THE LANCET

Supplementary appendix

This appendix formed part of the original submission and has been peer reviewed. We post it as supplied by the authors.

Supplement to: Moskowitz CH, Nademanee A, Masszi T, et al, for the AETHERA Study Group. Brentuximab vedotin as consolidation therapy after autologous stem-cell transplantation in patients with Hodgkin's lymphoma at risk of relapse or progression (AETHERA): a randomised, double-blind, placebo-controlled, phase 3 trial. *Lancet* 2015; published online March 19. http://dx.doi.org/10.1016/S0140-6736(15)60165-9.

Web Extra Material

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Table S1: Dose Modification Schedule

Toxicity	Grade 1	Grade 2	Grade 3	Grade 4
Non-hematologic	Continue at same dose level.	Continue at same dose level, except in the event of Grade 2 neuropathy. For Grade 2 neuropathy, withhold dose until toxicity is ≤ Grade 1 or has returned to baseline, then reduce the dose to 1.2 mg/kg and resume treatment.	Withhold dose until toxicity is ≤ Grade 1 or has returned to baseline, then resume treatment at the same dose level[a]. For Grade 3 or higher neuropathy, discontinue treatment.	Withhold dose until toxicity is ≤ Grade 1 or has returned to baseline, then reduce dose to 1.2 mg/kg and resume treatment[a].
Hematologic	Continue at same dose level.	Continue at same dose level.	Withhold dose until toxicity is ≤ Grade 2, or has returned to baseline, then resume treatment at the same dose level[b]. Consider growth factor support (G-CSF or GM-CSF) for treatment of neutropenia and prophylaxis in subsequent cycles.	Withhold dose until toxicity is ≤ Grade 2, then resume treatment at the same dose level. Consider growth factor support (G-CSF or GM-CSF) for treatment of neutropenia and prophylaxis in subsequent cycles. For the second occurrence of Grade 4 toxicity (if neutropenia, while receiving growth factor support), withhold dose until toxicity is ≤ Grade 2, then reduce the dose to 1.2 mg/kg and resume treatment[b].

a Patients who develop Grade 3 or 4 electrolyte laboratory abnormalities may continue study treatment without interruption.

b Patients who develop Grade 3 or 4 lymphopenia may continue study treatment without interruption.

G-CSF: granulocyte-colony stimulating factor; GM-CSF: granulocyte macrophage-colony stimulating factor

Table S2: PFS Analysis Components

Analysis	CT scans (per IRF)	CT Scans (per investigator)	Biopsy Reports	Lymphoma Assessments	Death
IRF	X		X		X
Investigator		X	X	X	X

Table S3: Subsequent Anti-Tumor Therapies

	Treatment Group	
	BV (n=165)	**Placebo (n=164)**
Subsequent treatment ever received, n (%)	51 (31)	85 (52)
Stem cell transplant*	13 (8)	24 (15)
Single-agent BV	8 (5)	72 (44)
Multi-agent therapy including BV	1 (1)	1 (1)
Multi-agent therapy	35 (21)	34 (21)
Single-agent therapy	22 (13)	22 (13)
Radiation	22 (13)	23 (14)
Donor lymphocyte infusion	2 (1)	1 (1)
Other treatment	1 (1)	2 (1)
First subsequent treatment, n (%)		
Allogeneic stem cell transplant	3 (2)	0 (0)
Single-agent BV	3 (2)	63 (38)
Multi-agent therapy including BV	1 (1)	0 (0)
Multi-agent therapy	27 (16)	12 (7)
Single-agent therapy	7 (4)	5 (3)
Radiation	10 (6)	4 (2)
Other treatment	0 (0)	1 (1)

* Transplant type: BV: 12/13 allogeneic; placebo: 23/24 allogeneic
BV: brentuximab vedotin

Table S4: Serious Adverse Events Occurring in ≥2 Patients on the BV Arm

	Treatment Group	
Preferred Term	**BV (n=167)**	**Placebo (n=160)**
Any Event, n (%)	41 (25)	20 (13)
Pneumonia	7 (4)	4 (3)
Pyrexia	6 (4)	2 (1)
Vomiting	5 (3)	1 (1)
Nausea	4 (2)	1 (1)
Hepatotoxicity	3 (2)	1 (1)
Peripheral sensory neuropathy	3 (2)	0 (0)
Acute respiratory distress syndrome	2 (1)	1 (1)
Constipation	2 (1)	0 (0)
Headache	2 (1)	0 (0)
Herpes zoster	2 (1)	1 (1)
Pneumonitis	2 (1)	0 (0)

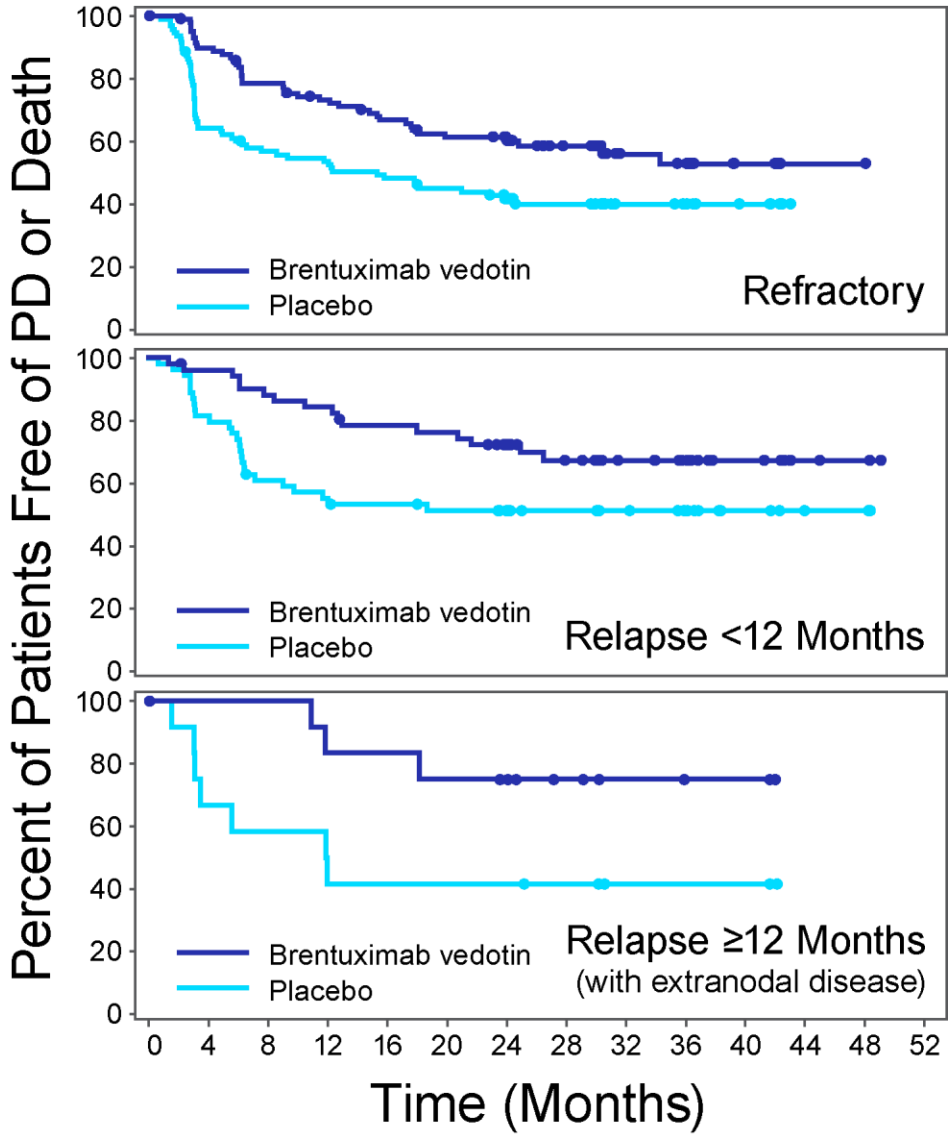
BV: brentuximab vedotin

Table S5: Summary of Deaths

	BV (n=167)	Placebo (n=160)
All Deaths, n (%)	28 (17)	25 (16)
Disease Related	18 (11)	17 (11)
Acute respiratory distress syndrome	0	1 (1)
Disease progression	5 (3)	9 (6)
Hodgkin lymphoma	13 (8)	7 (4)
Not Disease Related	9 (5)	7 (4)
Acute respiratory distress syndrome*	2 (1)	0
Aplastic anemia	0	1 (1)
Bladder cancer	1 (1)	0
Cardiac arrest	1 (1)	0
Graft versus host disease	0	3 (2)
Influenza	0	1 (1)
Lung infection	1 (1)	0
Myelodysplastic syndrome	1 (1)	1 (1)
Myocardial infarction	1 (1)	0
Pancreatic carcinoma	1 (1)	0
Pneumonia	0	1 (1)
Sepsis	1 (1)	0
Disease Relationship Unknown	1 (1)	1 (1)
Fungal pneumonia	0	1 (1)
Other	1 (1)	0
Death prior to progression per IRF, n (%)	4 (2)	3 (2)
Death prior to progression by INV, n (%)	5 (3)	3 (2)

*1 death occurred within 30 days of last dose of study treatment
BV: brentuximab vedotin; IRF: independent review facility; INV: investigator

Figure S1: Progression-Free Survival by Response to Frontline Therapy



Progression-free survival (PFS) by response to frontline therapy. Kaplan-Meier plots showing PFS per investigator between the brentuximab vedotin (BV) arm (dark blue) and the placebo arm (light blue) by response to frontline therapy: refractory (top), relapse in less 12 months (middle), and relapse at least 12 months after frontline therapy and with extranodal involvement (bottom). Symbols indicate censored patients.