V JORNADA GELL 2025
CLÍNICA DEL GRUPO DE ESTUDIO LATINOAMERICANO DE LINFOPROLIFERATIVOS

GELL
Grupo de Estudio Latinoamericano de Linfoproliferativos

Nuevo Proyecto del T cell Project: TCP 2.1

MASSIMO FEDERICO, STEFANO LUMINARI, and Co ..

MODENA/LECCE, ITALY

UNIMORE
UNIVERSITÀ DEGLI STUDI DI MODENA E REGGIO EMILIA

Associazione ANGELA SERRA per la Ricerca sul Cancro
Sede di Lecce "ITALIA MEMMI FERRARI"

Con el Aval:

Conflict of Interest Disclosure

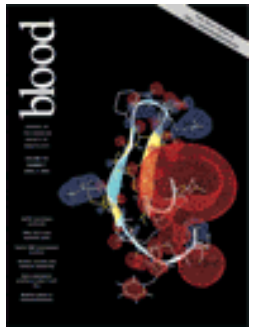
I hereby declare the following potential conflicts of interest concerning my presentation:

NONE

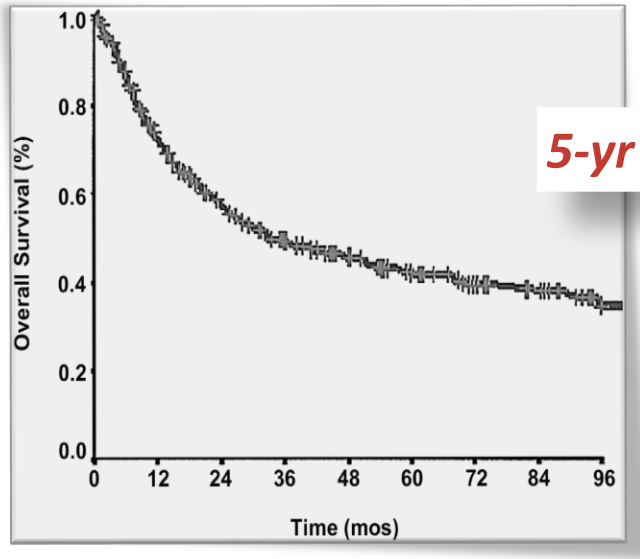
Peripheral T-cell lymphoma unspecified (PTCL-U): a new prognostic model from a retrospective multicentric clinical study

Andrea Gallamini, Caterina Stelitano, Roberta Calvi, Monica Bellei, Daniele Mattei, Umberto Vitolo, Fortunato Morabito, Maurizio Martelli, Ercole Brusamolino, Emilio Iannitto, Francesco Zaja, Sergio Cortelazzo, Luigi Rigacci, Liliana Devizzi, Giuseppe Todeschini, Gino Santini, Maura Brugiatelli, and Massimo Federico, for the Intergruppo Italiano Linfomi

Retrospective studies



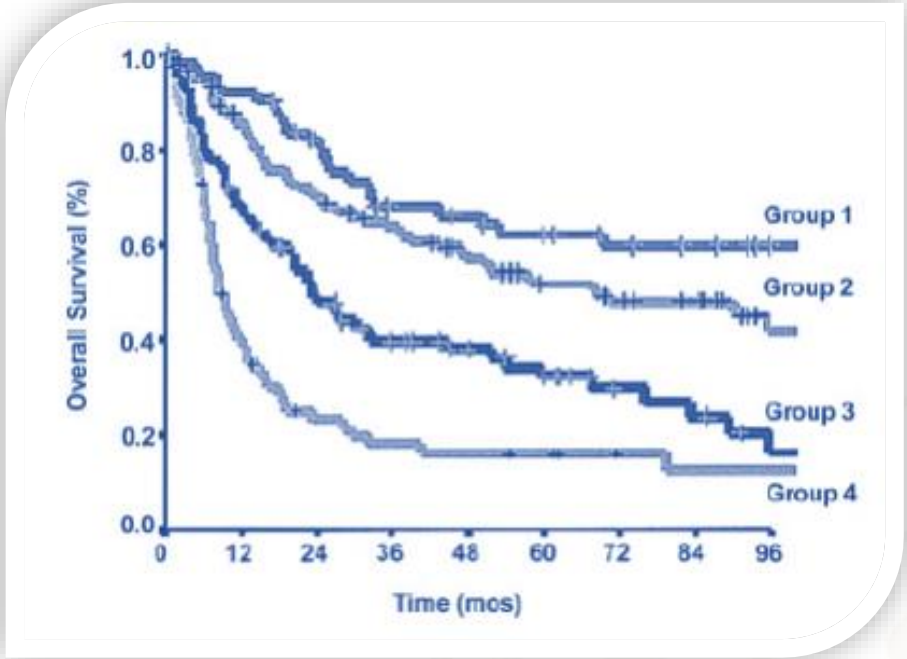
103(7), 2004



5-yr OS = 43.0%

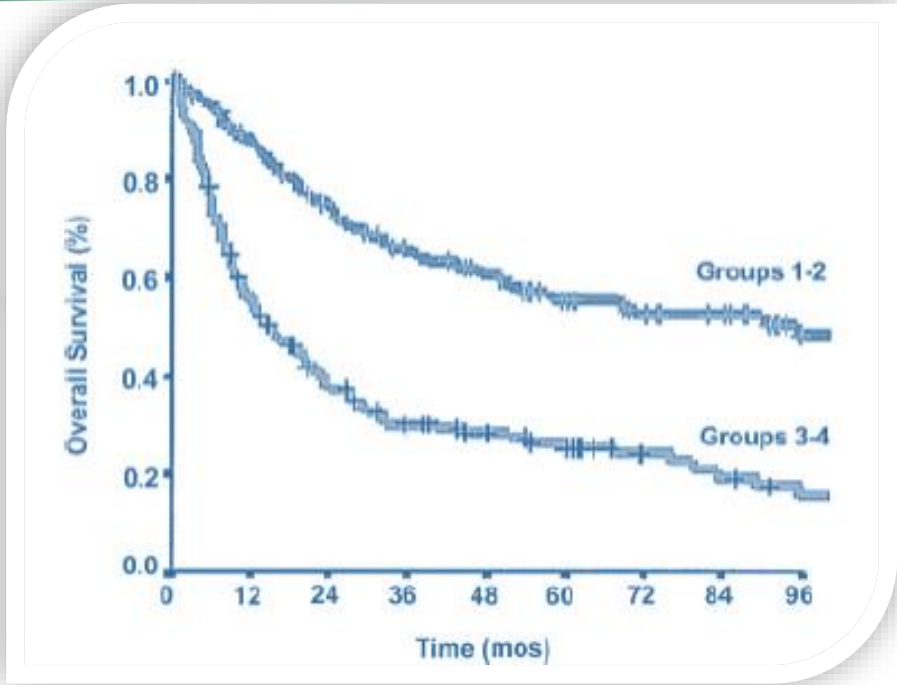
Patients	385
Median age	54 yr (15-96)
Median follow-up	42 mos
Treatment	
CHOP/CHOP like	78%
HDT-ASCT	12%

Factors	
Age	≤ 60 yrs *vs* > 60 yrs
ECOG-PS	0-1 *vs* 2-4
LDH	Normal *vs* Elevated
BM biopsy	Negative *vs* Positive



PIT

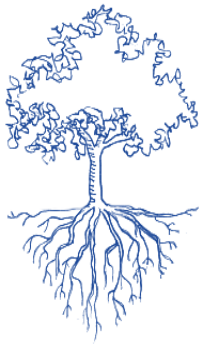
	Risk factors	Pts	
Group 1	0	64	
Group 2	1	108	
Group 3	2	83	
Group 4	3-4	67	*P=0.0000*
Group 1-2	***0-1***	***182***	
Group 3-4	***2-4***	***142***	***P=0.0000***



simplified PIT

International T-cell Project

- 1,314 cases with PTCL or NK/T cell lymphoma
  (161 excluded; 1,153 analyzed)
- Newly diagnosed 1990-2002
- 22 sites globally
- Expert Hematopathology review
- Correlation with clinical outcomes



International T-Cell Lymphoma Project

JOURNAL OF CLINICAL ONCOLOGY ORIGINAL REPORT

International Peripheral T-Cell and Natural Killer/T-Cell Lymphoma Study: Pathology Findings and Clinical Outcomes

International T-Cell Lymphoma Project

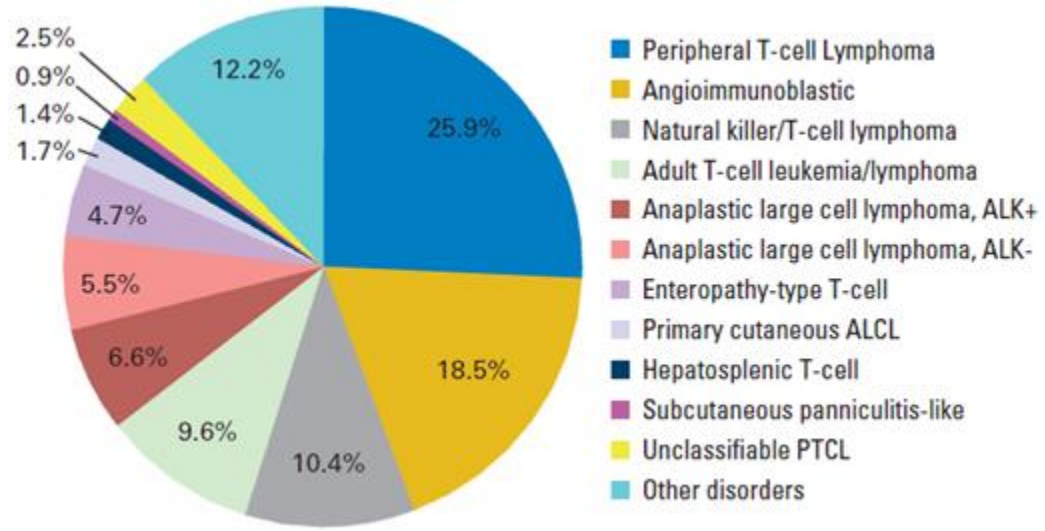


Fig 1. Distribution of 1,314 cases by consensus diagnosis.

Subtypes distribution among regions

Table 1. Major Lymphoma Subtypes by Geographic Region

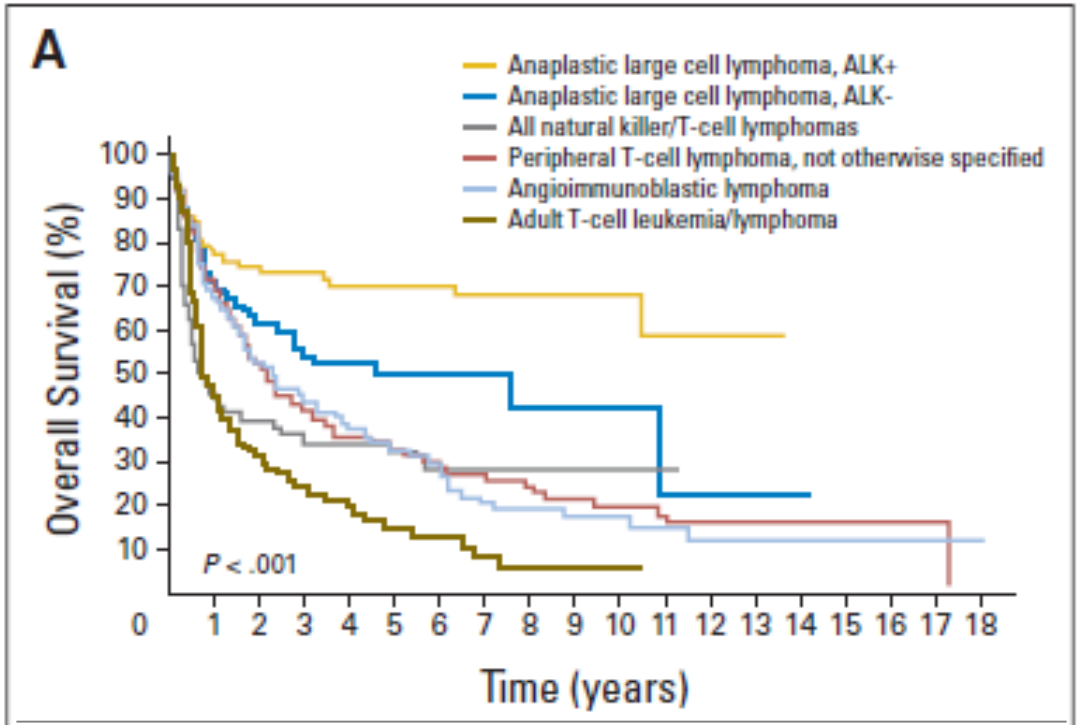
Subtype	% North America	% Europe	% Asia
PTCL-NOS	34.4	34.3	22.4
Angioimmunoblastic	16.0	28.7	17.9
ALCL, ALK positive	16.0	6.4	3.2
ALCL, ALK negative	7.8	9.4	2.6
NKTCL	5.1	4.3	22.4
ATLL	2.0	1.0	25.0
Enteropathy-type	5.8	9.1	1.9
Hepatosplenic	3.0	2.3	0.2
Primary cutaneous ALCL	5.4	0.8	0.7
Subcutaneous panniculitis-like	1.3	0.5	1.3
Unclassifiable T-cell	2.3	3.3	2.4

Abbreviations: PTCL, peripheral T-cell lymphoma; NOS, not otherwise specified; ALCL, anaplastic large-cell lymphoma; NKTCL, natural killer/T-cell lymphoma.

Overall survival

Vose et al.
2008

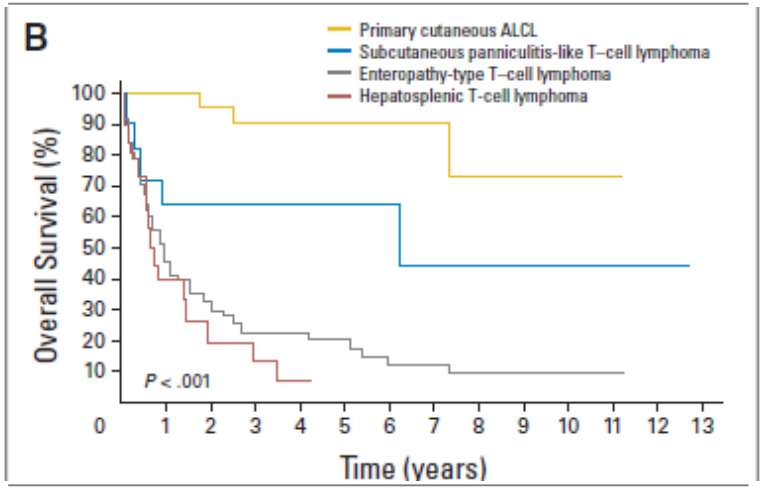
International T-Cell Lymphoma Project



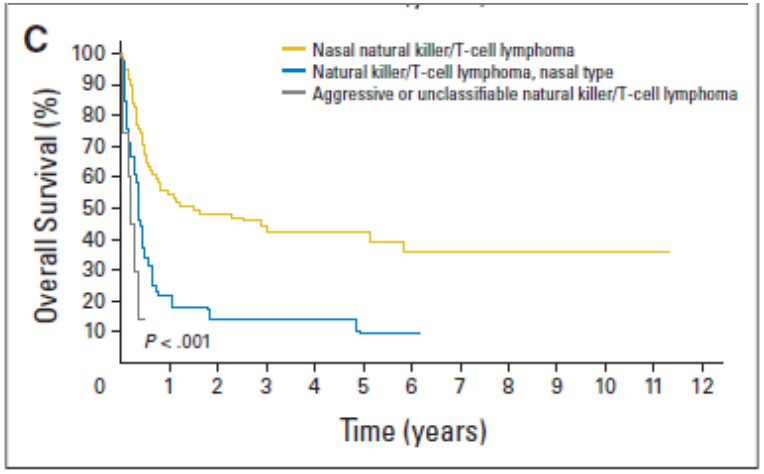
5-yr OS of most frequent subtypes

ALK+ ALCL	ALK– ALCL	PTCL-NOS	AITL	NKTCL	ATLL
70%	49%	32%	32%	32%	14%

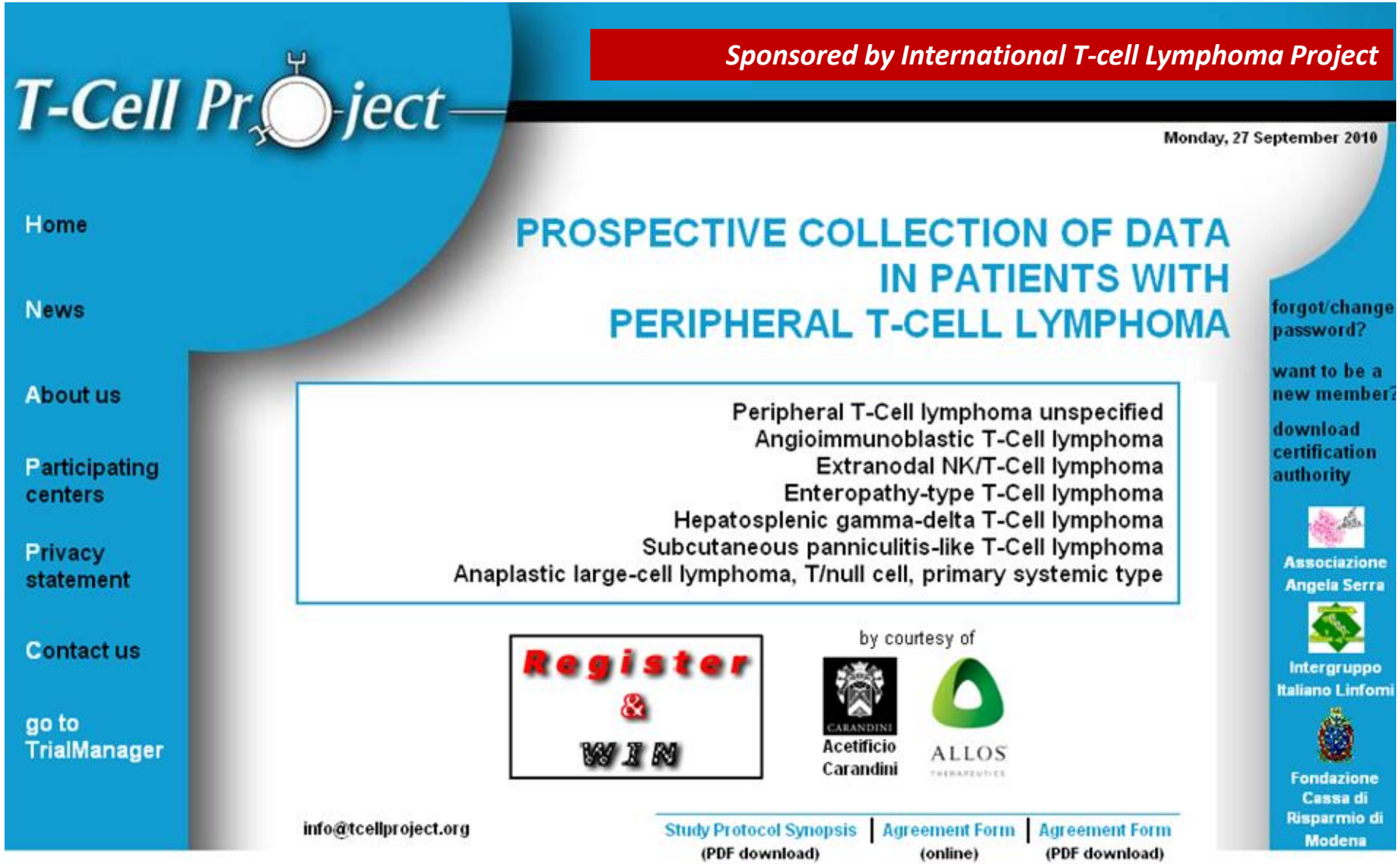
Less frequent subtypes



NKTCL



Study start: September 1, 2006



Why a prospective collection of data?

- to achieve a more controlled and homogeneous collection of data
- to have a very limited case exclusions
- to have homogeneity of inclusion criteria

Why a large cooperative study?

- to achieve a faster accrual
- to reduce time-dependent biases
- to limit selection biases

Parameters availability

Index	Cases (N=total)	Cases (N=used)	%	diagnosis year	publication year
IPI	3273	1385	42	1982-87	1993
ILI	987	429	43	1986-96	2000
FLIPI	4167	1795	43	1985-92	2004
FLIPI2	1057	939	89	2003-05	2009

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

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

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

Massimo Federico

Dept. of Diagnostic, Clinical and Public Health Medicine
Univesrity of Modena and Reggio Emilia

Registrations by Region

Sites

Recruiting	77	1695 Pts	100%
Active, Not Yet Recruiting	7	-	-

*active. not yet recruiting

USA
8 | 412 | 24%

MSKCC
MDACC
UNMC
Stanford
CCF
FHCRC
WUStL
Yale
SKCC*

Middle East
2 | 38 | 3%

Sheba Medical Center-Israel Haifa RAMBAM
Sourasky Medical Center-Israel*

Europe
56 | 7

ACCRUAL COMPLETED ON 2018

South America
7 | 342 | 20%

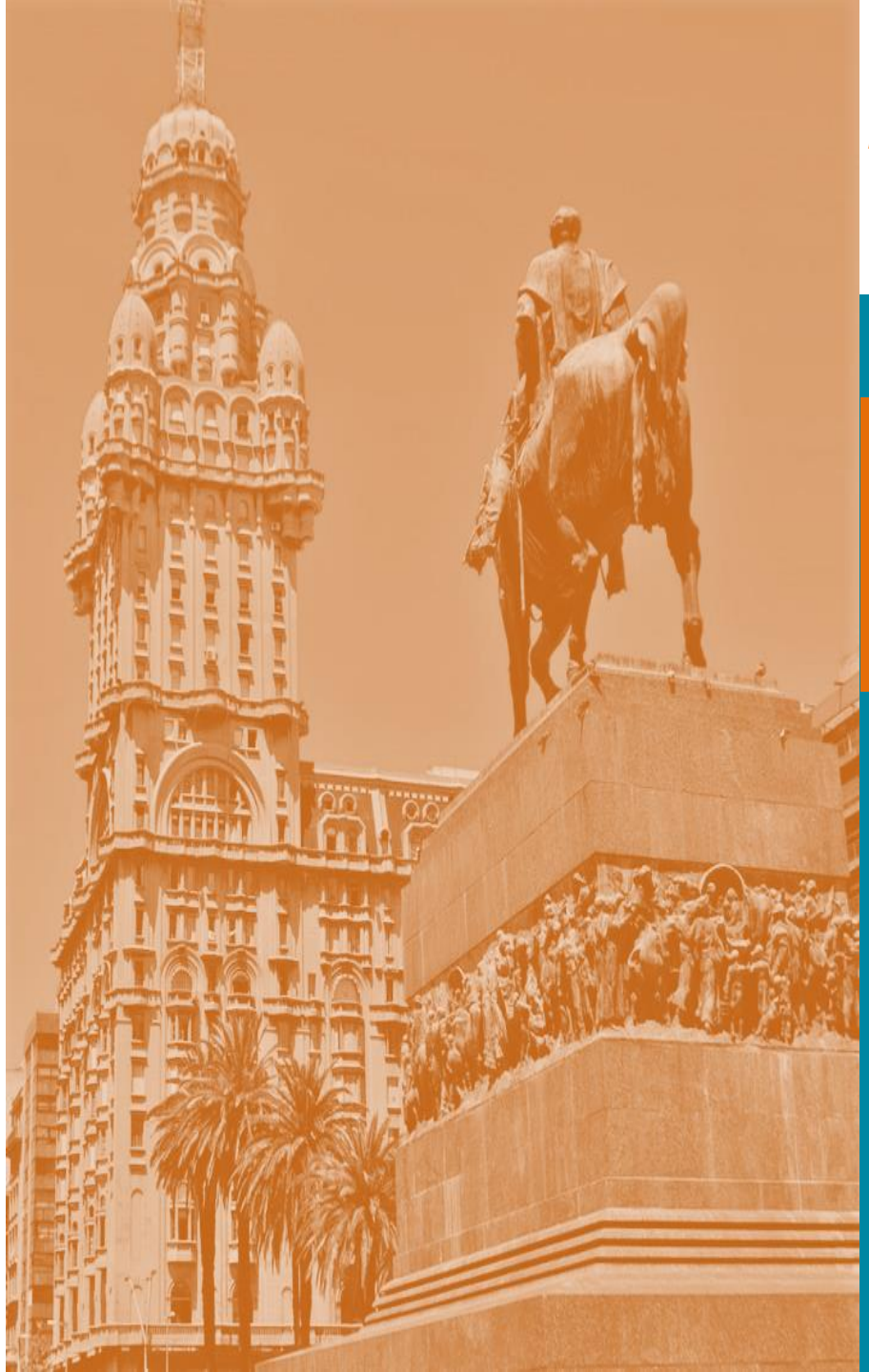
Argentina (3)
Brazil (2)
Chile (1)
Uruguay (1)

Asia
2 | 149 | 9%

SMC-South Korea
QMH-Hong Kong

Oceania
1 | 8 | <1%

Concord Hospital, Australia



Investigator Meeting

Montevideo ••• April 12-13, 2018

T-Cell Project

Report on the T-Cell Project

Massimo Federico
Monica Bellei
Stefano Luminari

Dipartimento di Medicina Diagnostica, Clinica e di Sanità Pubblica

Università di Modena e Reggio Emilia

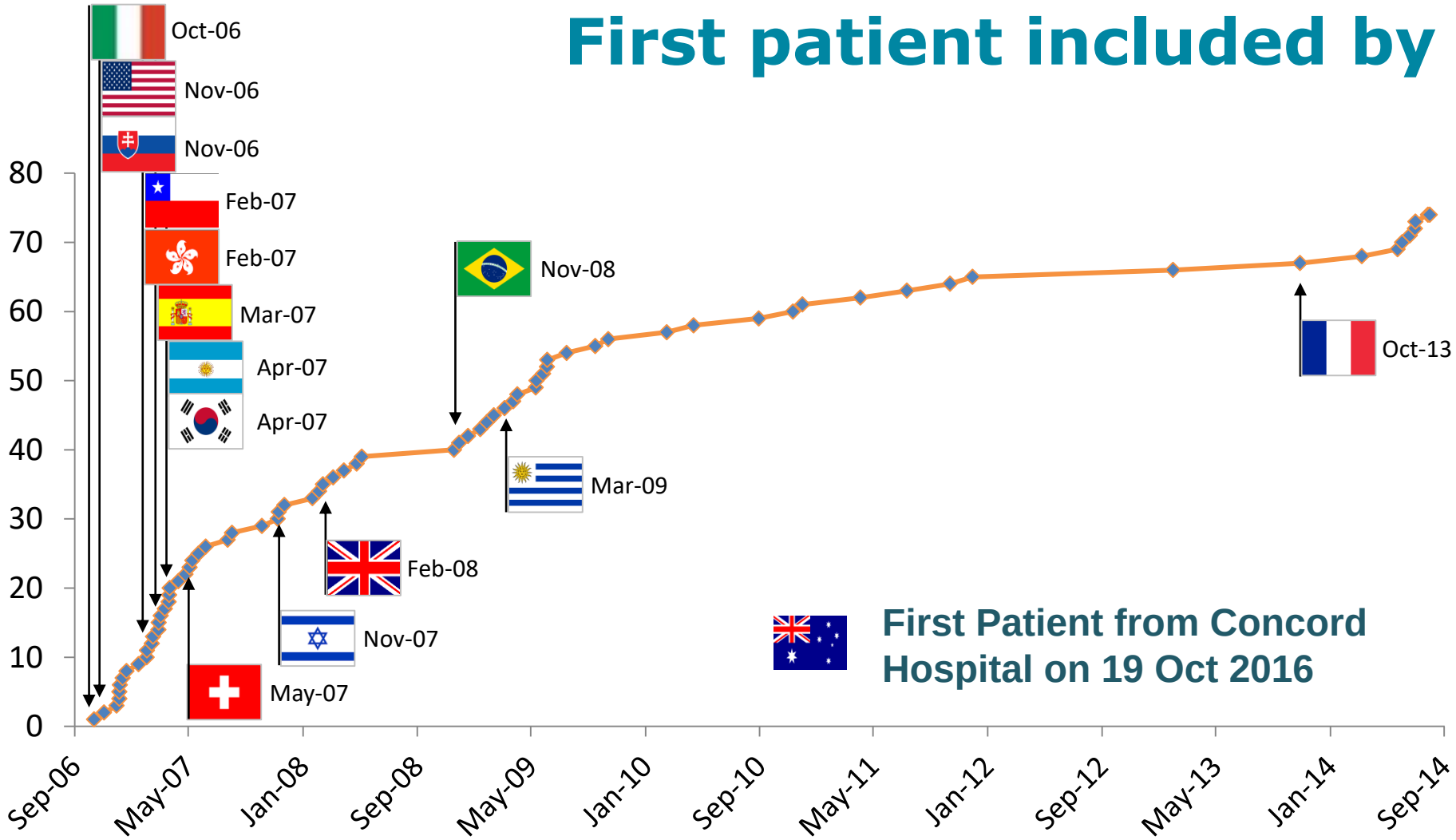
Status of the T-cell Project

(March 20, 2018)

- ✓ **89 authorized** sites
- ✓ **77 active** sites *(at least 1 Pt in)*
- ✓ **15 active** countries *(at least 1 Pt in)*
- ✓ **5 geographic areas**
  - Europe
  - North America
  - South America
  - Middle/Far East
  - Oceania

- ✓ **1,611 cases** of PTCL or NK/T-cell lymphoma registered

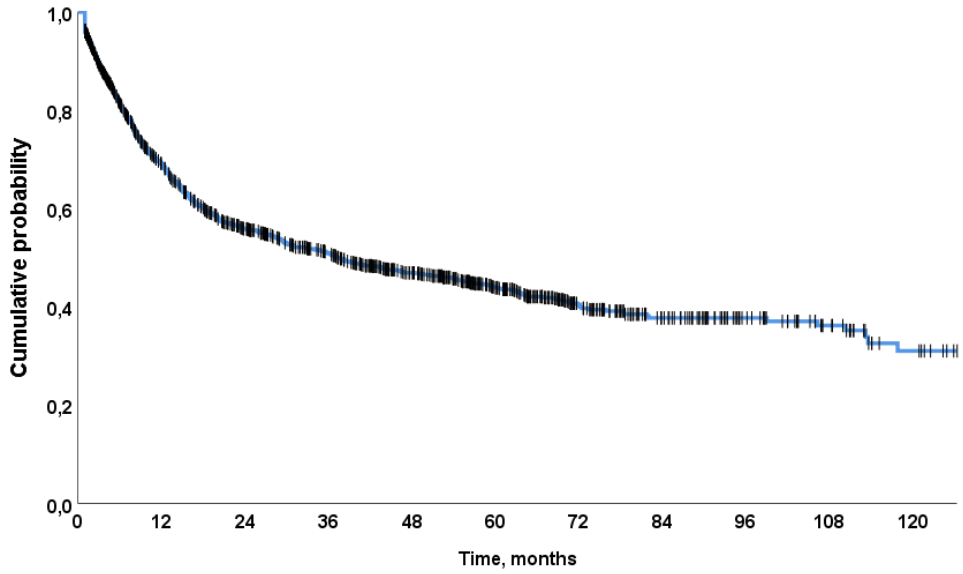
First patient included by Country



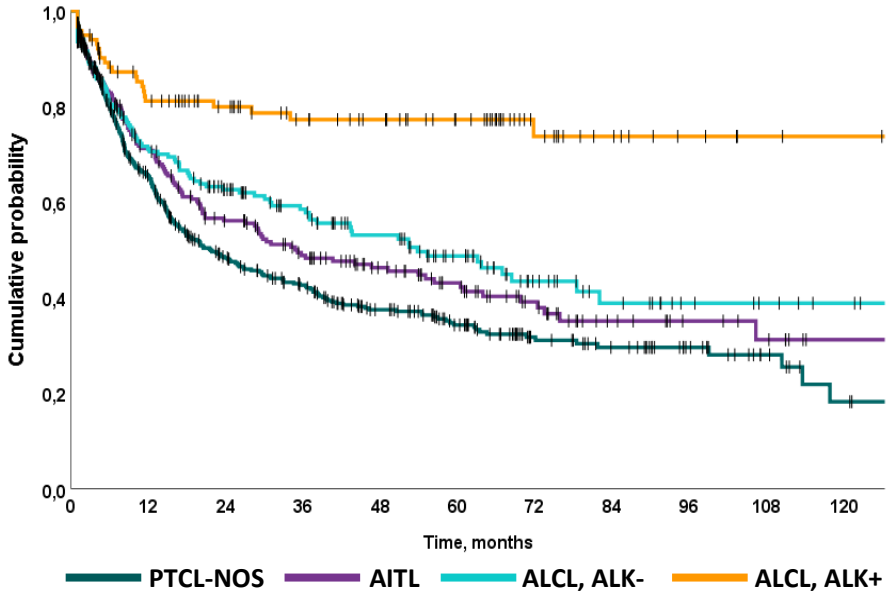
Active sites over time

25	33	39	51	56	59	62	65	65	66	67	74

Overall Survival

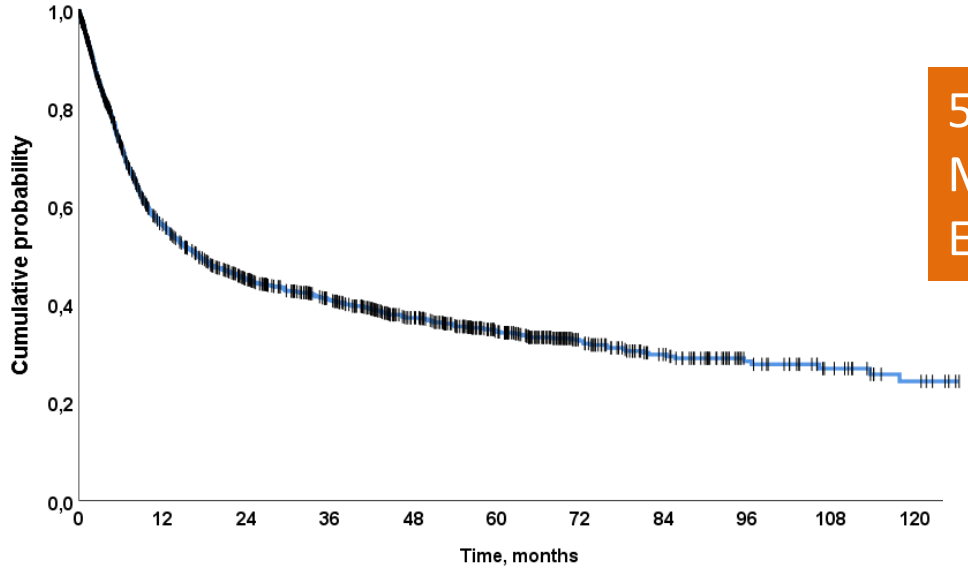


Median follow-up: **43 months**
5-yrs OS: **44%** (95% CI 41-47)
Median OS: **37 months** (95% CI 29-46)
Deaths: 690 (**47%**)
Main cause of death: Lymphoma (**68%**)



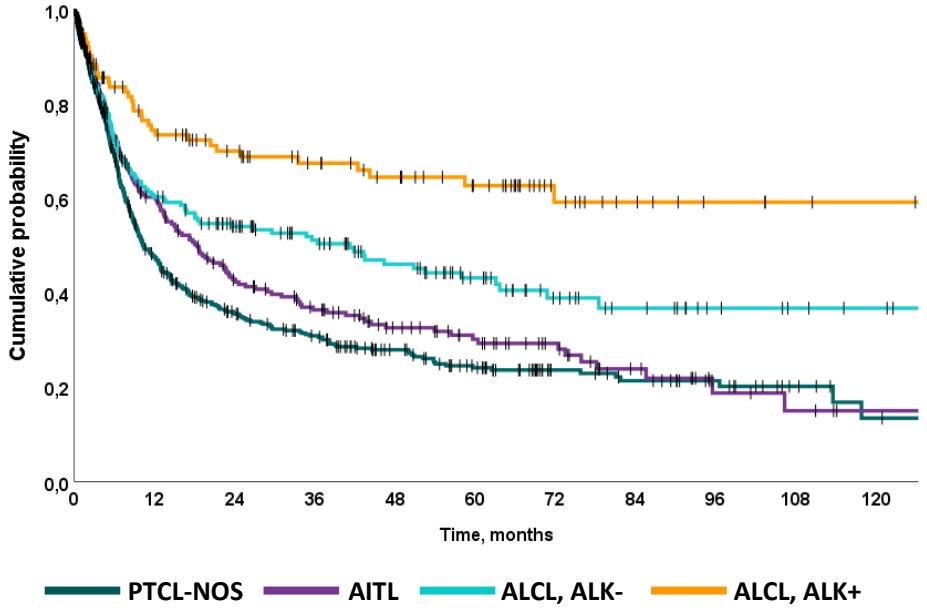
PTCL:	34%	OS at 5 yr
AILT:	42%	OS at 5-yr
ALCL –	49%	OS at 5-yr
ALCL +	77%	OS at 5-yr

Progression Free Survival



5-yrs PFS: **34%** (95% CI 31-37)
Median PFS: **17 months** (95% CI 14-20)
Events: 813 (**56%**)

PTCL:	24%	PFS at 5 yr
AILT:	30%	PFS at 5-yr
ALCL –	43%	PFS at 5-yr
ALCL +	63%	PFS at 5-yr



FIVE YEAR SURVIVAL

PIT (1989-2001): 43%

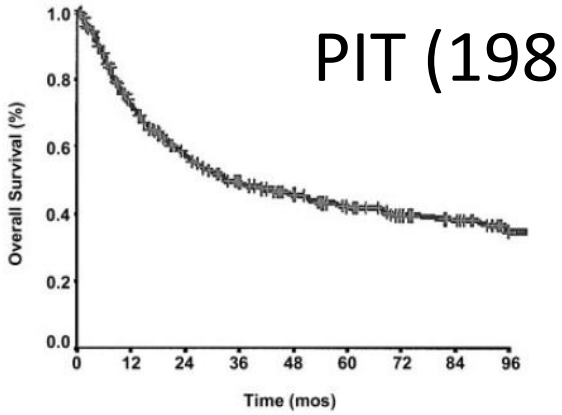


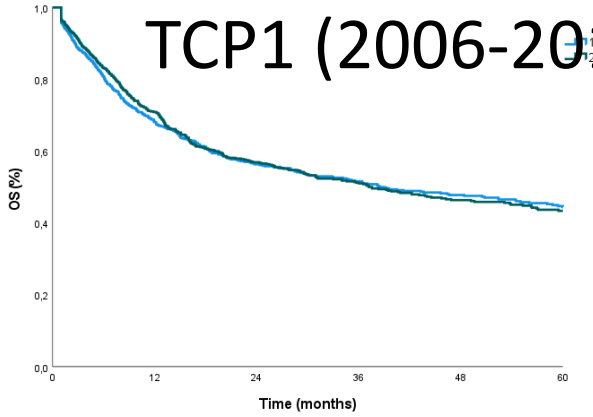
Figure 1. OS of 385 PTCL-U patients. Crosses mark censored cases.

ITCLP (1990-2002)

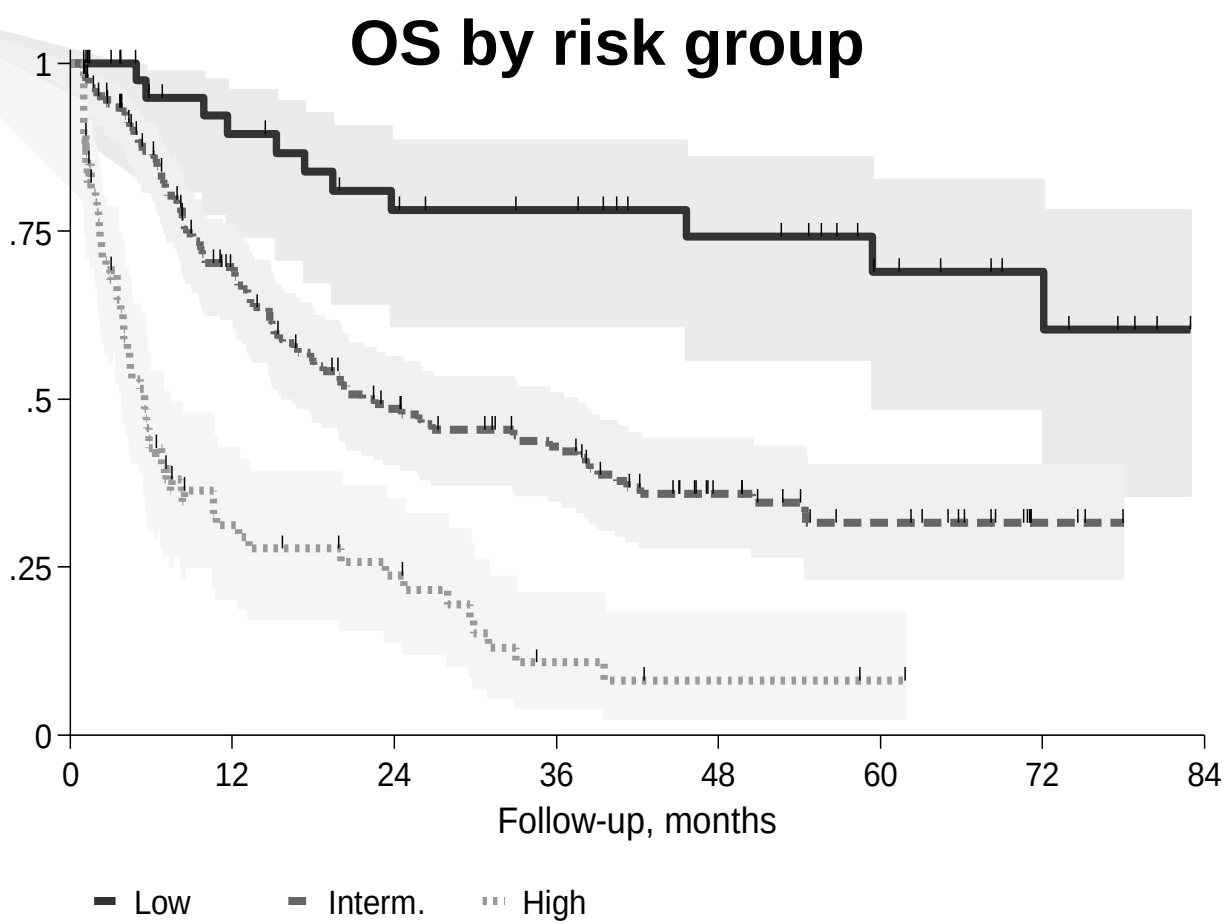
5-yr OS of most frequent subtypes

ALK+ ALCL	ALK– ALCL	PTCL-NOS	AITL	NKTCL	ATLL
70%	49%	32%	32%	32%	14%

TCP1 (2006-2018): 44%



PTCL NOS. A new prognostic model developed by the International T cell Project Network



ECOG PS	0-1
AA STAGE	1-2
Albumin Absolute N Count	> 3.5 g < 6,500

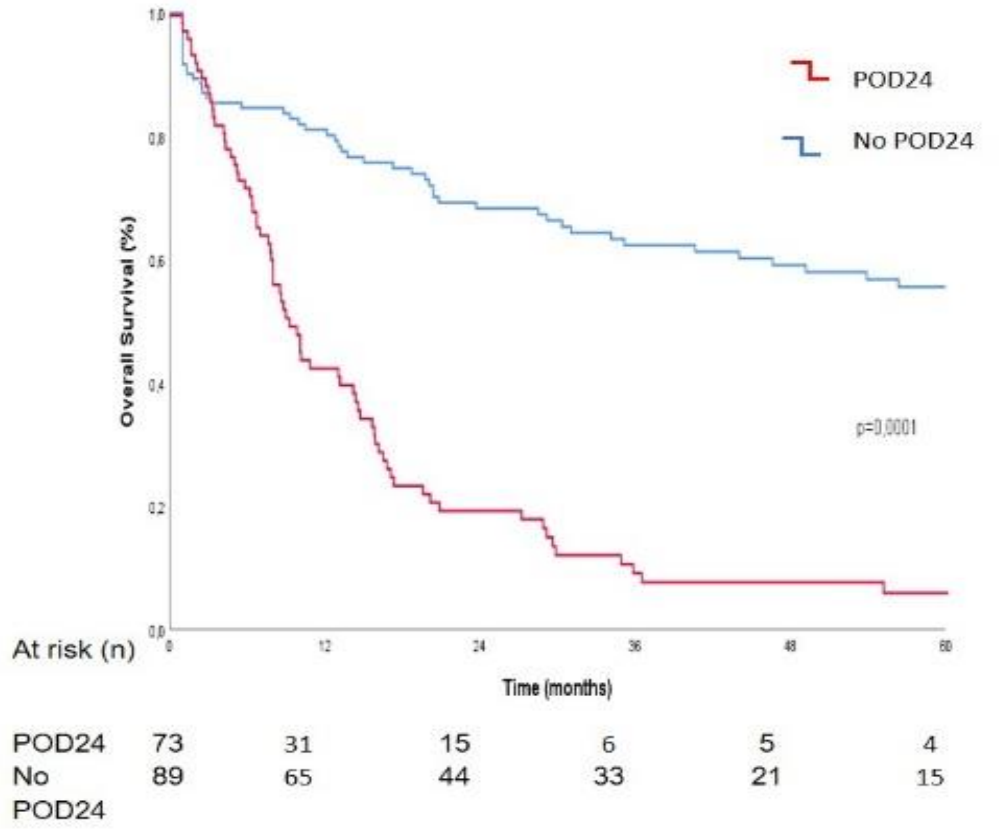
Low Risk	0 factors
Intermediate risk	1-2
High risk	3-4

Federico et al, BJH 2018

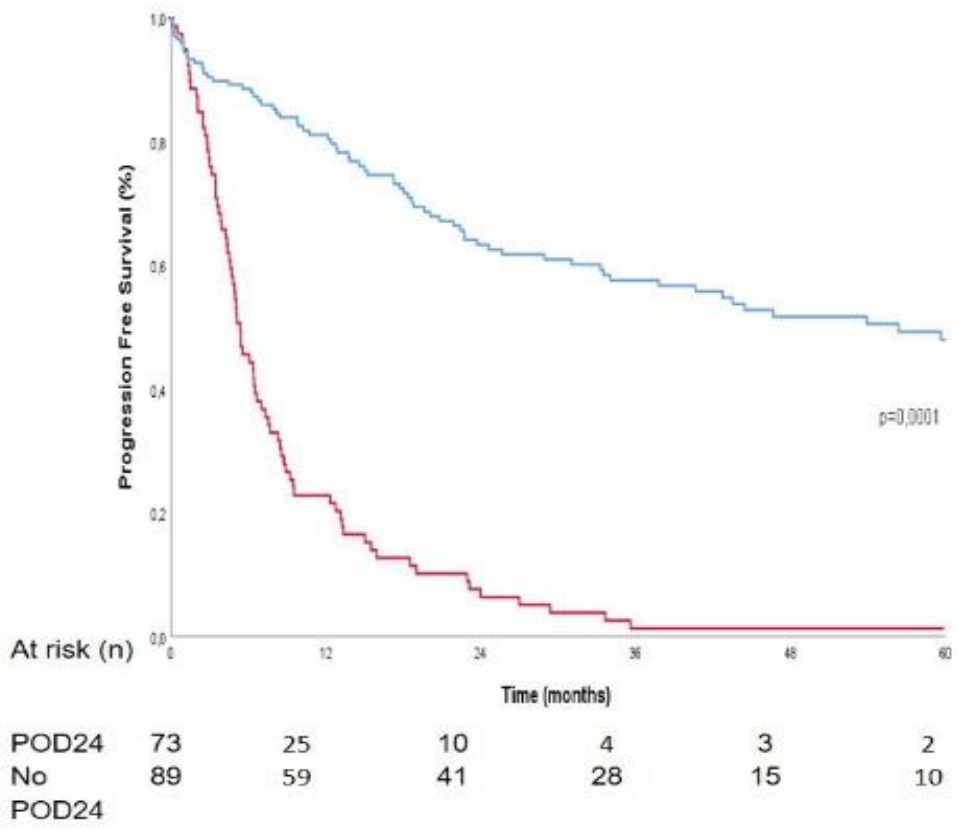
Treatment of Angioimmunoblastic T-Cell Lymphoma is still an unmet need for most patients: Final Report on 282 cases from the Prospective International T-Cell Lymphoma Project

blood
Leading the world in reporting basic and applied hematology research

a **OS**



b **PFS**



R. Advani, Blood 2021

REGULAR ARTICLE

T-Cell Project blood advances

The SALENTO prognostic model for limited-stage peripheral T-cell lymphoma from the International T-Cell Project Network

Greg Hapgood,[1] Monica Civallero,[2] Yana Stepanishyna,[3] Julie Vose,[4] Monica Elena Cabrera,[5] Ranjana H. Advani,[6] Stefano A. Pileri,[7] Martina Manni,[2] Steven M. Horwitz,[8] Francine M. Foss,[9] Felicitas Hitz,[10] John Radford,[11] Ivan Dlouhy,[12] Carlos Chiattone,[13] Won Seog Kim,[14] Tetiana Skrypets,[15] Arnon Nagler,[16] Judith Trotman,[17] Stefano Luminari,[2,18] and Massimo Federico,[2] on behalf of the International T-Cell Project

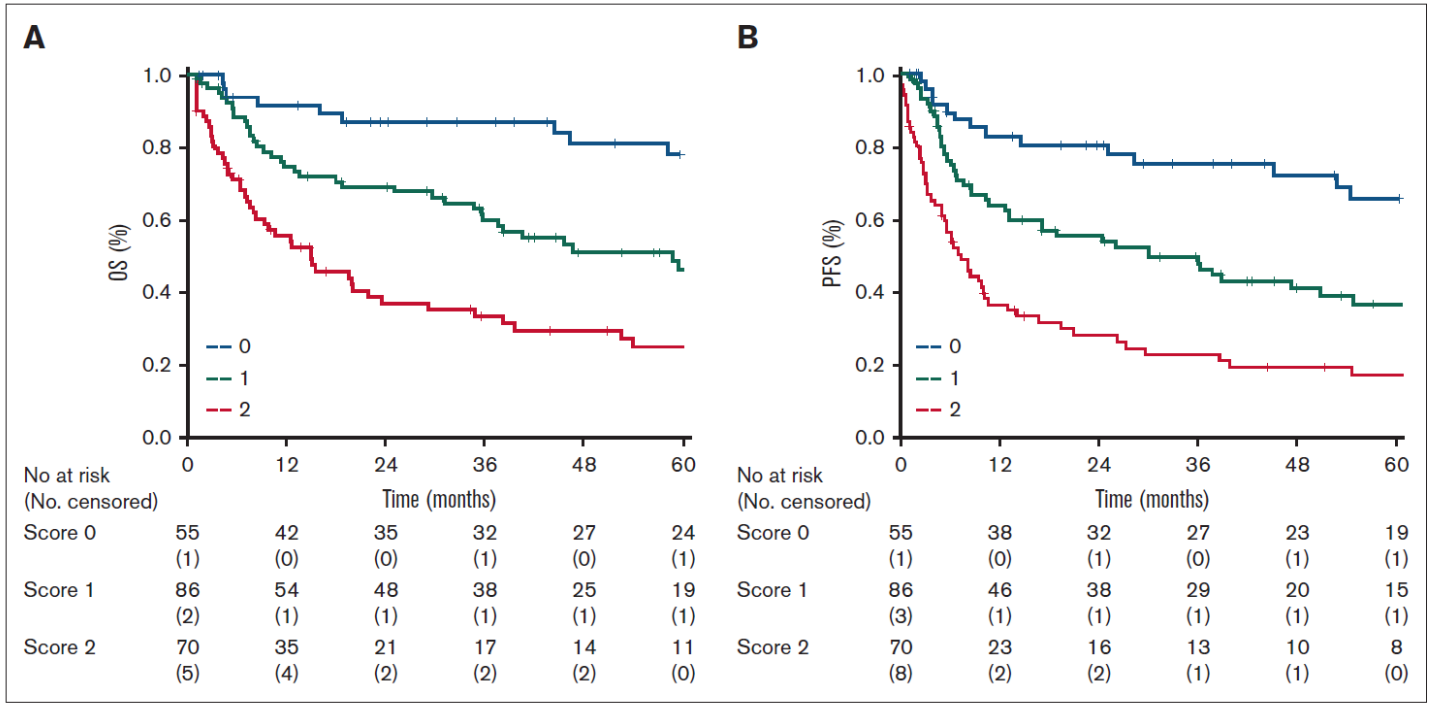


Figure 3. Kaplan-Meier curves. (A) Overall survival and (B) progression free survival by risk groups for all patients in the training sample (score 0 = 55 patients, score 1 = 86 patients, score 2 = 70 patients) identified by the Salento Model.

Age	> 60
LDH	> UNL
Albumin	< 35 g/L

Low Risk	0 factors
Intermediate risk	1
High risk	2-3

Received: 31 October 2023 | Accepted: 16 March 2024
DOI: 10.1111/bjh.19433

BJHaem
BRITISH JOURNAL OF HAEMATOLOGY

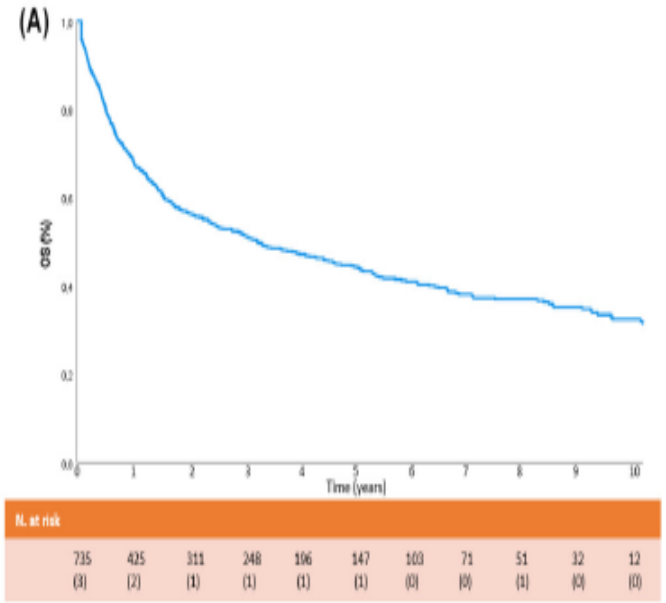
ORIGINAL PAPER

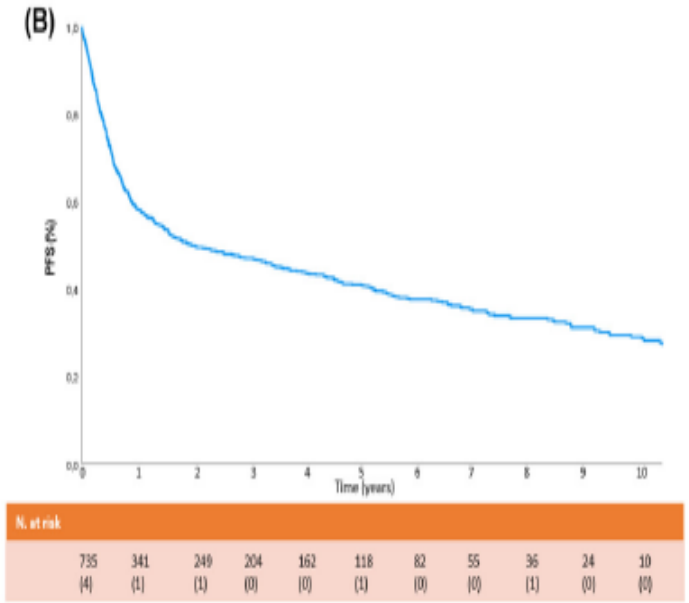
Haematological Malignancy – Clinical

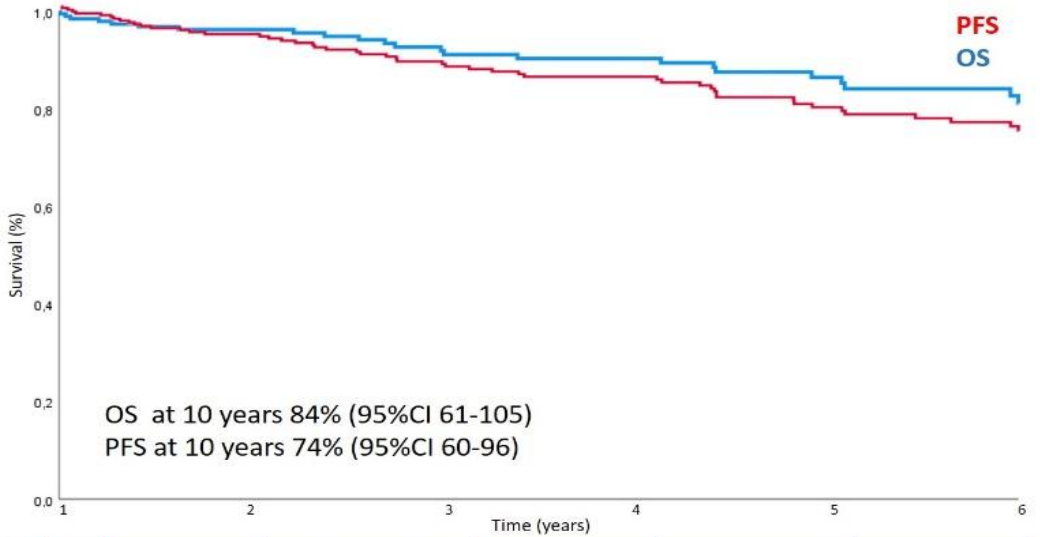
Long-term outcome of peripheral T-cell lymphomas: Ten-year follow-up of the International Prospective T-cell Project

M. Civallero[1] | J. G. Schroers-Martin[2] | S. Horwitz[3] | M. Manni[4] | Y. Stepanishyna[5] | M. E. Cabrera[6] | J. Vose[7] | M. Spina[8] | F. Hitz[9] | A. Nagler[10] | S. Montoto[11] | C. Chiattone[12] | T. Skrypets[13] | M. A. Perez Saenz[14] | G. Priolo[15] | S. Luminari[16] | A. Lymboussaki[1] | A. Pavlovsky[17] | D. Marino[18] | M. Liberati[19] | J. Trotman[20] | D. Mannina[21] | M. Federico[1] | R. Advani[2]

Ten-year overall survival and progression-free survival of long-term cohort patients alive and in remission after the initial 5 years







N. at risk						
OS	208 (0)	162 (0)	134 (0)	111 (0)	87 (0)	45 (0)
PFS	203 (0)	160 (0)	130 (0)	107 (1)	83 (1)	38 (0)

Investigator Meeting

Montevideo ••• April 12-13, 2018

LA CARTA DE MONTEVIDEO

International T-Cell non-Hodgkin's Lymphoma Study Group

La Carta de Montevideo

Peripheral T-cell non-Hodgkin lymphomas (PTCLs) are a heterogeneous group of rare lymphoproliferative disorders arising from mature T cells of post-thymic origin at different stages of differentiation with different morphological patterns, phenotypes, and clinical presentation. The current 2016 WHO classification for lymphoid neoplasms recognizes more than 20 biologically distinct subtypes of mature T and NK neoplasms, making the diagnosis and treatment of these lymphomas even more challenging.

In 2006, the International T-Cell Lymphoma Study Group launched the T Cell Project To verify if a prospective collection of data would allow to achieve more accurate information to better define prognosis of the most frequent subtypes (PTCL,NOS and AITL) and to improve knowledge on clinical and biological characteristics and outcome of the more uncommon subtypes. As of March 20, 2018, 77 Centers from 15 different Countries of 5 different Geografic Areas, including Europe, North America, South America, Middle/Far East, and Oceania registered 1,611 cases making this the largest series of of PTCL or NK/T-cell lymphoma ever collected.

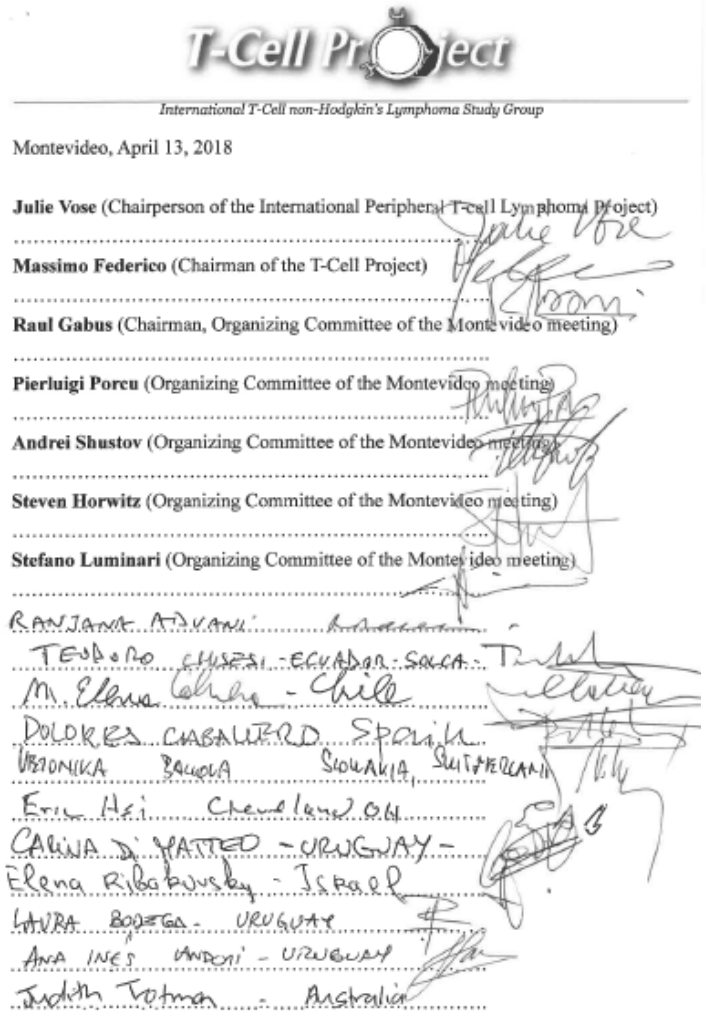
During the Montevideo Meeting held on April 12 and 13, 2018, the results of this study have been disclosed and a very positive feedback from the attendants was perceived.

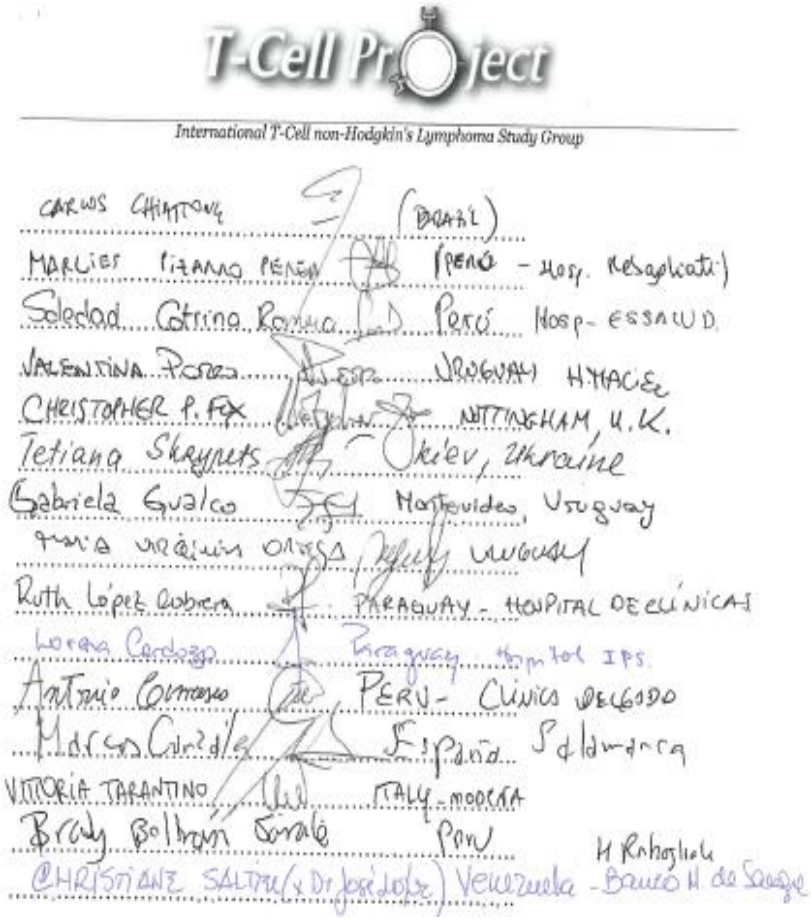
Thus, in order to continue to have a current view of the T-cell lymphomas scenario, the International T-cell Lymphoma Study Group decided to launch the T-cell Project 2.0, which adapts to changes made in diagnosis, staging and response evaluation.

In particular, the purpose of the new study is to better assess the clinical relevance of the new 2016 WHO Classification, the role of the 2014 Lugano Classification in staging and response assessment, the prognosis of different entities, the genomic landscape of different subtypes, and to investigate on most adequate treatment strategies for these neoplasms in the real-world population.

Given the relevance of this project and the benefits that patients all over the world can receive from such a large and qualified International Consortium, the undersigned representatives of respective Institutions approve the project and express their strong commitment in supporting the study in their own Institutions and Countries.

Montevideo, April 13, 2018





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"

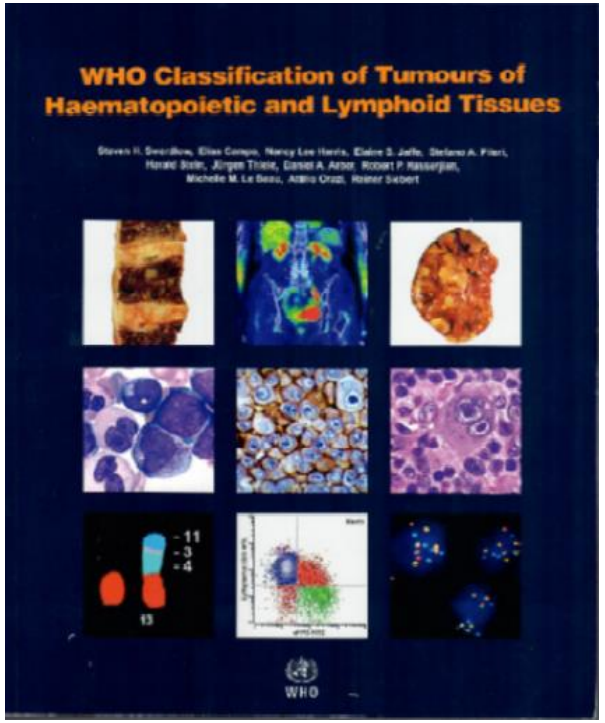
November 10, 1942

T-CELL PROJECT 2.0

Prospective, observational, international registry of patients with newly diagnosed peripheral T-cell lymphoma

SELECTION CRITERIA

NEW HISTOLOGIES (WHO 2016)



- Previously untreated patients with ***de novo*** diagnosis of peripheral T-cell or NK/T-cell lymphoma:
  - **T-cell large granular lymphocytic leukaemia**
  - **NK cells Chronic lymphoproliferative disorder**
  - **Aggressive NK-cell leukemia**
  - **Adult T-cell leukemia/lymphoma**
  - **Extra-nodal NK/T-cell lymphoma, nasal type**
  - **Intestinal T-cell lymphoma**
  - **Hepatosplenic T-cell lymphoma**
  - **Subcutaneous panniculitis-like T-cell lymphoma**
  - **Peripheral T-cell lymphoma, not otherwise specified**
  - **Angioimmunoblastic T-cell lymphoma and other nodal lymphomas of T follicular helper cell origin**
  - **Anaplastic large cell lymphoma, ALK-positive**
  - **Anaplastic large cell lymphoma, ALK-negative**
  - **Breast implant-associated anaplastic large cell lymphoma**

REGISTRATIONS BY REGION

USA
7 sites

170 sites in 25 countries

South America

Argentina	39 sites
Brazil	32 sites
Chile	4 sites
Peru	3 sites
Uruguay	1 site
Paraguay	1 site
Venezuela	1 site

Africa
Egypt 1 site

Oceania
Australia 17 sites

Europe

Italy	12 sites
UK	15 sites
Spain	12 sites
Turkey	5 site
Poland	3 sites
Switzerland	1 sites
Croatia	2 sites
Estonia	1 site
Romania	1 site
Ukraine	3 site
Netherlands	1 site
Greece	1 site

Asia

Israel	3 sites
India	1 site
South Korea	1 site
Kazakhstan	1 site
Japan	1 site

CURRENT STATUS OF TCP2.0 (by November 2025)

Total n° pts registered: **1475**

Out of study
Diagnosis not confirmed (N=51)

Total n° pts on study: **1424**

Patients enrolled after June 30, 2023 (N=294)

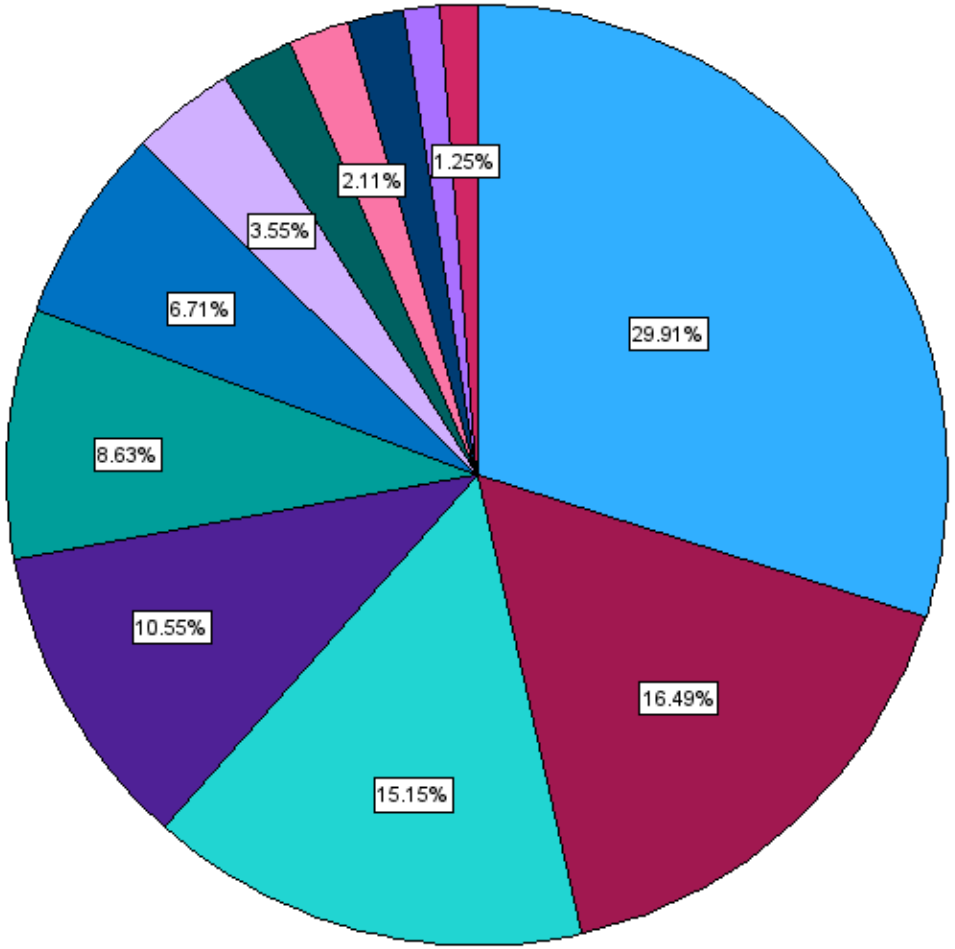
Total n° pts on study: **1130**

Recruiting sites: **148**

Recruiting countries: **28**

Geographic area: **5**

TCP 2



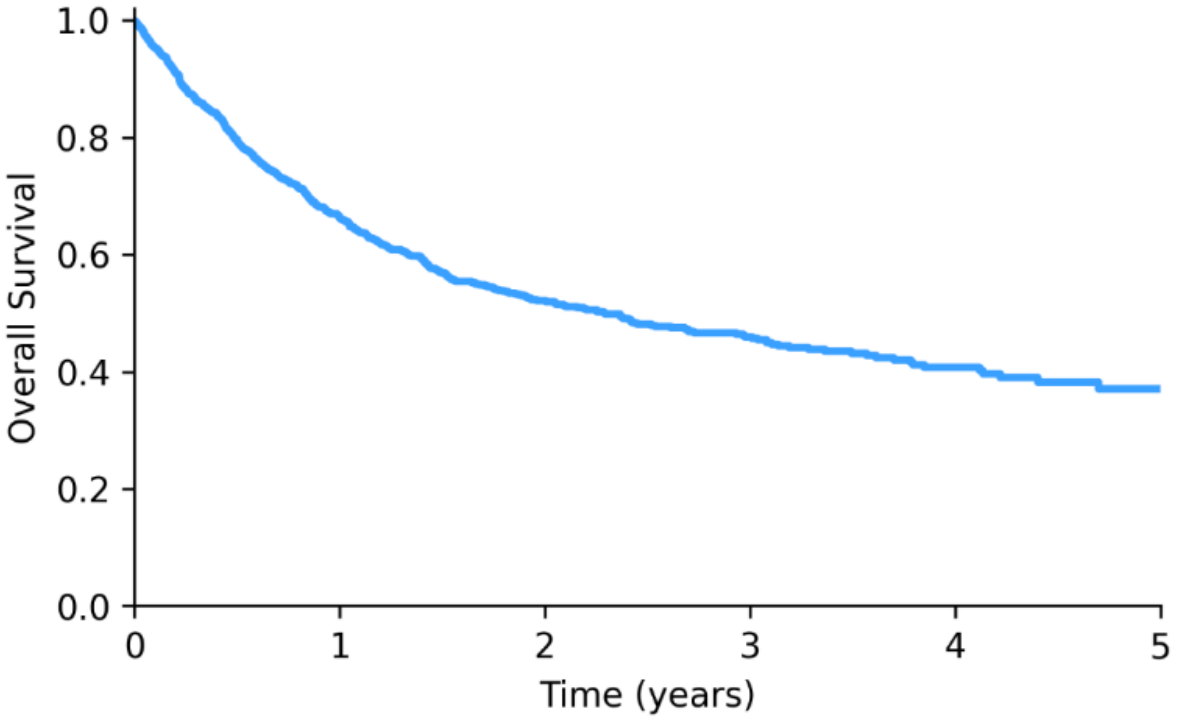
Distribution of 1,043 cases by local diagnosis

TCP 2

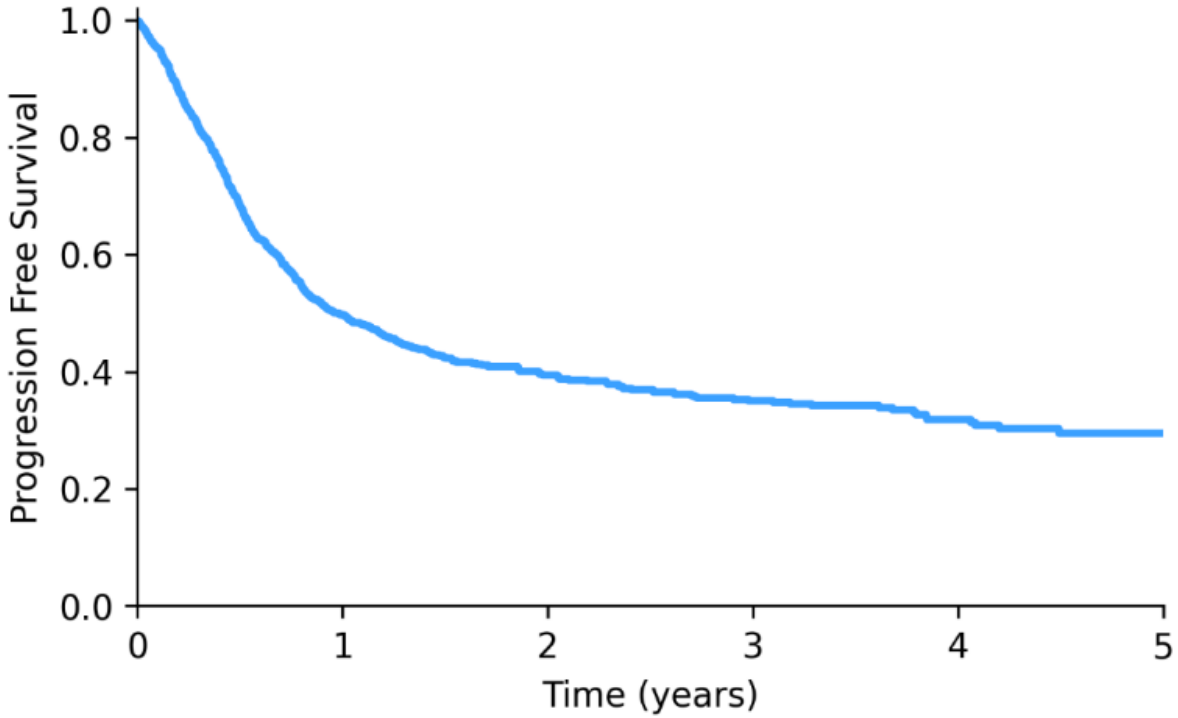
Subtype distribution among regions

Subtype	N (%)				
	Asia/Oceania (N=189, 18%)	Europe (N=166, 16%)	North America (N=61, 6%)	South America (N=627,60%)	TOTAL (N= 1043, 92.3%)
PTCL-NOS	61 (32.3)	62 (37.3)	17 (27.9)	172 (27.4)	312 (29.9)
AITL	39 (20.6)	33 (19.9)	11 (18)	75 (12)	158 (15.2)
NKTCL	19 (10.1)	12 (7.2)	8 (13.1)	71 (11.3)	110 (10.6)
ALCL, ALK+	9 (4.8)	17 (10.2)	6 (9.8)	38 (6.1)	70 (6.7)
ALCL, ALK-	41 (21.7)	18 (10.8)	4 (6.6)	109 (17.4)	172 (16.5)
ATLL	9 (4.8)	3 (1.8)	5 (8.2)	73 (11.6)	90 (8.7)
Enteropathy-type	0	5 (3.0)	0	21 (3.3)	26 (2.5)
Other minor subtypes	11 (5.8)	16 (9.6)	10 (16.4)	68 (10.8)	105 (10.1)

TCP 2 Overall and Progression Free Survival

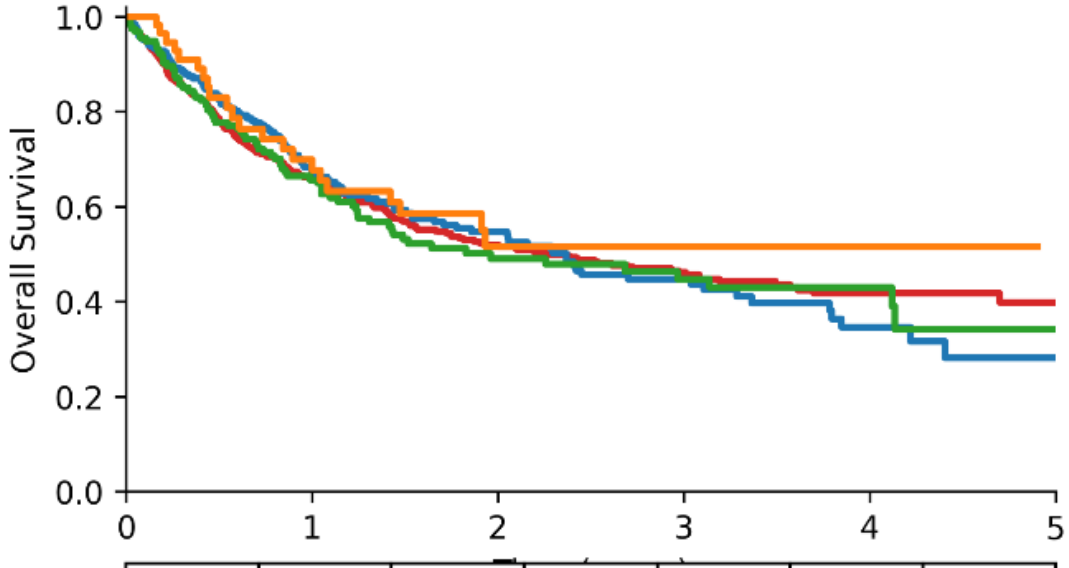


Time (year)	0	1	2	3	4	5
No. at risk	1130	570	310	189	85	17
OS%	99.9	66.3	52.1	45.9	40.8	37.1

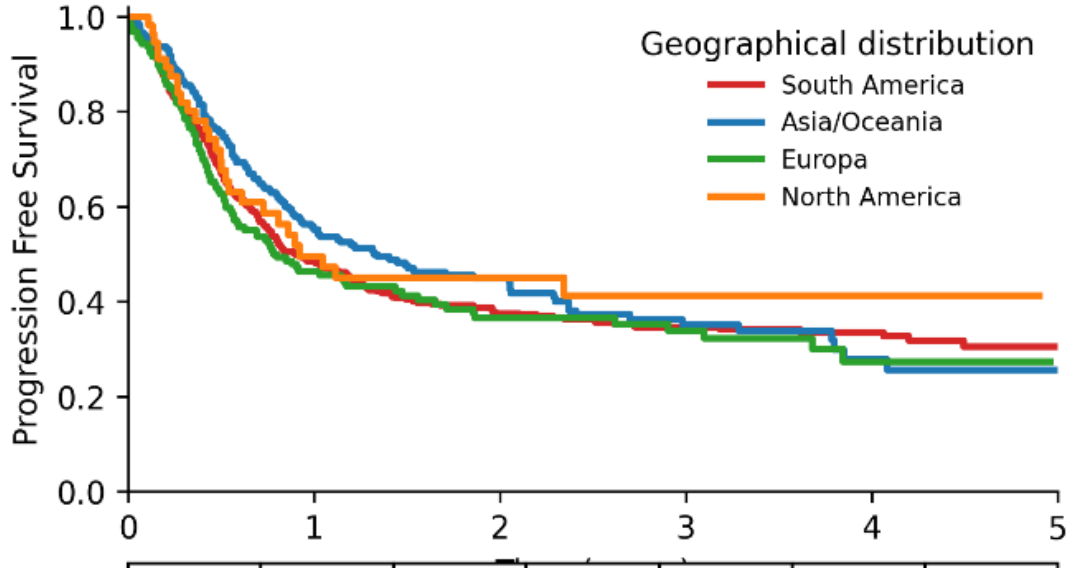


Time (year)	0	1	2	3	4	5
No. at risk	1130	423	238	146	69	14
PFS%	99.9	49.7	39.4	35.0	31.9	29.5

TCP 2 OS and PFS by Regions

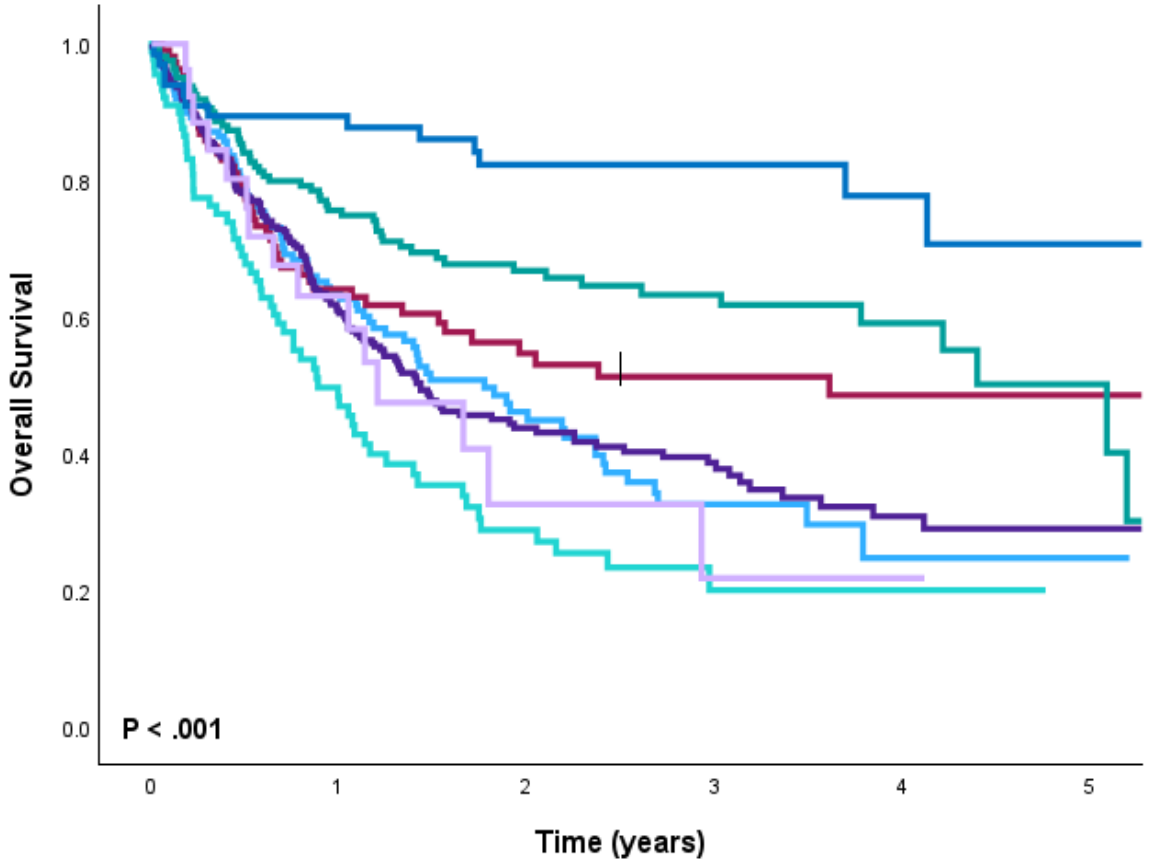


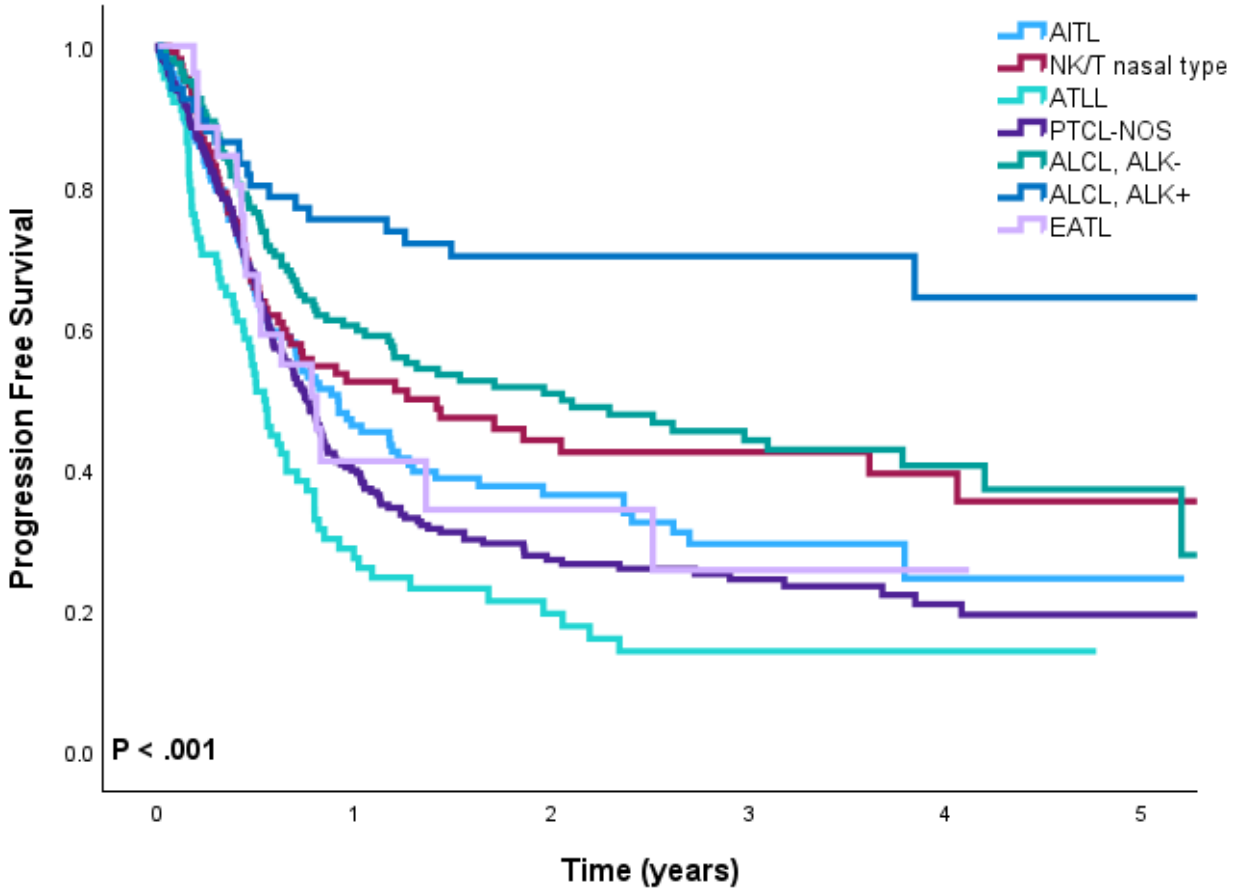
Time (year)	0	1	2	3	4	5
South America	634	324	174	110	51	12
OS%	100.0	65.9	51.9	46.2	41.8	39.9
Asia/Oceania	269	128	75	43	18	4
OS%	99.6	67.3	54.8	44.8	34.6	28.2
Europa	166	87	46	27	13	1
OS%	100.0	65.7	49.1	44.8	43.0	34.2
North America	61	31	15	9	3	0
OS%	100.0	67.7	51.6	51.6	51.6	51.6



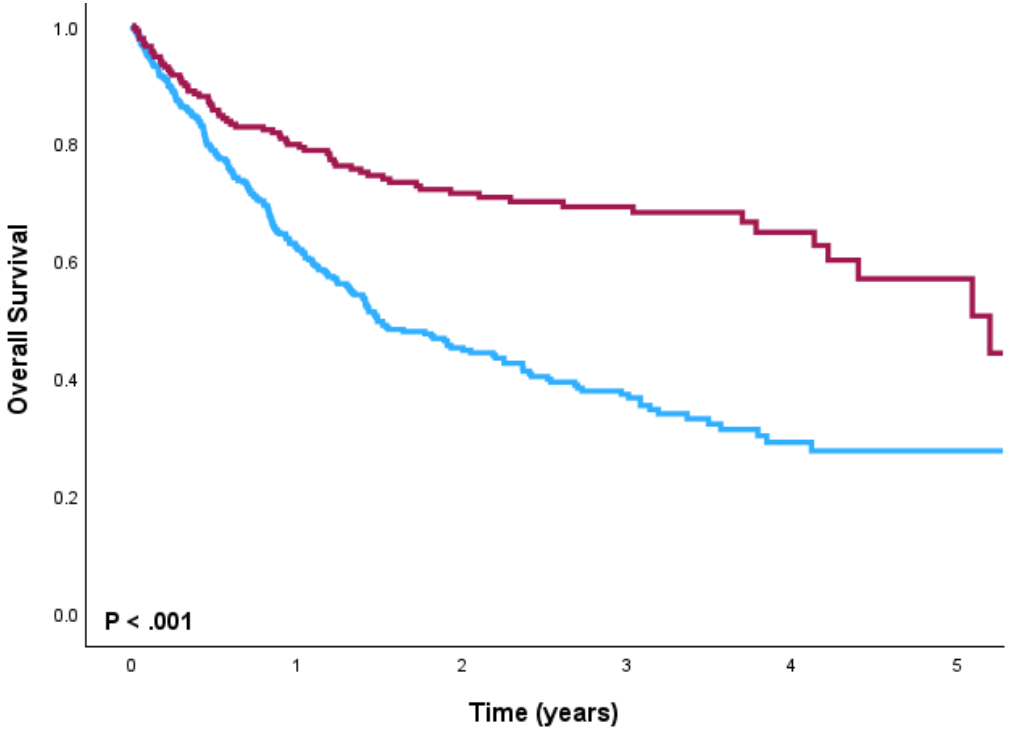
Time (year)	0	1	2	3	4	5
South America	634	239	128	86	44	11
PFS%	100.0	48.4	37.6	34.6	33.6	30.6
Asia/Oceania	269	102	60	31	13	3
PFS%	100.0	55.3	44.9	35.2	27.9	25.6
Europa	166	60	37	22	9	0
PFS%	99.4	46.4	36.6	33.9	27.4	27.4
North America	61	22	13	7	3	0
PFS%	100.0	49.6	45.1	41.3	41.3	41.3

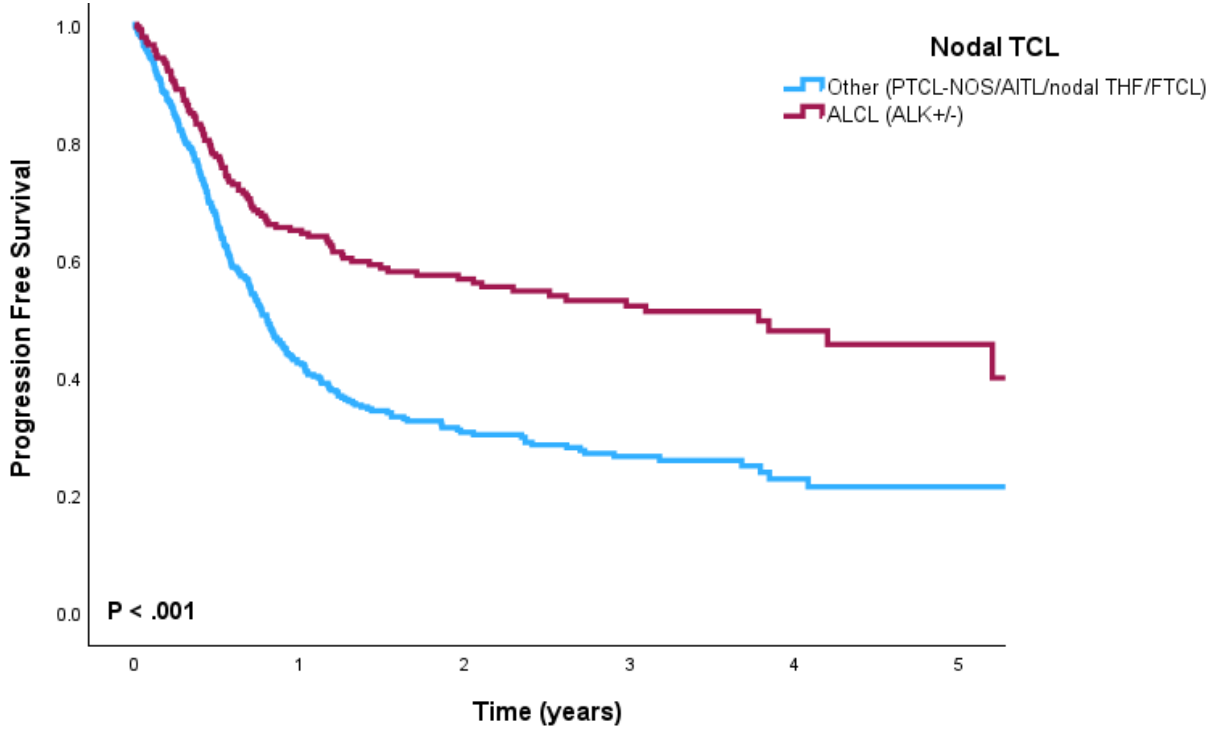
TCP 2 OS and PFS by histotypes





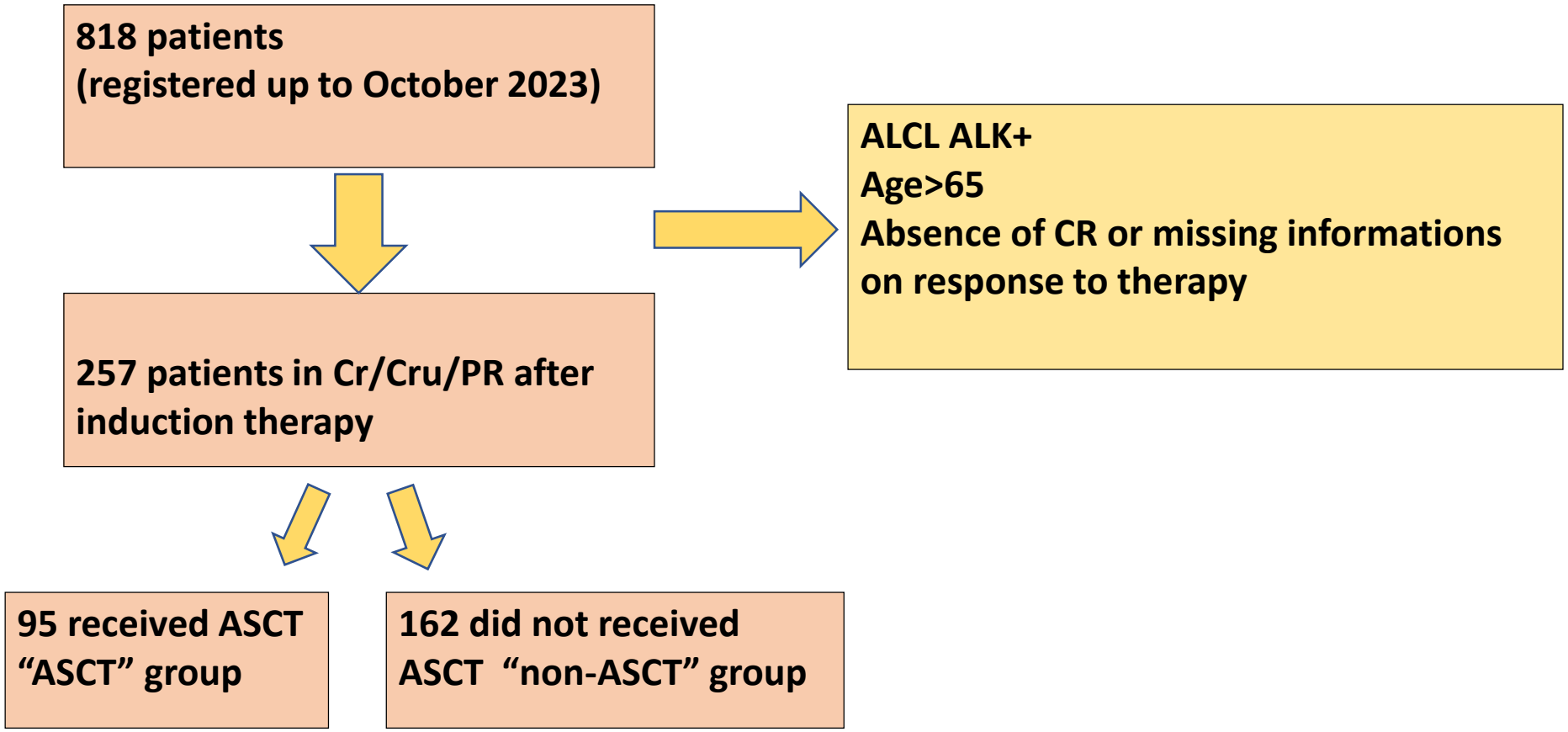
NODAL PTCLs: ALCL vs Other

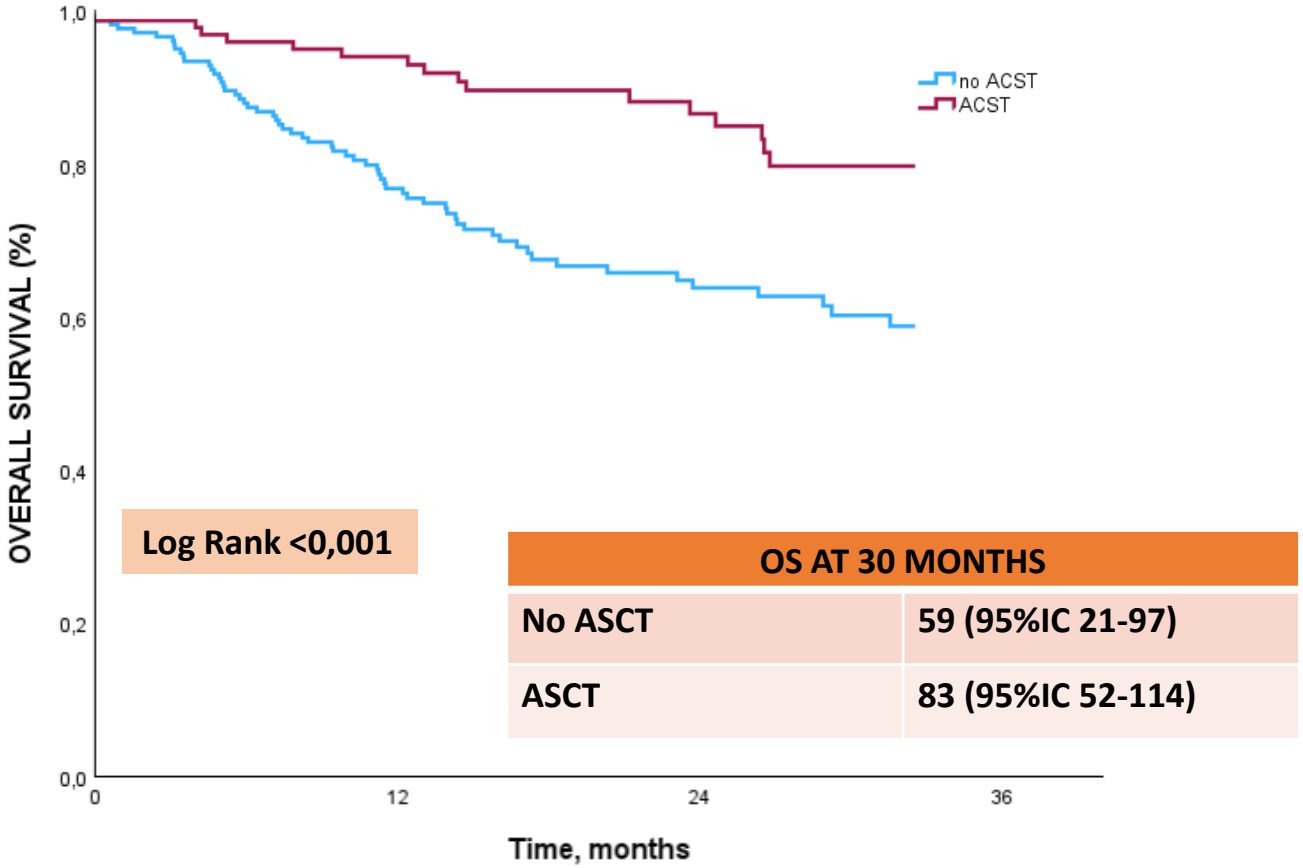




Transplant as consolidation in TCP2 (2018-2021)

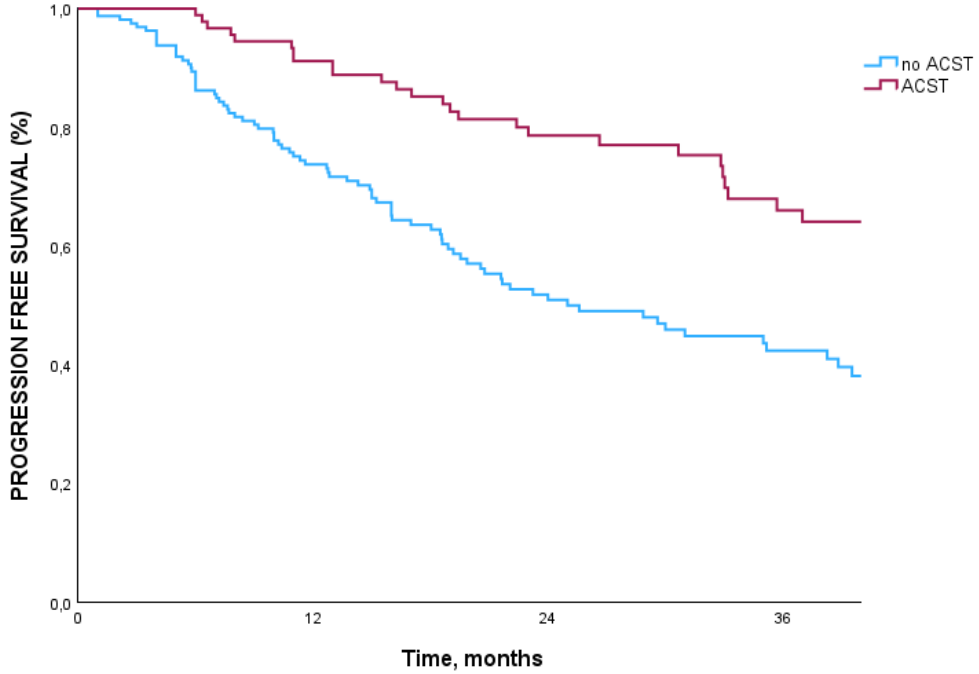
	Ntot	Transplant (N, %)
All patients	633	115 **(18,2%)**
All patients in CR/PR	387	111 **(28,7%)**
All patients in CR/PR and aged <70	337	106 **(31,4%)**


818 patients
(registered up to October 2023)
ALCL ALK+
Age>65
Absence of CR or missing informations on response to therapy
257 patients in Cr/Cru/PR after induction therapy
95 received ASCT
“ASCT” group
162 did not received ASCT “non-ASCT” group

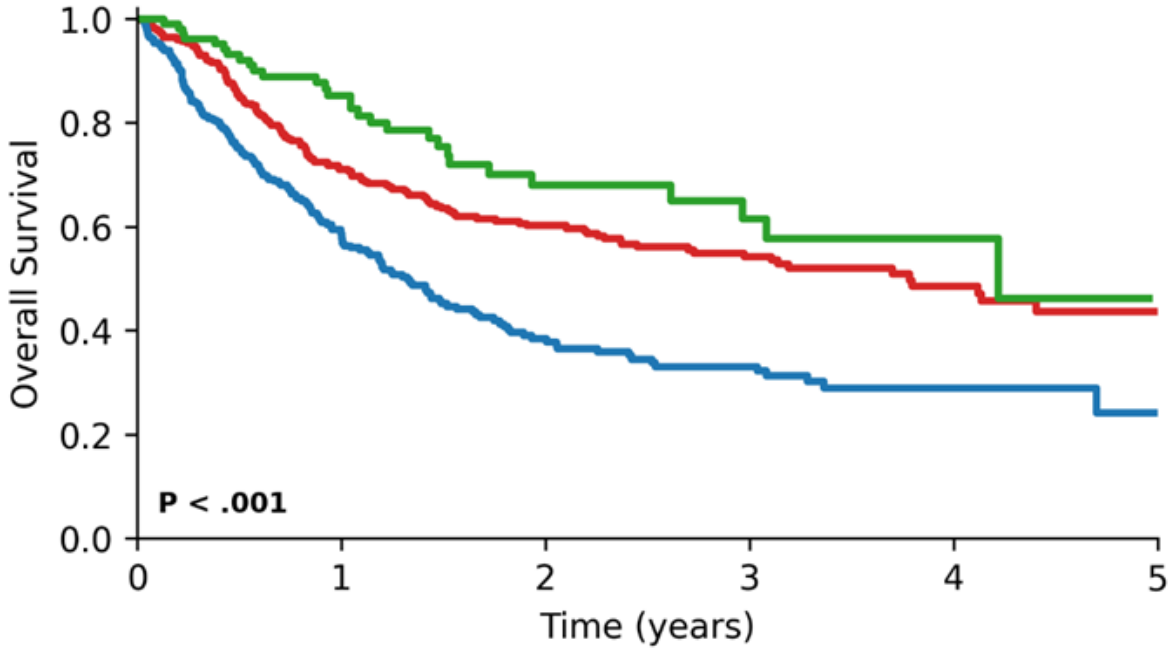


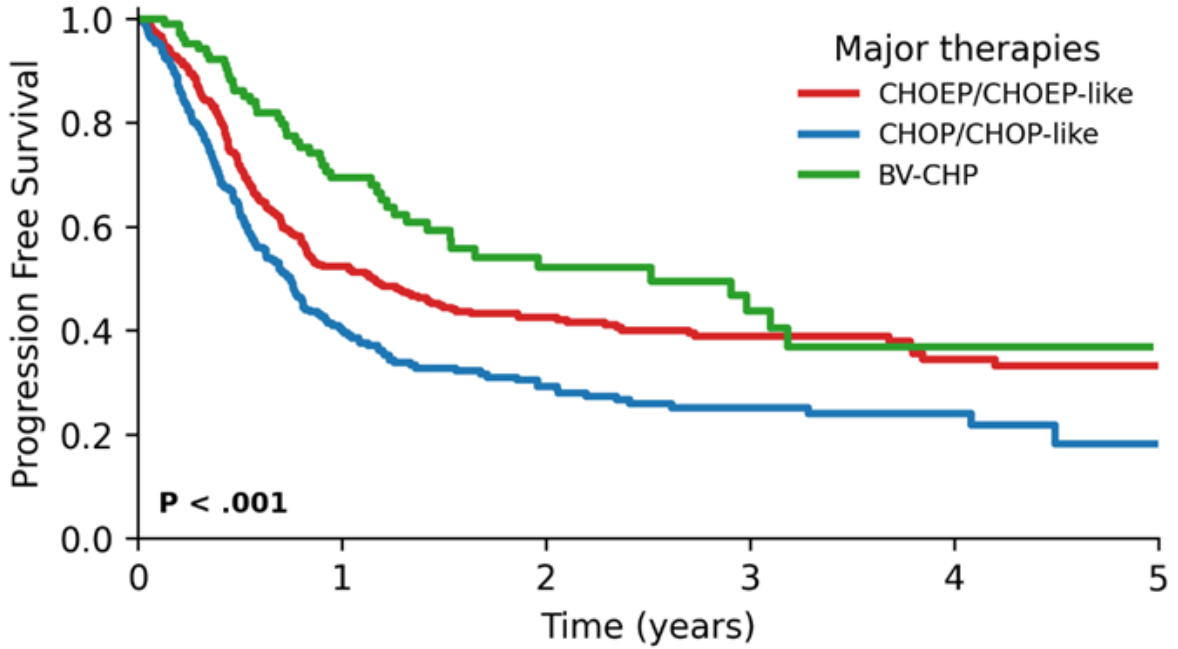
Log Rank <0,001

OS AT 30 MONTHS	
No ASCT	59 (95%IC 21-97)
ASCT	83 (95%IC 52-114)



TCP 2 OS and PFS by Regimens





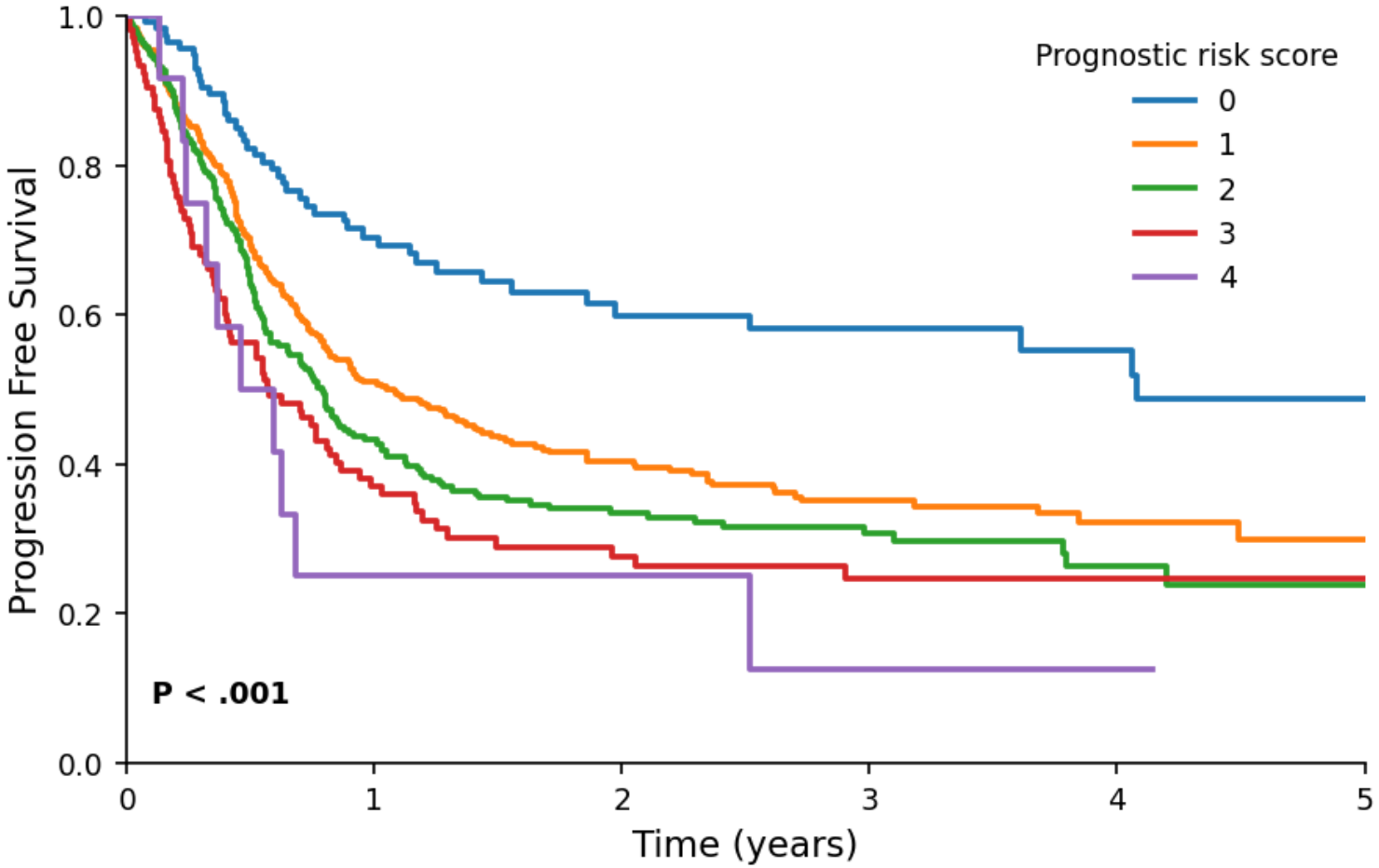
Time (year)	0	1	2	3	4	5
CHOEP/CHOEP-like	354	213	125	83	35	11
OS%	100.0	71.1	60.2	54.3	48.5	43.7
CHOP/CHOP-like	293	128	62	39	14	2
OS%	100.0	57.7	38.5	33.1	29.0	24.2
BV-CHP	108	68	32	17	8	0
OS%	100.0	85.3	68.0	61.5	57.7	46.1

Time (year)	0	1	2	3	4	5
CHOEP/CHOEP-like	354	157	93	62	28	9
PFS%	100.0	52.3	42.5	38.9	34.5	33.2
CHOP/CHOP-like	293	87	47	29	11	2
PFS%	100.0	40.1	29.3	25.2	24.1	18.3
BV-CHP	108	55	26	14	6	0
PFS%	100.0	69.4	52.2	43.9	36.8	36.8

Univariable and Multivariable models for association between prognostic variables and Progression Free Survival (PFS)

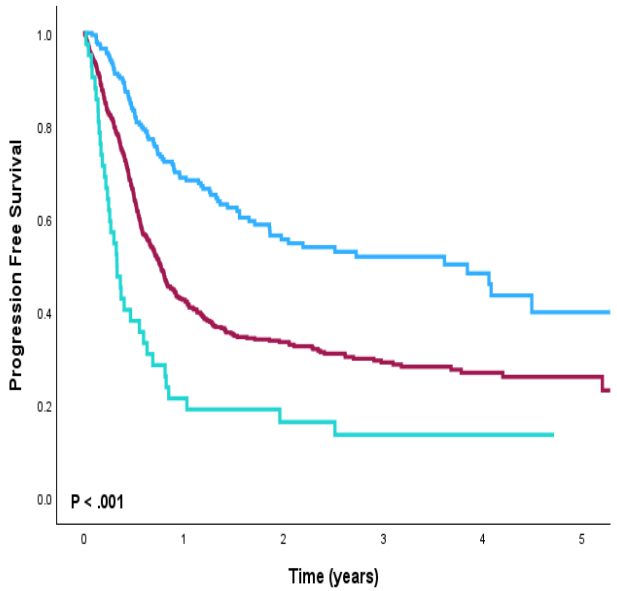
Variable	HR	95% CI	P	HR	95% CI	P
Age ≥ 65	1.76	1.47-2.11	**<0.001**	1.62	1.37-2.40	**<0.001**
Gender	1.06	0.89-1.27	NS			
ALCL (ALK+/ALK-) vs other	0.89	0.84-0.94	**<0.001**	0.59	0.85-1.00	**0.001**
Stage ≥3	2.10	1.67-2.65	**<0.001**	1.84	1.24-2.75	**<0.001**
B symptoms	1.23	1.03-1.47	**0.02**	1.00	0.40-1.31	NS
ECOG ≥2	2.17	1.78-2.64	**<0.001**	1.61	1.13-2.13	**<0.001**
LDH ≥ ULN	2.14	1.74-2.64	**<0.001**	0.027	1.00-1.79	NS
Beta2M > ULN	1.61	1.18-2.21	**0.003**			
Hemoglobin<12 g/dL	1.66	1.38-1.98	**<0.001**	0.27	0.11-0.98	NS
Albumin < 3.5 g/dL	1.84	1.51-2.23	**<0.001**	0.31	0.10-1.24	NS
Platelets <150 g/dL	1.74	1.43-2.12	**<0.001**	0.064	0.01-1.02	NS
BM involvement	0.57	0.46-0.70	**<0.001**	0.69	0.54-0.99	NS
Lymph nodes invol	1.08	0.88-1.33	NS			
Extranodal involvement	1.17	0.98-1.41	NS			
EBV	0.79	0.61-1.03	NS			

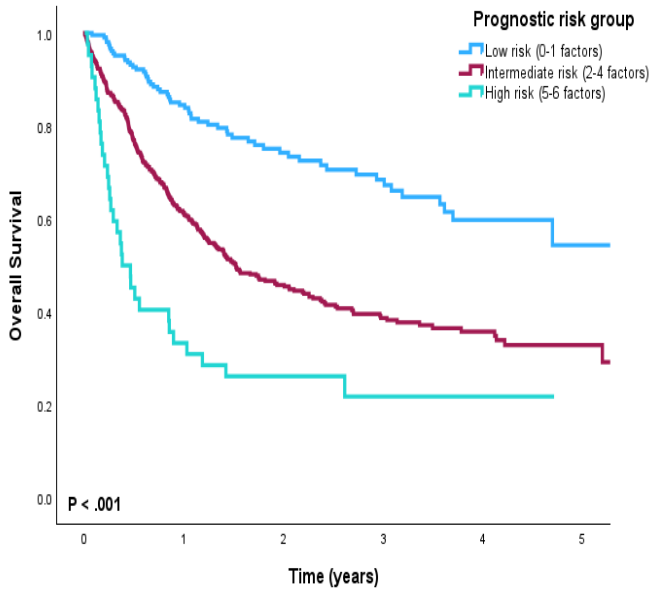
OUTCOME ACCORDING TO THE # OF ADVERSE RISK FACTORS



T-CELL PROJECT 2.0

OUTCOME ACCORDING TO THE TCP2 INDEX?





ECOG PS	0-1
AA STAGE	1-2
Age Histology	<65 ALCL

Low Risk	0-1 factors
Intermediate risk	2-4
High risk	5

TOWARDS TCP2.1

Chairman: Stefano Luminari
Co-Chairman: Pierluigi Porcu
Steering Committee: Christopher Fox, Miles Prince, Carlos Chiattone, Astrid Pavlovsky, Alejandro Martin, Alessandro Pulsoni, Socorro Maria Rodriguez

Subprojects (prospectively):

- PET assessment
- Geriatric assessment
- Virtual pathology review
- Role of ASCT
- Targeting EBV
- ctDNA assessment

MUCHAS GRACIAS POR SU ATENCION!