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Brentuximab Vedotin in PTCL: Other than ALCL

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CD30 Expression in TCL other than ALCL

Series	Definition of +	Subtype	CD30+ % (N)
Sabbatini 2013	≥ 25%	PTCL-NOS	52% (45/87)
		AITL	21% (9/42)
		ENKTCL	70% (7/10)
		MF	13% (4/32)
		ALL Types	43% (83/192
Went 2006	≥ 30%	PTCL-NOS	3% (4/145)
		AITL	0% (0/42)

Sabbatini et al Haematologica. 2013 August; 98(8): e81–e82
Went et al. J Clin Oncol. 2006 Jun 1;24(16)

Phase 2: Brentuximab in R/R PTCL Patients

	AITL N=13	PTCL N=22	ALL N=35
Med Age	64 (55-79)	64.5 (33-83	64 (33-83)
CD30 Expression			
Positive	9 (69)	17 (77)	26 (74)
Negative	2 (15)	4 (18)	6 (17)
Response to most recent Rx			
Refractory	9 (69)	17 (77)	26 (74)
Relapsed	4 (31)	5 (23)	9 (26)
Median Prior RX	3 (1-4)	2 (1-9)	2 (1-9)

Horwitz SM, et al. *Blood*. 2014;123:3095-3100.

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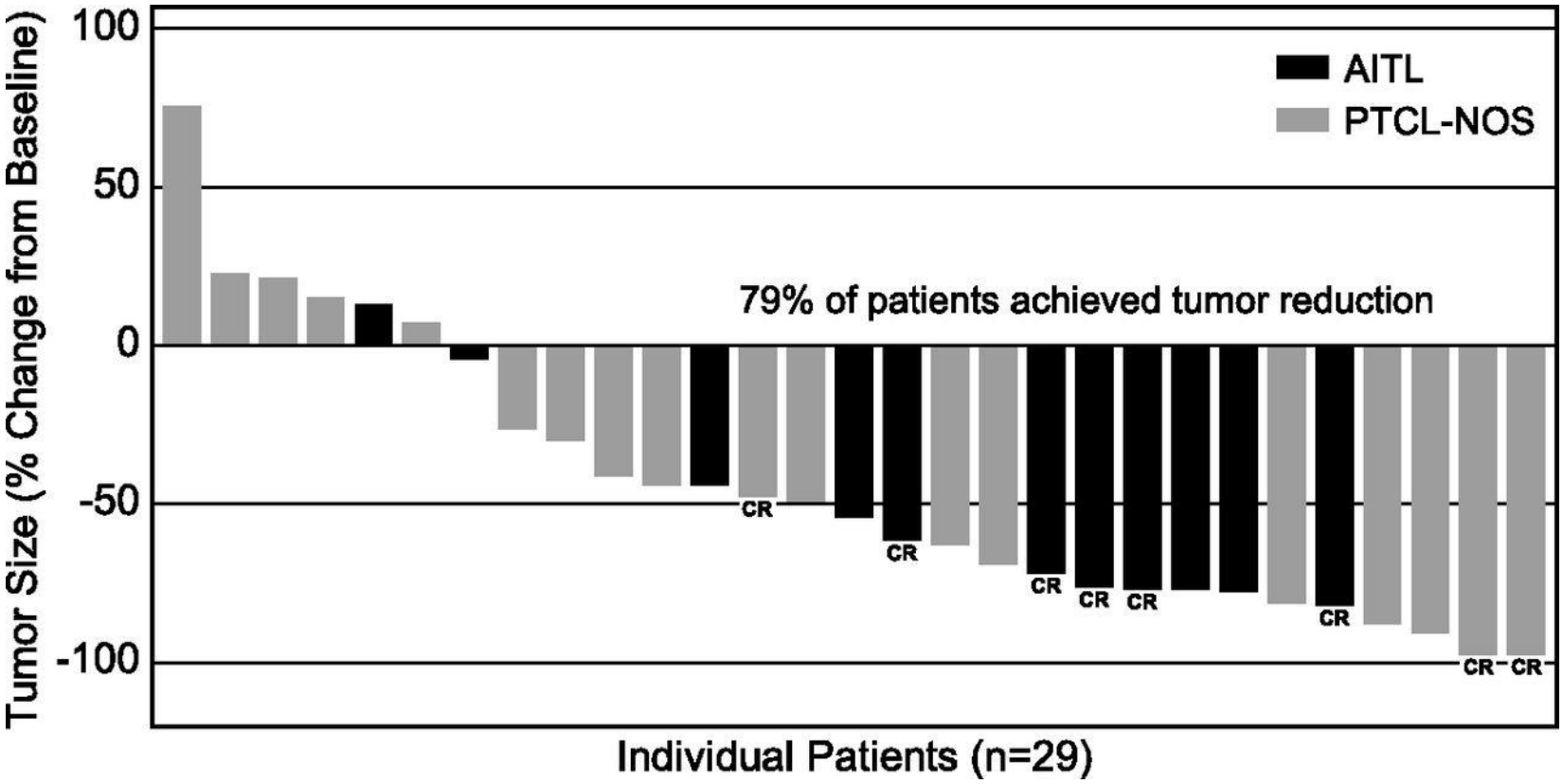
Phase 2: Brentuximab in R/R PTCL Response

Clinical Response, n(%)	AITL (n=13)	PTCL-NOS (n=22)	Total
ORR	7 (54)	7 (33)	14 (41)
CR	5 (38)	3 (14)	8 (24)
PR	2 (15)	4 (19)	6 (18)
SD	3 (23)	3 (14)	6 (18)
PD	3 (23)	11 (52)	14 (41)

- Grade 3/4 AEs: neutropenia (14%), peripheral sensory neuropathy (9%), and hyperkalemia (9%)

Horwitz SM, et al. *Blood*. 2014;123:3095-3100.

Maximum tumor size reduction from baseline.



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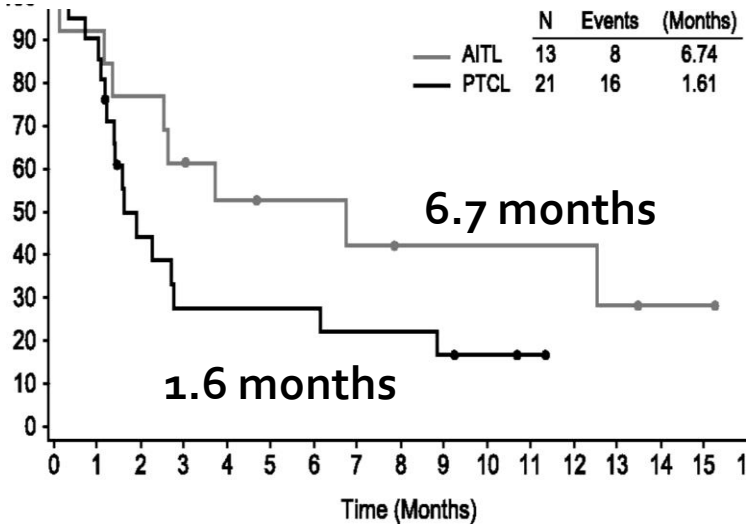
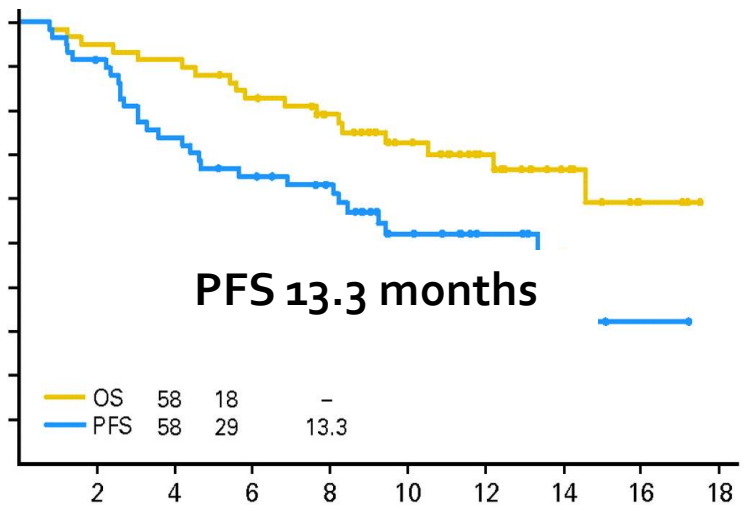
Progression Free Survival: Relapsed/Refractory PTCL

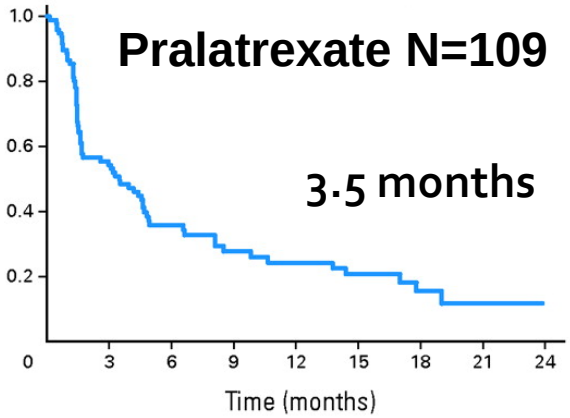
Brentuximab: PTCL N=21, AITL N=13



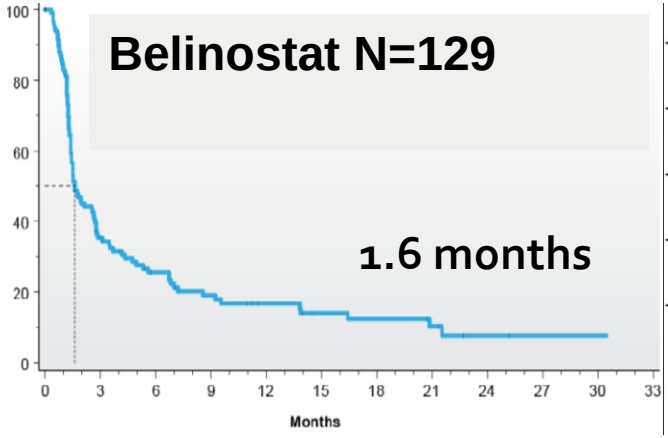
Brentuximab ALCL N=56



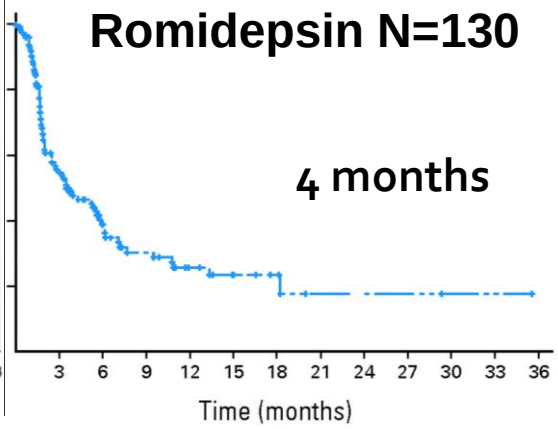
Pralatrexate N=109



Belinostat N=129

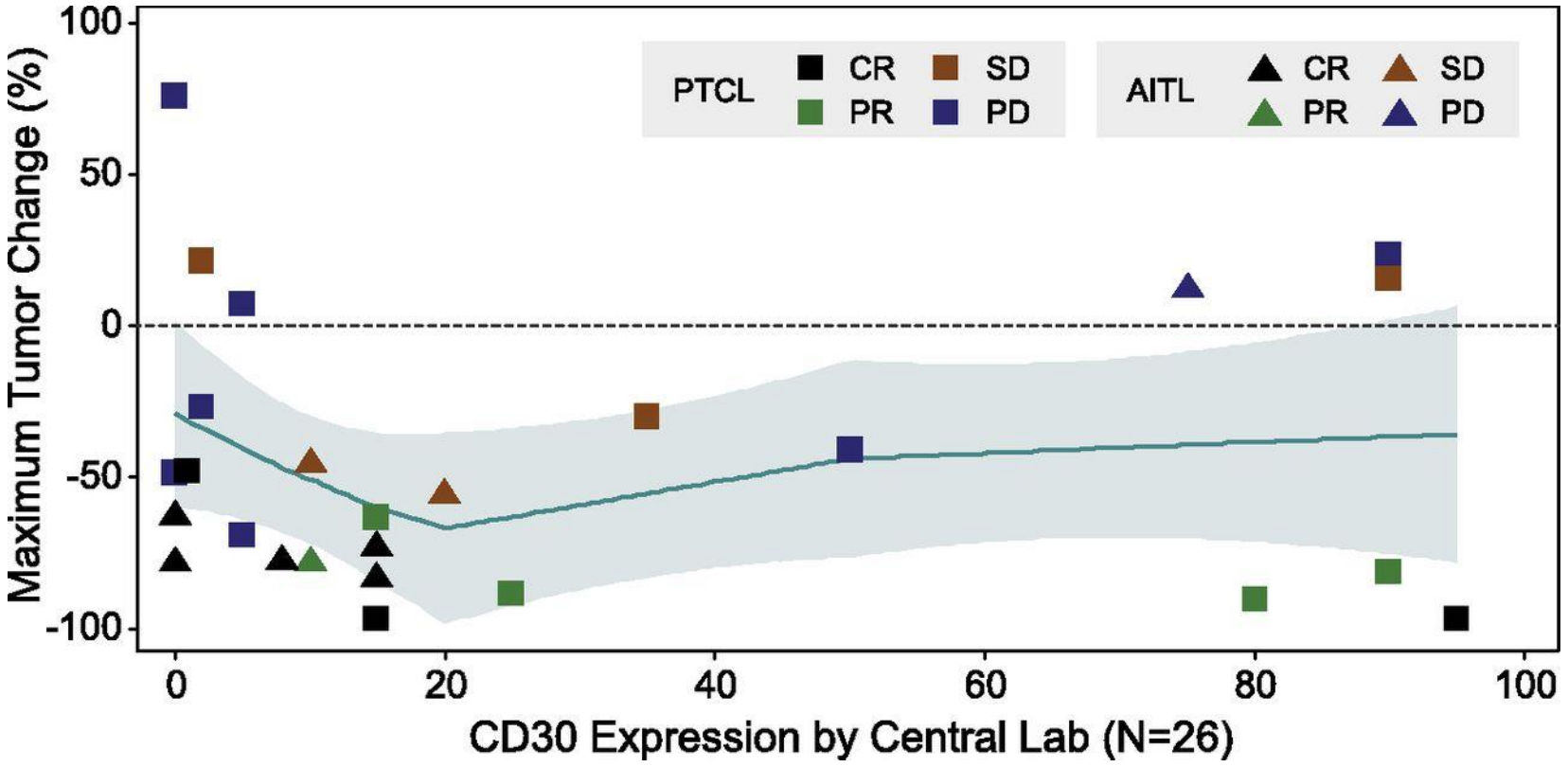


Romidepsin N=130



Horwitz S M et al. Blood 2014;123:3095-3100,Pro B, et al. J Clin Oncol. 2012;30:2190-2196,O' Connor OA, et al. *J Clin Oncol*. 2011;29:1182-1189,Coiffier B, et al. *J Clin Oncol*. 2012;30 :631-636,O'Connor OA et al ASCO 2013,

Maximum tumor size decrease by quantitative CD30 expression.



Steven M. Horwitz et al. Blood 2014;123:3095-3100

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Retrospective Multicenter Study of Relapsed or Refractory PTCL Patients treated with BV: Named Patient Program in France

Histological subtypes	CD30 expression score					
	0 (<5%)	I (5%-24%)	II (25%-49%)	III (50%-75%)	IV (>75%)	NA °
Systemic ALCL (n=24)						
ALK+ ALCL (n=9)			1*	1*	3	4
ALK- ALCL (n=15)					14	1
Other non-ALCL systemic PTCL (n=14)						
PTCL-NOS (n=11)	1	1	3	3	2	1
EATL (n=1)				1		–
ATLL (n=1)	1					–
AITL (n=1)		1				–

ORR in systemic TCL

ALCL (n=24) 62%

Non-ALCL (n=14), 21%

(*P*=0.04)

Mathilde Lamarque et al. Haematologica 2016;101:e103-e106

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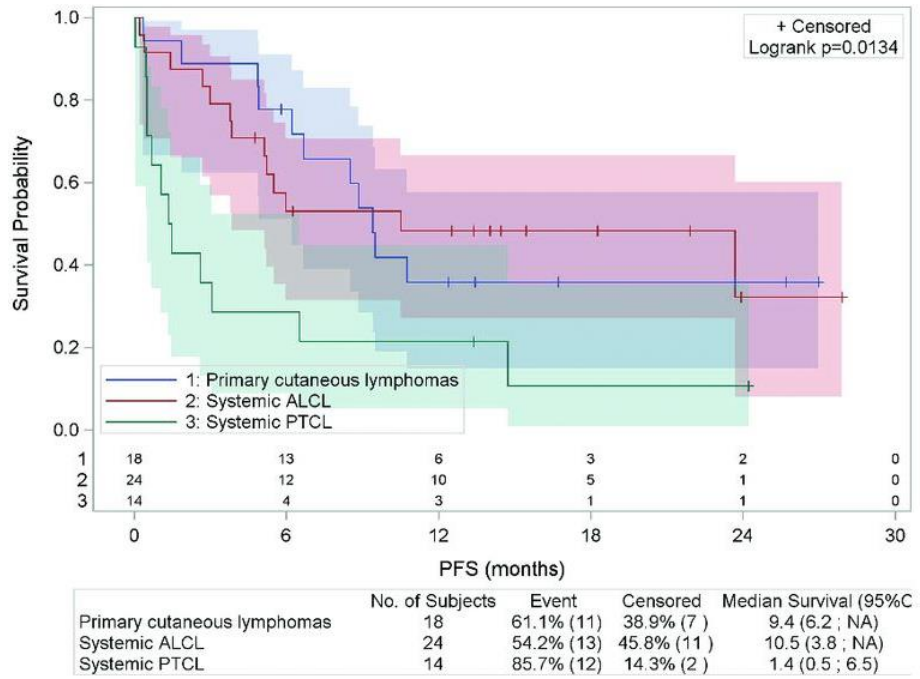
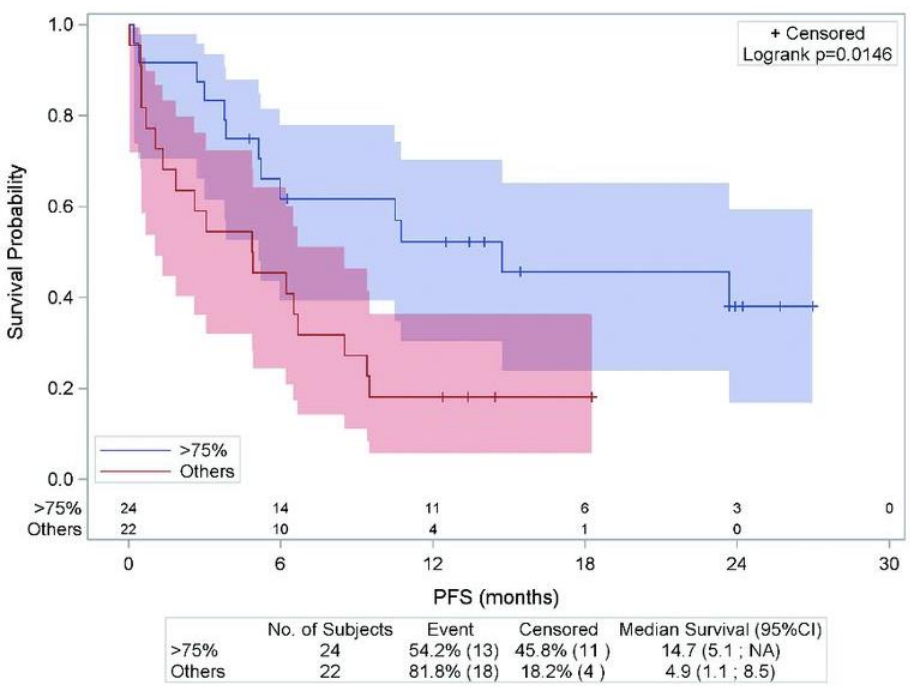
Progression-free survival:

- Histological subtypes
- CD30 expression (>75% vs. others)

A



	No. of Subjects	Event	Censored	Median Survival (95%C
Primary cutaneous lymphomas	18	61.1% (11)	38.9% (7)	9.4 (6.2 ; NA)
Systemic ALCL	24	54.2% (13)	45.8% (11)	10.5 (3.8 ; NA)
Systemic PTCL	14	85.7% (12)	14.3% (2)	1.4 (0.5 ; 6.5)



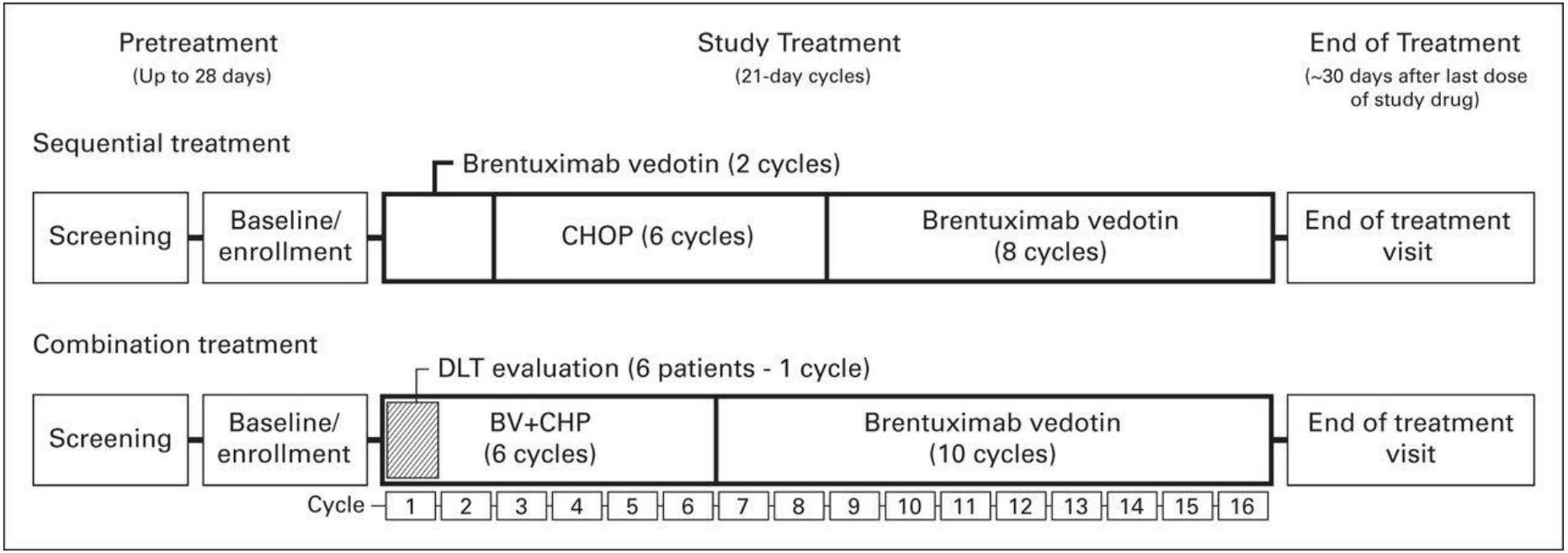
	No. of Subjects	Event	Censored	Median Survival (95%CI)
>75%	24	54.2% (13)	45.8% (11)	14.7 (5.1 ; NA)
Others	22	81.8% (18)	18.2% (4)	4.9 (1.1 ; 8.5)

PFS was longer for primary cutaneous lymphomas and systemic ALCL > systemic PTC: PFS was longer for patients with CD30 score IV than for the remaining patients (14.7 *vs*. 4.9 months; *P*=0.01)

Mathilde Lamarque et al. Haematologica 2016;101:e103-e106

haematologica
Journal of the European Hematology Association
Published by the Ferrata Storti Foundation

BV + CHP-BV, BV- CHOP-BV : Schema



Michelle A. Fanale; *JCO* **2014,** 32, 3137-3143.

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Patients – Demographic and Disease Characteristics

	Total, N=26
Age in years (range)	56 (21–82)
Gender (M/F)	11/15
IPI score ≥2, n (%)	18 (69)
Stage III/IV disease, n (%)	19 (73)
Disease Diagnosis, n (%)	
Systemic ALCL	19 (73)
ALK negative	16
ALK positive	3
Other peripheral T-cell lymphomas, n (%)	7 (27)
Peripheral T-cell lymphoma NOS, n	2
Angioimmunoblastic T-cell lymphoma, n	2
Adult T-cell leukemia/lymphoma, n	2
Enteropathy-associated T-cell lymphoma, n	1

Michelle A. Fanale; *JCO* **2014,** 32, 3137-3143.

Activity – Summary of Clinical Response at the End of Combination Therapy

- The objective response rate to treatment with brentuximab vedotin was 100% and CR rate was 88%
- 1 pt with PR converted to CR during brentuximab vedotin monotherapy

	ALCL, (N=19)	Non-ALCL[b], (N=7)	Total, (N=26)
Clinical Response[a] n (%)			
Complete Response (CR)	16 (84)	7 (100)	23 (88)
Partial Response (PR)	3 (16)	0	3 (12)

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Treatment Discontinuations by Treatment Period

	Brentuximab vedotin + CHP (N=26)	Brentuximab vedotin (N=21)	Total (N=26)
Discontinuation of treatment, n (%)	5 (19)	10 (48)	15 (58)
Reason for treatment discontinuation, n (%)			
Progressive disease	0	3 (14)	3 (12)
Investigator decision	1 (4)	2 (10)	3 (12)
Adverse event	3 (12)	3 (14)	6 (23)
Patient decision, non-AE	1 (4)	2 (10)	3 (12)

- 23 of 26 pts (88%) completed all 6 cycles of brentuximab vedotin + CHP
- 21 of 26 pts (81%) went on to receive brentuximab vedotin monotherapy; of which, 11 pts (42%) received all 16 cycles

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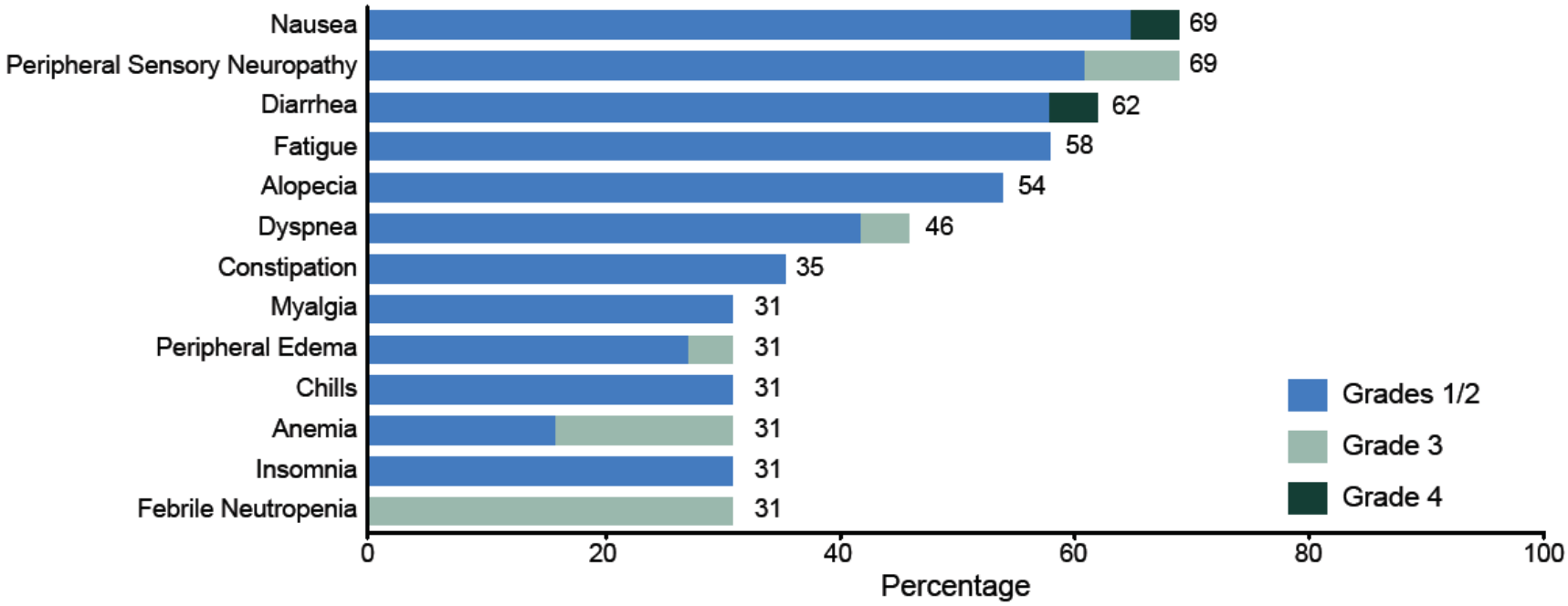
Safety – Adverse Events Occurring in at Least 30% of Patients (N=26)



- No deaths occurred within 30 days of study treatment
- Adverse events with a severity of at least Grade 3 (≥10% incidence) were febrile neutropenia (31%), neutropenia (23%), anemia (15%), and pulmonary embolism (12%)

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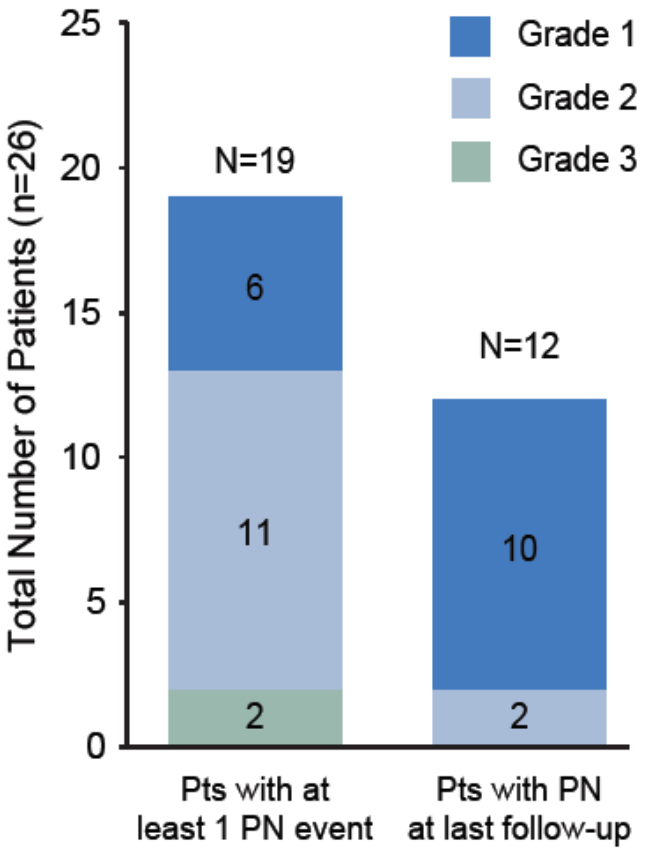
Resolution of Peripheral Neuropathy

- 73% of pts (19/26) experienced PN, the majority of whom had symptoms ≤Grade 2
- No Grade 4 PN was observed
- 95% of patients (18/19) had complete resolution or some improvement of PN symptoms at last follow-up:
  - 7/19 (37%) had complete resolution[a]
  - 11/19 (58%) had some improvement[b]
- The majority of pts with ongoing neuropathy (10/12) had a maximum severity of Grade 1 at last follow-up
- The median time to resolution of neuropathy was 1.3 months



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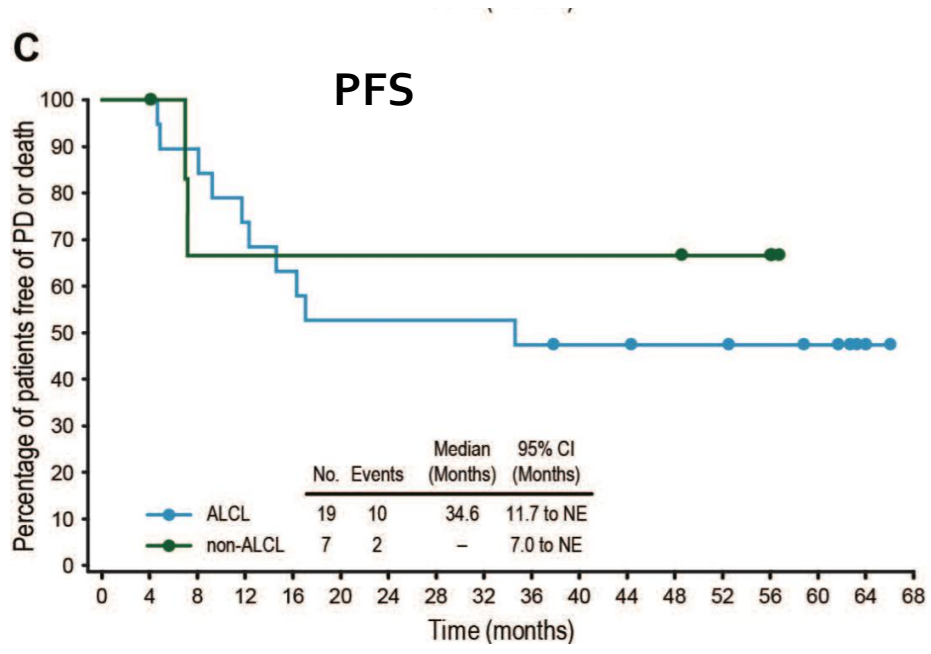
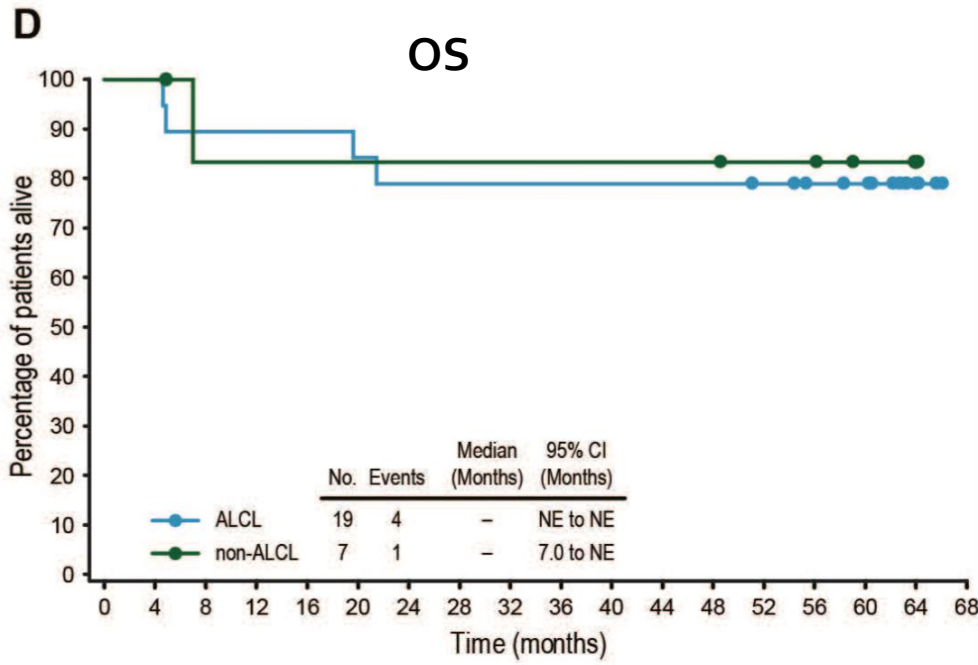
BV + CHP-BV
5 Year PFS, OS





Michelle A. Fanale; *Blood* **2018**

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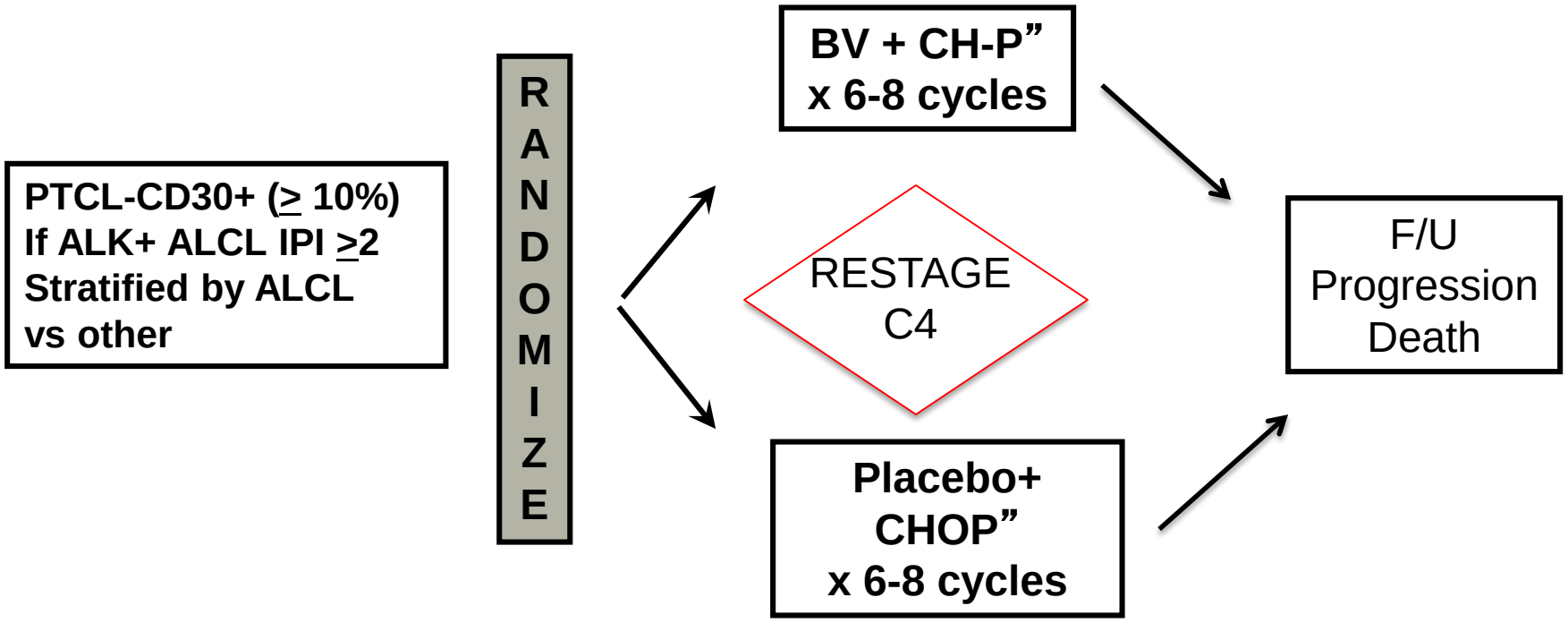
Echelon-2

A Phase 3 Study of Brentuximab Vedotin and CHP Versus CHOP in the Frontline Treatment of Patients with CD30-positive PTCL



Primary endpoint is PFS
400+ pts

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Brentuximab Vedotin in PTCL: Other than ALCL

- Limited single agent experience from prospective studies
- Activity but less than for ALCL
  - ORR
  - PFS
- ? AITL > PTCL-NOS
- Anecdotal responses in EATL, NK/T, ATL, HSTCL
- Level of CD30 expression?
- Best activity may be as part of combination therapy
  - Phase 1/2
  - Echelon 2