POST-NEW ORLEANS 2022
Novità dal Meeting della Società Americana di Ematologia

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Milano
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2-3-4 Febbraio 2023

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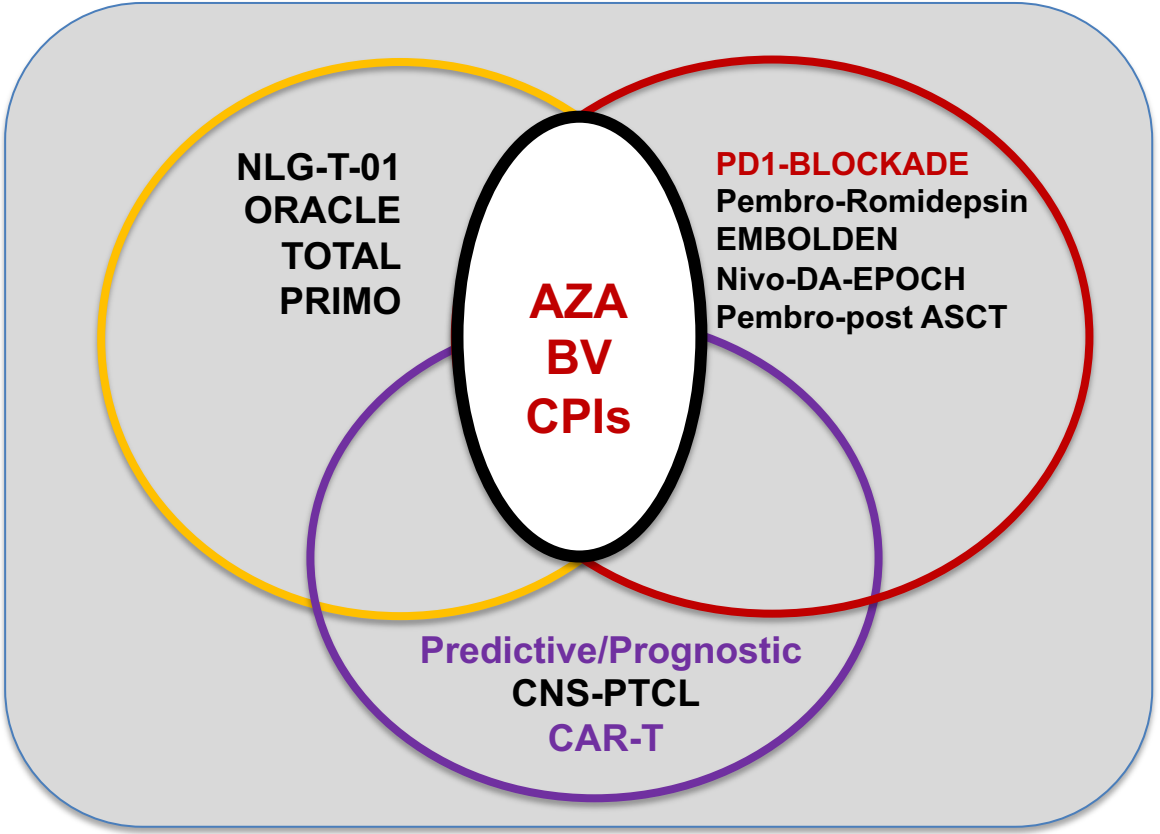
Come da nuova regolamentazione della Commissione Nazionale per la Formazione Continua del Ministero della Salute, è richiesta la trasparenza delle fonti di finanziamento e dei rapporti con soggetti portatori di interessi commerciali in campo sanitario.

- Posizione di dipendente in aziende con interessi commerciali in campo sanitario **(Nada)**
- Consulenza ad aziende con interessi commerciali in campo sanitario **(Nada)**
- Fondi per la ricerca da aziende con interessi commerciali in campo sanitario **(Nada)**
- Partecipazione ad Advisory Board **(Roche, BMS-Celgene, Incyte, Takeda, MSD)**
- Titolarietà di brevetti in compartecipazione ad aziende con interessi commerciali in campo sanitario **(Nada, purtroppo)**
- Partecipazioni azionarie in aziende con interessi commerciali in campo sanitario **(Nada, come sopra)**
- Altro **(Trovate tutto su OnlyFans)**

Update of 1L and RR-PTCL trials

CNS risk in PTCL



Anti-PD1 takeover in PTCL ?

User-friendly CAR-T for RR-PTCL ?

614 The 'big five' upfront trials in PTCL (plus one): Questions & Answers

Study	Sponsor	Design	PTS	ALK+ ALCL	Question	Outcome
NLG-T0-1	Nordic Lymphoma Group (NLG)	Phase 2	160	NO	PFS & OS Bi-weekly CHOEP+ ASCT	**5yr OS: 51%** **5yr PFS: 44%**
ACT-1 (young) CHOP+ASCT+/- ALZ (low dose) **ACT-2** (elderly) CHOP +/- ALZ (higher dose)	NLG German Lymphoma Group (GLG)	Phase 3	131 116	NO	EFS improvement with CHOP+ ALZ	**ACT-1: No difference** (BUT better outcome in ALZ treated pts with ERB4 pathway upregulation; mainly females) **ACT-2: No difference**
AlloSCT vs. ASCT	GLG	Phase 3	104	NO	Upfront consolidation with allo better than auto ?	**No difference** Allo-SCT less relapses but higher TRM
ECHELON-2 (CHP-BV vs. CHOP)	Seattle Genetics/ Takeda	Phase 3	452	YES	CHP-BV better than CHOP ?	**CHP-BV better than CHOP in ALCL** Not powered for other PTCL sybtypes
Ro-CHOP (CHOP+ Romi vs. CHOP)	LYSA/ Celgene	Phase 3	421	NO	Ro-CHOP better than CHOP ?	**No difference** Some TFH Lymphomas with long lasting CRs
PTCL13 Ro-CHOEP+ASCT	FIL PTCL13	Phase 1b/2	86	NO	Ro-CHOEP 18 months PFS: 70%	**18-month PFS: 46.2%** (95%CI:35.0–56.7) 18-months OS: 73.1% (95%CI:61.6–81.7)

Relander T, et al.

614 Long-Term Follow-up of Clinical Outcome Determinants and Correlative Biological Features from the Nordic NLG-T-01 Trial

No ALK+ALCL
No Leukemic T-NHL

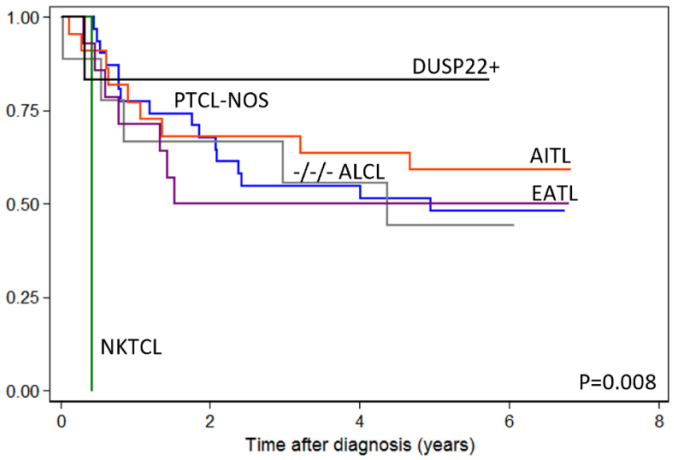
CHO(E)P-14 x 3-6 cycles
(n = 160)
ORR: 82%
CR: 51%

PR or CR

BEAM or BEAC + Autologous SCT
(n = 115 [72%])

5yr OS: 51%
5yr PFS: 44%

NLG-T-01
Overall survival



	10-yr OS	10-yr PFS	10-yr DSS
ALK-ALCL, DUSP22r	83%*	66%**	100%
ALCL triple neg	42%	46%	66%
AITL	46%	39%	32%
PTCL-NOS	39%	32%	47%
EATL	29%	29%	33%

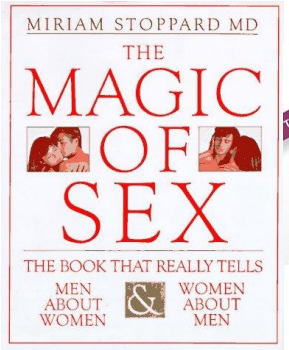
*1 event: septic death in CR under ASCT
**2 events: 1 septic death in CR under ASCT; 1 relapse after 5-Yrs CR, 2nd cCR
DSS: disease specific survival

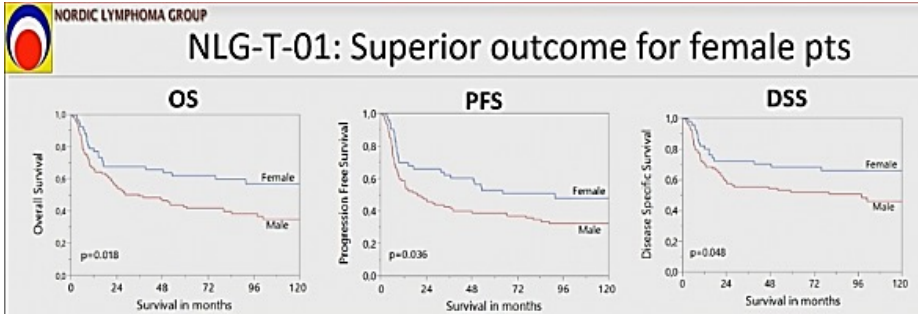
NLG-T-01: Long-term follow-up
Causes of death

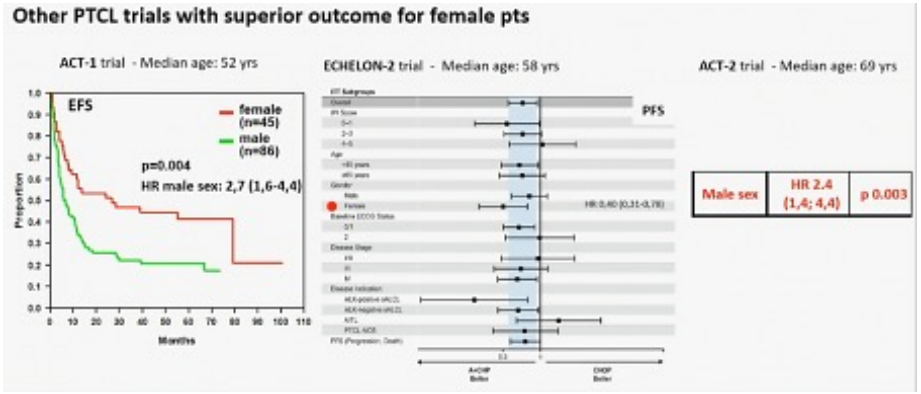
	Time from diagnosis			
Causes of death	<24 mo	24 - 59 mo	≥ 60 mo	Total
Lymphoma	56 (86,2%)	8 (50,0%)	4 (50,0%)	68 (76,4%)
Toxicity	8 (12,3%)	1 (6,3%)	0 (0,0%)	9 (7,9%)
2nd malignancy	0 (0,0%)	4 (25,0%)	1 (12,5%)	5 (2,3%)
Other causes	1 (1,5%)	3 (18,8%)	2 (25,0%)	6 (6,7%)
Unknown	0 (0,0%)	0 (0,0%)	1 (12,5%)	1 (1,1%)
N of deaths	65	16	8	89

Median age: 57 yrs
(range: 22 - 47)

- After 10 yrs of FU: long term survival in about 40% of patients with PTCL (ALK+ALCL excluded)
- Adverse prognosis: hi-IPI (age; PS≥ 2)
- The magic of sex: Females superior outcomes (also ACT-1 and ECHELON-2)
- Favorable outcome for ALK-negative ALCL with rearranged DUSP22; triple negative (DUSP22, TP63, ALK) ALCL had an intermediate outcome

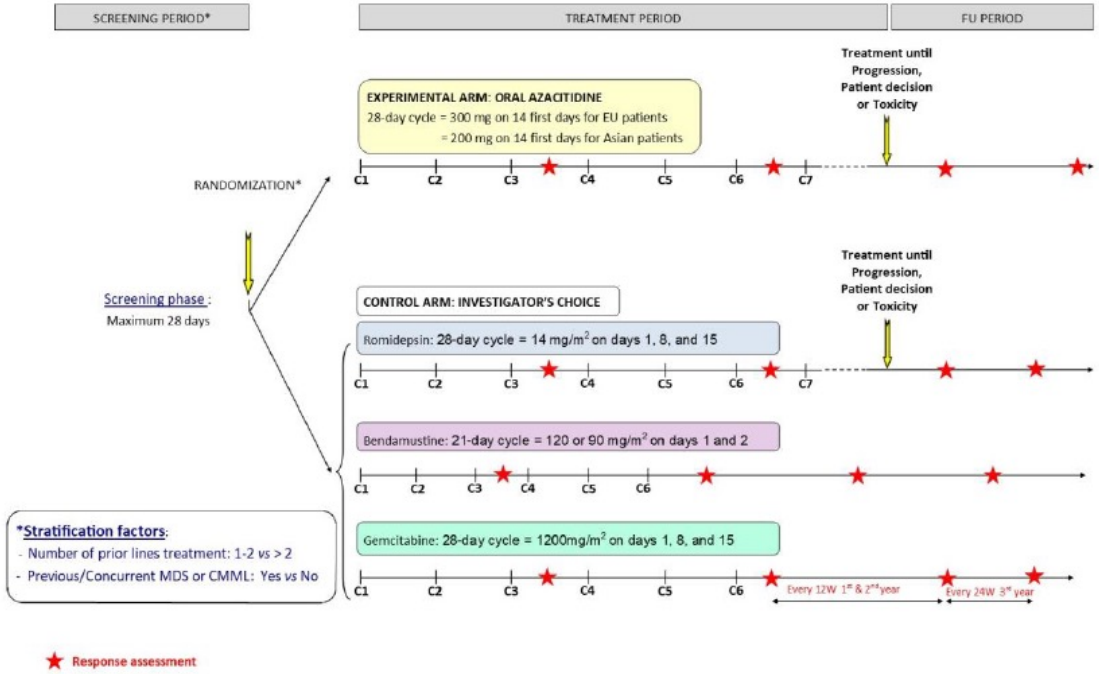




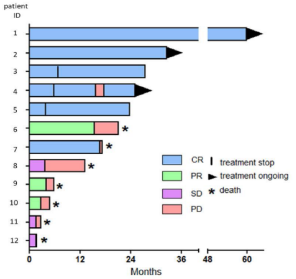


Relander T, et al.

959 Oral Azacytidine in Patients with Relapsed/Refractory Angioimmunoblastic T-Cell Lymphoma: Final Analysis of the Oracle Phase III Study



- T follicular helper peripheral T-cell Lymphomas (TFH PTCL) represent up to 40% of non cutaneous PTCL
- They are characterized by frequent mutations in *TET2*, *DNMT3A* and *IDH2*, impacting DNA methylation
- Preliminary reports suggest an efficacy of 5-azacitidine in relapsed/refractory TFH PTCL



Lemonnier et al, Blood 2018

Key inclusion criteria

- Aged ≥18y
- TFH PTCL (WHO 2016):
  - AITL
  - Follicular PTCL
  - Nodal PTCL with TFH phenotype
- ECOG 0-3
- **Relapsed/refractory lymphoma after≥ 1 previous line**
- Adequate hematopoietic function

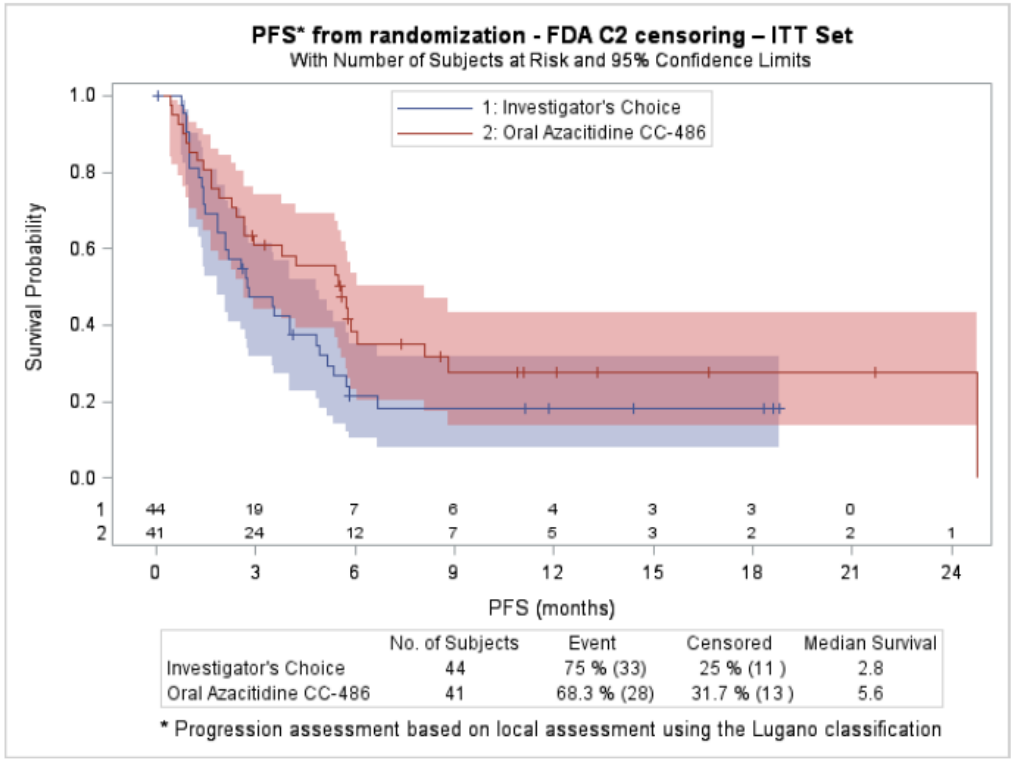
ORACLE: Baseline characteristics

	azacitidine CC-486	Investigator treatment choice	romidepsin	bendamustine	gemcitabine
N	42	44	4	16	24
median age (IQR)	70.5 (65-77)	68 (58.5-73.5)	68.5 (62.5-71.5)	63.5 (53-68)	72 (64-78)
Sex male	22 (52%)	28 (64%)	3 (75%)	10 (62.5%)	15 (62.5%)
ECOG 2-3	11 (26%)	9 (20%)	0 (0%)	4 (25%)	5 (20%)
Bone marrow involvement	12/37 (32%)	17/40 (42,5%)	1/4 (25%)	8/16 (50%)	8/20 (40%)
Associated MDS/CMML	0	1 (2%)	0	0	1 (4%)
IPI 4-5	13/42 (31%)	14/42 (33%)	0/4	5/15 (33%)	9/23 (39%)
Previous line number					
1-2 vs ≥3	34 (81%) vs 8 (19%)	37 (84%) vs 7(16%)	4 (100%) vs 0 (0%)	14 (88%) vs 2 (12%)	19 (79%) vs 5 (21%)
1	24 (57%)	14 (32%)	4 (100%)	3 (19%)	7 (29%)
2	10 (24%)	23 (52%)	0 (0%)	11 (69%)	12 (50%)
refractory patients	20 (48%)	28 (64%)	1 (25%)	13 (80%)	14 (58%)

ORACLE: Response rate

	CC-486 N=42	Investigator's choice N=44	
3 months (or PTD cycle 1-3)			
Overall response rate	**14 (33%)** [19.6%-49.5%]	**19 (43.2%)** [28.3%-59%]	p =0.33
Complete response rate	**5 (11.9%)** [4%-25.6%]	**10 (22.7%)** [11.5%-37.8%]	p =0.18
6 months (or PTD cycle 4-6)			
Overall response rate	**13 (31%)** [17.6-47.1%]	**10 (22.7%)** [11.5%-37.8%]	p =0.40
Complete response rate	**5 (11.9%)** [4%-25.6%]	**7 (15.9%)** [6.6%-30.1%]	p =0.56

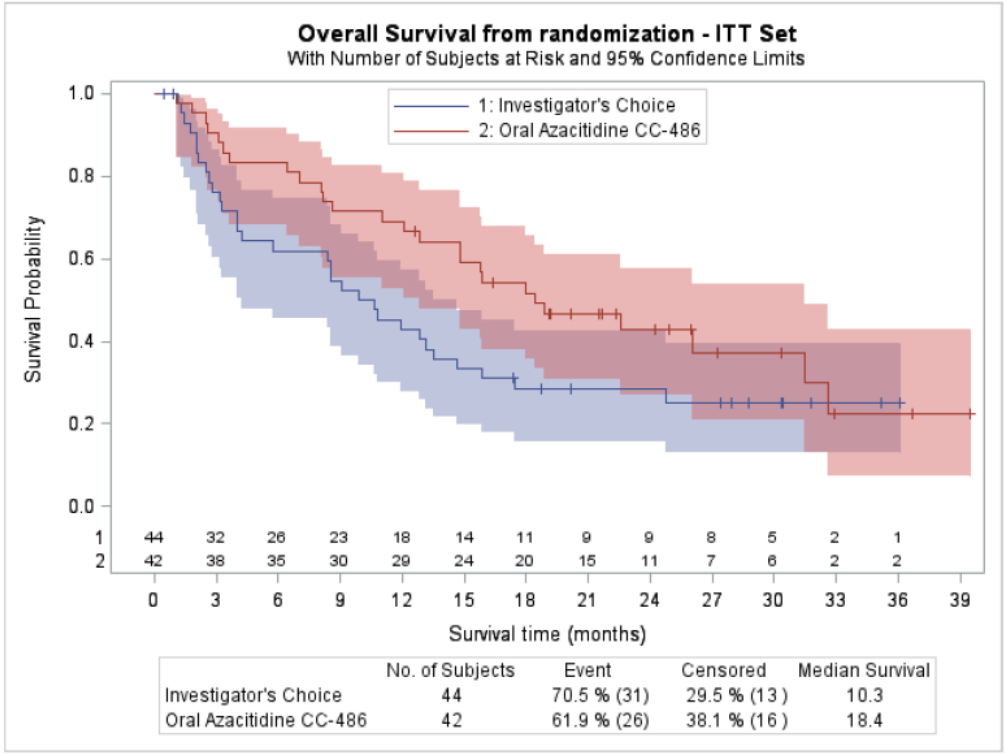
Dupuis J , et al.



	Investigator's choice	CC-486
median	2.8 months	5.6 months
95% CI	1.9 - 4.8 months	2.7 - 8.1 months

P=0.0421

prespecified p=0.025

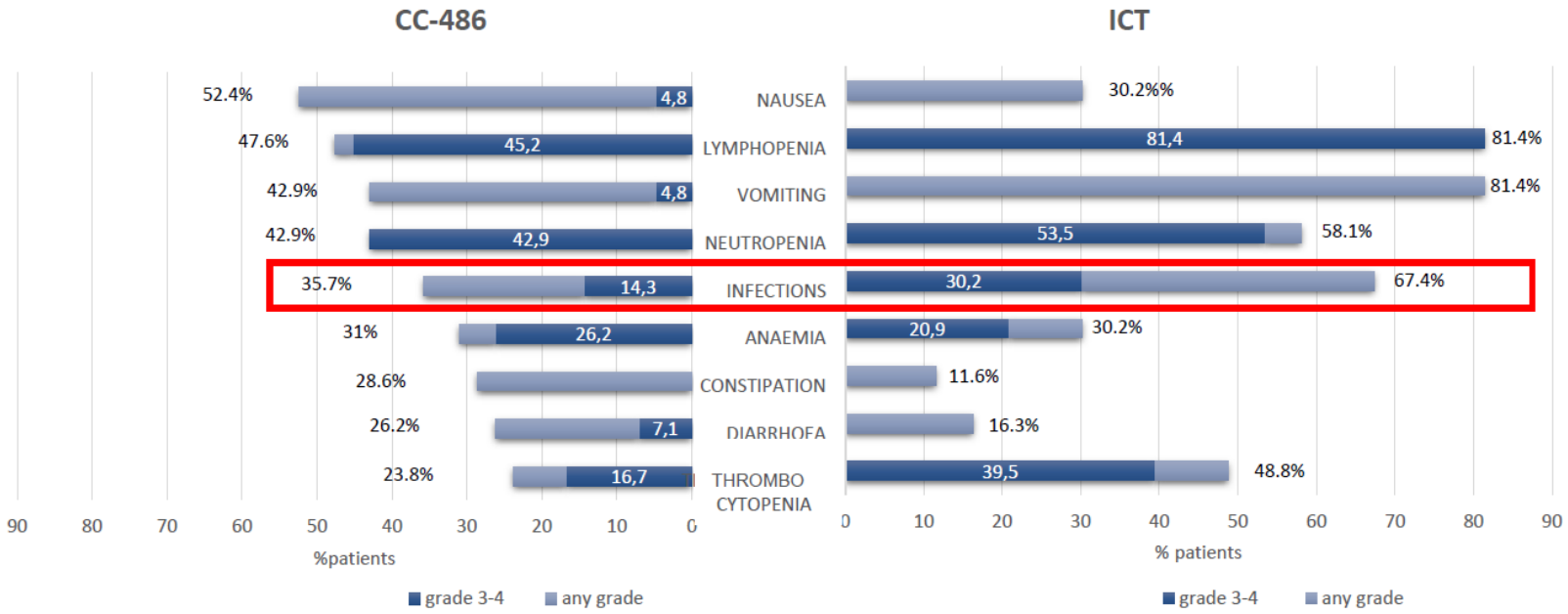


	Investigator's choice	CC-486
median	10.3 months	18.4 months
95% CI	4.2 – 13.5 months	12.9 – 31.5 months

P=0.0166*

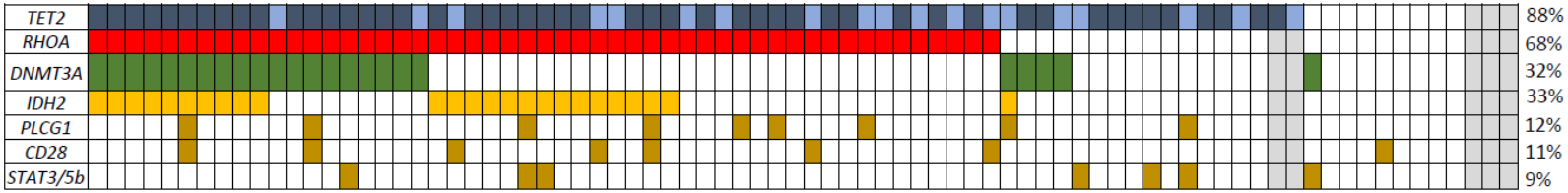
* Descriptive p value

ORACLE: TEAE occurring in >20% patients



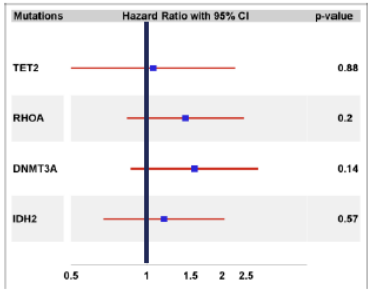
Dupuis J , et al.

Recurrent mutations do not have prognostic impact

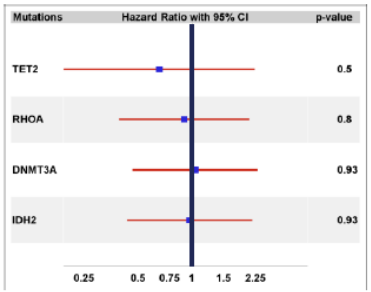


PFS

TFH PTCL

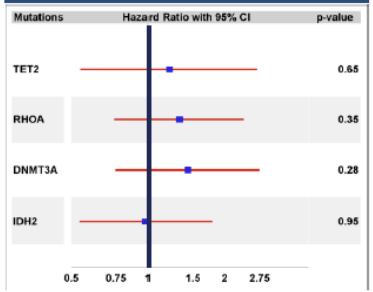


CC-486 arm

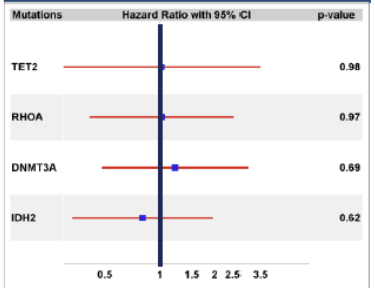


OS

TFH PTCL

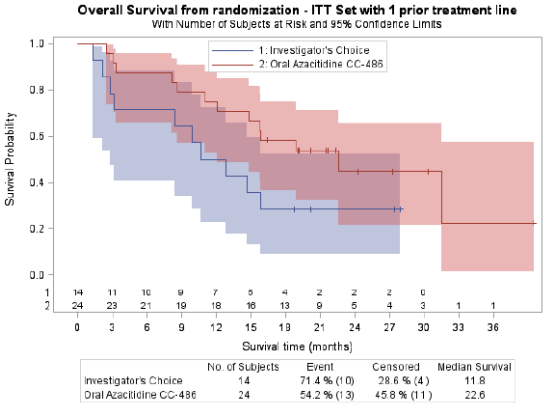


CC-486 arm

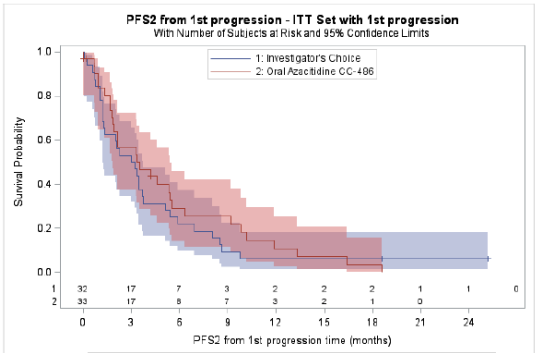


ORACLE Study_ASH 2022

Dupuis J , et al.



	No. of Subjects	Event	Censored	Median Survival
Investigator's Choice	14	71.4 % (10)	28.6 % (4)	11.8
Oral Azacitidine CC-486	24	54.2 % (13)	45.8 % (11)	22.6



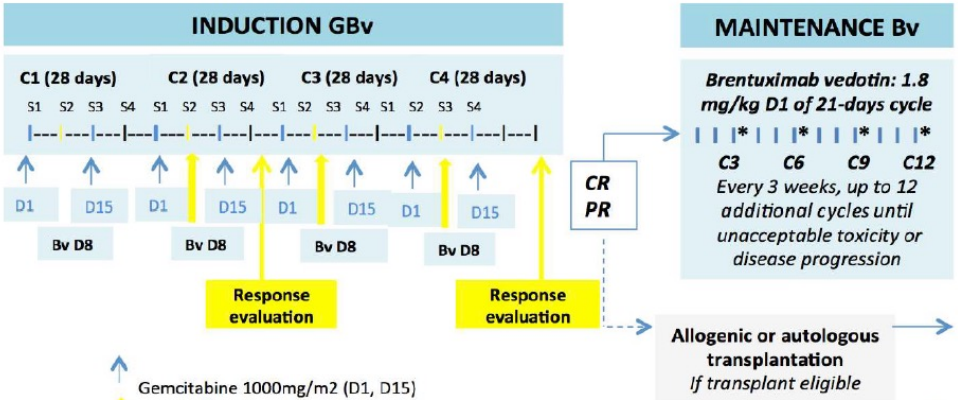
	No. of Subjects	Event	Censored	Median Survival
Investigator's Choice	32	93.8 % (30)	6.3 % (2)	3.1
Oral Azacitidine CC-486	33	87.9 % (29)	12.1 % (4)	3.5

- Unbalanced population between the two arms ?
  Similar trend than in the study population
- Could 5-azacitidine sensitize the lymphoma to next treatment ?
  Similar PFS 2
- ORR/CR could not reflect the benefit of CC-486?

Conclusion

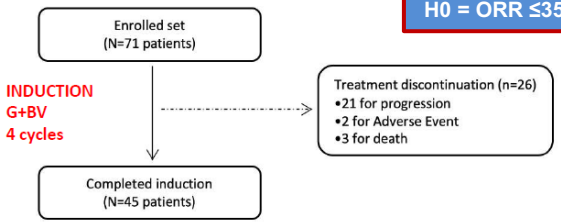
- **CC-486 has a favorable safety profile**
- **The study did not meet the primary endpoint**
- **However, the study, with 42 patients treated with CC-486, might be underpowered to detect a clinically meaningful difference in PFS**
- **A prolonged survival was observed in patients treated by CC-486**
- **These results support the development of combination based on 5-azacitidine in TFH PTCL**

956 Addition of Brentuximab Vedotin to Gemcitabine in Relapsed or Refractory T-Cell Lymphoma: Final Analysis of a Lysa Multicenter, Phase II Study. "the TOTAL Trial"



Age , median (range; years)	66 (20-79)
Male/female (n)	47/24
Histology (%)	
AILT	31
PTCL-TFH	7
PTCL-nos	7
ALCL-Alk negative	14
ALCL-Alk positive	6
EATL	3
PTCL unclassified	3
PTCL (pending histology review)	29
Disease stage (%)	
Stage I-II	8
Stage III-IV	92
ECOG (%)	
0	31
1-2	69

@4 Cycles G+BV

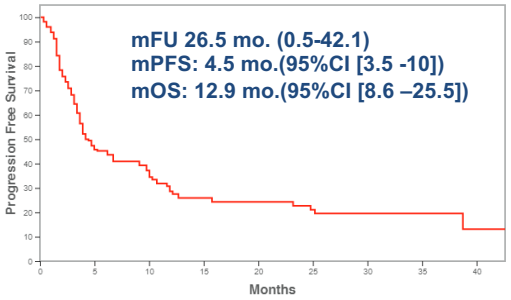


H0 = ORR ≤35%

Response (n= 71) Intention-to-treat as by Local Investigator	N	%
CR+PR	34	46.6
CR	14	19.7
PR	19	26.7

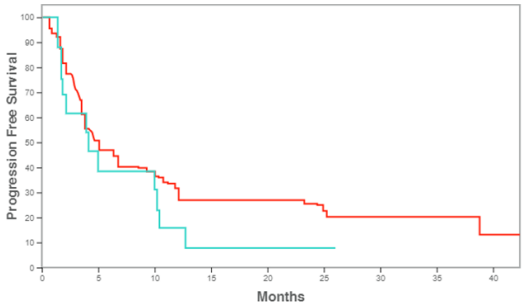
Previous line of treatment (%)	
1 line	80
2 lines	16
3 lines	4
Prior therapy* (%)	
CHOP/CHOP like regimen	100
ASCT transplantation	16
Epigenetic modifiers	7
Time from diagnosis to enrollment months; median (range)	9.4 (2-131)
Refractory to last prior therapy (%)	39

Progression-free survival



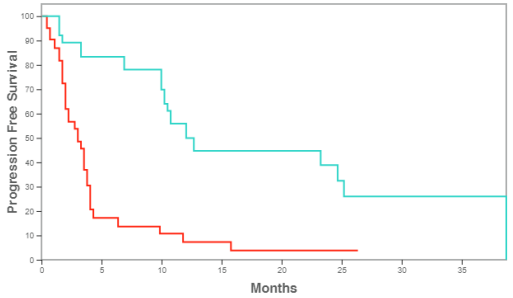
Curves	N	Median (95% CI)
Brentuximab vedotin + Gemcitabine	71	4.5 (3.5-10)

Progression-free survival according to CD30: T cells: All patients



Curves	N	Median (95% CI)
> 10	-	5.1 (0-0)
<= 10	-	4.1 (0-0)

Progression-free survival: Non ALCL patients



Curves	N	Median (95% CI)
sCD30 level > 120 ng/mL	30	3.2 (2-4)
sCD30 level <= 120 ng/mL	18	12.5 (10.1-25.2)

DOR - 33 pts in PR/CR: 15.8 mo (95%CI [10.4 –(-)])

Figure 1A (n=71)

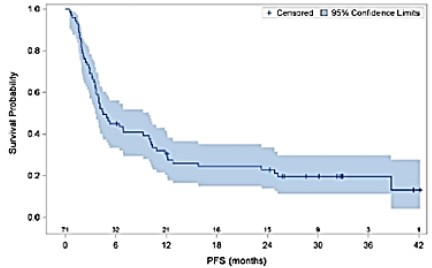


Figure 1B (non ALCL pts)

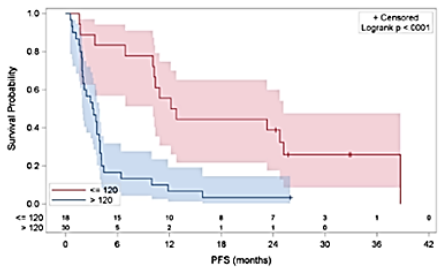


Table 1 CD30 evaluation in non-ALCL pts

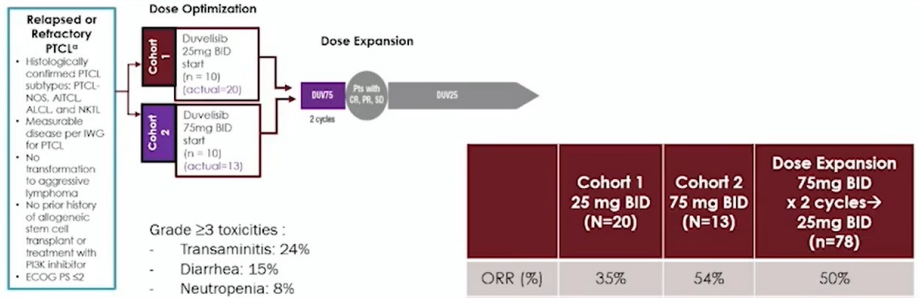
	Baseline serum sCD30 (ELISA) (n=48)		p	CD30 on tumor cells (IHC) (n=44)		p
	≤120 ng/mL	>120 ng/mL		≤10%	>10%	
n	18	30		13	31	
ORR	77.8%	13.3%	*<0.001*	46.2%	38.7%	*0.65*
PFS	12.5 m (10.1-25.2)	3.2 m (2.0-4.0)	*<0.001*	4.1 m (1.7-10.3)	4.1 m (3.1-10.9)	*0.53*
OS	29.6 m (13.4-39.3)	7.3 m (3.9-10.8)	*<0.001*	9.0 m (5.0-25.5)	13.4 m (7.3-29.6)	*0.44*
n	14	4		6	12	
DOR	24.0 m (10.4-38.7)	10.9 m (6.4-15.8)	*0.019*	10.3 m (4.9-NA)	17.7m (10-25.2)	*0.32*

NA : non achieved, m : months

Tournilhac O, et al.

4225 Duvelisib in Patients with Relapsed/Refractory Peripheral T-Cell Lymphoma from the Phase 2 Primo Trial Expansion Phase: Impact of Prior Treatment and Expanded Safety Analysis

PRIMO: Duvelisib Single Agent in PTCL



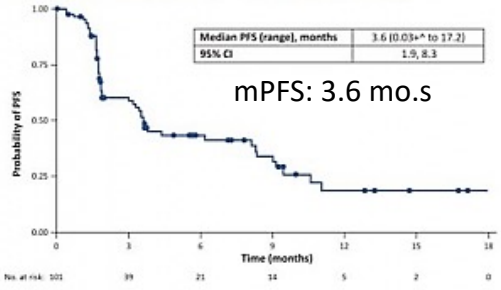
	Cohort 1 25 mg BID (N=20)	Cohort 2 75 mg BID (N=13)	Dose Expansion 75mg BID x 2 cycles→ 25mg BID (n=78)
ORR (%)	35%	54%	50%
CR (%)	25%	31%	32%

Grade ≥3 toxicities :
- Transaminitis: 24%
- Diarrhea: 15%
- Neutropenia: 8%
- Rash: 16%

Table 2. Preliminary Results: Adverse events of special interest (all grades, all causality) by prior regimen and time on treatment subgroups

Adverse event of special interest, n (%)	1 prior regimen (N = 26)	2 prior regimens (N = 22)	3+ prior regimens (N = 53)	Tx Duration ≤2 cycles (N = 101)	Tx Duration >2-4 cycles (N = 56)	Tx Duration >4 cycles (N = 31)
Infections	8 (30.8)	7 (31.8)	26 (49.1)	27 (26.7)	9 (16.1)	10 (32.3)
Colitis	0	0	1 (1.9)	0	0	1 (3.2)
Cutaneous reactions	10 (38.5)	12 (54.5)	13 (24.5)	20 (19.8)	16 (28.6)	7 (22.6)
Diarrhea	4 (15.4)	6 (27.3)	21 (39.6)	20 (19.8)	8 (14.3)	7 (22.6)
Neutropenia/ neutrophil count decreased	10 (38.5)	6 (27.3)	17 (32.1)	29 (28.7)	8 (14.3)	8 (25.8)
Pneumonia	1 (3.8)	0	2 (3.8)	2 (2.0)	0	1 (3.2)
Pneumonitis	1 (3.8)	0	1 (1.9)	1 (1.0)	1 (1.8)	0
Transaminase elevation	17 (65.4)	9 (40.9)	18 (34.0)	34 (33.7)	17 (30.4)	4 (12.9)

PFS PER IRC ASSESSMENT – PRIMO EP (N=101)



mPFS: 3.6 mo.s

. Incidence of infections increased with number of prior therapies; transaminase elevations decreased as treatment duration increased

Table 1. Preliminary Outcomes by Prior Regimens and Prior Anticancer Therapy

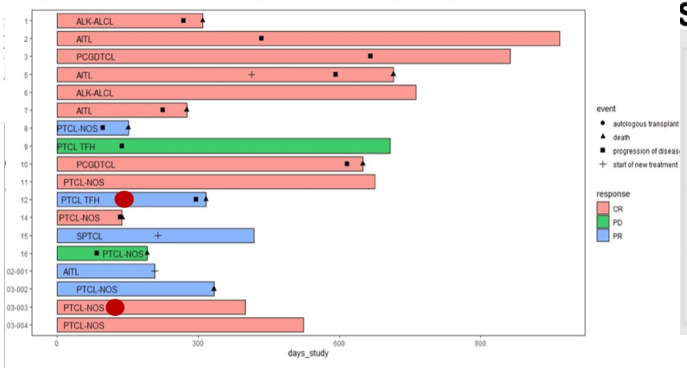
OUTCOME	PRIMO-EP (N=101)
ORR by IRC, n (%) [95% CI]	49 (48.5) [38.8–58.3]
CR by IRC, n (%) [95% CI]	34 (33.7) [24.4–42.9]
Response (CR + PR) by number of prior regimens, %	
1 prior regimen (n=26)	34.6
2 prior regimens (n=22)	63.6
3+ prior regimens (n=53)	49.1
BOR by prior therapy, (% of subgroup): CR / PR / SD	
Prior CHOP/R-CHOP	37.8 / 5.4 / 2.7
Prior CHOEP/EPOCH	27.0 / 27.0 / 0
Prior Salvage Chemotherapy CHOP/R-CHOP or CHOEP/EPOCH	44.7 / 7.9 / 0
Prior BV or BV-chemo	32.4 / 10.8 / 0
Prior SCT	22.7 / 27.3 / 0

958 Results from a Phase I Trial Using Nivolumab in Combination with Dose Adjusted EPOCH in Newly Diagnosed Peripheral T-Cell Lymphomas

Table 1: Baseline characteristics of 18 patients treated with Nivo + EPOCH

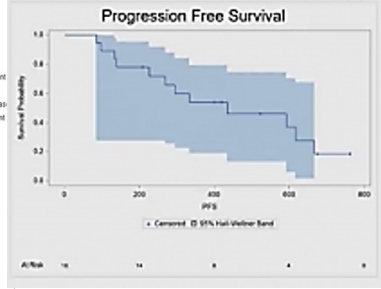
Baseline Characteristics	N=18 (%)
Subtype	
Peripheral T-cell lymphoma NOS	7 (38.9%)
T-cell lymphomas with a FH phenotype	6 (33%)
Primary cutaneous γ/δ T-cell lymphoma	2 (11.1%)
Anaplastic large cell lymphoma, ALK-	2 (11.1%)
Subcutaneous panniculitis like T-cell lymphoma (SPTCL)	1 (5.6%)
Median Age	66.0
Sex, M	10 (58.8%)
ECOG PS	
0-1	7 (38.9%)
2	11 (61.1%)
Stage	
III	1 (5.6%);
IV	17 (94.4%)
LDH, greater than normal	10 (55.6%)
Extranodal sites, 2 or more	7 (41.2%)
IPI	
Low (0-1)	3 (17%)
Intermediate (2-3)	6 (33%)
High (4-5)	9 (50%)
CD30 expression >10%	2 (11%)
EBV+ (defined as any EBER positivity or elevated viral load)	6 (33%)

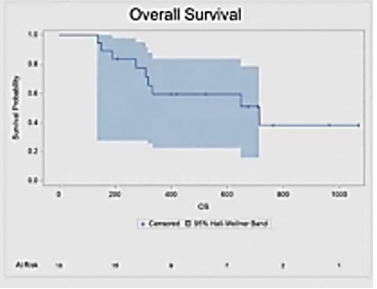
Figure 1: End of induction response and corresponding duration of response



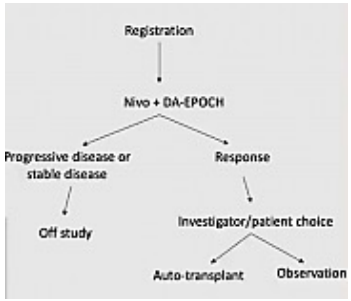
Primary objective: INV-assessed ORR

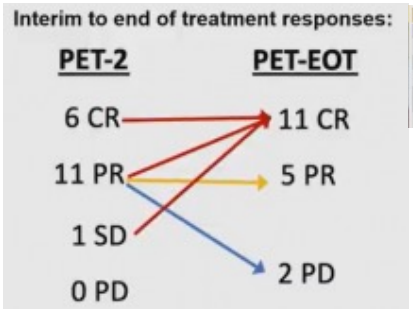
Survival Analysis





mPFS (n=18) : 14.5 mo.s
mOS (n=18) : 23.8 mo.s





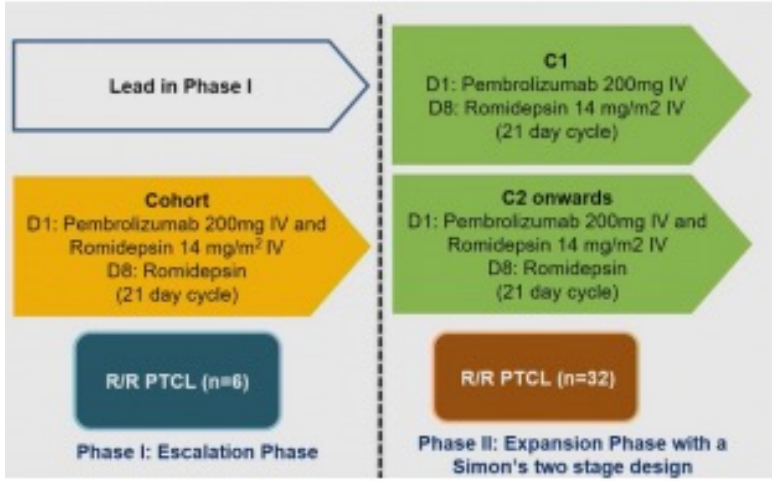
Drug	Dose	Days
Nivolumab (IV)	360 mg	1
Etoposide (CIV)	50 mg/m2/d	1-4
Doxorubicin (CIV)	10 mg/m2/d	1-4
Vincristine (CIV)	0.4 mg/m2/d	1-4
Cyclophosphamide (IV)	750 mg/m2	5
Prednisone (PO)	60 mg/m2/d	1-5

Summary of immune related adverse events

	All patients (N=18)	Nivo + EPOCH Cycle 1 (N=12)	Nivo + EPOCH Cycle 2 (N=6)
Any grade irAEs	14 (78%)	10 (83%)	2 (33%)
Grade >2 irAEs	7 (39%)	9 (75%)	0
Discontinuation of Nivo due to irAEs	8 (44%)	8 (67%)	0

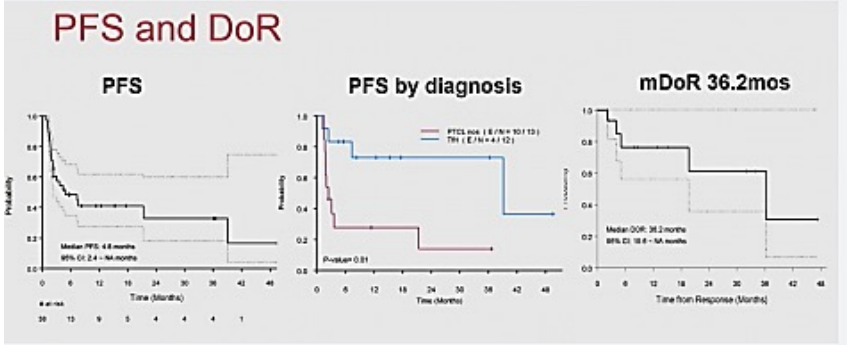
irAE = immune related adverse event; Nivo = nivolumab

960 Updated Results of an Investigator-Initiated Phase II Study of Pembrolizumab and Romidepsin for Patients with Relapsed or Refractory T-Cell Lymphoma (TCL) with Survival Analysis

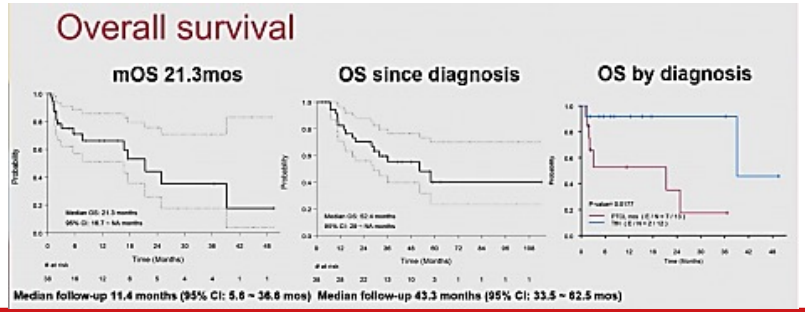


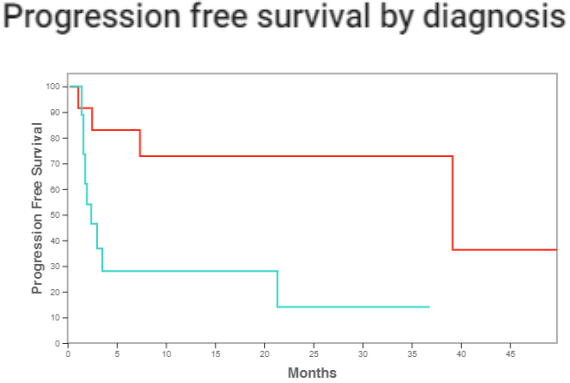
Two patients experienced hyper-progression within the first 10 days of treatment

960 Updated Results of an Investigator-Initiated Phase II Study of Pembrolizumab and Romidepsin for Patients with Relapsed or Refractory T-Cell Lymphoma (TCL) with Survival Analysis



Curves	N	Median (95% CI)
Pembrolizumab + Romidepsin	38	4.8 (2.4-0)





Curves	N	Median (95% CI
T-follicular helper cells	12	39.2 (0-0)
Peripheral T-cell lymphomas-not otherwise specified	13	2.4 (0-0)

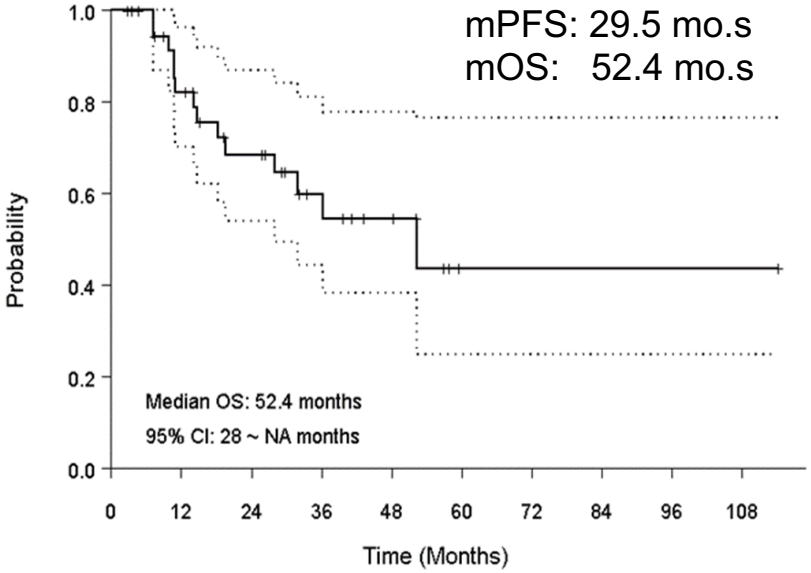
	P-value
Peripheral T-cell lymphomas-not otherwise specified vs T-follicular helper cells	0.01

960 Updated Results of an Investigator-Initiated Phase II Study of Pembrolizumab and Romidepsin for Patients with Relapsed or Refractory T-Cell Lymphoma (TCL) with Survival Analysis

Table 1 Demographics for Phase I and II	TCL (n= 38)
Age (Median; range in years)	67 (32-82)
<60 n (%)	5 (13.2)
≥60 n (%)	33 (86.8)
Gender, n (%)	Male: 22 (57.9)
	Female: 16 (42.1)
Race, n (%)	Caucasian: 24 (63.2)
	Black: 7 (18.4)
	Other: 3 (7.9)
	Asian: 4 (10.5)
Bone marrow involvement, n (%)	16 (42.1)
Elevated LDH, n (%)	26 (68.4)
ECOG ≥2, n (%)	20 (52.6)
Stage 3 or 4, n (%)	24 (63.2)
Disease status, n (%)	Relapse: 7 (18.4)
	Refractory: 31 (81.6)
Prior therapies	
CHOP/CHOP Protocol	10
CHOEP	10
EPOCH	3
BV with CHP or CHEP or Benda	8
Others: ABVD, Cisplatin, DeVIC, Gemcitabine, SMILE	7
Prior SCT, n (%)	9 (23.7)
Histologic classification, n (%)	TFH (AITL, PTCL with TFH): 12 (31.6)
	PTCL:13 (34.2)
	Mycosis Fungoides (MF) large cell transformation (LCT): 4 (10.5)
	ALCL: 4 (10.5)
	ENK/T cell: 3 (7.9)
	EATL: 2 (5.3)

ORR: 39.5%
CR: 34.2%

Figure 1: Overall Survival



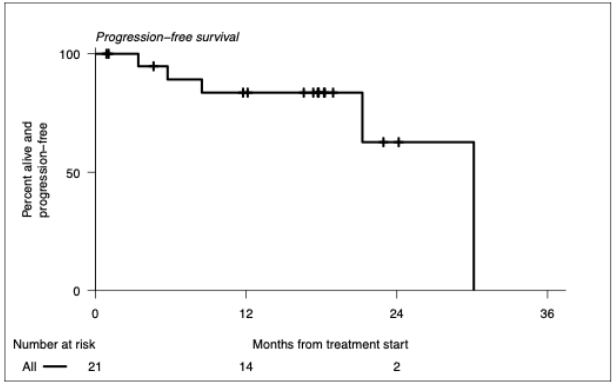
490 A Phase 2 Study of Pembrolizumab (MK-3475) after Autologous Stem Cell Transplantation in Patients with T-Cell Non-Hodgkin Lymphoma

Table 1: Patient Characteristics

	Total n = 21 (%)
Age at registration	
Median (range)	58 (33 - 73)
Histology	
Peripheral T-Cell Lymphoma	11 (52)
Angioimmunoblastic T-Cell Lymphoma	4 (19)
Extranodal NK/T-cell lymphoma, nasal type	3 (14)
ALK-negative Anaplastic Large Cell Lymphoma	2 (10)
Monomorphic epitheliotropic intestinal T-cell lymphoma	1 (5)
Sex	
Female	9 (43)
Male	12 (57)
Race	
Asian	1 (5)
Black or African American	2 (10)
White	10 (48)
Other	8 (38)
ECOG PS	
00- Fully Active	4 (19)
01- Restricted	16 (76)
02- Ambulatory and Capable of Self Care	1 (5)
No. prior treatments	
Median (range)	1
1	15 (71)
2	2 (10)
3	4 (19)
EBV status at diagnosis	
Negative	6 (29)
Positive	5 (24)
Missing	10 (48)
Conditioning regimen	
Carmustine/Cytarabine/Etoposide/Melphalan (BEAM)	14 (67)
Busulfan/Cyclophosphamide/Thiotepa	1 (5)
Missing	6 (29)
Disease status before ASCT	
Complete Response	19 (90)
Partial Response	2 (10)
Disease status at study entry (post-ASCT)	
Complete Response	20 (95)
Stable Disease	1 (5)

Pembrolizumab at 200 mg IV q3/52 for up to 8 cycles

Figure 1: Progression free survival

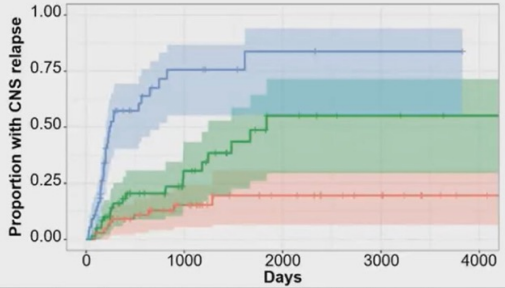


62% of patients were progression-free at 18 months post-transplantation

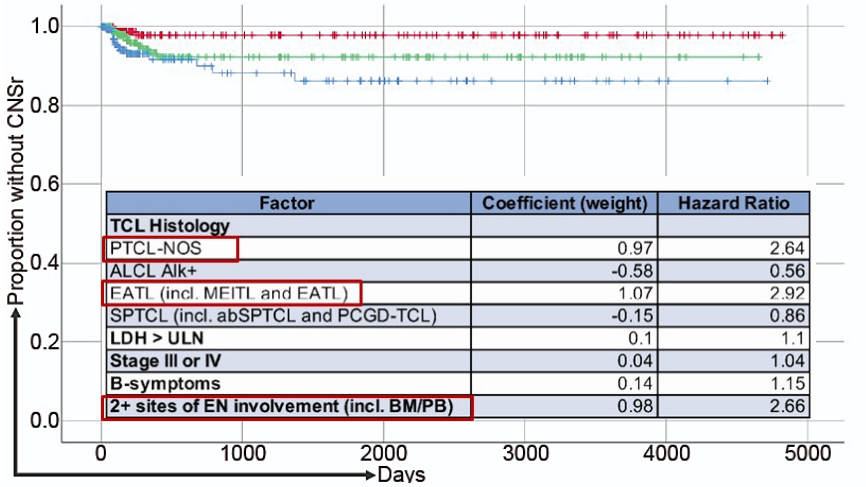
Merrill MH, et al.

615 CNS Relapse in T-Cell Lymphoma Index: A Risk Score to Predict Central Nervous System Relapse in Patients with T-Cell Lymphomas

CITI risk terciles based on Training dataset



Risk	CITI	n	Cumulative incidence	Hazard ratio	95% CI	P-value
Low	X≤0.14	67	19.6%	Reference	N/a	
Intermediate	0.14<X≤1.11	60	55.1%	2.51	1.16-5.39	0.019
High	1.11<X	55	83.7%	8.74	4.26-17.90	<0.001



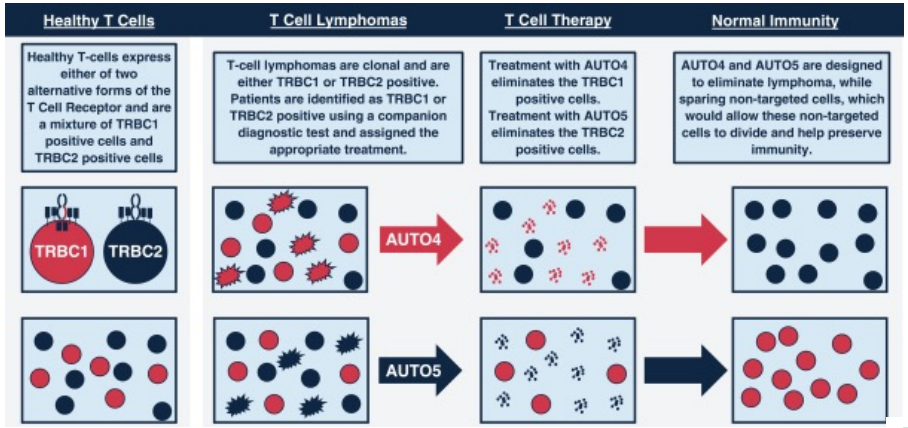
Factor	Coefficient (weight)	Hazard Ratio
TCL Histology		
PTCL-NOS	0.97	2.64
ALCL Alk+	-0.58	0.56
FATL (incl. MEITL and EATL)	1.07	2.92
SPTCL (incl. abSPTCL and PCGD-TCL)	-0.15	0.86
LDH > ULN	0.1	1.1
Stage III or IV	0.04	1.04
B-symptoms	0.14	1.15
2+ sites of EN involvement (incl. BM/PB)	0.98	2.66

Risk	Cumulative incidence	Hazard ratio	95% CI	p-value
Low	1.9%	Reference	N/a	N/a
Intermediate	4.9%	3.35	0.93-12.02	p=0.057
High	7.3%	5.72	1.64-19.95	p=0.002

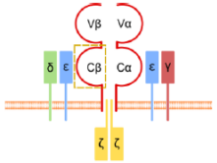
Treatment	Coefficient	Hazard Ratio
Frontline etoposide	0.427	1.532
SCT in first remission	-0.831	0.435
CNS Prophylaxis	0.444	1.559

Mature T cells express either TRBC1 or TRBC2
T-Cell Lymphomas are also clonal and express either TRBC1 or TRBC2

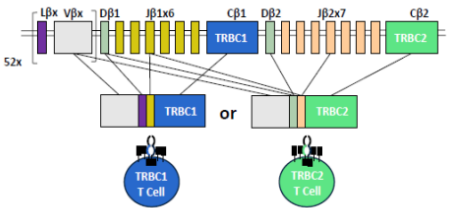
4634 First in Human Study of AUTO4, a TRBC1-Targeting CAR T-Cell Therapy in Relapsed/Refractory TRBC1-Positive Peripheral T-Cell Lymphoma



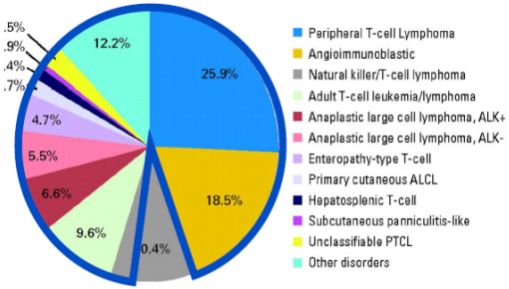
Structure of the T Cell Receptor or TCR



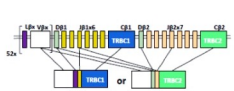
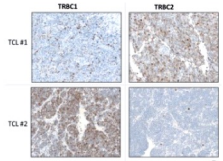
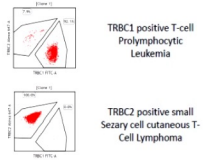
Duplication of β chain constant region gene



istribution of cases by subtype



Subtypes that are TRBC1 or TRBC2 positive

Next Generation Sequencing	Immunohistochemistry	Flow Cytometry
		
NGS sequencing <250 bp		TRBC1 positive T-cell Prolymphocytic Leukemia TRBC2 positive small Sezary cell cutaneous T-Cell Lymphoma
T cell clonality NGS assay currently used in AUTO4 Phase 1	FFPE specific antibodies can discriminate between TRBC1 and TRBC2 patient tumors	Flow specific antibodies can discriminate between TRBC1 and TRBC2 in patient tumors

Companion Diagnostic Test

Designed to stratify patients into TRBC1 and TRBC2 derived cancers

› ~ 40% of T cell lymphomas are TRBC1+

TRBC1+ patients
AUTO4
TRBC1 programmed T cell product candidate

AUTO5
TRBC2+ patients
TRBC2 programmed T cell product candidate

› ~ 60% of T cell lymphomas are TRBC2+

4634 First in Human Study of AUTO4, a TRBC1-Targeting CAR T-Cell Therapy in Relapsed/Refractory TRBC1-Positive Peripheral T-Cell Lymphoma

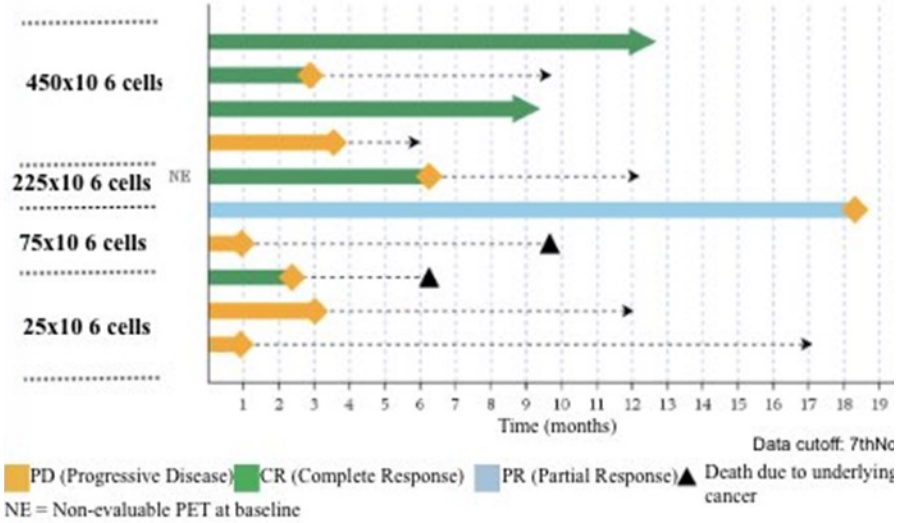
Baseline Characteristics

	Total (N=10)
Age, median (range)	55 (34 – 63)
Median prior lines of treatment (range)	3 (1 – 5)
Stage of Lymphoma at screening	
I/II	2 (20%)
III/IV	8 (80%)
Lymphoma Subtype, n (%)	
Peripheral T-cell lymphoma NOS	5 (50%)
Anaplastic large cell lymphoma, ALK-negative	1 (10%)
Angioimmunoblastic T cell lymphoma (AITL)	4 (40%)
Prior Autologous Stem Cell Transplant, n (%)	3 (30%)
CD30+ Immunophenotype for T-Cell NHL, n (%)	5 (50%)*
ECOG 0/1, n (%)	3 (30%), 7 (70%)
Bridging therapy YES, n (%)	7 (70%)

*3/5 received Brentuximab as bridging therapy or prior line treatment; 1/5 ALCL

Data cutoff: 7thNov2

Efficacy



PTCL @ ASH 2022 …take the long way home…

Study (setting)	Response rates	Survival
UPFRONT		
NGL-T01		5yr OS: 51% 5yr PFS: 44%
Nivo-DA-EPOCH ***DA-EPOCH****	*ORR:* 88% *CR:* 61% *ORR:* 78.0% CRR: 61%	mPFS: 14.5 mo.s mOS: 23.8 mo.s 2-yr PFS: 47.1% 2-yr OS: 61.9%
REL/REF		
ORACLE (CC 486)	*ORR*: 22.7% *CR*: 15.9%	mPFS: 5.6 mo.s mOS: 18.4 mo.s
TOTAL (GEM+BV)	*ORR*: 46.6% CR: 19.7%	mPFS: 4.5 mo.s mOS: 12.9 mo.s
PRIMO (Duvelisib)	*ORR*: 48.5% CR: 33.7%	mPFS: 3.6 mo.s
Pembro-Romidepsin	*ORR*: 39.5% *CR*: 34.2%	mPFS: 29.5 mo.s mOS: 52.4 mo.s

Results of single agents in the R/R setting !

	ORR (CR)	Median PFS
1. Pralatrexate; (n=111)	29% (15)	3.5 m
2. Romidepsine; (n=130)	25% (15)	4 m
3. Bendamustine; (n=60)	50% (28)	3.6 m
4. Belinostat; (n=129)	25% (11)	1.6 m
5. Brentuximab Vedotin; (n=39)*	69% (44)	6.7m
6. Alisertib; (n=102)	34%	4 m
7. Gemcitabine (n=30)	35% (22)	3 m
8. Azacytidine+romidepsine (n=11)	73%	

	ORR (CR)	Median PFS
1. ICE(n=40)	70% (35)	6 m
2. GemDexCis (n=51)	80% (47)	4 m
3. ESHAP (n=22)	32% (18)	2.5 m

*Maeda, 2017

PTCL @ ASH 2022 …take the long way home…

1° Line	>1 Line
1. Updated diagnostics: Entity-specific approaches - ALK-negative ALCL (DUSP22r, TP63r) - Follicular T-cell lymphoma - Nodal PTCL with TFH phenotype	*1. Eligible & no previous transplant* *- Salvage + ASCT (± allo-SCT)* *(GDP, ICE, ESHAP, Gifox….)*
2. ***Enroll into a clinical study !***	*2.* ***Enroll into a clinical study !***
3. CHO(E)P (21/14) x4/6 ± ASCT (± allo-SCT)	*3.* If ASCT failure or ineligible (individual approach) - BV, Gem ± BV, Benda ± BV - Lenalidomide (AITL ?) - Belinostat (?)
4. DA-EPOCH x4/6 ± ASCT (± allo-SCT)	
5. BV-CHP ± ASCT	