Supplemental Material

Final data from the phase 3 ALCANZA study of brentuximab vedotin vs physician's choice in cutaneous T-cell lymphoma

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Supplemental tables

Supplemental Table 1. Patient baseline characteristics (ITT population)

	Brentuximab vedotin (n = 64)	Physician's choice (n = 64)	Overall (N=128)
Age, years (range)	62 (51-70)	59 (48-67)	60 (48-69)
Sex, n (%)			
Male	33 (52)	37 (58)	70 (55)
Female	31 (48)	27 (42)	58 (45)
Race			
White	56 (88)	53 (83)	109 (85)
Other	5 (8)	10 (16)	15 (12)
Not reported	3 (5)	1 (2)	4 (3)
ECOG PS, n (%)			
0	43 (67)	46 (72)	89 (70)
1	18 (28)	16 (25)	34 (27)
2	3 (5)	2 (3)	5 (4)
CD30 expression, median % (range)*	32.5 (12.5-67.5)	31.3 (12.0-47.5)	31.3 (12.5-60.0)
Time since initial diagnosis (months)	42.2 (12.8-87.4)	37.0 (12.3-102.7)	40.9 (12.7-96.8)
Time since progression on last therapy (months)†	2.4 (1.4-7.9)	1.3 (0.9-3.7)	1.9 (1.1-3.8)
Lines of previous therapy			
Total	4.0 (2.0-7.0)	3.5 (2.0-5.5)	4.0 (2.0-6.0)
Skin-directed	1.0 (1.0-2.0)	1.0 (1.0-2.0)	1.0 (1.0-2.0)
Systemic	2.0 (1.0-4.0)	2.0 (1.0-3.0)	2.0 (1.0-4.0)
MF, n (%)	48 (75)	49 (77)	97 (76)
Disease stage‡§			
IA-IIA	15/48 (31)	18/49 (37)	33/97 (34)
IIB	19/48 (40)	19/49 (39)	38/97 (39)
IIIA-IIIB	4/48 (8)	2/49 (4)	6/97 (6)
IVA1	0	1/49 (2)	1/97 (1)
IVA2	2/48 (4)	8/49 (16)	10/97 (10)
IVB	7/48 (15)	0	7/ 97 (7)

C-ALCL, n (%)	16 (25)	15 (23)	31 (24)
Disease stage‡			
Skin			
T_1	1/16 (6)	4/15 (27)	5/13 (16)
T_2	3/16 (19)	5/15 (33)	8/31 (26)
T_3	12/16 (75)	6/15 (40)	18/31 (58)
Node			
N_0	10/16 (63)	11/15 (73)	21/31 (68)
N_1	2/16 (13)	1/15 (7)	3/31 (10)
N_2	2/16 (13)	1/15 (7)	3/31 (10)
N_3	2/16 (13)	2/15 (13)	4/31 (13)
Visceral			
M_0	12/16 (75)	14/15 (93)	26/31 (84)
M_1	4/16 (25)	1/15 (7)	5/31 (16)

Data cut-off for baseline patient characteristics: August 16, 2017.

C-ALCL indicates primary cutaneous anaplastic large-cell lymphoma; CD30, cluster of differentiation 30; ECOG PS, Eastern Cooperative Oncology Group performance status; ITT, intent-to-treat; MF, mycosis fungoides.

*Based on average CD30 expression among all biopsies for each patient's baseline visit.†Excluding radiotherapy. ‡Percentage in each subcategory in the total column is based on the number of patients in each disease subtype. §One patient in each group had incomplete staging data and are not included in the table.

Supplemental Table 2. Subsequent antineoplastic treatment (ITT population)

	Brentuximab vedotin (n = 64)	Physician's choice (n = 64)
Patients with ≥1 subsequent antineoplastic treatment, n (%)	50 (78)	48 (75)
Type of treatment, n (%)*		
Skin-directed therapy	26 (52)	30 (63)
Radiotherapy	15 (30)	20 (42)
Phototherapy	13 (26)	13 (27)
Topical steroids	3 (6)	6 (13)
Other	0	0
Topical chemotherapy	0	0
Topical retinoids	0	0
Systemic therapy	44 (88)	45 (94)
Chemotherapy	34 (68)	27 (56)
Other	28 (56)	23 (48)
Methotrexate	14 (28)	10 (21)
Brentuximab vedotin	12 (24)	33 (69)
Immunotherapy	12 (24)	9 (19)
Other	9 (18)	5 (10)
Bexarotene	6 (12)	6 (13)
Histone deacetylase inhibitor	6 (12)	4 (8)
Non-topical retinoids	3 (6)	0
Photopheresis	1 (2)	1 (2)
Denileukin diftitox	0	0
Other/unknown	1 (2)	4 (8)

Abbreviations are explained in supplemental Table 1.

*Percentages are based on the number of patients with ≥1 subsequent antineoplastic treatment in the ITT population in each arm.

Supplemental Table 3. Patient response per IRF in MF patients by baseline TNMB stage per investigator (ITT population)

	Patients, n (%)							
	Brentuximab vedotin (n = 64)				Physician's choice (n = 64)			
	Total	ORR4	ORR	CR	Total	ORR4	ORR	CR
MF	48 (75)	24 (50)	31 (65)	5 (10)	49 (77)	5 (10)	8 (16)	0
Skin								
T1	5 (10)	1 (20)	1 (20)	0	1 (2)	0	1 (100)	0
T2	13 (27)	7 (54)	10 (77)	1 (8)	20 (41)	4 (20)	4 (20)	0
T3	25 (52)	13 (52)	16 (64)	4 (16)	24 (49)	1 (4)	3 (13)	0
T4	5 (10)	3 (60)	4 (80)	0	4 (8)	0	0	0
Node								
N0	25 (52)	14 (56)	18 (72)	4 (16)	23 (47)	2 (9)	5 (22)	0
N1	6 (13)	2 (33)	2 (33)	0	4 (8)	0	0	0
N2	0	NA	NA	NA	3 (6)	0	0	0
N3	5 (10)	4 (80)	4 (80)	1 (20)	9 (18)	0	0	0
NX	12 (25)	4 (33)	7 (58)	0	10 (20)	3 (30)	3 (30)	0
Visceral								
M0	41 (85)	22 (54)	27 (66)	5 (12)	48 (98)	5 (10)	8 (17)	0
M1	7 (15)	2 (29)	4 (57)	0	0	NA	NA	NA
MX*	0	NA	NA	NA	1 (2)	0	0	0
Blood								

B0	43 (90)	23 (53)	28 (65)	4 (9)	41 (84)	4 (10)	6 (15)	0
B1	4 (8)	1 (25)	2 (50)	1 (25)	7 (14)	1 (14)	2 (29)	0
B2[†]	0	NA	NA	NA	1 (2)	0	0	0
BX[‡]	1 (2)	0	1 (100)	0	0	NA	NA	NA

CR indicates complete response; IRF, independent review facility; NA, not available; ORR, overall response rate; ORR4, objective response rate lasting ≥4 months; TNMB, tumor-node-metastasis-blood. All other abbreviations are explained in supplemental Table 1.

*One patient in the physician's choice arm had no biopsy performed to confirm visceral staging, and had no response.

[†]One patient in the physician's choice arm had confirmed blood stage B1 at screening, and B2 at baseline.

[‡]One patient in the brentuximab vedotin arm had incomplete blood staging data, and had a partial response.

Supplemental Table 4. Patient response per IRF in C-ALCL patients by baseline TNMB stage per investigator (ITT population)

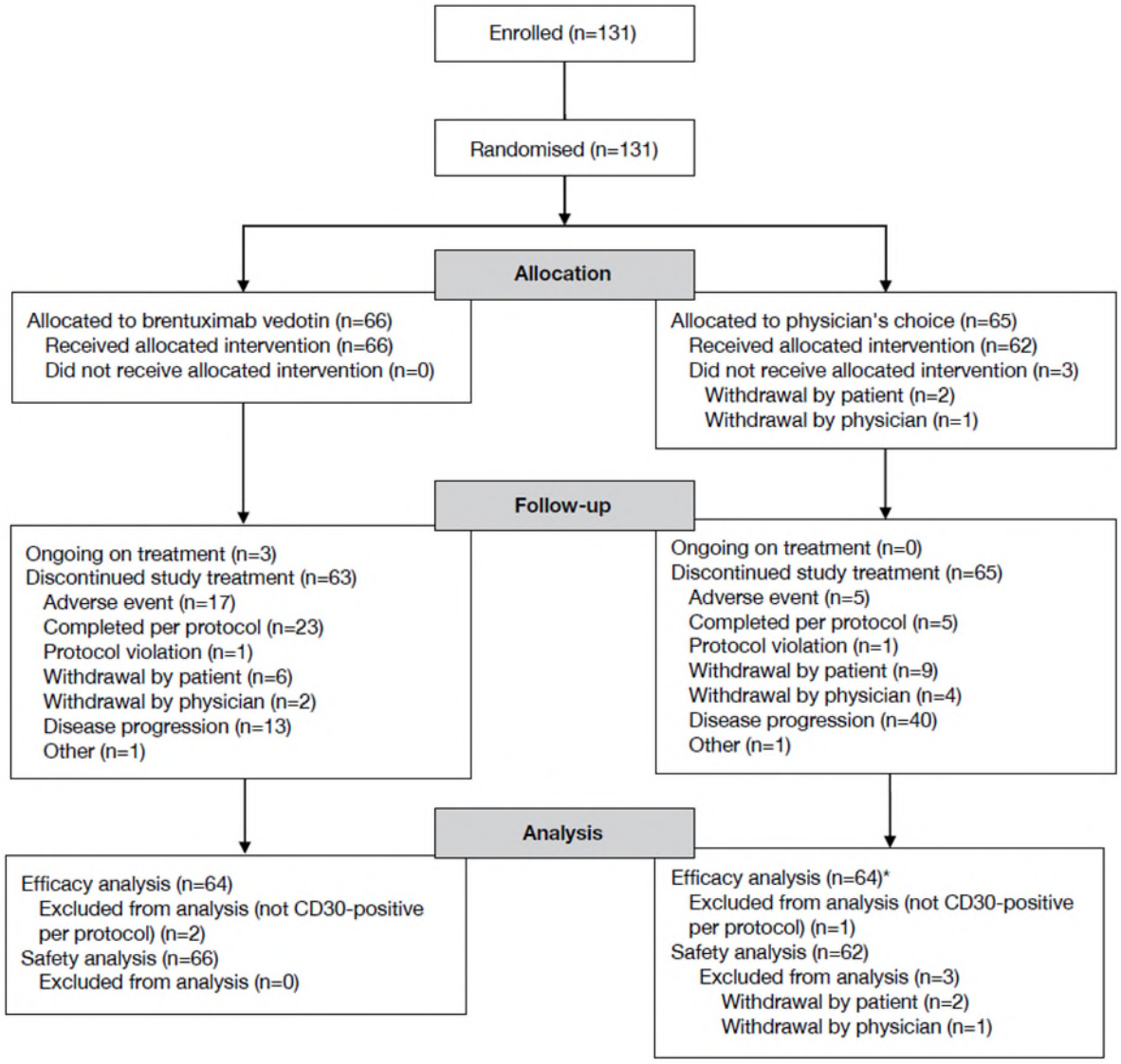
	Patients, n (%)						
	Brentuximab vedotin (n = 64)			Physician's choice (n = 64)			
	Total	ORR4/ ORR*	CR	Total	ORR4	ORR	CR
C-ALCL	16 (25)	11 (69)	6 (38)	15 (23)	3 (20)	5 (33)	1 (7)
Skin							
T1	1 (6)	1 (100)	1 (100)	4 (27)	1 (25)	2 (50)	0
T2	3 (19)	3 (100)	1 (33)	5 (33)	0	1 (20)	0
T3	12 (75)	7 (58)	4 (33)	6 (40)	2 (33)	2 (33)	1 (7)
Node							
N0	10 (63)	8 (80)	4 (40)	11 (73)	3 (27)	5 (45)	1 (9)
N1/ N2[†]	2 (13)	1 (50)	1 (50)	1 (7)	0	0	0
N3	2 (13)	1 (50)	0	2 (13)	0	0	0
Visceral							
M0	12 (75)	9 (75)	5 (42)	14 (93)	3 (21)	5 (36)	1 (7)
M1	4 (25)	2 (50)	1 (25)	1 (7)	0	0	0
M2	0	0	0	0	NA	NA	NA

Abbreviations are explained in supplemental Tables 1 and 3.

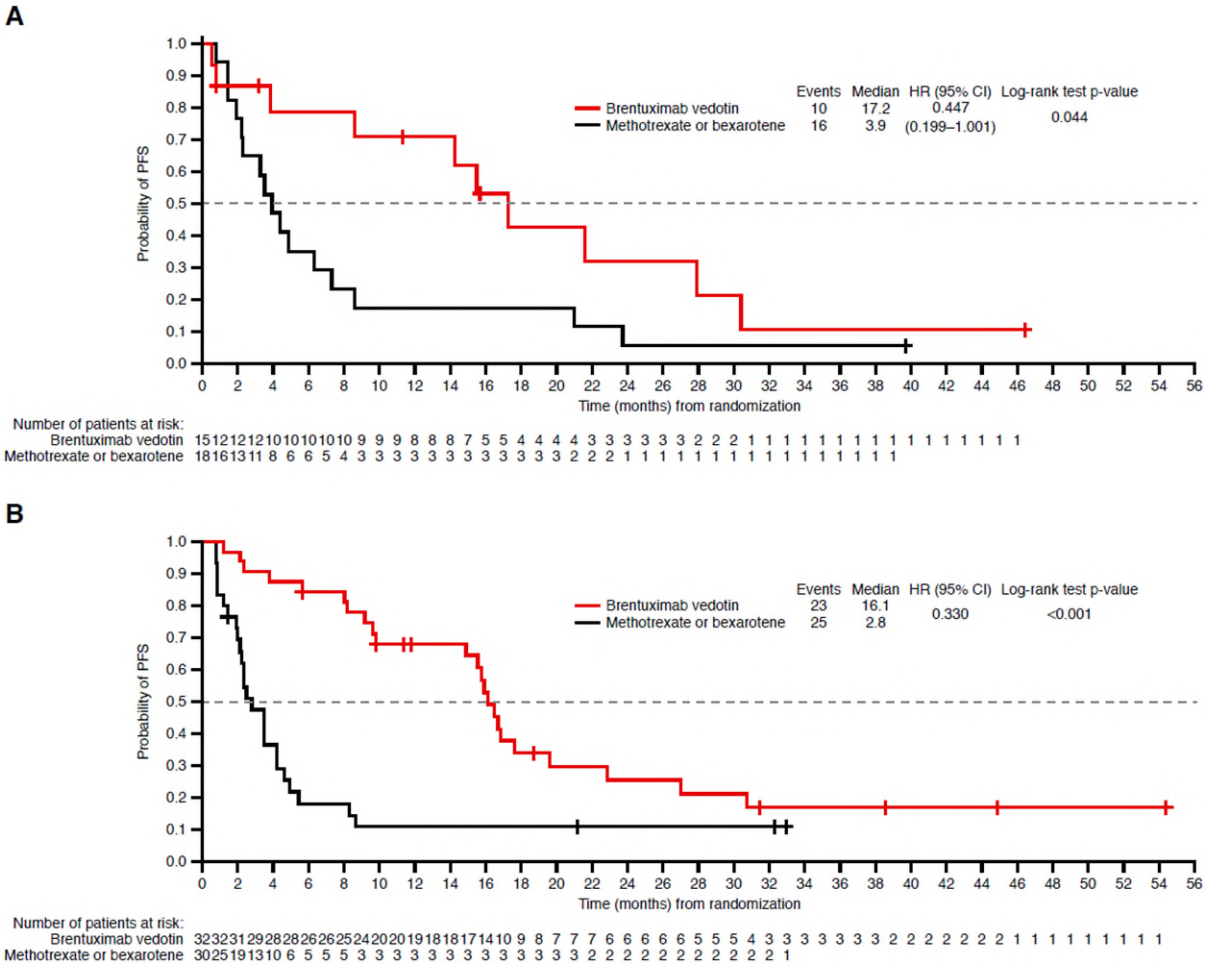
*ORR4 and ORR were the same for the brentuximab vedotin arm.

[†]N1 and N2 had identical results across both the brentuximab vedotin and physician choice arms.

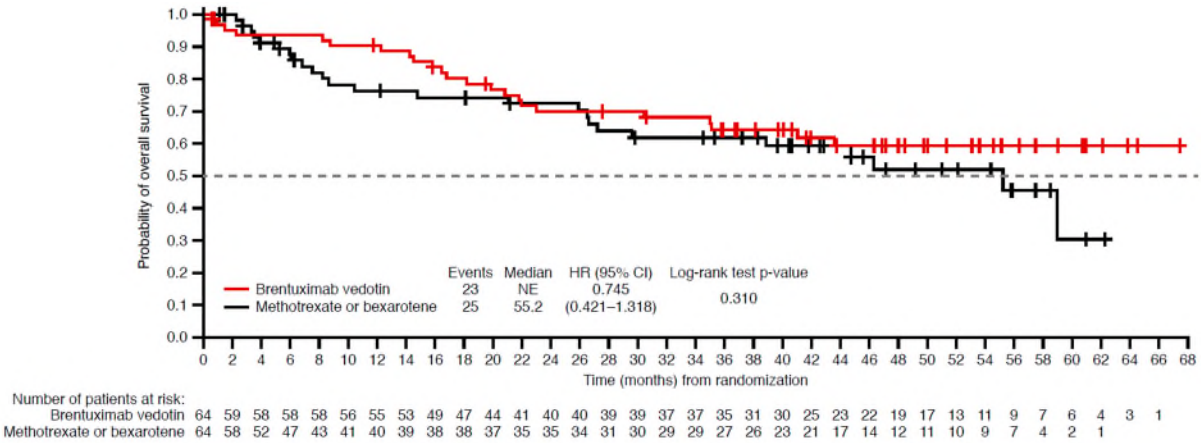
Supplemental figures



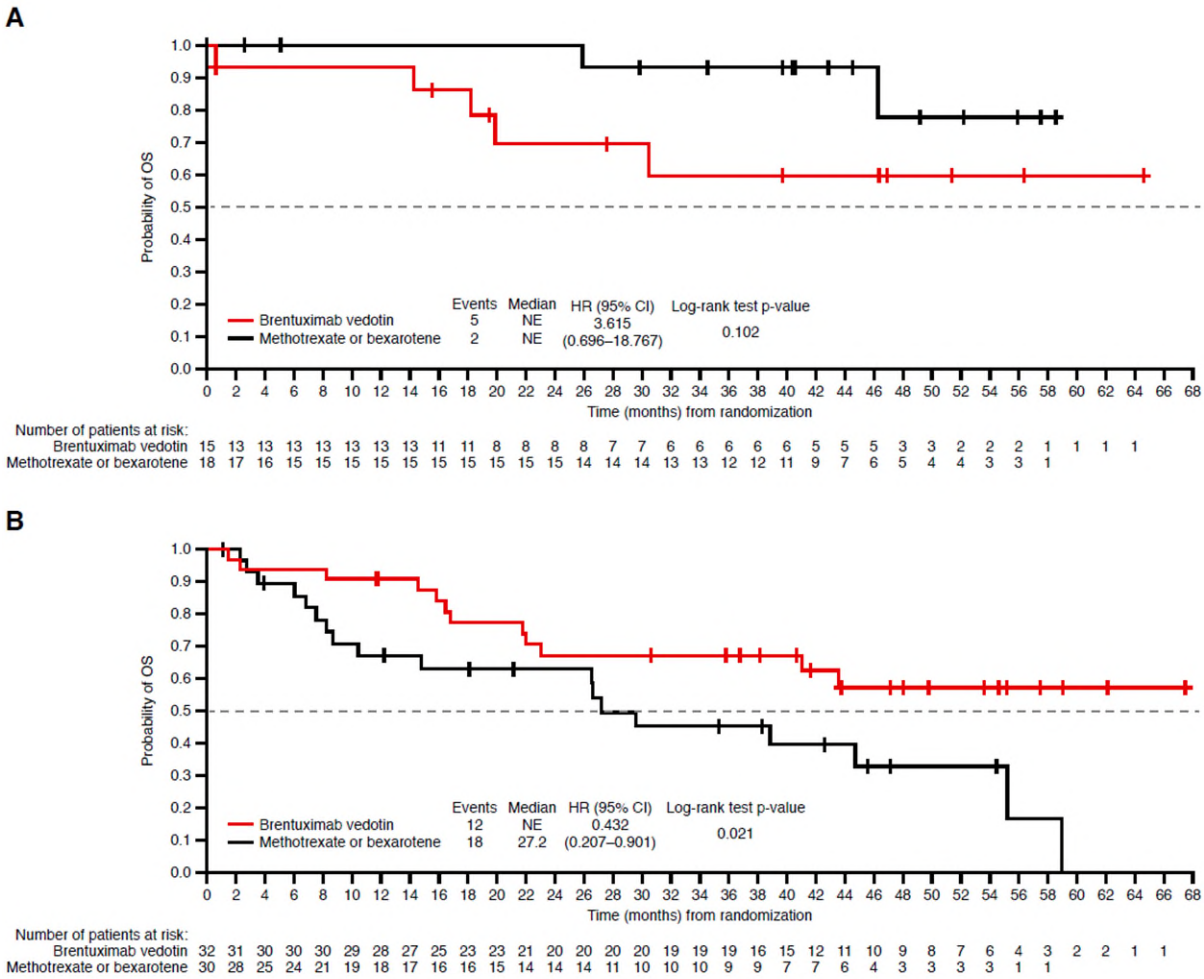
Supplemental Figure 1. CONSORT flow diagram.[15] Flow diagram of patients through enrollment, intervention allocation, follow-up, and data analysis in the brentuximab vedotin and physician's choice arms. Reprinted from The Lancet, Vol 390, Prince HM, et al. Brentuximab vedotin or physician's choice in CD30-positive cutaneous T-cell lymphoma (ALCANZA): an international, open-label, randomised, phase 3, multicentre trial, pp555–566, Copyright 2017, with permission from Elsevier. https://www.thelancet.com/.



Supplemental Figure 2. PFS per IRF by MF stage in the ITT population. (A) Patients with early stage MF. (B) Patients with advanced stage MF. PFS was defined as the time from randomization until disease progression per IRF or death due to any cause, whichever occurs first. Patients who were lost to follow-up, withdrew consent, or discontinued treatment due to undocumented disease progression after the last adequate disease assessment were censored at last disease assessment. CI indicates confidence interval; HR, hazard ratio; PFS, progression-free survival.



Supplemental Figure 3. OS (ITT population). OS was defined as the time from randomization to the date of subject death due to any cause. NE indicates not evaluable; and OS, overall survival. All other abbreviations are explained in supplemental Figure 1.



Supplemental Figure 4. OS by MF stage in the ITT population. (A) Patients with early stage MF. (B) Patients with advanced stage MF. OS was defined as the time from randomization to the date of subject death due to any cause. Abbreviations are explained in supplemental Figures 1 and 2.