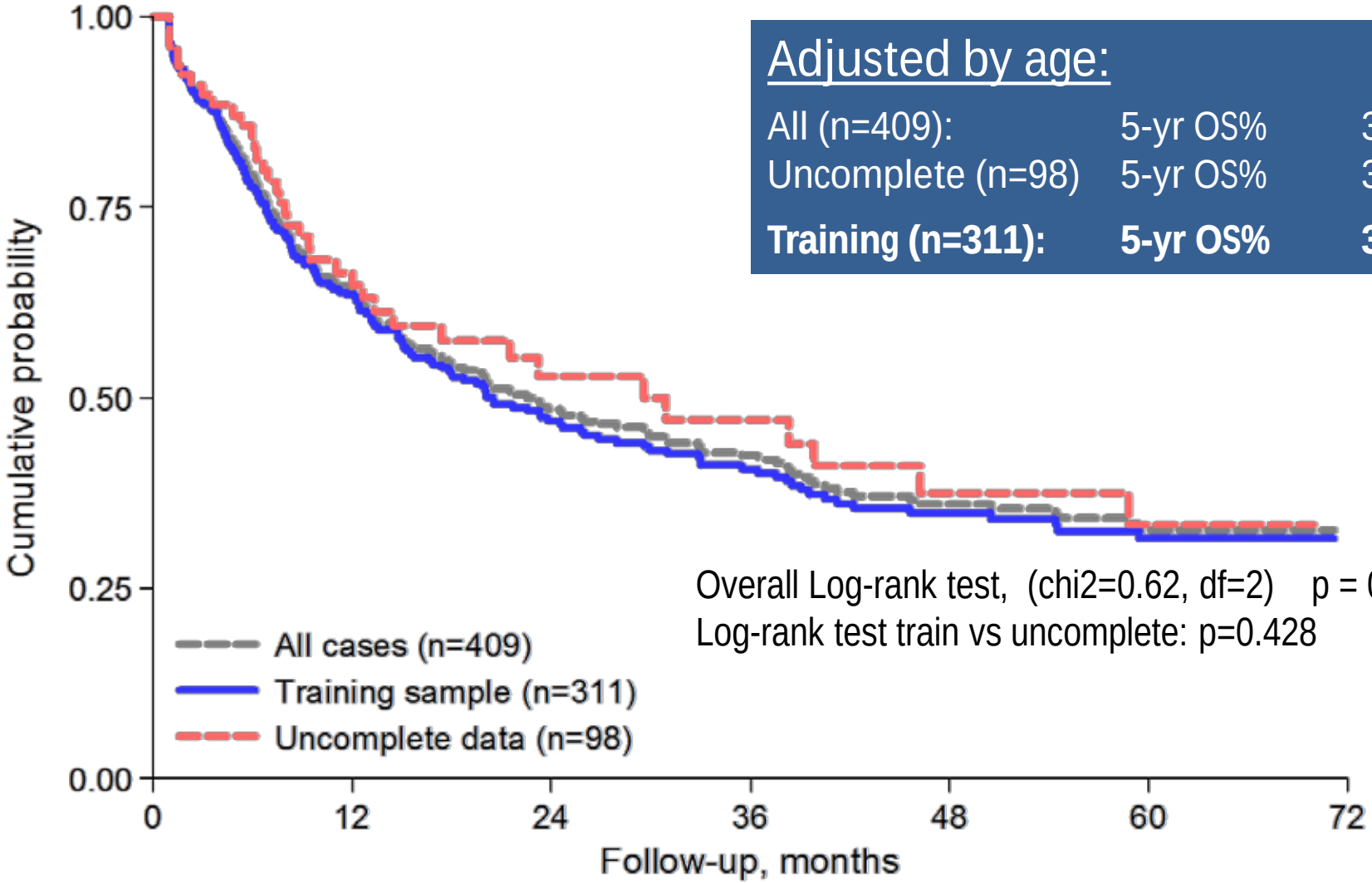
Flow chart, PTCL-NOS



Overall Survival of PTCL-NOS by IPI



Overall survival PTCL-NOS



Adjusted by age:

All (n=409):	5-yr OS%	33
Uncomplete (n=98)	5-yr OS%	33
Training (n=311):	**5-yr OS%**	**32**

Overall Log-rank test, (chi2=0.62, df=2) p = 0.733
Log-rank test train vs uncomplete: p=0.428

Variables with potential prognostic impact

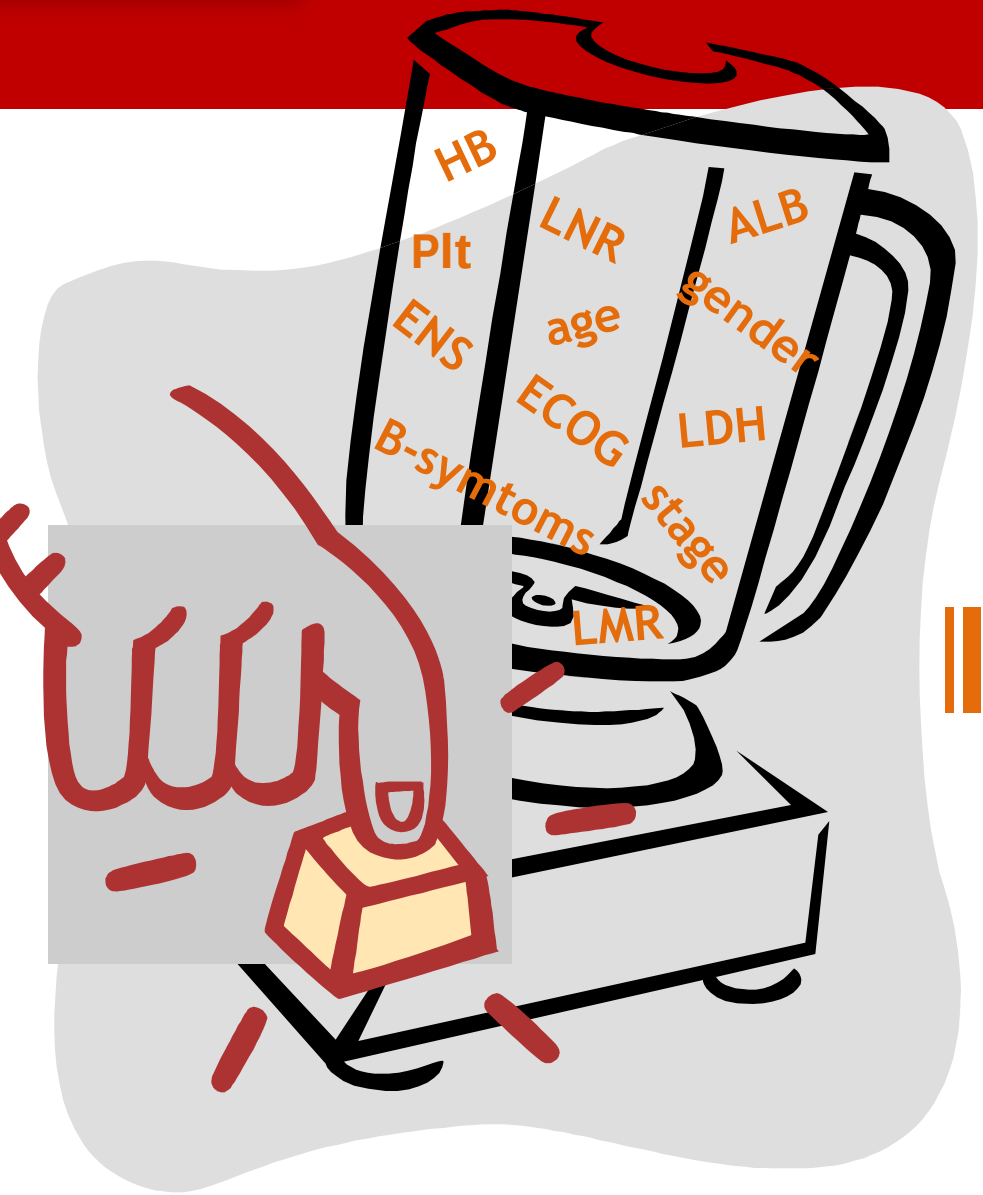
- chosen from literature among those reported with a prognostic impact on survival in this subset

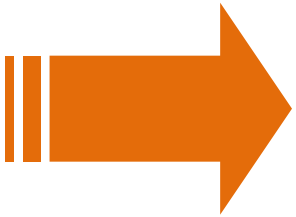
	Variable
1.	Age>60 yrs
2.	LDH >ULN
3.	Albumin, <3.5 g/dL
4.	Hemoglobin <12, g/dL
5.	Platelets <150/mm^3
6.	Lymphocyte to Monocyte Ratio (LMR) ≤2.1
7.	Neutrophil to Lymphocyte Ratio (NLR) >6.5
8.	ECOG Performance Status >1
9.	Stage III-IV
10.	B-symptoms
11.	Extra nodal sites>1
12.	Male Gender

OS: univariate Cox regression Training sample(n=311)

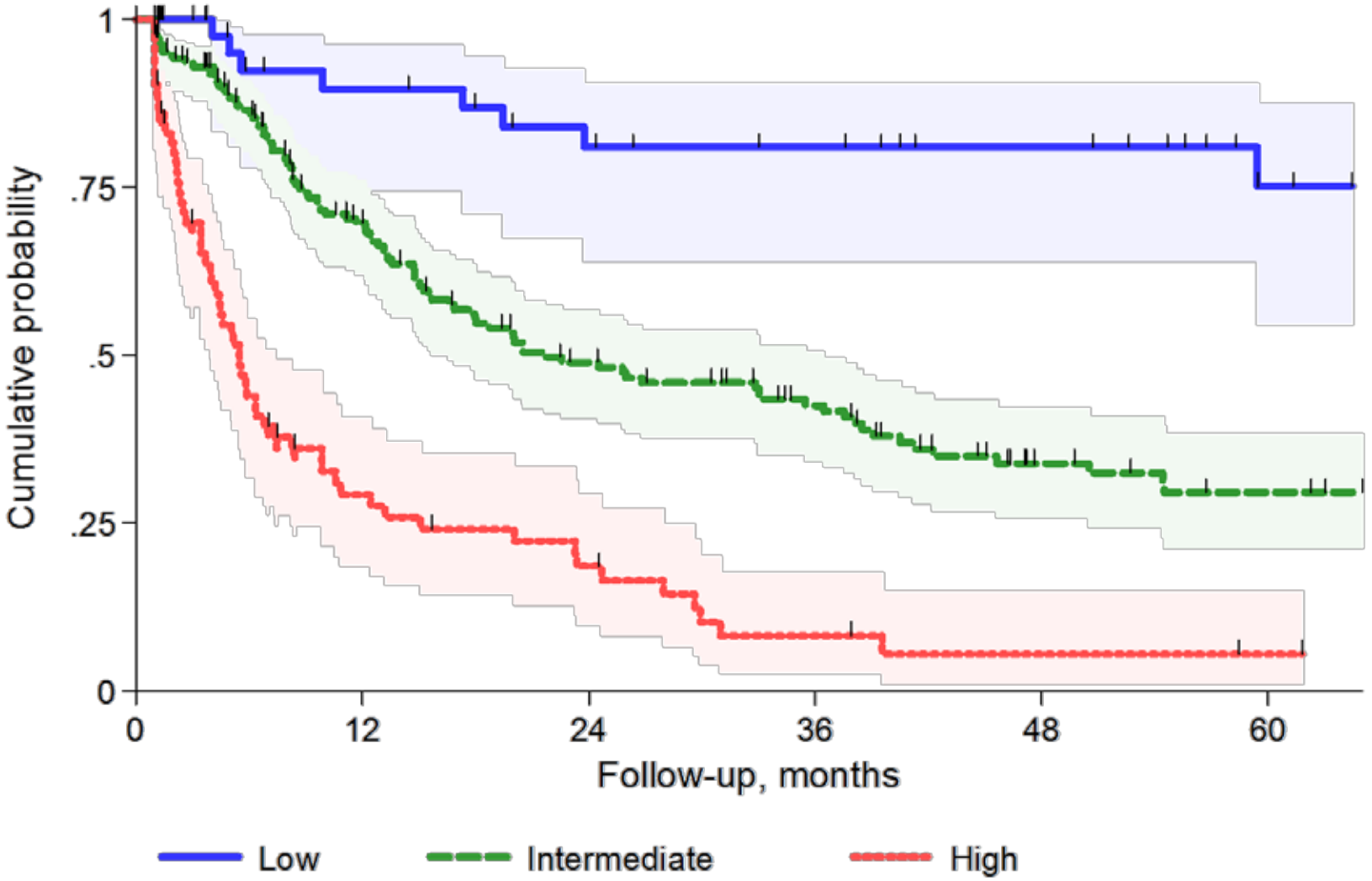
Factor	%	HR	CI95	P
Age >60	55	**1.25**	**0.92-1.70**	0.151
Male gender	62	**1.52**	**1.09-2.12**	0.013
PS > 1	26	**2.60**	**1.89-3.57**	<0.001
Stage III-IV	76	**2.18**	**1.44-3.29**	<0.001
ENS >1	28	**1.17**	**0.84-1.62**	0.354
B symptoms	44	**1.79**	**1.32-2.42**	<0.001
LDH > ULN	53	**1.98**	**1.45-2.72**	<0.001
Hb < 12 g/dL	39	**1.43**	**1.05-1.94**	0.022
Albumin <3.5 g/dL	38	**2.63**	**1.94-3.58**	<0.001
LMR <2.1	41	**1.55**	**1.15-2.10**	0.005
NLR >6.5	21	**2.24**	**1.60-3.13**	<0.001
Plt <150/mm^3	21	**1.52**	**1.07-2.18**	0.020

TCP Model: The Winners are…

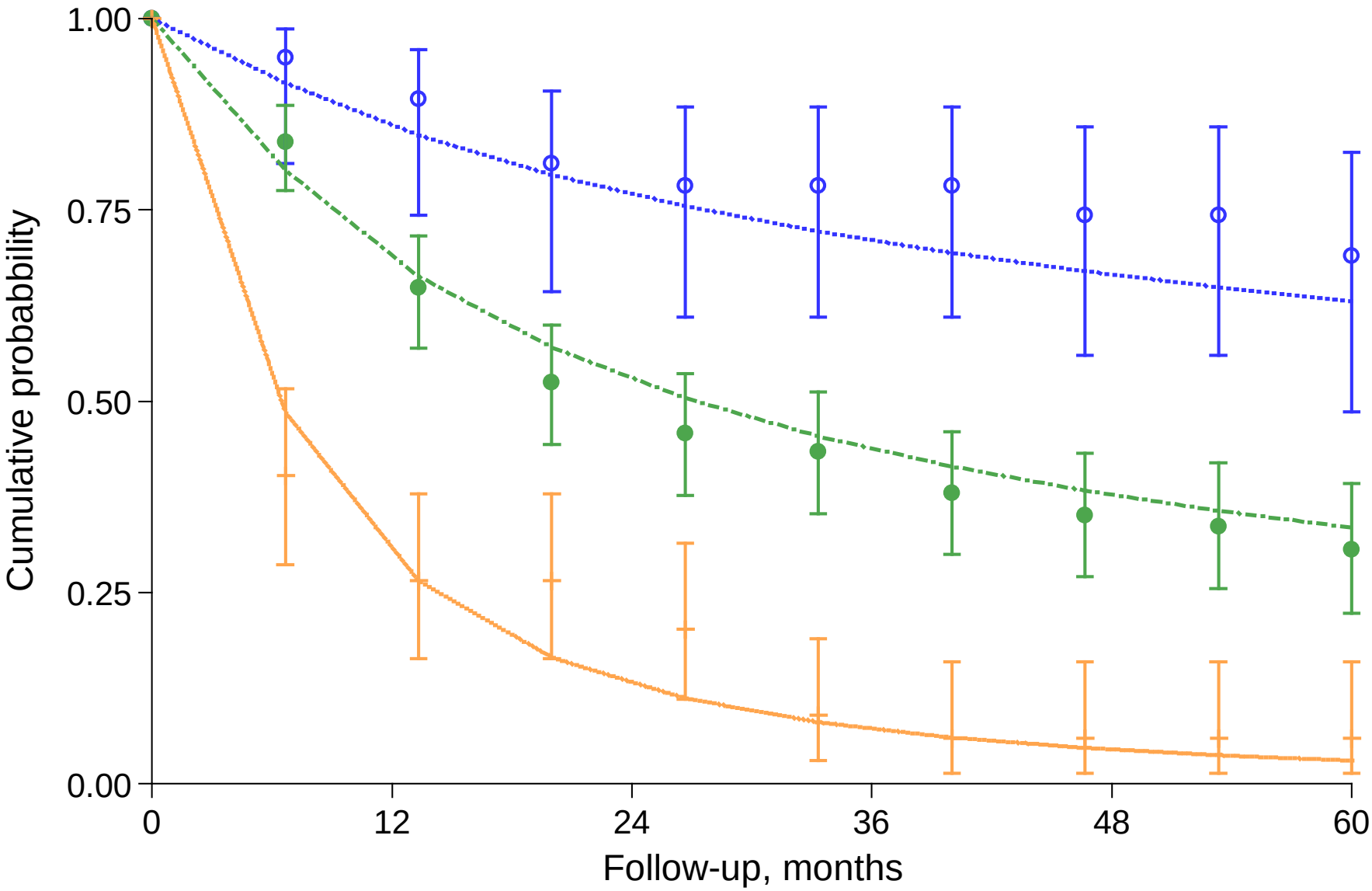




OS by score (training, n=310)



Calibration (score with ANC>6500)



Now this is not the end. It is not even the beginning of the end. but it is, perhaps, the end of the beginning.

The Lord Mayor's Luncheon, Mansion House

"The End of the Beginning"

November 10, 1942

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