Brentuximab Vedotin in PTCL-NOS/AITL

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2012…2015 T-Cell Lymphomas

We Are Illuminating The Darkest of Tunnels

Bologna, Italy

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- CD30 Expression in PTCL
- Brentuximab Vedotin in PTCL/AITL
- Concurrent Therapy of Brentuximab Vedotin plus CHP in Non-ALCL CD30+ PTCL
- ECHELON-2 Design and Potential Role of Other Combinations

CD30 Expression in Non-ALCL PTCL

Diagnosis	CD30 IHC Scores 0	1+	2+	3+	4+	≥ 2+
PTCL-NOS	36%	13%	21%	13%	18%	52%
AITL	51%	21%	12%	9%	0%	21%
NK/TCL nasal type	20%	10%	30%	10%	30%	70%
EATL type 1 (classical)			22%		78%	100%
EATL type 2	100%					0%

Scoring scale:
1+ = < 25%
2+ = 25-50%
3+ = 50-75%
4+ = > 75%

Sabattini, E…Pileri, SA, *Haematologica*, 2013

Patient Demographics in Phase II Brentuximab Vedotin Non-ALCL PTCL Trial

Enrolled patients with any locally assessed level of CD30 expression by IHC BerH2 Ab

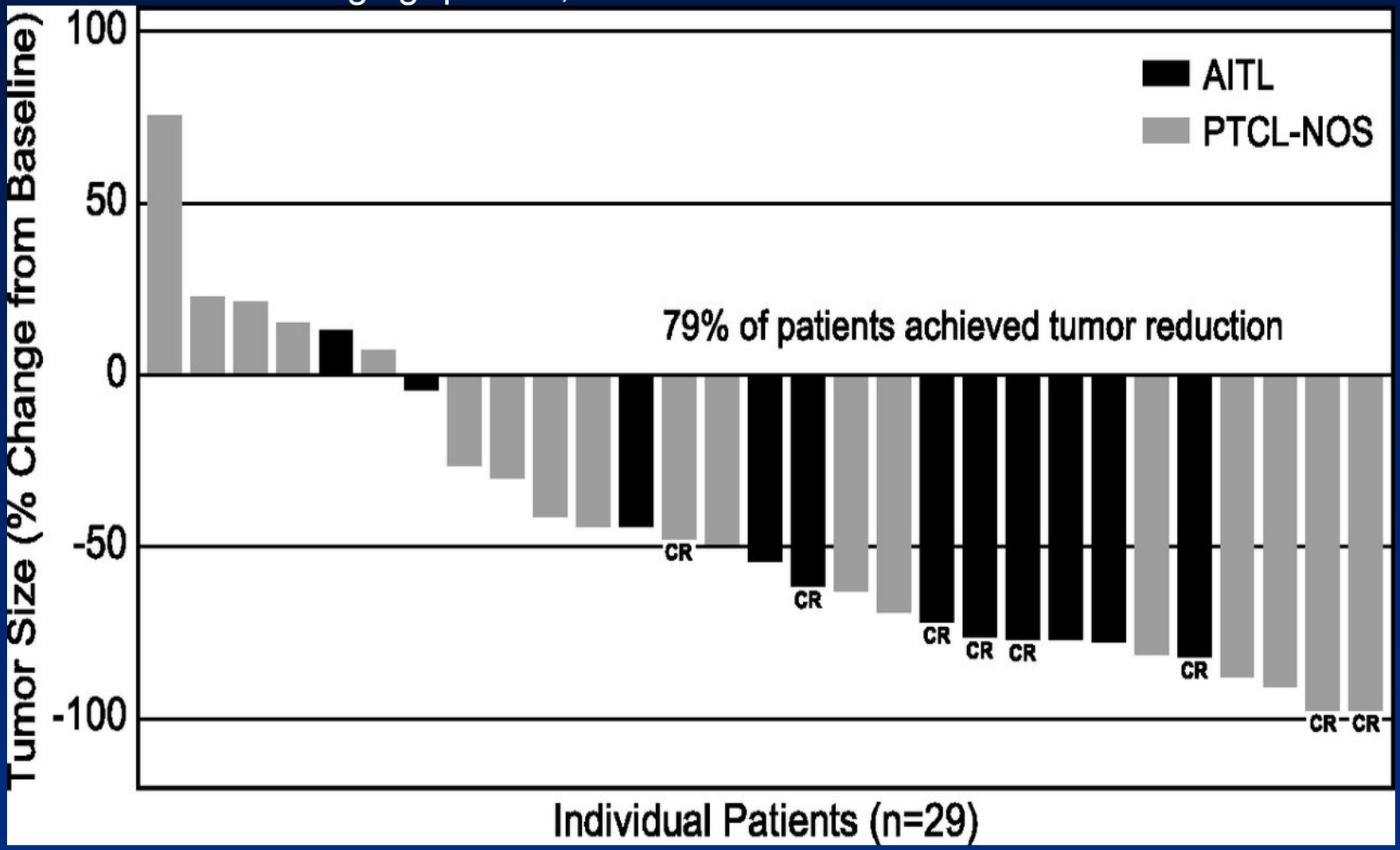
Excluded Sezary syndrome and MF including transformed MF

	AITL (N= 13)	PTCL-NOS (N=22)
Median age (yrs)	64	64.5
Median time from dx to first dose (mo)	13.2 (3.2-52.6)	9.5 (1.1-78.2)
CD30 status + – N/A or missing	 69% 15% 15%	 77% 18% 5%
Refractory to frontline tx	69%	77%
Refractory to last tx	69%	59%
Median prior tx	3 (1-4)	2 (1-9)
Prior ASCT	15%	5%

Horwitz, SM, et al, *Blood*, 2014

Brentuximab Vedotin Efficacy in Non-ALCL PTCL

Pts dosed at 1.8 mg/kg q 3 wks, if SD or better could continue until PD



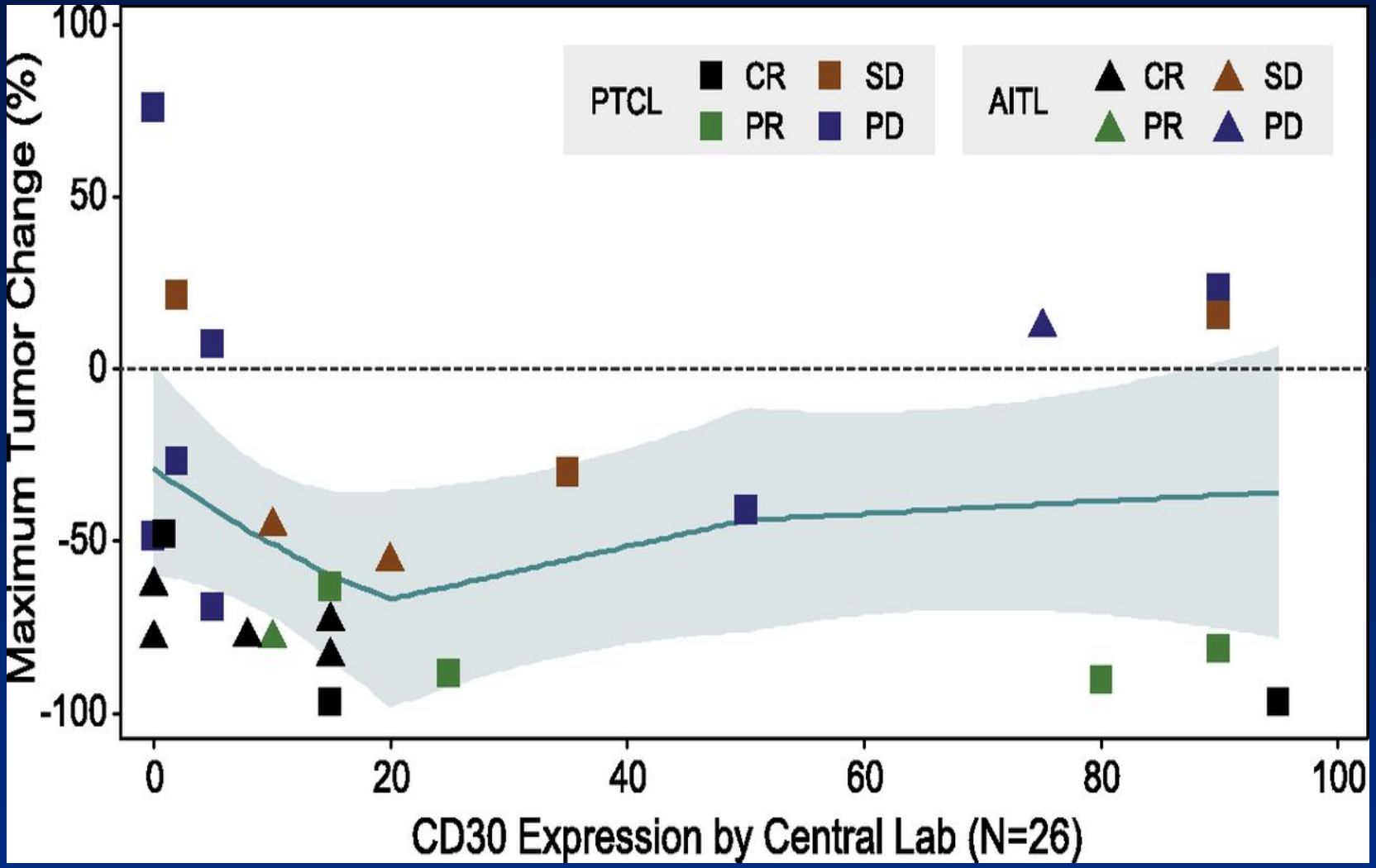
Horwitz, SM, et al, *Blood*, 2014

Brentuximab Vedotin Relative Outcomes in AITL versus PTCL

	AITL (n=13)	PTCL-NOS (n=21)	Total (n=34)
ORR	54%	33%	41%
CR	38%	14%	24%
PR	15%	19%	18%
SD	23%	14%	16%
PFS	6.74 mo	1.61 mo	2.6 mo

Horwitz, SM, et al, *Blood*, 2014

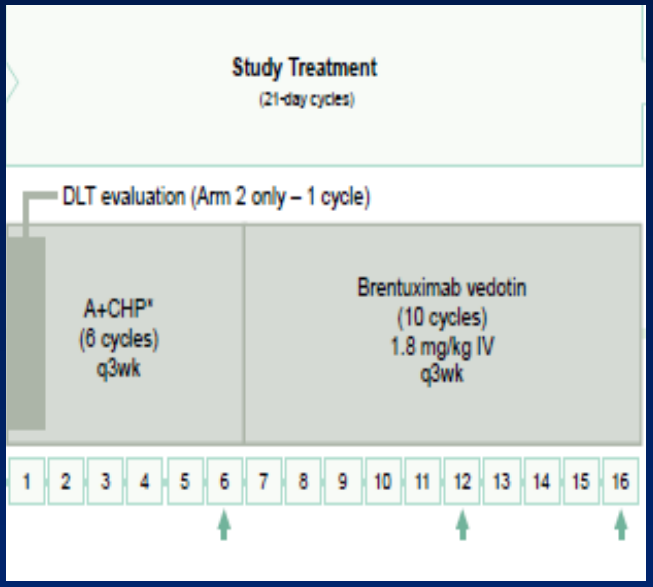
Level of CD30 Expression Did Not Correlate with Disease Response



Horwitz, SM, et al, *Blood*, 2014

Phase I Trial of Brentuximab Vedotin plus CHP for Front-Line Therapy for sALCL and other CD30+ T-Cell Lymphomas (TCL)

Patient Characteristics	N=26
Age	56 (21–82)
Gender, n	11 M / 15 F
IPI score ≥ 2	69%
Stage III/IV disease	73%
Diagnosis	
sALCL, %	73%
ALK +/-, n	16/3
Other peripheral TCL	27%
Peripheral TCL NOS, n	2
Angioimmunoblastic TCL, n	2
Adult T-cell leukemia/lymphoma, n	2
Enteropathy-associated TCL, n	1



ALK+ ALCL patients needed IPI of ≥ 2 to enroll

Non-ALCL pts needed CD30 expression of ≥ 1% to enroll

Fanale, M et al, *JCO*, 2014

Levels of CD30 Expression for Non-ALCL Patients Enrolled

Diagnosis	CD30 Expression by IHC
Adult T-cell leukemia/lymphoma	25%, 98%
AITL	25%, 50%
PTCL-NOS	50%, 80%
EATL	60%

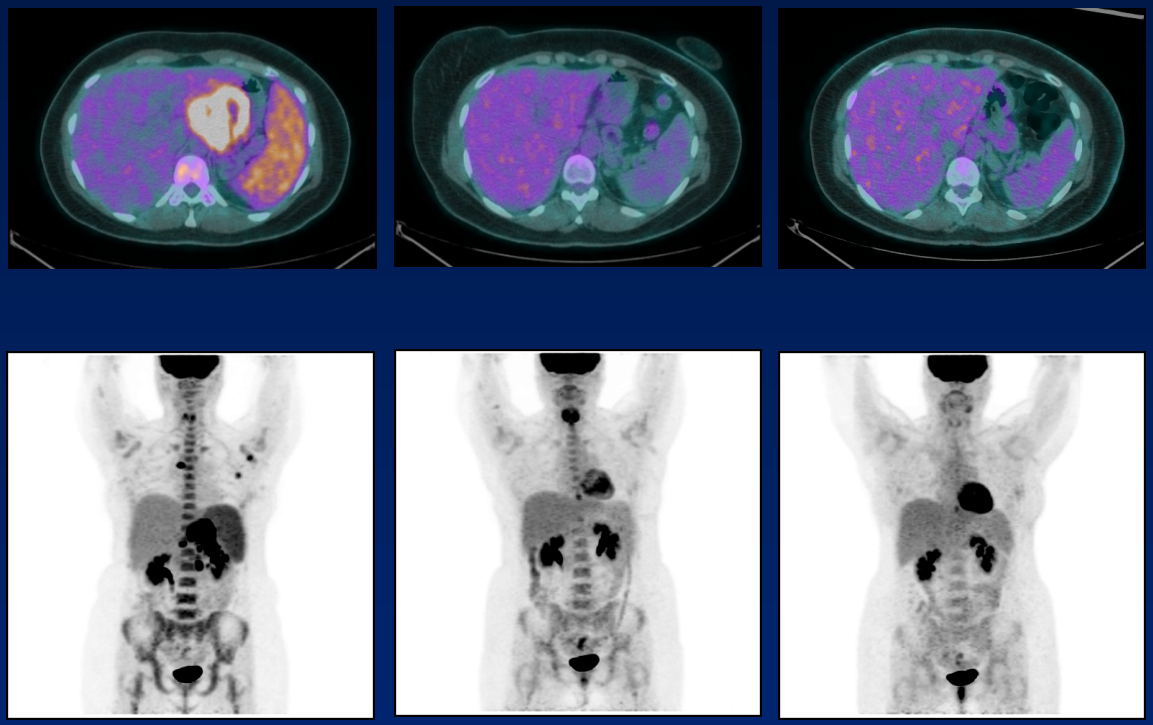
Fanale, M et al, *JCO*, 2014

Responses to Front-line Concurrent Therapy with Brentuximab Vedotin Plus CHP

Key Response Results	sALCL (N=19)	Non-ALCL (N=7)	Total (N=26)
ORR, %	100%)	100%	100%
CR	84%	100%	88%
PR	16%	-	12%

Fanale, M et al, *JCO*, 2014

Case: 37F with PTCL-NOS, CD30+ Treated with Brentuximab Vedotin plus CHP Phase I Trial



Baseline Cycle 6 Cycle 12

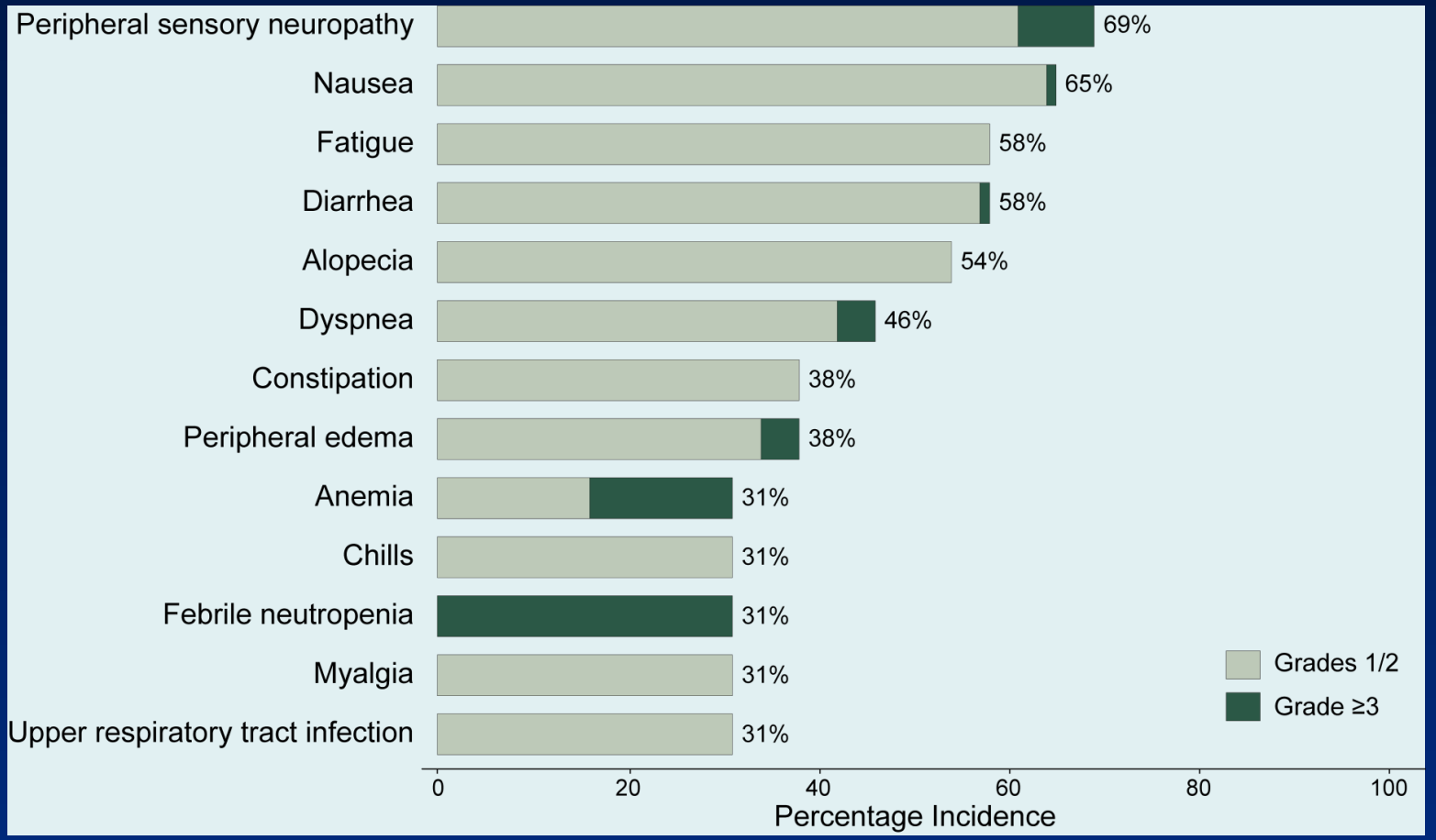
- Stage IV
- IPI score of 2

Treatment

Brentuximab vedotin with CHP (6 cycles)
- PR (Cycle 2)
- CR (Cycle 6)

Single-agent brentuximab vedotin (10 cycles)
- Remains in CR 31 mo into follow-up

Treatment Emergent AEs Occurring in ≥ 30%

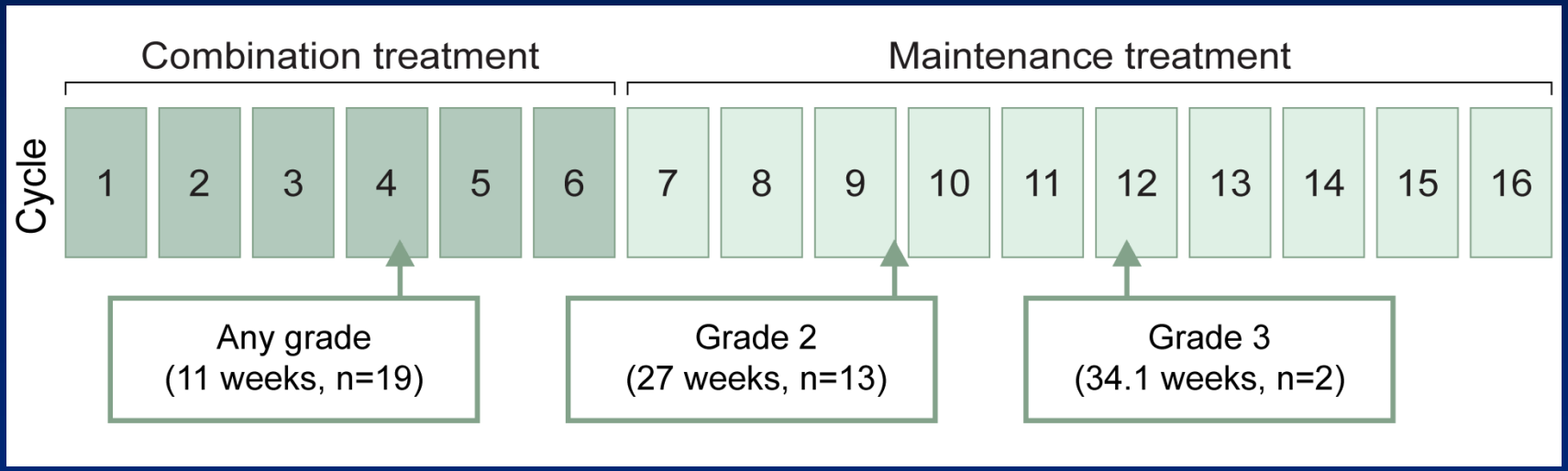


Fanale, M et al, *JCO*, 2014

Peripheral Neuropathy with Front-line Concurrent BV plus CHP Therapy

- Treatment-emergent peripheral neuropathy occurred in 19/26 patients (73%)*
  - 2/19 patients (11%) had Grade 3 events; no Grade 4 events

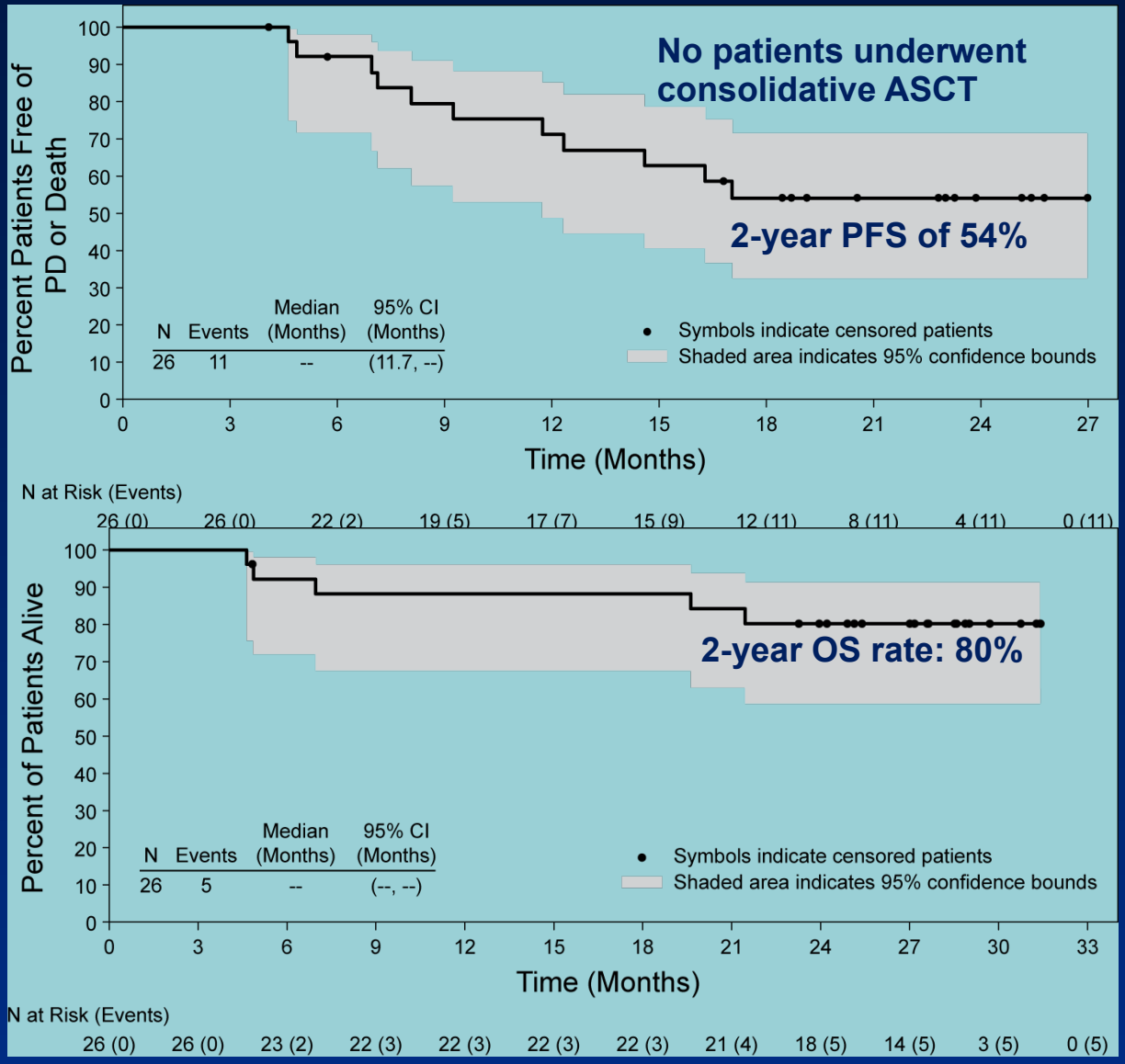
Median Time to Onset



- 17 of 19 patients (89%) had complete resolution or some improvement in symptoms
  - Median time to improvement was 3.5 months (range, 0–6)

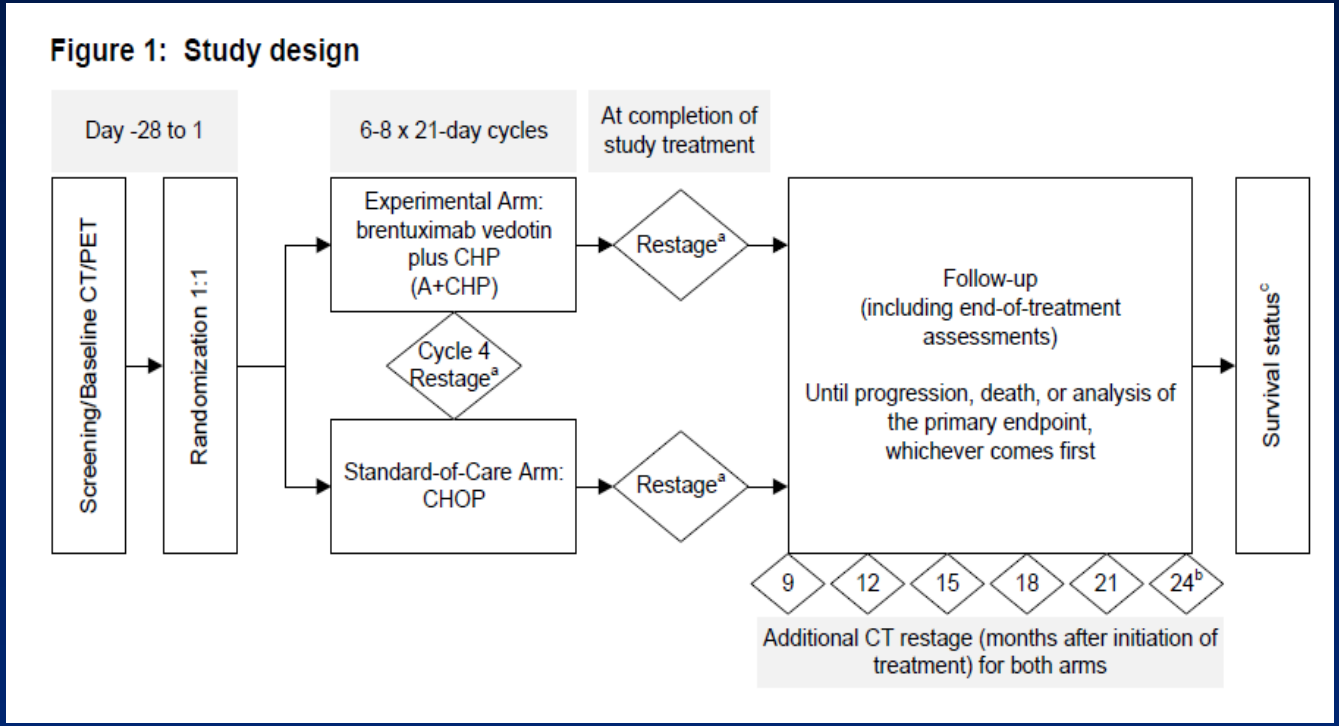
Fanale, M et al, *JCO*, 2014

PFS and OS with Front-line CHP plus Brentuximab Vedotin



Fanale, M et al, *ESMO*, 2014

Current and Next Steps of Brentuximab in Non-ALCL PTCL



450 pts to be randomized (~75% ALCL) and non-ALCL PTCL need 10% CD30+ by IHC

Double-blinded, placebo controlled

Consolidative SCT or RT allowed after 6 cycles

Powered for PFS of 23.9 vs 16.5 mo (CHP +BV vs CHOP)

Modest CR rates in relapsed PTCL-NOS

Good tolerability allows for evaluation of doublet-based approaches

Investigator-initiated trial with dual TORCi (MLN0128)

Rationale supported by everolimus data previously reported by Witzig, T et al.

Other potential agents include PD-1 inhibitors