GIORNATE EMATOLOGICHE VICENTINE

XI edizione

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Palazzo Bonin Longare - Vicenza

Linfomi T Update Diagnostico - Terapeutico

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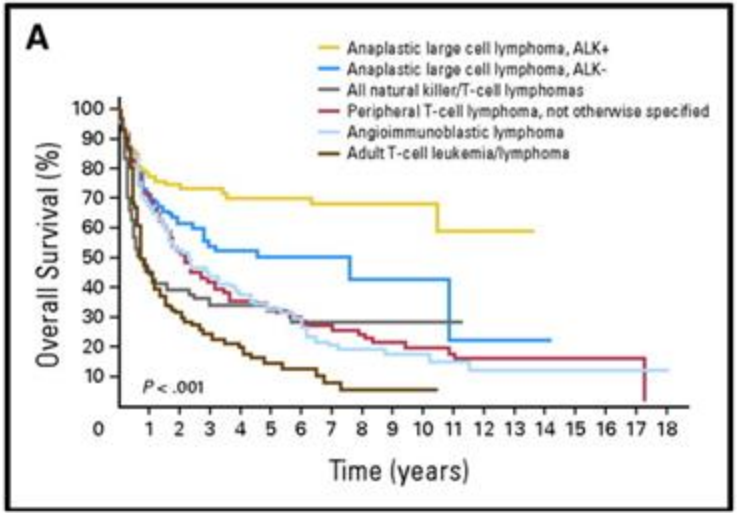
Disclosure of Cinzia Pellegrini

Company name	Research support	Employee	Consultant	Stockholder	Speakers bureau	Advisory board	Other
Roche					x		x
Gilead					x		x
Takeda						x	
Janssen-Cilag						x	
Abbvie					x		x
BeOne					x		

PTCL - Background

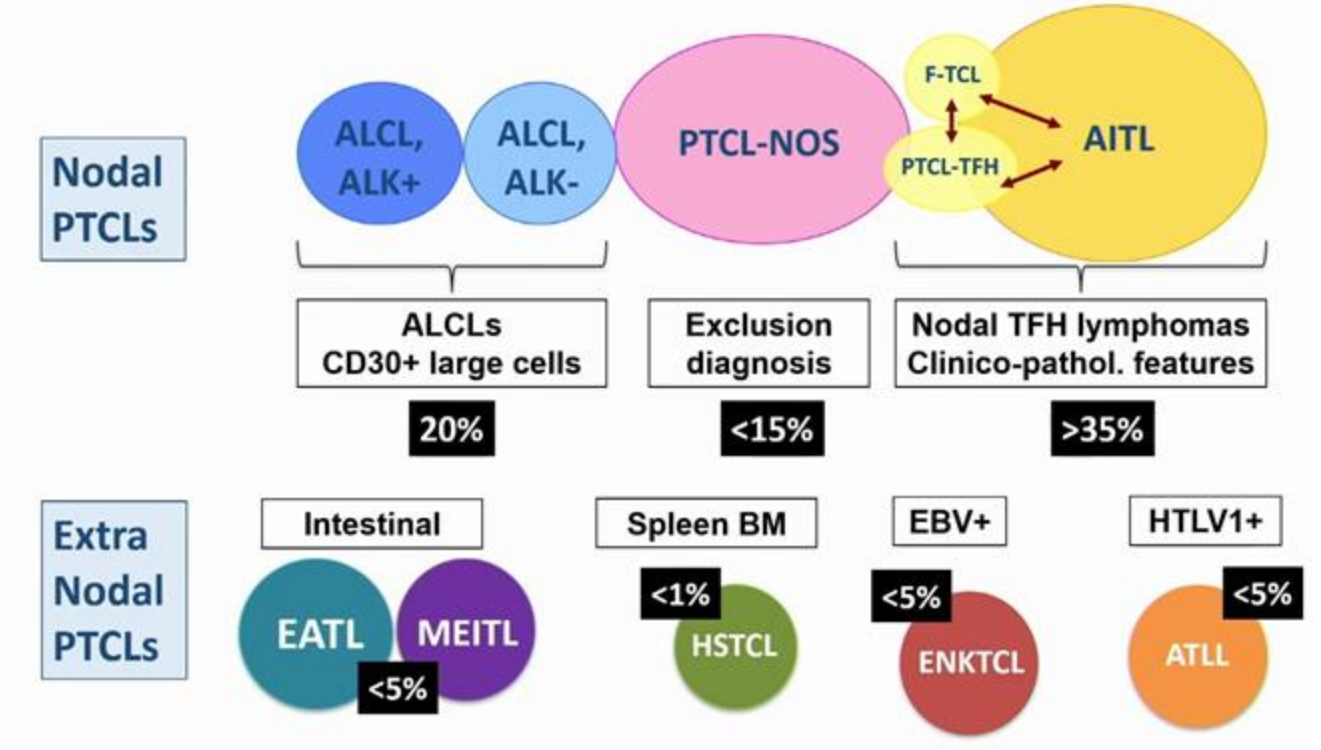
- PTCLs are **rare** and very **heterogenous** lymphoproliferative disorders-accounting for 15% of all NHLs
- There are more than 30 different subtypes of PTCLS (WHO 2022; ICC 2022)
- **25% of patients are primary REFRACTORY to first line**
- Except for ALK+ ALCL, other subtypes have **poor OS with standard therapies with a 5 years OS of 15-20%**



Molecular characterization→ to identification of subtypes with different prognoses →development of novel pathway-directed and subtype-specific therapies

Vose et al. JCO 2008;26:4124

Histological subtypes



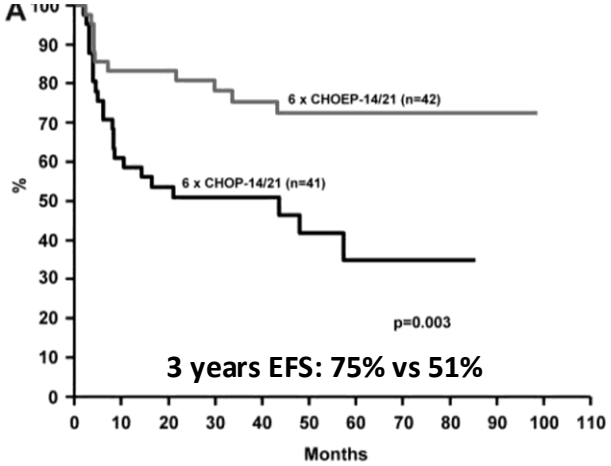
Outline of the discussion

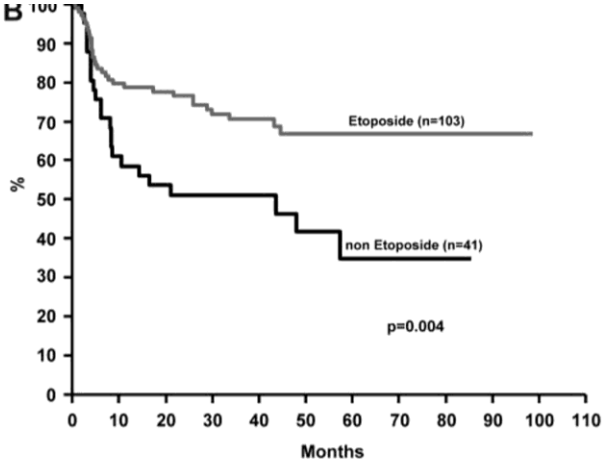
First line treatment

- The role of etoposide
- The role of consolidation with stem cell transplantation
- The role of novel agents in combination to standard chemotherapy

CHOEP is better than CHOP?

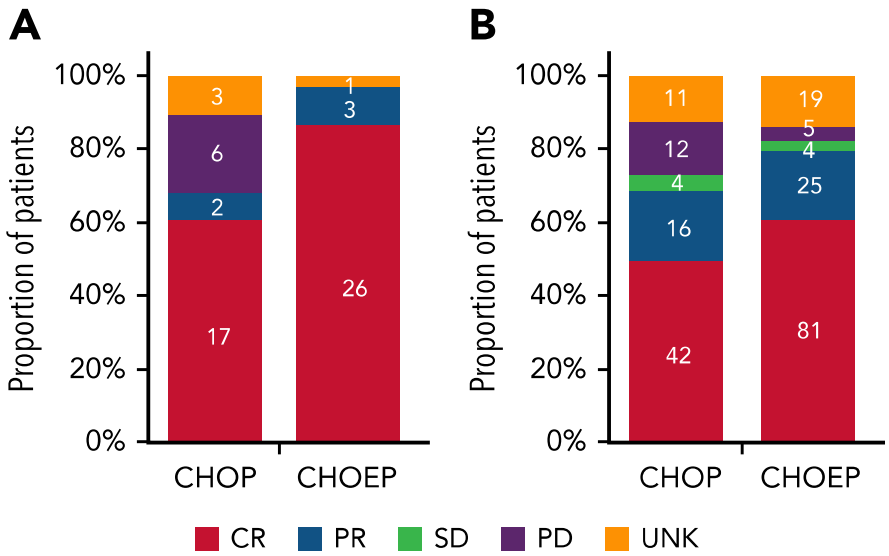
- Etotopside improved 3-EFS in patients < 60 years
- 6 cycles of CHOP remains the standard for patients > 60 years





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

CHOEP is better than CHOP?



- In advanced stage PTCL, the addition of Etoposide to CHOP improved OS in ALK+ ALCL but not in ALK-, AITL,PTCL-NOS
- Consolidation with ASCT in first line setting significantly increased OS in ALK-ALCL, AITL, and PTCL-NOS

Brink M et al. Blood 2022 Sep 1;140(9):1009-1019

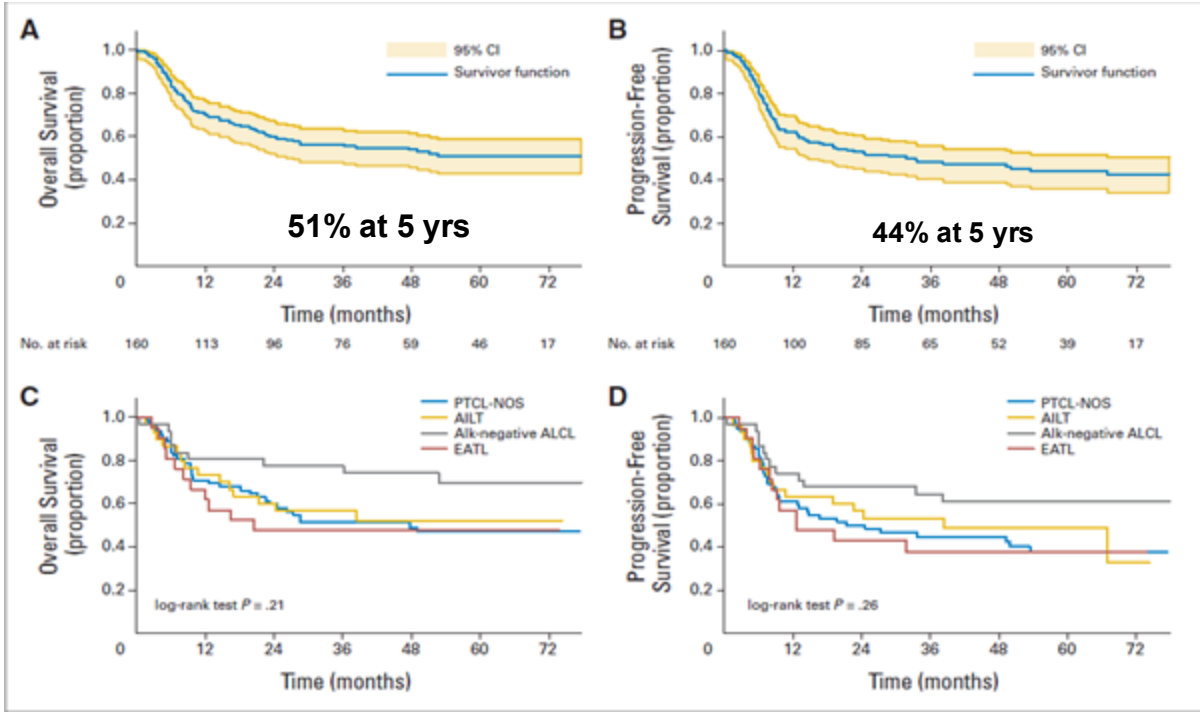
Cautionary notes about consolidative auto-SCT in PTCL

- There are no RCT demonstrating that consolidative auto-SCT improves outcome in PTCL
- There is retrospective evidence ‘for’ and ‘against’
- There are few prospective trials – diverse subtype inclusion

  however,
- The relapse risk remains high with CHOP(like) chemotherapy alone thus, it is ‘considered’ in most subtypes (exception ALK-pos ALCL)

Upfront transplant in PTCL: Nordic NLG-T-01 Phase 2 study

n=160 (PTCL-NOS n=62, 39%)



All patients

5 y OS by Subtype

ALK-	70%
AITL	52%
NOS	47%
EATL	48%

5 y PFS by Subtype

ALK- 61%

AITL 49%

NOS 38%

ETL 38%

D' Amore F. et al JCO 2012

Randomized study of Auto versus NO Auto-HSCT post CR in nodal PTCLs (TRANSCRIPT)

- 18-69 y
- Fit enough for ASCT
- PTCL-NOS
- TFH TCLs
- ALK-negative ALCL
- PS 0-2

→ CHOP
CHOEP
CHP-BV*

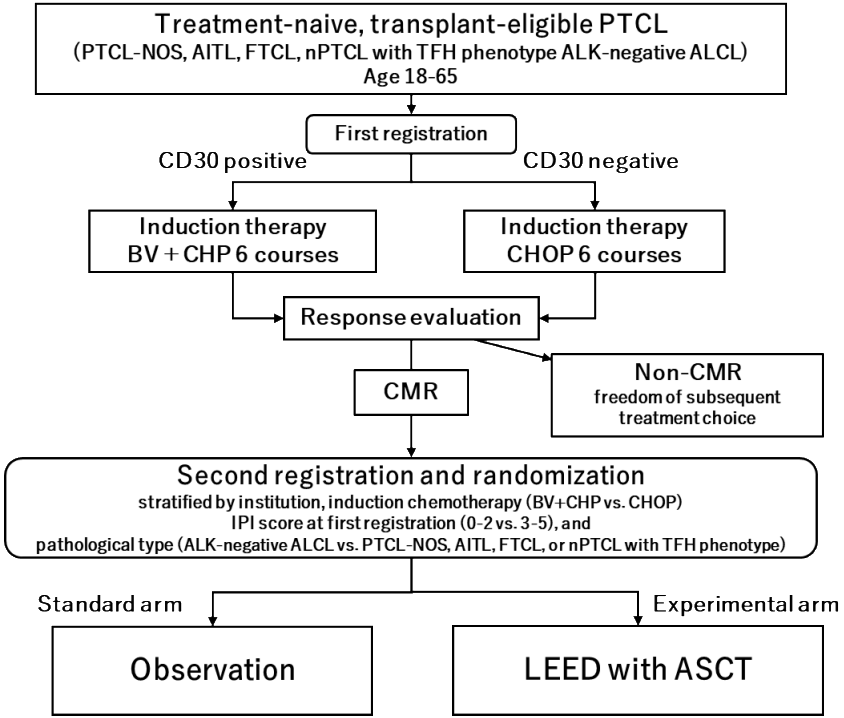
*ALK-neg ALCL only

→ CHOP
CHOEP
CHP-BV* } + ASCT (if CR)

- Enrollment goal n= 204
- Primary endpoint PFS in CR patients
- August 2022 activated (NCT05444712)
- Dr. Bachy PI (France)

JCOG2210, TRANSER STUDY

142 patients from
52 Hospitals



Ryosuke K. Japan ese Journal of Clinical Oncology Febb 2025

CHOP+ X = CHOP

Experimental regimen	Trial design	Outcomes	Reference
Romidepsin-CHOP	PIII	CR 41%; 2Y PFS 42%	Bachy et al. JCO 2022
Alemtuzumab-CHOP	PIII	CR 52%; 3Y EFS 35%	ACT-1 (Young) d'Amore ASH 2018
Alemtuzumab-CHOP	PIII	CR 60%; 3Y EFS 27%	ACT-2 (Elderly) ACT-2 Wulf Leukemia 2021
Lenalidomide-CHOP	PII	CR 41%; 2Y PFS 42%	Lemonnier et al. Blood Adv 2021
Lenalidomide-CHOEP	PII		Stuver BJH 2023
Denileukin diftitox-CHOP	PII	CR 55%; 2Y PFS 43%	CONCEPT Foss et al. Leuk Lymphoma 2013
Vorinostat-CHOP	PI		Oki 2013
Belinostat-CHOP	PI		Johnston Exp Hematol Oncol 2021
Chidamide-CHOP			Lu 2016
Azacytidine-CHOP	PII		Ruan Blood 2023
Everolimus-CHOP	PII		Kim 2016
Pralatrexate-CHOP	PI		Fol-CHOP Iyer Blood Adv 2024
Pralatrexate-CEOP	PII		Advani BJH 2016
Bortezomib-CHOP	PII		Kim EJC 2012
Bevacizumab-CHOP	PII	CR 49%; 1YPFS 44%	Ganjoo Leuk Lymphoma 2014
VIP-reinforced ABVD	PIII	CR 44%; 2Y EFS 45%	GOELAMS-LTP95 Simon et al. BJH 2010
Pralatrexate-CEOP	PII	CR 52%; 2Y PFS 39%	Advani et al. BJH 2016
Modified HyperCVAD	PII	CR 46%; 2Y PFS 46%	Hapgood et al. Leuk Lymphoma 2019
GEM-P	PII	CR 46%; 2Y PFS 38%	CHEMO-T Gleeson et al. Lancet Haematol 2018
PEGS	PII	CR 24%; 2Y PFS 12%	SWOG S0350 Mahadevan et al. Cancer 2013
CEOP/IVE/GDP	PII		Cai Genome Med 2020
ICED	PII		ROSE Kim Front Oncol 2023

CHOP+ X = CHOP

X: is it efficient enought? Or something wrong with CHOP?

Drug (n)	Dose as Single Agent	Daily DI as Single Agent (mg/kg/day)	Dose in Combination	Daily DI with CHOP (mg/kg/day)	% Dose Intensity	Reference
Romidepsin	14 mg/kg D 1, 8 and 15 Q28 day	1.5 mg/kg/day	12 mg/kg D 1 and 8	1.1 mg/kg/day	28% Reduction in DI	Bachy et al., 2021
Brentuximab vedotin	1.8 mg/kg Q21 days	0.9 mg/kg/day	1.8 mg/kg D 1	0.9 mg/kg/day	100% of planned DI	Horwitz et al. 2019 & 2022
Vorinotstat	400 mg PO QD	400 mg/day	300 mg PO tid days x 5 days	214 mg/day	47% Reduction in DI	Oki et al. 2013
Everolimus	10 mg PO QD	10 mg/day	5 mg D 1-14 Q 21 D	3.3 mg/day	66% Reduction in DI	Kim et al. 2013
Denilukein difitox	18 mcg/kg/day x 5 day Q21 D	2.1 mcg/kg/day (or 4.2 mcg/kg/day)	18 mcg/kg D 1 and 2 Q 21D	1.7 mcg/kg/day	80% of planned DI	Foss et al. 2013
Bortezomib	1.3 mg/m2 Days 1, 4, 8 and 11 Q 21 D	0.25mg/kg/day	1.6 mg/m2 Days 1 & 8	0.15 mg/kg/day	40% Reduction in DI	Lee et al., 2008
Chidamide	50 mg TIW x 3 wks Q21 D	9.5 mg/day	30 mg Days 1, 4 and 8 Q 21 days	4.3 mg/day	55% Reduction in DI	Lu et al. 2016

Courtesy of Owen O'Connor

Phase 3 ECHELON-2 CHP-BV vs CHOP in CD30+ PTCLs

Eligibility
- Treatment naïve
- CD30+ PTCL (≥10% cells)
- Targeting 75% ALCL (ALK+ IPI ≥ 2)

R

- CHOP x 6-8
- Brentuximab vedotin + CHP x 6-8

CHP–BV vs CHOP
Improved PFS √
Improved OS √
Comparable toxicity √
Rapid FDA approval 2018 √

Primary endpoint:
PFS= death, subsequent therapy to treat residual or PD

***Events do not include consolidative RT/SCT**

Total 552	A+CHP (N=226)	CHOP (N=226)
Disease diagnosis, n (%)		
sALCL	162 (72)	154 (68)
ALK+	49 (22)	49 (22)
ALK-	113 (50)	105 (46)
PTCL-NOS	29 (13)	43 (19)
AITL	30 (13)	24 (11)
ATLL	4 (2)	3 (1)
EATL	1 (0)	2 (1)

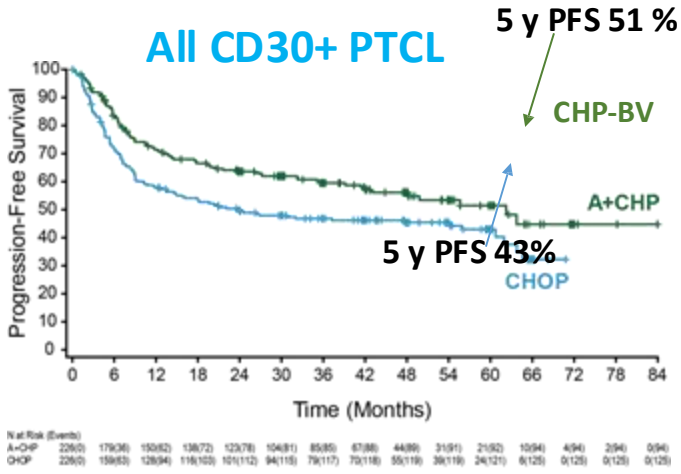
ALCL represents 70% of enrolled patients

PTCL-NOS n=72 (13%)
AITL n=54 (~10%)

Horwitz et al. ASH 2018; Horwitz et al. Lancet Oncology 2019

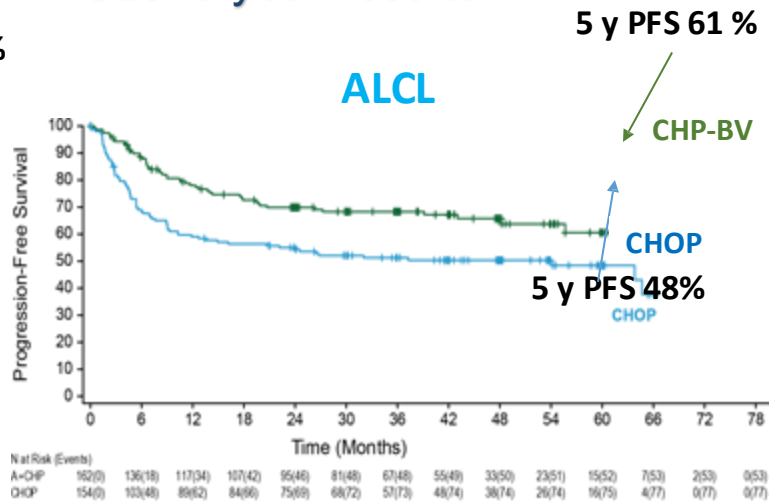
CHP-BV in CD30+ PTCLs: 5 year results

All CD30+ PTCL



	N	Events	Medians (Months)	HR (95% CI)	p-value*
A+CHP	226	94	62.26	0.70 (0.53, 0.91)	0.0077
CHOP	226	125	23.75		

ALCL



	N	Events	Medians (Months)	HR (95% CI)	p-value*
A+CHP	162	53	-	0.55 (0.39, 0.79)	0.0009
CHOP	154	77	54.18		

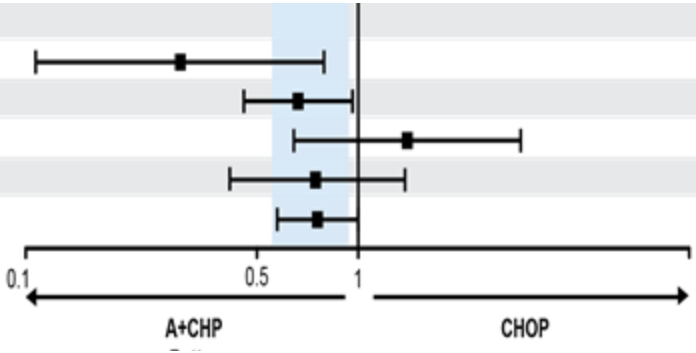
	5 y PFS CHP-BV	5 y PFS CHOP
ALK-negative	49%	39%
ALK- positive	87%	67%

Horwitz et al Ann. Oncology 2022

What is the evidence for CHP-BV in CD30+ non-ALCL PTCLs?

CHP-BV vs CHOP subgroup analyses

Disease Indication			
ALK-positive sALCL	5/49	16/49	0.29 (0.11, 0.79)
ALK-negative sALCL	50/113	60/105	0.65 (0.44, 0.95)
AITL	18/30	13/24	1.40 (0.64, 3.07)
PTCL-NOS	19/29	31/43	0.75 (0.41, 1.37)
PFS (PD, Death)	84/226	103/226	0.75 (0.56, 1.00)



CHP-BV better

CHOP better

Challenges:

1) Unplanned subgroup analysis

2) Small patient numbers

- AITL: n=54; PTCL-NOS n=72

3) Definition of CD30 + was ≥ 10%

Horwitz et al Lancet Oncology, 2019

CHP-BV in CD30+ non-ALCL PTCLs: SGN35-02 STUDY

FRONTLINE BRENTUXIMAB VEDOTIN AND CHP (A+CHP) IN PATIENTS (PTS) WITH PERIPHERAL T-CELLLYMPHOMA WITH LESS THAN 10% CD30 EXPRESSION: RESULTS FROM THE PHASE 2 SGN35-032 STUDY

Seventy pts received ≥1 dose of study drug as of June 30, 2023.
Median age was 63.5 years, 57% were male, and 90% had ECOG ≤1. Most had stage IV disease (63%) and were in the CD30 1% to <10% cohort per local CD30 (55%).
Median treatment duration was 18 weeks (range, 0-24 weeks)

Table 1. Endpoints per BICR by cohort

	CD30 <1%	CD30 1% to <10%
Per local CD30[a]	N=29	N=36
ORR, % (95% CI)	79 (60.3, 92.0)	78 (60.8, 89.9)
CR rate, % (95% CI)	66 (45.7, 82.1)	67 (49.0, 81.4)
Per central CD30[a]	N=19	N=25
ORR, % (95% CI)	63 (38.4, 83.7)	80 (59.3, 93.2)
CR rate, % (95% CI)	53 (28.9, 75.6)	68 (46.5, 85.1)

a Analysis performed among EE set, a subset of all treated pts with postbaseline response assessment or discontinue treatment.

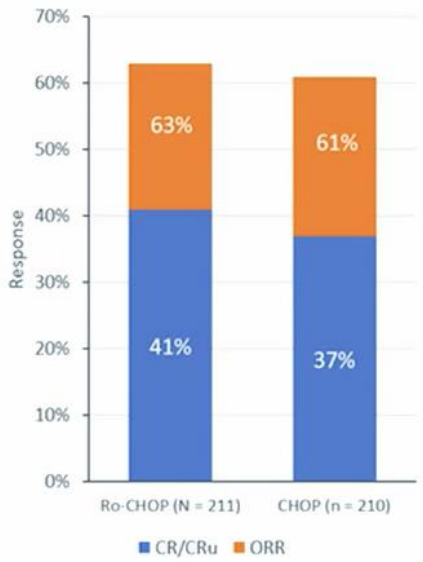
ORR 77%
with
CR 65%

In pts with non-sALCL PTCL with <10% CD30 expression, A**+CHP as frontline therapy appears effective and has a safety profile consistent with label.**

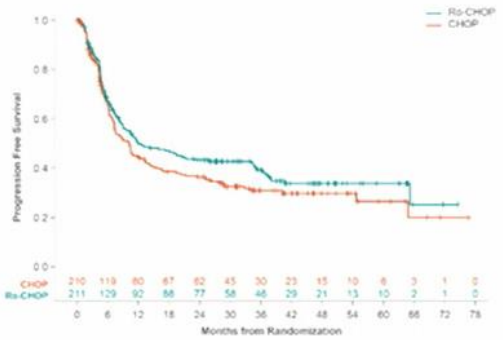
Swaminathan Padmanabhan Iyer et Al, Poster session ASCO 2024

Ro-CHOP Efficacy

Ro-CHOP: Response at End of Treatment

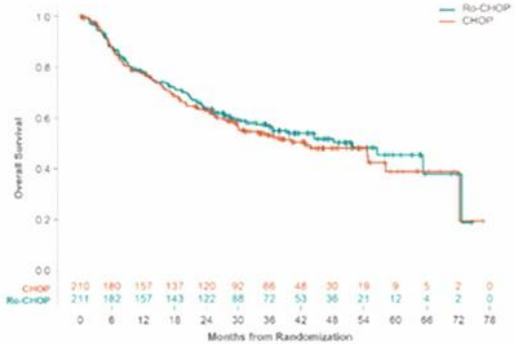


Ro-CHOP: PFS by independent RAC (ITT Population)*



	Ro-CHOP (n = 211)	CHOP (n = 210)
PFS, median (95% CI), mo	12.0 (9.0-25.8)	10.2 (7.4-13.2)
HR (95% CI)	0.81 (0.63-1.04)	
P value	0.096	

Ro-CHOP: OS (ITT Population)



	Ro-CHOP (n = 211)	CHOP (n = 210)
OS, median (95% CI), mo	51.8 (35.7-72.6)	42.9 (29.9-NR)
HR (95% CI)	0.90 (0.68-1.20)	
P value	0.477	

Bachy et al. JCO 2022; Camus et al. JCO 2024

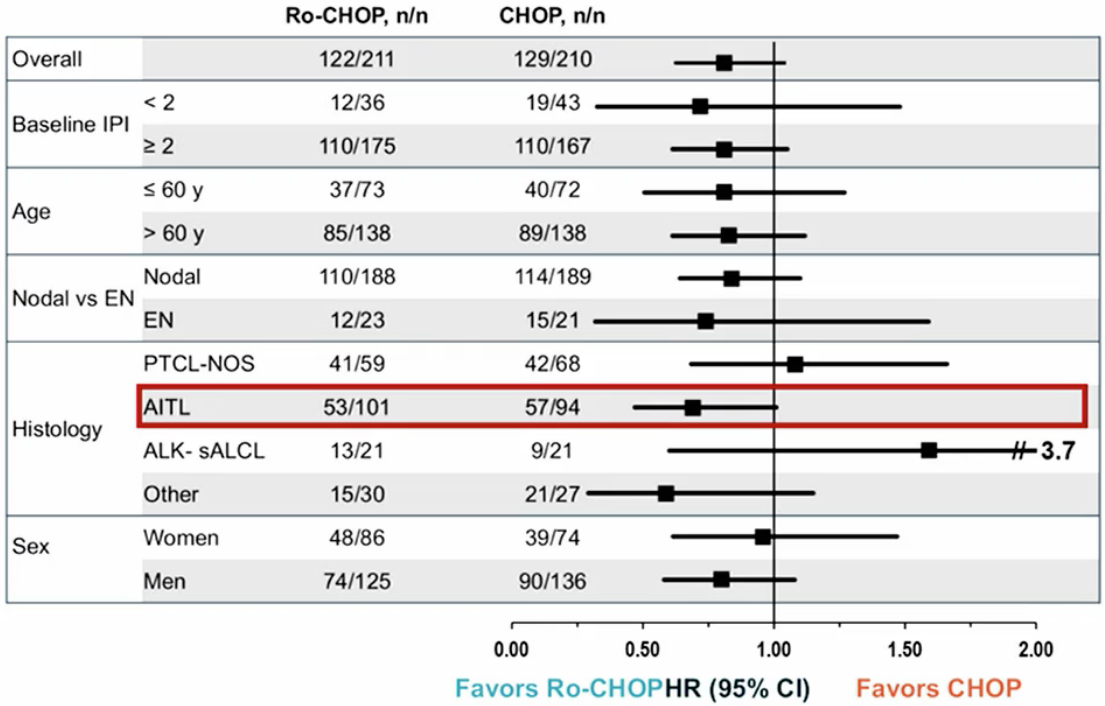
Ro-CHOP

TEAEs and Dosing	Ro-CHOP	CHOP
Grade 4	74%	42%
Grade ≥ 3	94%	70%
• Thrombocytopenia	50%	10%
• Neutropenia	49%	33%
• Anemia	47%	17%
• Leukopenia	32%	20%
• Febrile neutropenia	21%	10%
Discontinued due to AEs	8%	NR
Dose Reduction	37%	NR
Dose Interruption	63%	NR
Dose Intensity <90%	15%	9%

!

Courtesy of Owen O'Connor

Ro-CHOP
Subgroup Analysis of PFS (ITT population) –Outcomes in AITL

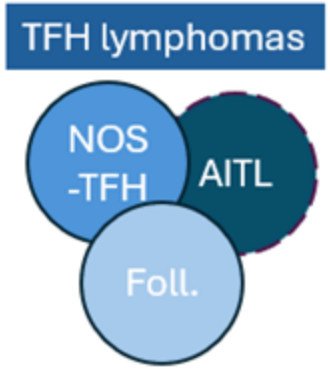


CHOP +/- Romidepsin
Update 5 years

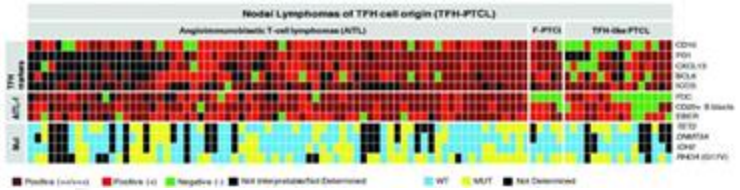
Regimen	No.	PFS	PFS by Subtype
Ro-CHOP[7,12]	421		
Ro-CHOP	211	Median PFS—12.0 months	Median PFS TFH—19.5 months Non-TFH—8.7 months Median OS TFH—65 months PTCL-NOS—25.8 months
CHOP	210	Median PFS—10.2 months	Median PFS TFH—10.6 months Non-TFH—9 months

Bachy et al. JCO 2022; Camus et al. JCO 2024

T-Follicular Helper Lymphomas and Role of Epigenetic Modifiers



- -Recurrent mutations in TET2, RHOA, IDH2, DNMT3A



Azacitidine + CHOP: Phase II Study

Key Eligibility

- Untreated PTCL
  - Nodal T-cell lymphoma with T-follicular helper (TFH) phenotype (WHO 2016 classification)
    - Angioimmunoblastic T-cell lymphoma
    - Follicular T-cell lymphoma
    - PTCL/NOS, T-follicular helper (TFH) variant
  - PTCL-NOS
  - Anaplastic large cell lymphoma, ALK negative
  - Anaplastic large cell lymphoma, ALK positive with IPI >2
  - Adult T-cell leukemia / lymphoma

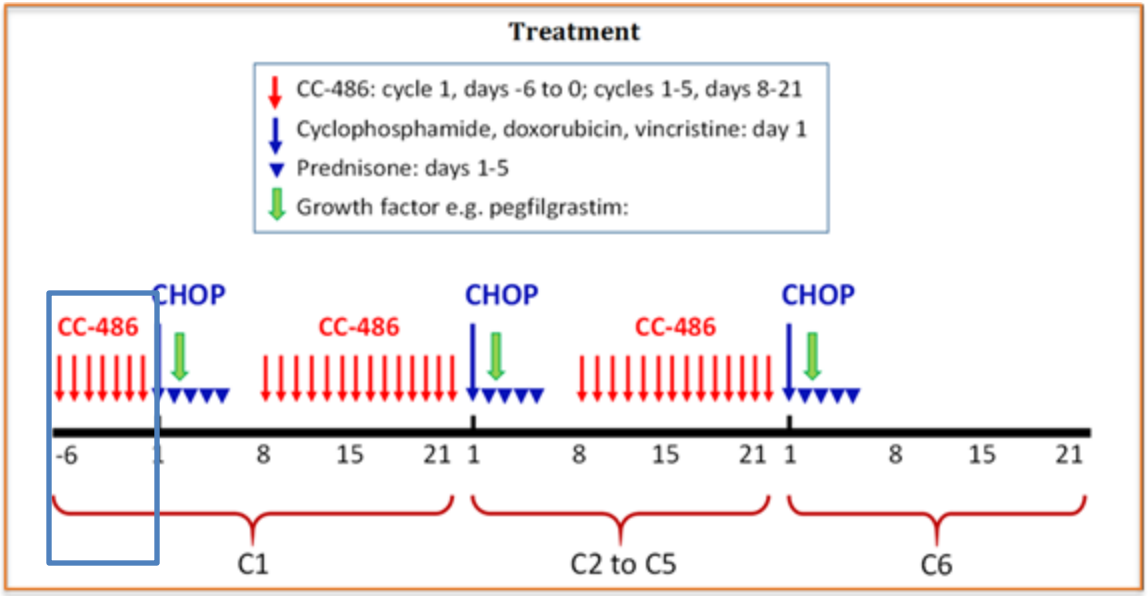
17/20

Objectives

1st – CRR; 2nd – ORR, safety and survival
Exploratory genomic, transcriptomic and methylomic biomarkers

Sample Size = 20

Simon's two-stage design (alpha=10%, power=80%)



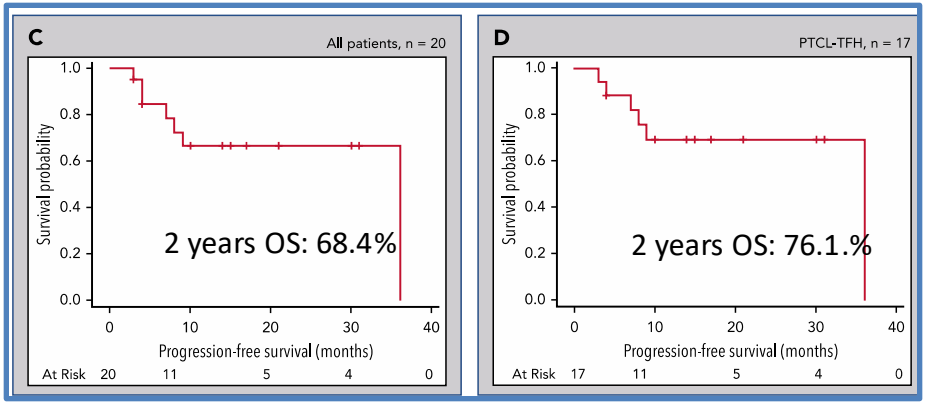
- CC486 at 300 mg daily from day -6 to day 0 for cycle 1 priming, and on days 8-21 following cycles 1-5.
- Patients in CR/PR following 6 cycles of treatment have the option to proceed to consolidative HSCT.

Ruan et al.Blood Adv. 2023

Azacitidine + CHOP: Phase II Study

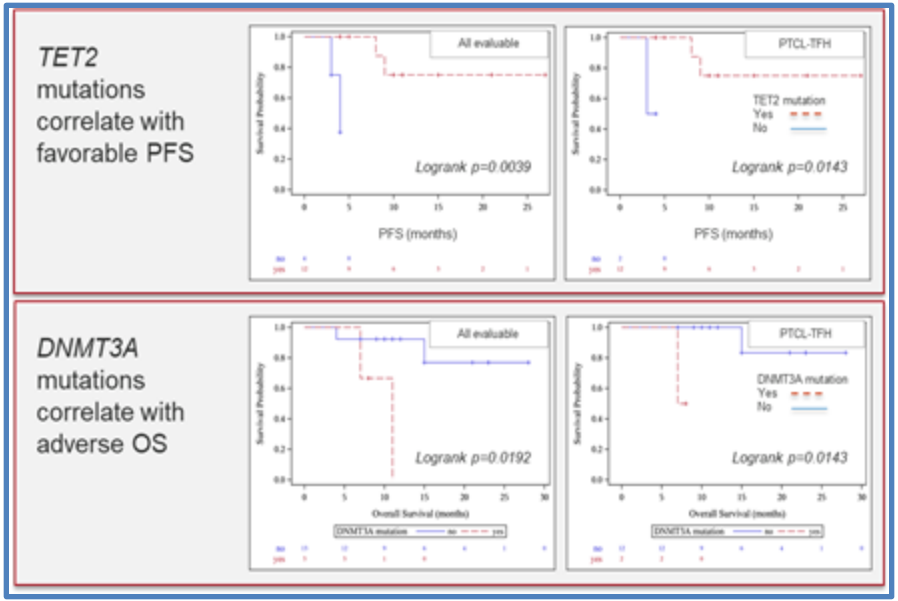
- All population ORR (n=20): 75% (75% CR)
- PTCL-THF ORR (N=17): **88% (88% CR)**

Overall Survival



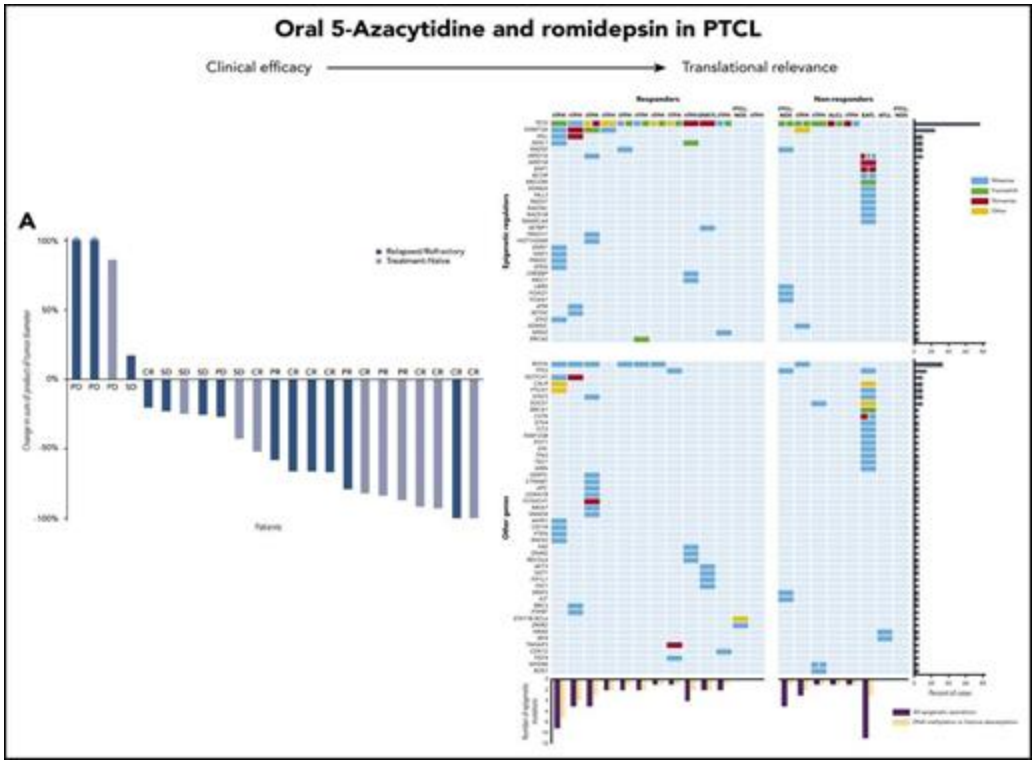
50% received Auto-Transplant

TET2 mutations associated with CR and favorable PFS



Ruan et al. Blood Advances 2023

Non-CHOP Approaches



Phase 2 study n=25 relapsed/refractory AND treatment naïve PTCLs

→ **Treatment naïve n=11 (TFH/AITL n=8)**
ORR 70% CR 50% (n=10 evaluable)

→ **Relapsed/refractory n=14***
ORR 54% CR 38% (13 evaluable)
*includes 5 pts from expansion ph 1

TFH PTCL n=17
ORR 80% CR 60%

Grade 3/4
Thrombocytopenia 48%
Neutropenia 40%
Febrile neutropenia 12%

Falchi et al. Blood 2021

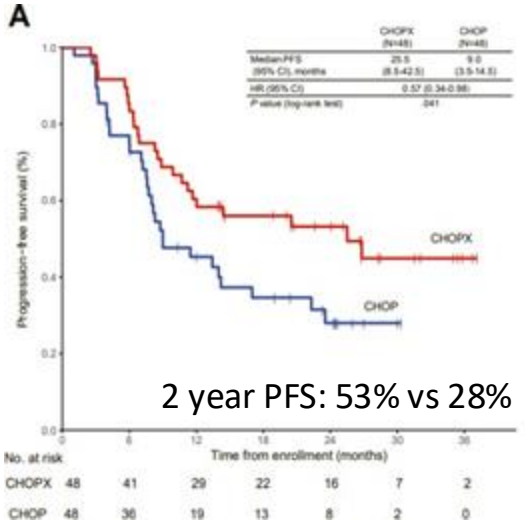
Phase III Study: Guidance-03

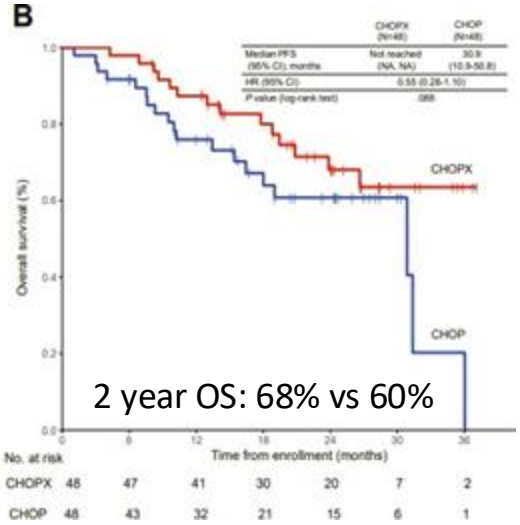
Targeted agents plus CHOP compared with CHOP as the first-line treatment for newly diagnosed patients with peripheral T-cell lymphoma (GUIDANCE-03): an open-label, multicentre phase 2 clinical trial

Ming-Ci Cai,[a,j] Shu Cheng,[a,j] Hong-Mei Jing,[b,j] Yan Liu,[a,j] Guo-Hui Cui,[c] Ting Niu,[d] Jian-Zhen Shen,[e,j] Liang Huang,[f] Xin Wang,[g] Yao-Hui Huang,[a] Li Wang,[a,h] Peng-Peng Xu,[a] and Wei-Li Zhao[a,h,*]

CHOP X 1 Cycle → **CHOP X** X 5 Cycles

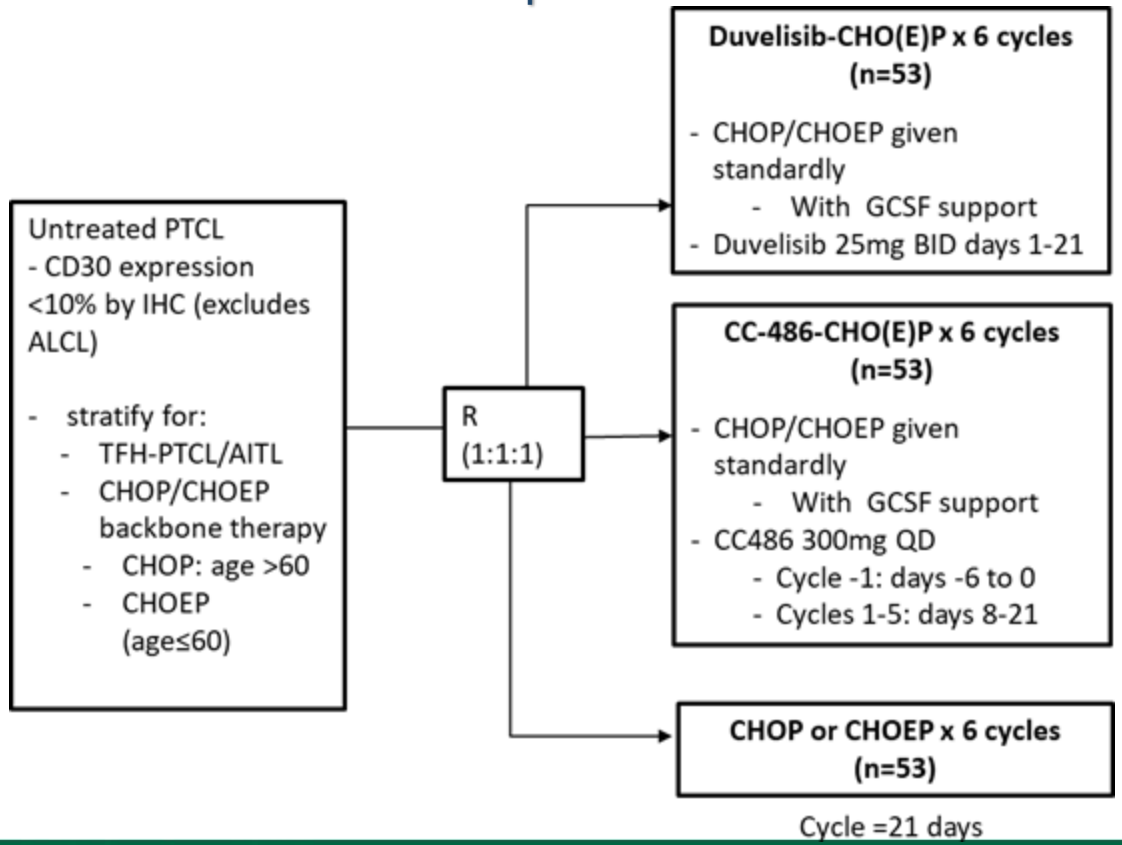
CHOP **X**
-P53^{mut}- decitabine
-TET2/KMT2D ^{mut} azacytidine
-CREBBP/EP300 ^{mut} tucidinostat
-with out mutation above: Lenalidomide





Lancet Regional Health Western Pacific 2024;50:101160,

A051902: A randomized phase II study of duvelisib or 5-azacitidine in addition to CHOP or CHOEP in comparison to CHOP/CHOEP



- Primary Objective:
  - To compare the PET CR rate of duvelisib or 5-azacitidine in combination with CHOP/CHOEP compared to CHOP/CHOEP
- Primary Endpoint:
  - **25% difference PET CR rate**
- Correlative Studies:
  - Monitoring MRD
  - Gene Expression Profiling and Custom Capture Sequencing
  - Patient Reported Outcomes
  - PET/CT Evaluation

NCT04803201

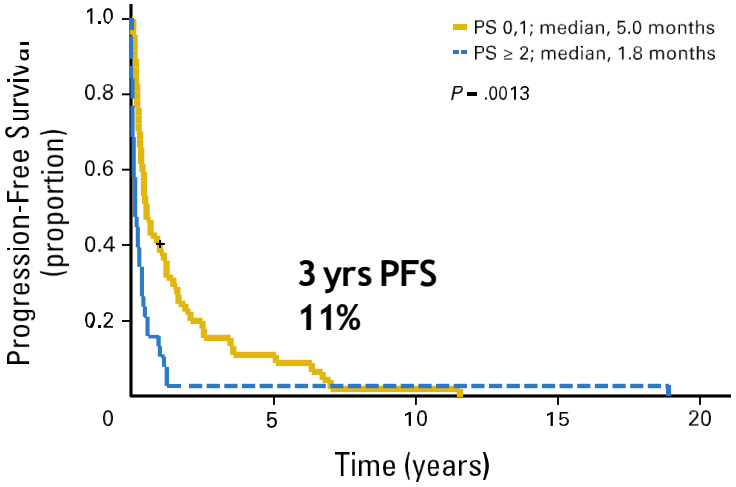
Conclusions FIRST LINE THERAPY

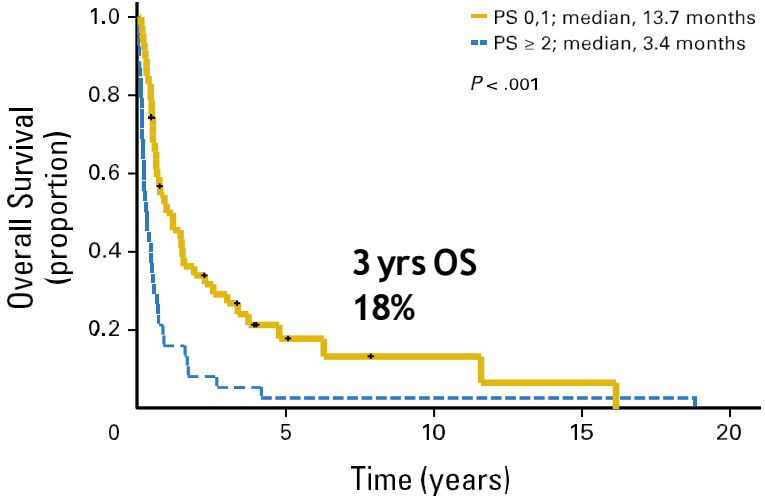
- Advances in understanding the biology and molecular mechanisms of PTCL have led to improved classification and treatment strategies
- Treatment approaches have become more targeted, offering the potential for better patient outcomes
- BV-CHP has changed the treatment landscape in ALCL
- Intensification regimens-safe and effective
- Recent studies highlight the sensitivity of TFHL to epigenetic therapies
- Future research should prioritize evaluating new treatments for specific subtypes or molecularly defined subgroups

Outcome of Relapsed/Refractory nodal PTCL lymphomas failing first-line therapy

N=153, only 7% ALCL ALK pos.

1980-2011





No New drugs, ONLY chemotherapy, exclusion of patients candidate at transplantation

Mak V, Journal of Clinical Oncology 2013

Outcome of R/R TCL and NKCL: PETAL CONSORTIUM 2010-2021

Retrospective study N=925 Including Mature TCL and NKTCL

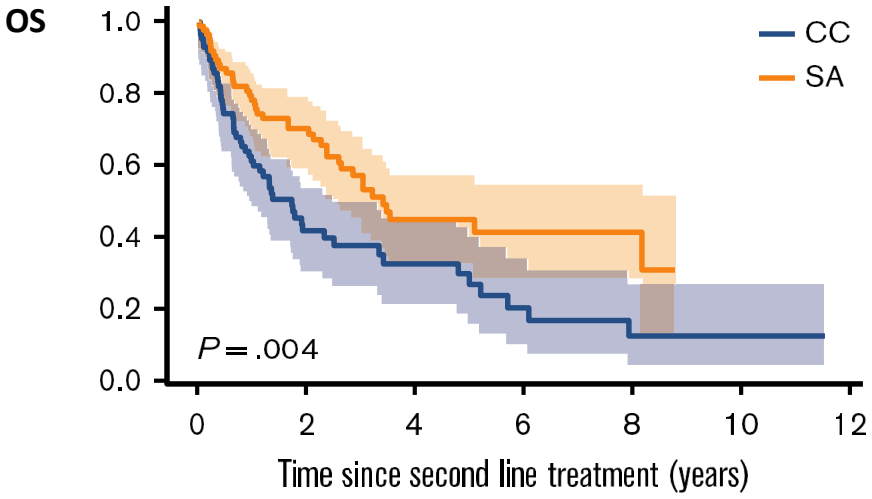
N=763 survival analyses from the start second therapy

Second-line therapies:
Chemotherapy CC : 60%
New Drugs SA (Antifolate, ADC, Signaling inhibitors, and Epigenetic modifiers): 35%

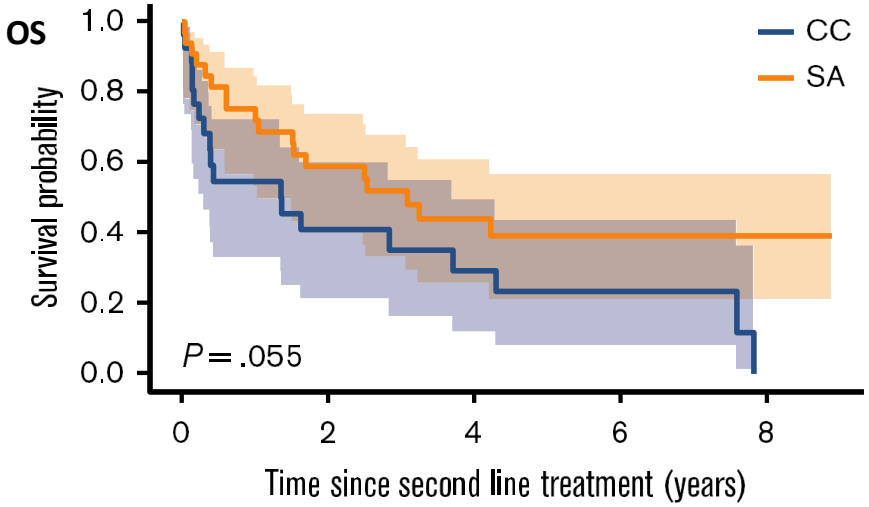
ALL pts Overall CR rate: 35%

Overall TX consolidation: 20%

AITL



ALK– ALCL



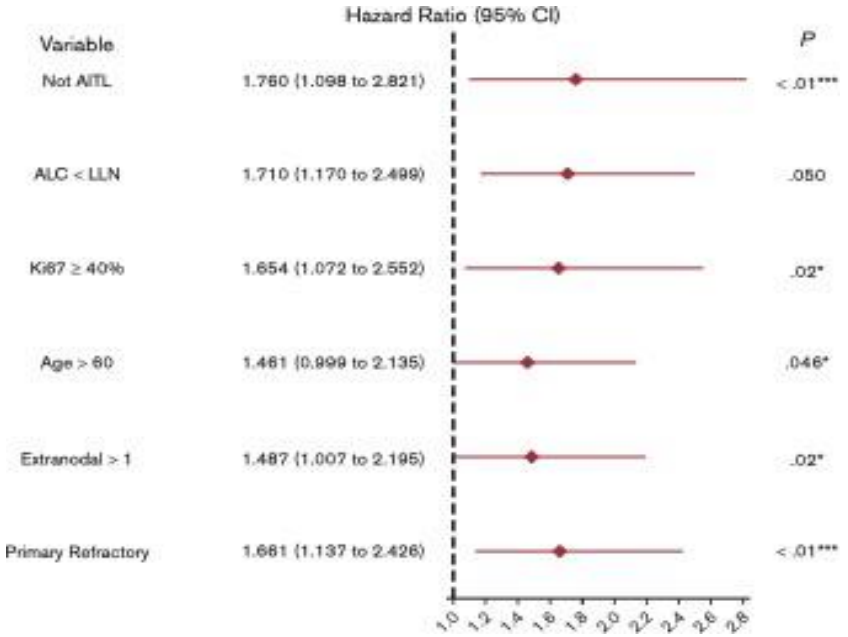
Han JX, Blood Advance 2025

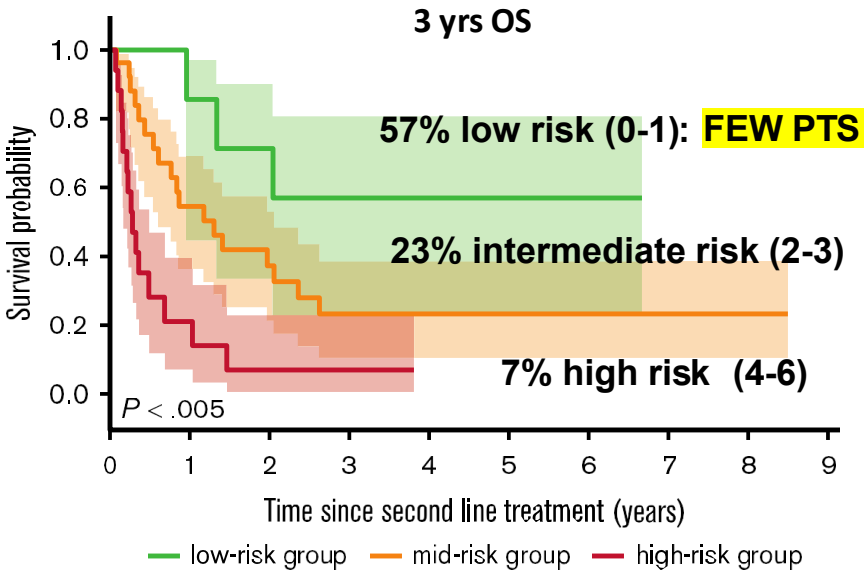
Outcome of R/R TCL and NKCL: PETAL CONSORTIUM (2010-2021)

Retrospective study N=925 Including Mature TCL and NKTCL

N=763 survival analyses from the start second therapy

PIRT score: performed on 248 pts





Han JX, Blood Advance 2025

Chemotherapy Drugs

Drug	N°pts	Histological Subtype	ORR%/CR%	Median PFS Median DOR	Median OS
Gemcitabine	39	51% PTCLNOS 49% MF	55%/30% 48%/16%	-	-
ICE **Tay T 2022**	60	PTCL 43% AITL 28% ALCL 22% Others 7%	68%/45%	**4,4 months**	20 months
Bendamustine **(alkyl/purine analog)** **prospective** **Damaj J 2012**	**60**	**PTCLNOS 38%** AITL 53% ALCL 3,5% Others 6%	**50%/28%**	**3,63 months** 3,5 months	**6,27 months**
Pralatrexate **O'Connor OA 2011**	**111**	**PTCLNOS 53%** AITL 12% ALCL 15% Others 20%	**29%/**14% 32% PTCL-NOS 35% ALCL 8% AITL	**3,5 months** 10,5 months	14,5 months

New drugs

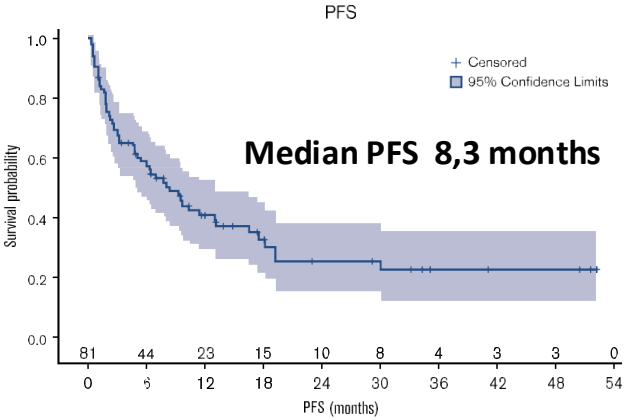
Drug class	Target	DRUGS Name	Main Efficacy
Anti CD30 targeting therapies	CD30	Brentuximab	ALCL Alk + and Alk neg> CD30+ TCL
Signaling Pathways Inhibition	ALK Inhibitors	Crizotinib, Alectinib	ALCL ALK POS
	Jak Inhibitors	Ruxolitinib/ Golidocitinib	JAK2mutated/STAT3+
	PI3-Kinase Inhibitors	Duvelisib Tenalisib Linperlisib	TFH> others
EPIGENETIC	HDAC Inhibition	Romidepsin, Belinostat, Chidamide	TFHL > others
	Hypomethylating Agents	Azacytidine, Decitabine	
	EZH1/EZH2 Inhibitors	Valemetostat	
Immunomodulators		Lenalidomide	TFHL > others

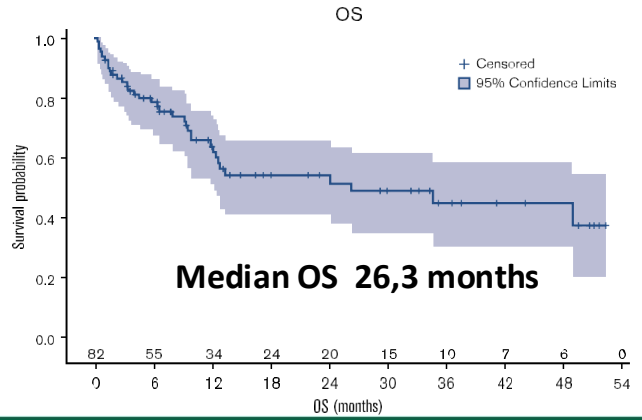
Brentuximab+Bendamustine

ORR 68%, CR rate 49%

Variable	N=82
Median	60 25-86
Subtype	TFH 51% PTCLNOS 16% ALCL 27% Others 8%
CD30 Expression (>5%)	Pos 63% Neg 21% Missing 9%
Previous Exposition to Brentuximab	11%
Previous SCT	30%

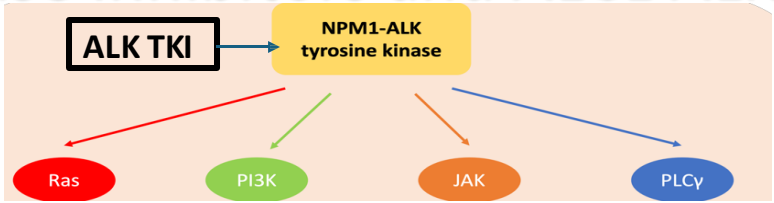
30% consolidated with transplantation
(6 Autologous and 16 AlloSCT)



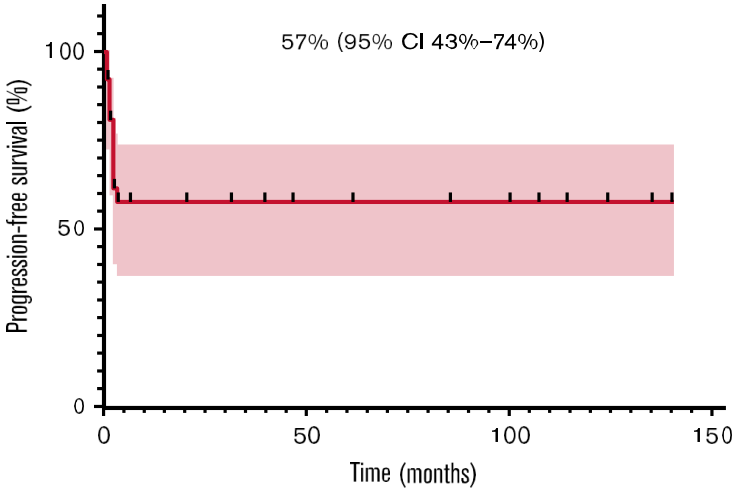


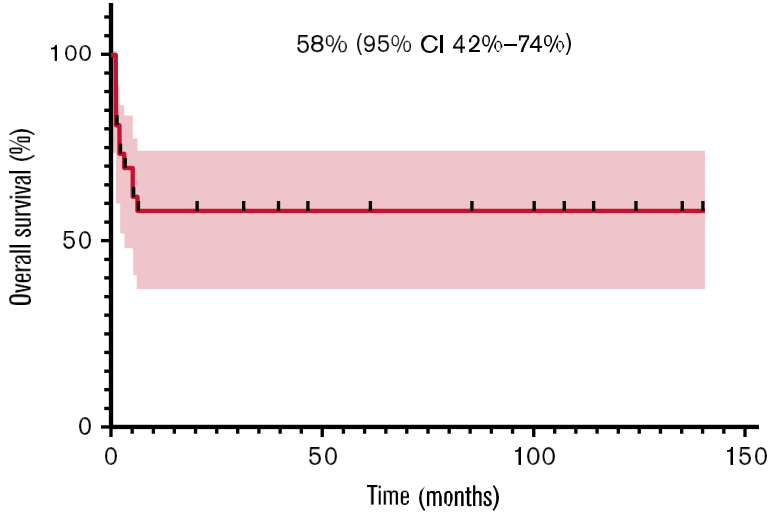
Aubrais R, Blood Advance 2023

ALK Tyrosine Kinase Inhibitors and ALCL ALK +

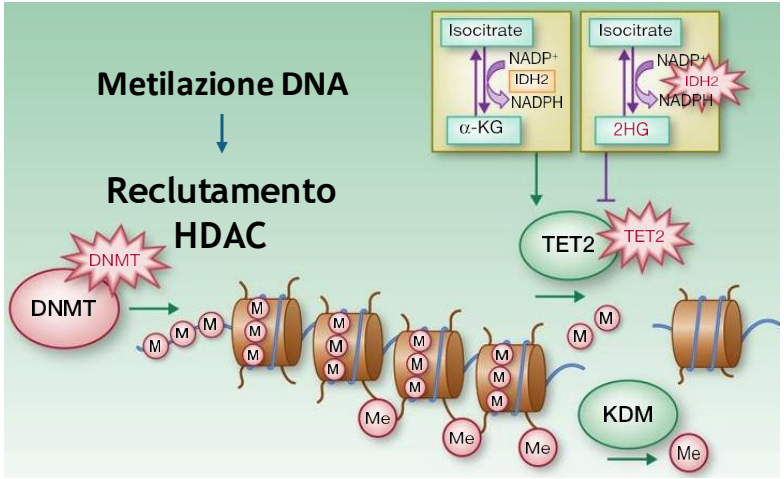


Crizotinib: N=27 (N=25 ALCL ALK+, N=1 DLBCL ALK pos; n=1 Plasmoblastic); median previous therapies 2

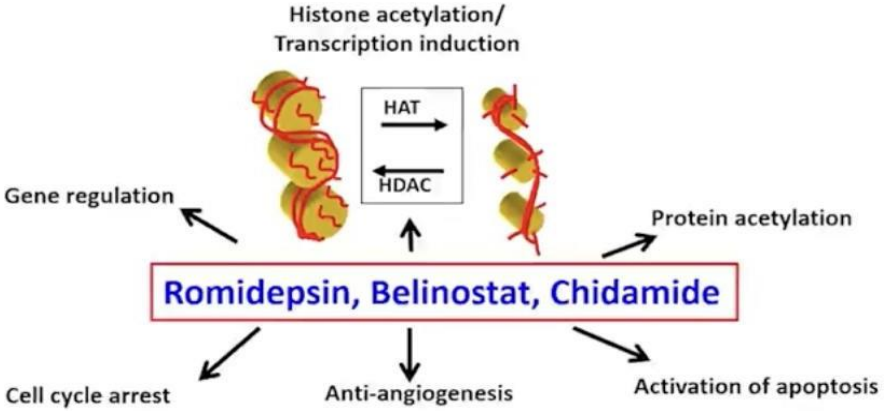




Rindone G. Blood Advance 2023



HDAC Inhibitors in Phase II trials

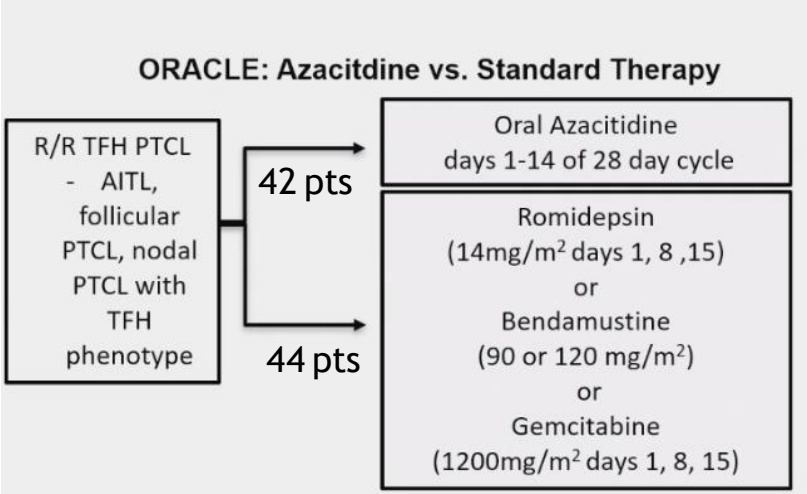


	Romidepsin* ORR (%) /CR (%)	mPFS mDOR	Belinostat ORR (%) /CR (%)	mPFS mDOR	Chidamide ORR (%)/CR%	mPFS mDOR
Overall	25%/15%	4 mo 17 mo	26%/11%	1.6 mo 13.6 mo	28%/14%	2.1 mo 10 mo
AITL	30%/19%		45%		50%/40%	
PTCLNOS	29%/14%		23%		22%/7%	
ALK-negative	24/19%		15%		45%/36%	

* Withdrawn 2021 for PTCL

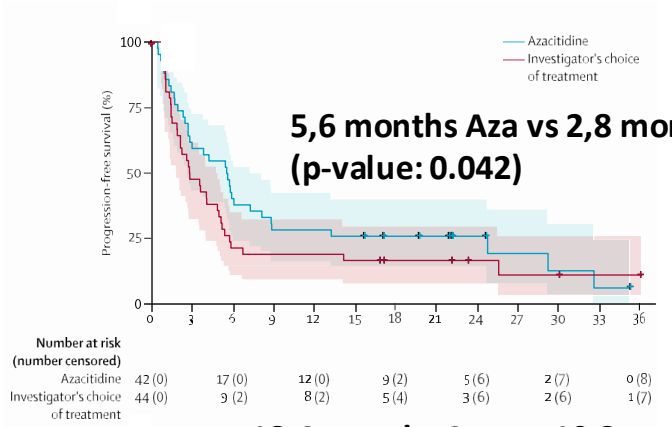
Coiffier JCO 2012; O'Connor et al. JCO 2015; Shi et al. Ann Onco 2015

ORACLE STUDY: ORAL AZACYTIDINE VERSUS INVESTIGATOR'S CHOICE in T-FHL Lymphomas

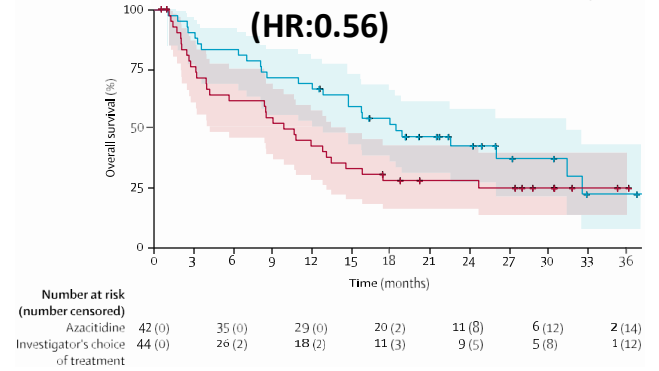


CR RATE: 12% Aza vs 23% other therapies
Median Duration of Response: 10,4 months versus 3,4 months

The primary endpoint, PFS advantage, was not met (p-value < 0.025)



5,6 months Aza vs 2,8 months others (p-value: 0.042)



18.4 months Aza vs 10,3 months others (HR:0.56)

Depuis J, Lancet Hematology 2024

VALENTINE-PTCL01 (VALEMETOSTAT: EZH1 andEZH2 Inhibitor phase II study

Variable	N= 133
Age, years	69 (58-74)
Sex (Male/Female)	68%/32%
ECOG (0-1/2-3)	93%/7%
Subtypes ALCLpos/ALCLneg TFH Lymphomas PTCL NOS Others	 2%/5% 40% 34% 19%
Previous Lines	2 (1-3)
Previous any type Tx	26%

Zinzani P, Lancet Oncology 2024

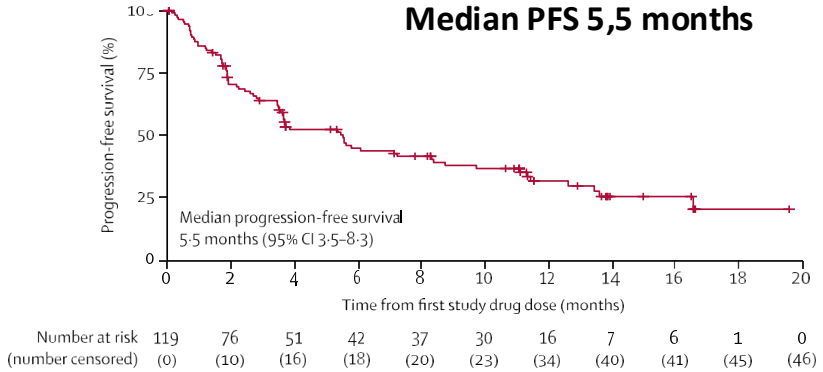
Study Endpoint: Objective RESPONSE

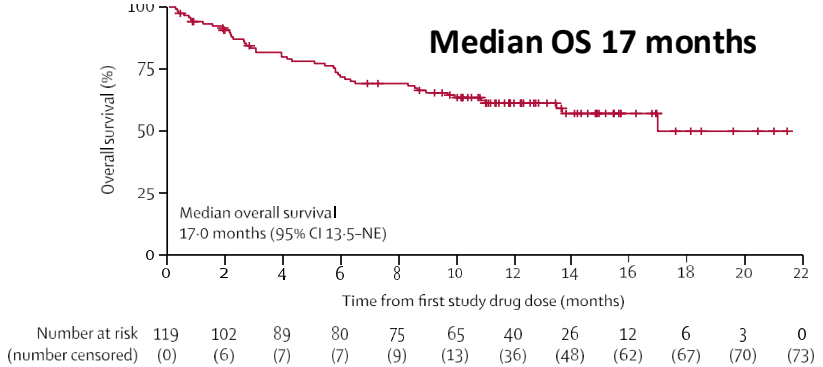
Response and Outcome in Nodal R/R TCL

Variable	ORR/CR	DOR
Entire population	52%/27% (PET/CT)	11,9 months
TFH	54%	
PTCL-NOS	32%	
ALCL	33%	

Median time to first response 8 weeks
Median DOR 11,9 months
Low incidence of treatment discontinuation
10% (!!! Thrombocytopenia).
8% proceed to AlloSCT

Median FUP 12,3 months





Zinzani P, Lancet Oncology 2024

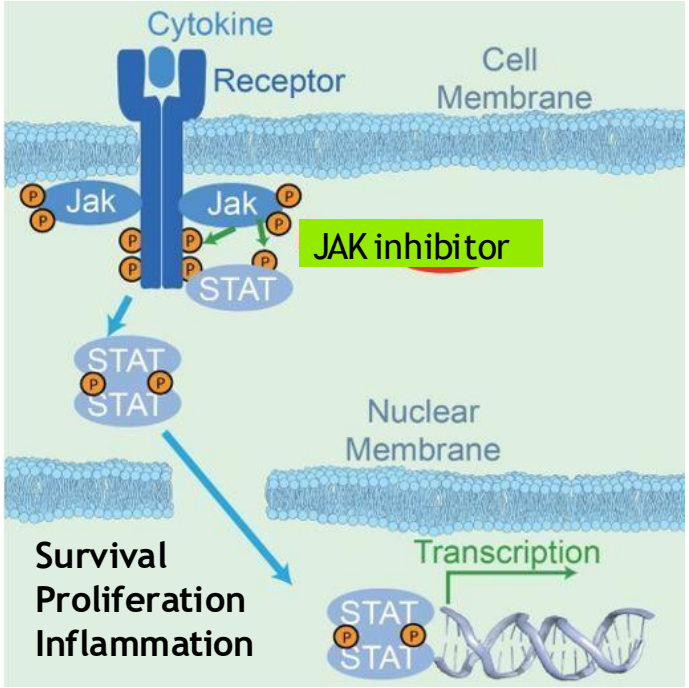
PI3K Inhibitors

Drug	N°	ORR%/CR%	Subtype response	Median PFS	Subgroups mPFS
Duvelisib* δ/γ (PRIMO TRIAL)	**123**	48%/33%	AITL 62% PTCLNOS 49% ALCL 15%	3,5 months	AITL: 8,3 months PTCLNOS: 3,5 months ALCL:1,6 months.
Linperlisib δ**	35	48%/33%	AITL: 62% PTCL: 39% ALCL: 25%	3,6 months	

*** pts that proceed to SCT : 15%; !!! Infections (4.4% fatal treatment related events);**
**** pts that proceed to SCT: 14%; only one death wound infection not drug related**

Neha Metha Shah 625 Abstract; ASH 2024; Lyer PS ASH 2024

GOLIDOCITINIB, A SELECTIVE JAK1 INHIBITOR in R/R TCL



Variable	N=88
Age, median age(years)	58 (51-67)
PTCL-NOS	57%
AITL	18%
ALCL	11%
Others	13%
Previous therapies	
Chemotherapy	100%
HDAC	50%
CD30-target therapies	10%
Others	1%

Dose: 150 mg orally until PD or Toxicity

Song Y et. al. Lancet Oncology 2024

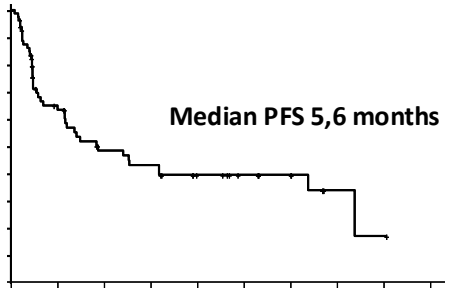
GOLIDOCITINIB, A SELECTIVE JAK1 INHIBITOR in R/R TCL

ORR and ORR by Subtype	%
All pts ORR/CR rate	44%/24%
PTCL-NOS (23/50)	46% (23/50)
AITL	56% (9/16)
ALCL	10% (1/10)

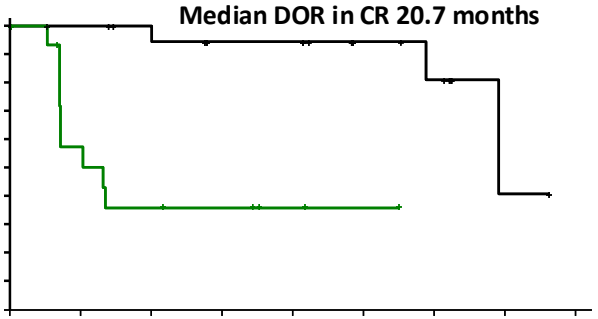
Prior HDAC Inhibitor	
Yes	24/44 (55%)
No	15/44 (34%)

Median DoR (months) 20·7 months
Median follow-up time (months) (IQR) 12· 5 months
Discontinuation drug 9%

PFS



DOR



Song Y et. al. Lancet Oncology 2024

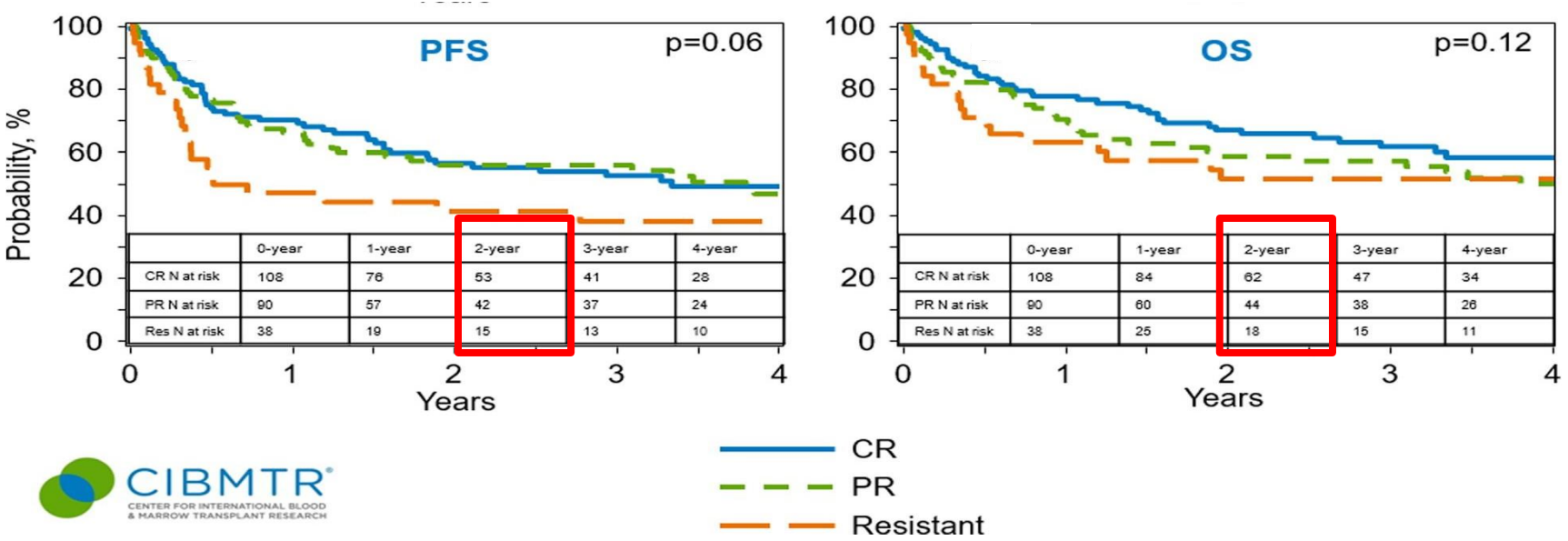
Allogeneic SCT

Patients fit, consider comorbidities, Any donor

AITL	PTCL	ALCL alk -neg	ALCL alk -pos
Sensitive Relapse: yes **Refractory Relapse:** yes (in case of low burden)	**Sensitive Relapse:** yes **Refractory Relapse:** no	**Sensitive Relapse:** yes **Refractory Relapse:** ?	**Sensitive Relapse:** yes ? **Refractory Relapse:** yes

-**Consolidation of "first remission" only in specific "subtype"** : **APPROVED INDICATIONS:** Hepatosplenic and ATLL Lymphomas/Acute, **TO BE DEFINED:** Advanced NKTCL; Monomorphic epiteliotrophic Intestinal T-cell lymphomas

Allogeneic SCT in Angioimmunoblastic



CIBMTR
CENTER FOR INTERNATIONAL BLOOD & MARROW TRANSPLANT RESEARCH

N=246 (56% matched Sibling/46% MUD)

Epperla N, Journal of Hematology and Oncology 2019

Management of R/R PTCL

- Eligible for a Clinical trial;
- Evaluation **Expression CD30 and Mutations;**
- Eligible or not eligible for Allogeneic SCT (in case ot not eligible, consider drugs with limited toxicity for long-term treatment);
- **ALCL pos:**
  - BV if not refractory; ALK inhibitors > AlloSCT (if eligible)
- **ALCL neg:**
  - BV (if not refractory) + Benda > AlloSCT (if eligibile)
- **T-Follicular Helper Lymphomas and PTCL-NOS**
- BV if CD30+
- CT
- TFH: Aza > AlloSCT (if eligible)

SSD LINFOMI E SDR LINFOPROLIFERATIVE CRONICHE

Prof. Pier Luigi Zinzani