Brentuximab Vedotin in Combination with CHP in Patients with Newly-Diagnosed CD30+ Peripheral T-cell Lymphomas: 2-Year Follow-up

MA Fanale; SM Horwitz; A Forero-Torres; NL Bartlett; RH Advani; B Pro; RW Chen; A Davies; T Illidge; D Huebner; DA Kennedy; AR Shustov

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Disclosures

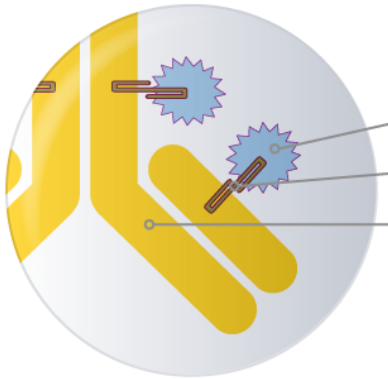
- Seattle Genetics, Inc. provided research funding to the institutions of RHA, NLB, RC, AD, MAF, AF, SMH, TI, BP, and ARS.
- NLB, RHA, RC, MAF, TI, SMH, ARS, AD, and BP have acted as consultants for Seattle Genetics, Inc. and MAF and ARS have received honoraria from Seattle Genetics, Inc.
- AF, RC, and ARS have participated in a Seattle Genetics, Inc. speakers' bureau.
- NLB, RC, MAF, and BP have received travel expenses from Seattle Genetics, Inc.
- DAK is an employee of and has equity ownership in Seattle Genetics, Inc.
- Takeda Pharmaceuticals International Co. provided research funding to the institutions of RHA and SMH.
- RHA, TI, and SMH have acted as consultants for Takeda Pharmaceuticals International Co.
- TI and AD have received honoraria from Takeda Pharmaceuticals International Co.
- DH is an employee of and has equity ownership in Takeda Pharmaceuticals International Co.

Background

- Peripheral T-cell lymphomas (PTCLs) are aggressive non-Hodgkin lymphomas
  - Some tumors express CD30, including systemic anaplastic large cell lymphoma (sALCL), where expression is pathognomonic
- Frontline treatment usually consists of anthracycline-containing regimens such as CHOP
  - Complete remission (CR) rate 39–53%[a,b,c]
  - 5-year overall survival (OS) rate 12–49%[d]
- Brentuximab vedotin is an antibody-drug conjugate that has shown efficacy in a pivotal study of patients with relapsed or refractory sALCL[e]
  - Objective response rate 86% (CR rate 57%)

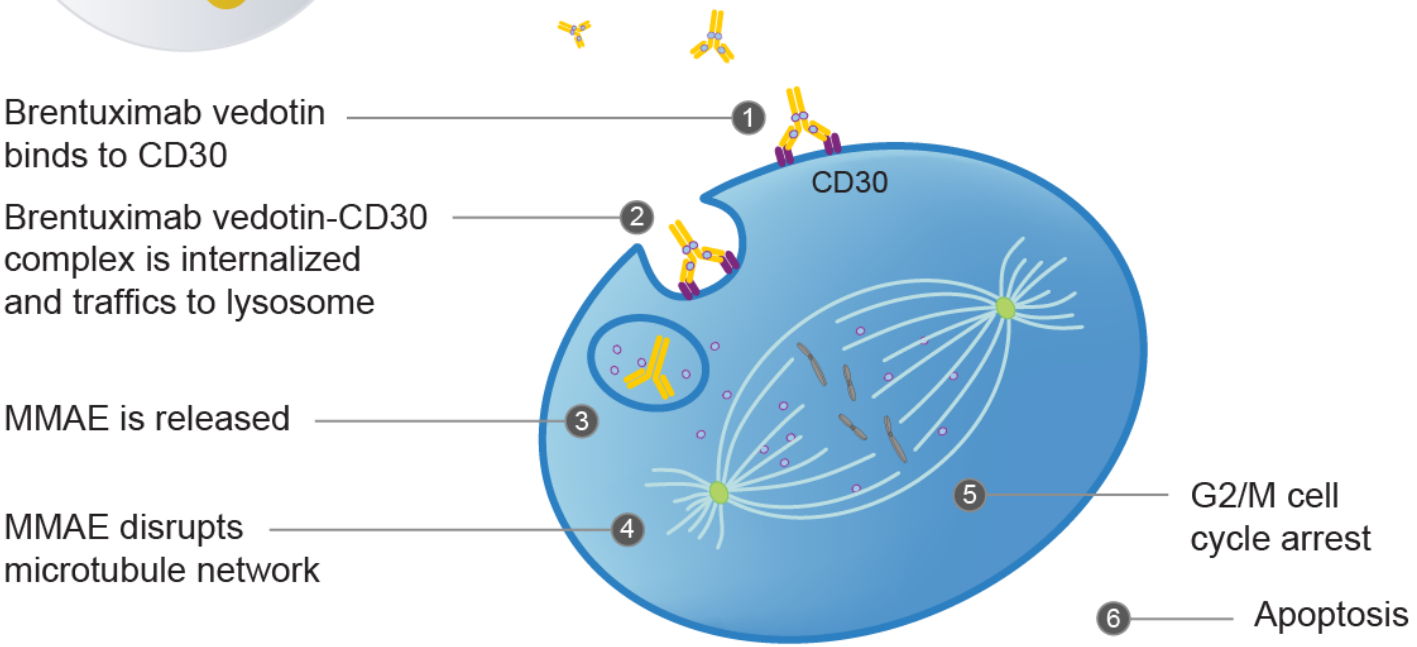
a Savage et al. Blood 2008; 111: 5496-504
b Reimer et al. J Clin Oncol 2009; 27: 106-13
c D'Amore et al. J Clin Oncol 2012; 30: 3093-9
d Vose et al. J Clin Oncol 2008; 26: 4124-30
e Pro et al. J Clin Oncol 2012; 30: 2190-96

Mechanism of Action



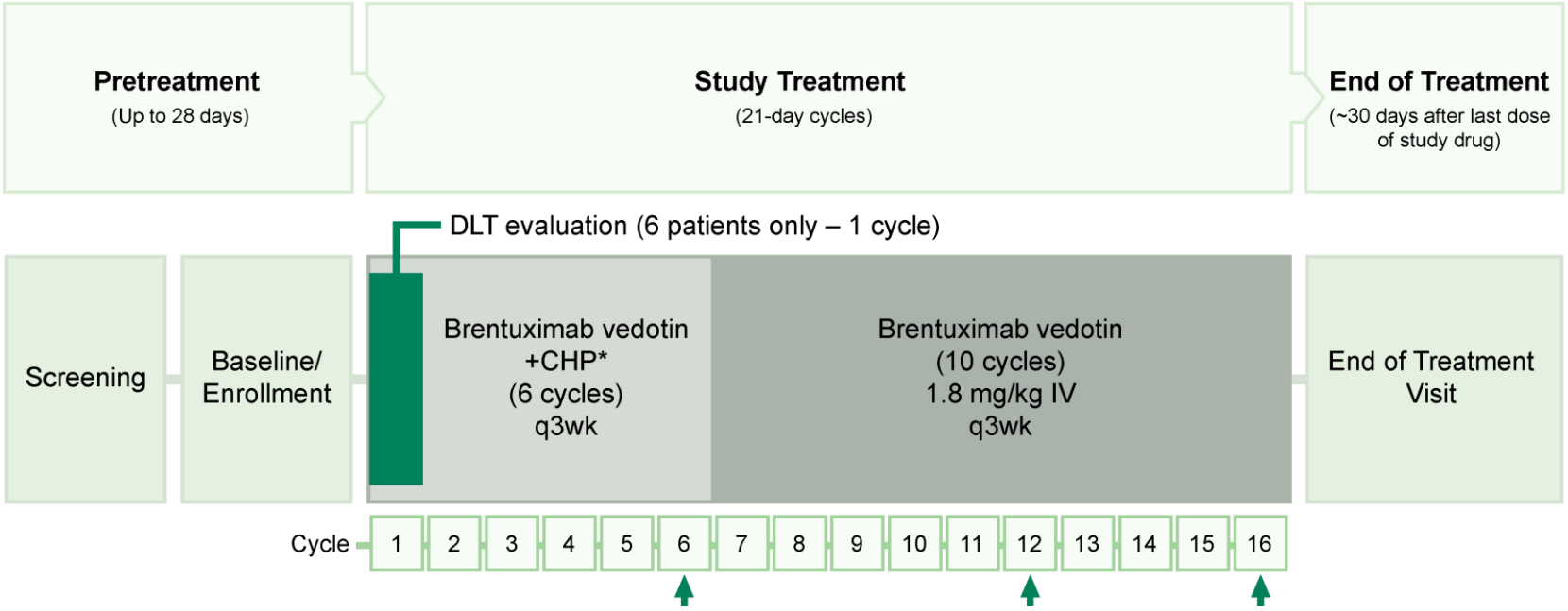
Brentuximab vedotin antibody-drug conjugate (ADC)

- Monomethyl auristatin E (MMAE), microtubule-disrupting agent
- Protease-cleavable linker
- Anti-CD30 monoclonal antibody



Study Design

- Phase 1, multicenter study conducted in the US and Europe (ClinicalTrials.gov #NCT01309789)



- Patients followed for survival and disease status every 3 months after EOT
- Primary results have been reported previously (Fanale et al., J Clin Oncol, *in press*)
  - This presentation updates response durability and peripheral neuropathy resolution in patients treated with combination treatment (brentuximab vedotin + CHP)

* CHP=CHOP without vincristine

Patient and Disease Characteristics

	Total N=26
Age*, years	56 (21–82)
Gender, n	11 M / 15 F
IPI score ≥2, n (%)	18 (69)
Stage III/IV disease, n (%)	19 (73)
Diagnosis	
sALCL, n (%)	19 (73)
ALK +/-, n	16/3
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

* Median (range)

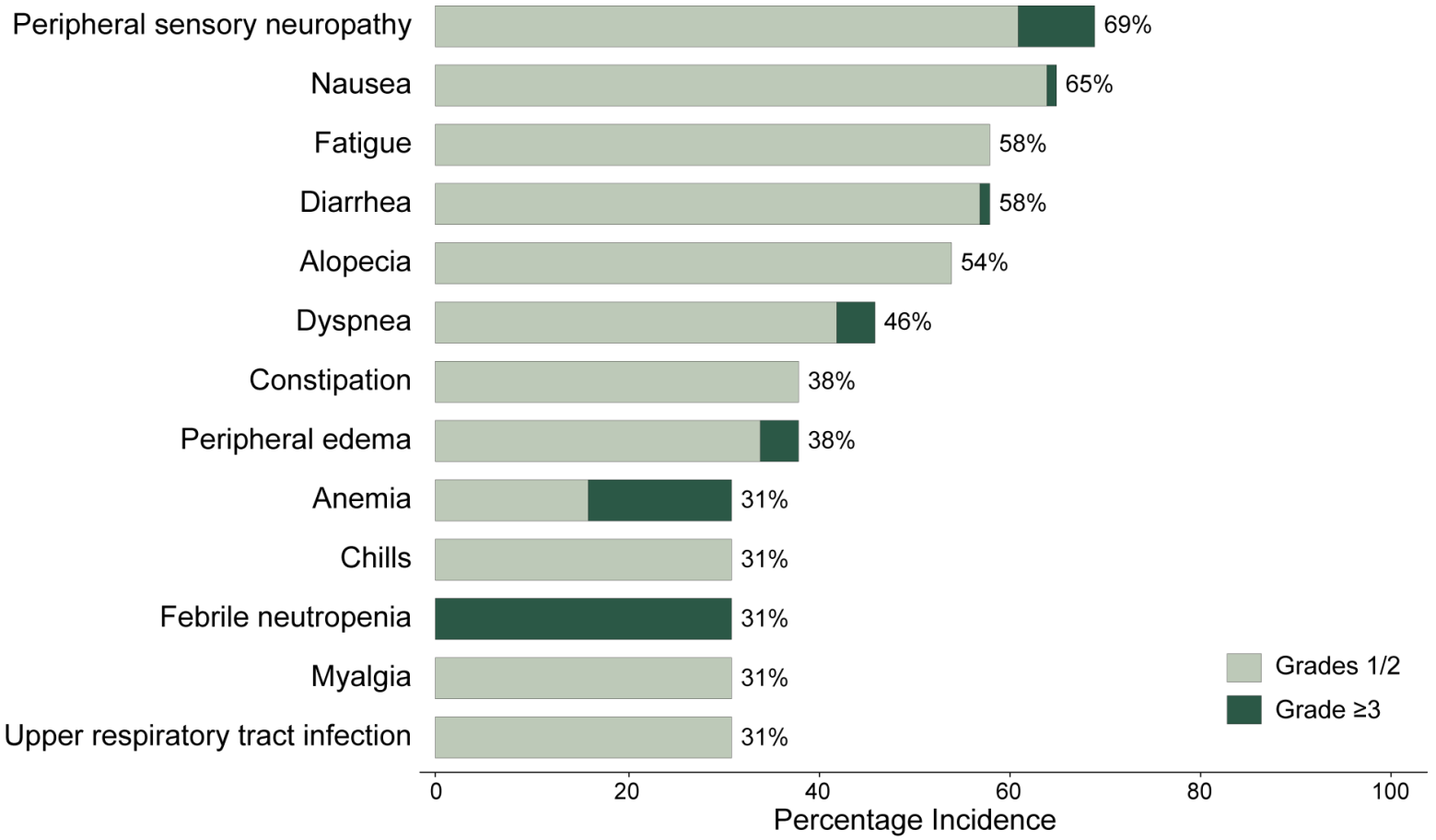
Exposure

- 23 of 26 patients (88%) received all 6 cycles of brentuximab vedotin + CHP
- 21 patients received maintenance treatment with single-agent brentuximab vedotin
  - 11 of 21 (52%) received 16 total cycles of brentuximab vedotin
- Median number of brentuximab vedotin cycles including maintenance was 13 (range, 3–16)
- 40 of 309 brentuximab vedotin doses (13%) were reduced
  - Relative dose intensity 95%

Treatment Discontinuation

Reason for treatment discontinuation	Total N=26 n (%)
Completed treatment	11 (42)
Progressive disease	3 (12)
Adverse event	6 (23)
Peripheral sensory neuropathy	3 (12)
Abdominal pain	1 (4)
Asthenia	1 (4)
Peripheral motor neuropathy	1 (4)
Investigator decision	3 (12)
Patient decision, non-AE	3 (12)

Adverse Events*



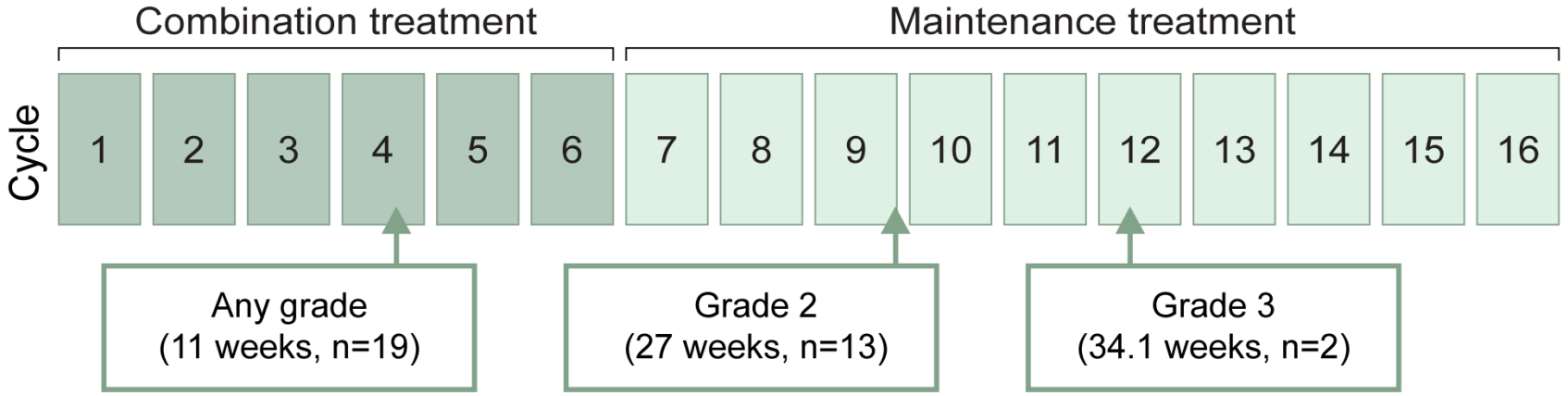
- No deaths occurred within 30 days of study treatment

* Treatment-emergent AEs occurring in at least 30% of patients (N=26)

Peripheral Neuropathy

- 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)

* Standardized MedDRA Query analysis

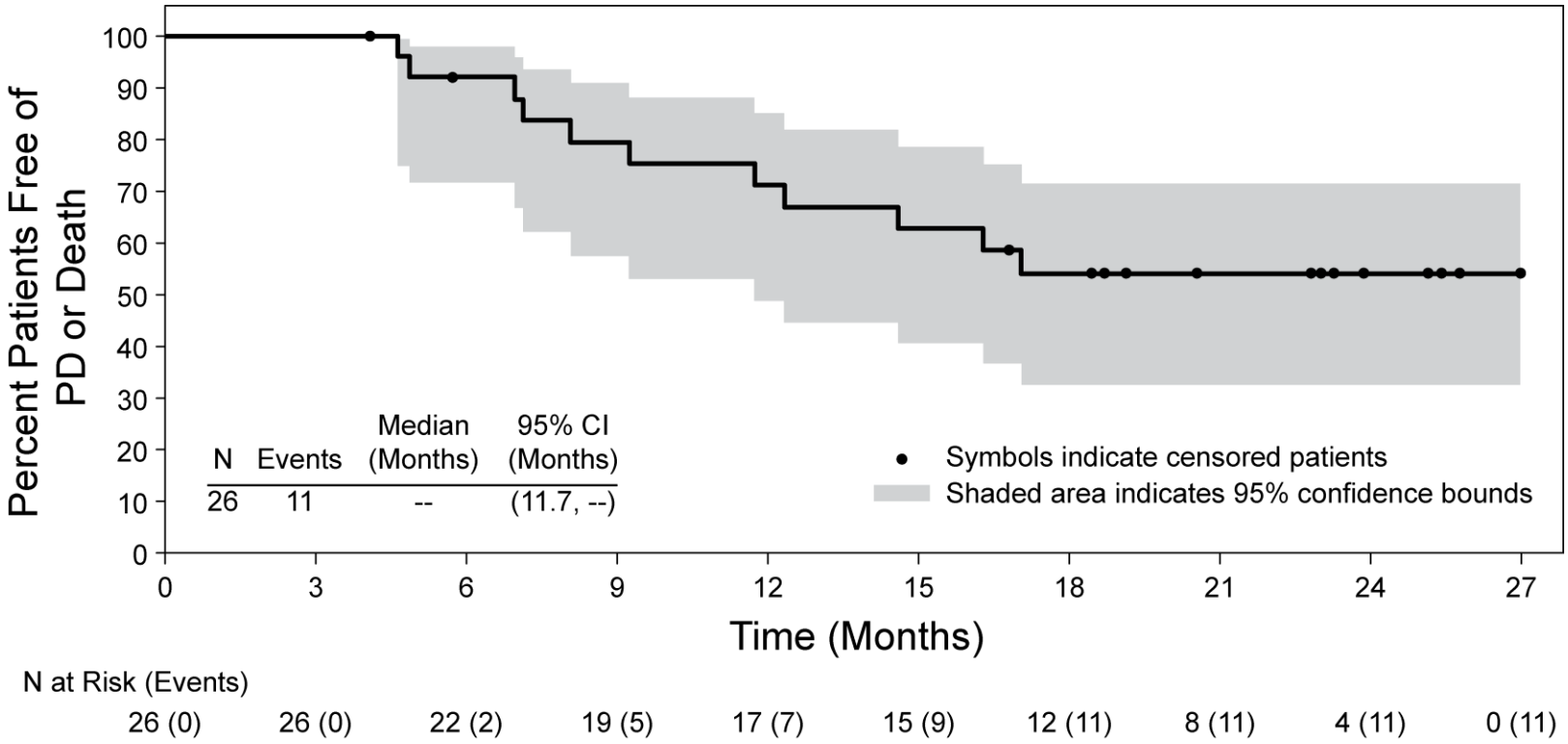
Clinical Response

	sALCL (N=19)	Non-ALCL (N=7)	Total (N=26)
Objective Response*, n (%)	19 (100%)	7 (100%)	26 (100%)
Complete Remission	16 (84%)	7 (100%)	23 (88%)
Partial Remission	3 (16%)	--	3 (12%)

- 1 patient with PR converted to CR during maintenance

* Response per investigator at end of combination treatment (Cycle 6) or at latest assessment for 3 patients who discontinued prior to Cycle 6 (Cheson 2007)

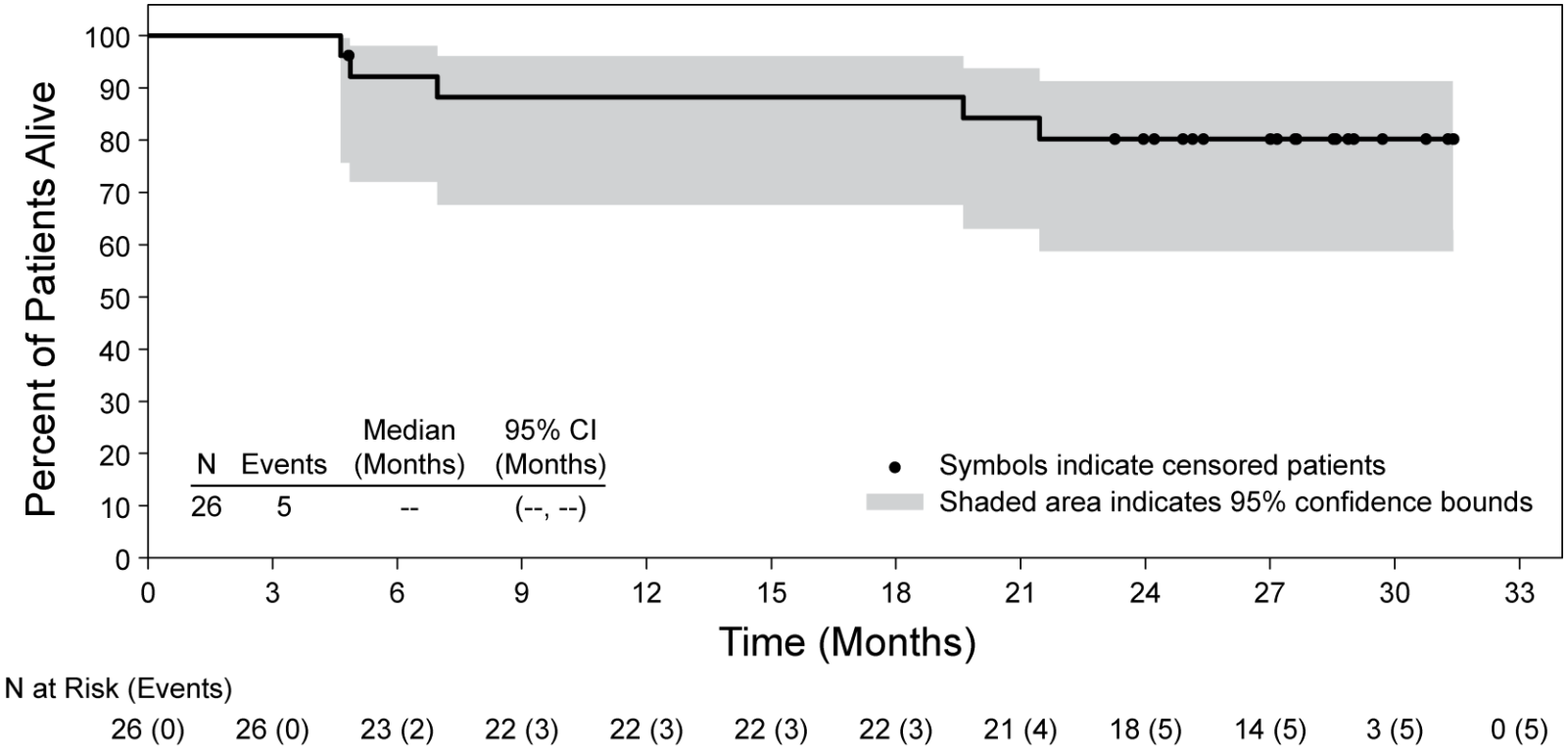
Progression-Free Survival



- Median observation time from first dose: 27.1 months
- Estimated 2-year PFS rate: 54% (95% CI 32%, 71%)
- 10/19 ALCL patients and 5/7 non-ALCL patients remain free of disease progression or death
- No patients went on to receive a consolidative stem cell transplant*

* Subsequent treatment data missing for 5 patients

Overall Survival



- Estimated 2-year OS rate: 80% (95% CI 59%, 91%)
- 15 of 19 patients with sALCL patients and 6 of 7 non-ALCL patients remain alive
  - All deaths disease related except one case of respiratory failure in which disease-relatedness was unknown
- 4 patients received subsequent brentuximab vedotin treatment after progression*
- After progression, 3 patients received stem cell transplants (2 allogeneic, 1 autologous)*

* Subsequent treatment data missing for 5 patients

Conclusions

- Brentuximab vedotin + CHP exhibited manageable toxicity
- Substantial and durable antitumor activity was observed in both sALCL and non-ALCL patients
  - Objective response rate 100%, CR rate 88%
  - Estimated 2-year PFS rate 54%
  - Estimated 2-year OS rate 80%
- ECHELON-2, a randomized phase 3 study comparing 6–8 cycles of brentuximab vedotin + CHP with CHOP in the frontline treatment of patients with CD30+ PTCL (including sALCL), is currently enrolling patients (ClinicalTrials.gov #NCT01777152)