SUPPLEMENTARY APPENDIX

Brentuximab Vedotin with Chemotherapy for CD30-Positive Peripheral T-cell Lymphoma (ECHELON-2): a global, double-blind, randomised, phase 3 trial.

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*Authors on the Steering Committee contributed equally to the oversight of the study, including study design and maintaining the quality of study conduct.

†Listed in Part I

This appendix has been provided by the authors to give readers additional information about their work.

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Part I - ECHELON-2 investigators

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Part II - Methods text not included in full paper

Text S1. Study design

Biomarker Measurements

Histologically confirmed CD30-positive disease and histologic subtype were determined by local pathology assessment in a CD30-qualified laboratory to enable enrolment.

By local assessment, tissue from the diagnostic biopsy was confirmed for CD30 positivity by immunohistochemistry (anti-CD30 BerH2 antibody). The 3 following criteria must have been met to declare CD30 positivity:

1. CD30 detected in 10% or greater of neoplastic cells (in cases where enumeration of neoplastic cells was not possible, total lymphocytes may have been used).
2. CD30 staining at any intensity above background.
3. Membranous, cytoplasmic, and/or golgi pattern of expression of the CD30 antigen.

ALK status was also assessed by local pathology for subjects with a diagnosis of sALCL.

Submission of the tumour block or unstained slides from a diagnostic biopsy was also required prior to randomisation for subsequent central confirmation of CD30 expression, disease histologic subtype, and ALK status for subjects with a diagnosis of sALCL. The diagnostic specimen was to be from a malignant lymph node or extranodal tissue obtained by core or excisional/incisional biopsy.

Full Eligibility Criteria

Inclusion Criteria

1. Subjects with newly diagnosed, CD30-positive peripheral T-cell lymphoma per the Revised European-American Lymphoma World Health Organization 2008 classification by local assessment. Eligible histologies were limited to the following:

    - ALK-positive sALCL with an IPI score greater than or equal to 2

- ALK-negative sALCL
- PTCL-NOS
- AITL
- Adult T-cell leukaemia/lymphoma (ATLL; acute and lymphoma types only, must have been positive for human T-cell leukaemia virus 1)
- Enteropathy-associated T-cell lymphoma (EATL)
- Hepatosplenic T-cell lymphoma

2. Fluorodeoxyglucose (FDG)-avid disease by PET and measurable disease of at least 1·5 cm by CT, as assessed by the site radiologist.
3. Age greater than or equal to 18 years.
4. An Eastern Cooperative Oncology Group (ECOG) performance status less than or equal to 2.
5. The following required baseline laboratory data:

- bilirubin ≤1·5X upper limit of normal (ULN) or ≤3X ULN for subjects with Gilbert's disease or documented hepatic involvement with lymphoma
- alanine aminotransferase (ALT) and aspartate aminotransferase (AST) ≤3X ULN or ≤5X ULN for subjects with document hepatic involvement with lymphoma
- serum creatinine ≤2X ULN
- absolute neutrophil count (ANC) ≥1000/μL (unless documented bone marrow involvement with lymphoma)
- platelet count ≥50,000/μL (unless documented bone marrow involvement with lymphoma)

6. Females of childbearing potential must have had a negative serum or urine beta human chorionic gonadotrophin (β-hCG) pregnancy test result within 7 days prior to the first dose of study treatment and must have agreed to use an effective contraception method during the study and for at least 6six months following the last dose of study drug. Females of non-childbearing potential were those who are postmenopausal greater than one year or who have had a bilateral tubal ligation or hysterectomy.
7. Males who had partners of childbearing potential must have agreed to use an effective contraceptive method during the study and for six months following the last dose of study drug.
8. Subjects or their legally authorized representative must have provided written informed consent.

Exclusion Criteria

1. History of another primary invasive cancer, hematologic malignancy, or myelodysplastic syndrome that has not been in remission for at least three years.
2. Current diagnosis of any of the following:

- Primary cutaneous CD30-positive T-cell lymphoproliferative disorders and lymphomas. Cutaneous ALCL with extracutaneous tumour spread beyond locoregional lymph nodes were eligible (previous single-agent treatment to address cutaneous and locoregional disease was permissible)
- Mycosis fungoides (MF), including transformed MF

3. History of progressive multifocal leukoencephalopathy (PML).
4. Cerebral/meningeal disease related to the underlying malignancy.
5. Prior treatment with brentuximab vedotin.
6. Baseline peripheral neuropathy ≥ Grade 2 (per the National Cancer Institute-Common Terminology Criteria for Adverse Events, Version 4·03) or subjects with the demyelinating form of Charcot-Marie-Tooth syndrome.
7. Left ventricular ejection fraction less than 45% or symptomatic cardiac disease (including symptomatic ventricular dysfunction, symptomatic coronary artery disease, and symptomatic arrhythmias), or myocardial infarction within the past six months, or previous treatment with complete cumulative doses of doxorubicin or other anthracyclines.
8. Any active Grade 3 (per the NCI CTCAE, Version 4·03) or higher viral, bacterial, or fungal infection within two weeks prior to the first dose of study treatment; any known human immunodeficiency virus

(HIV) infection, hepatitis B surface antigen-positive status, or known or suspected active hepatitis C infection.

9. Current therapy with other systemic anti-neoplastic or investigational agents.
10. Females who were pregnant or breastfeeding.
11. Subjects with a known hypersensitivity to any excipient contained in any of the drug formulations of study treatments.
12. Subjects with known urinary outflow obstruction.

Concomitant Therapy and Dose Modifications

The use of G-CSF was permitted at the discretion of the treating physician based upon institutional standards. In May 2015, the Independent Data Monitoring Committee recommended that Seattle Genetics remind investigators to administer G-CSF in accordance with American Society of Clinical Oncology or European Society of Medical Oncology guidelines. Dose modifications of blinded study treatment (brentuximab vedotin or vincristine), cyclophosphamide, doxorubicin, or prednisone due to hematologic and non-hematologic toxicity were allowed per institutional standards at the discretion of the investigator and included discontinuation of a treatment component. Recommended dose modifications for study treatment-associated neuropathy are described in appendix Table S1.

Text S2. Statistical Analysis

Missing data was not imputed, with the exception of adverse event dates, subsequent anti-cancer therapy start date, and death date. Subjects with missing values of a variable other than the time-to-event endpoints (PFS and OS) were excluded from the analysis of that endpoint. Censoring rules were applied to the estimation of the distribution of the time-to-event endpoints.

Randomisation of approximately 450 subjects (225 subjects per treatment arm) over 42 months was planned to achieve (with 95% probability) 238 events in approximately 60 months assuming 42 months of subject accrual, given an anticipated dropout rate of 5%, and 18 months of PFS follow-up after randomisation of the last subject. The study was powered on the assumption that 238 PFS events would provide approximately 80% power to detect a hazard ratio of 0.6895 using the log-rank test and an overall one-sided alpha level of 0.025 (i.e., two-sided alpha level of 0.05).The study was initially designed to randomise 300 subjects, but in March 2015, the sample size was recalculated to increase the likelihood of observing the specified number of PFS events for appropriate power of the final analysis. The protocol was amended again in May 2018 to allow for earlier analysis of the primary endpoint in August 2018 if the protocol-specified 238 events had not been reached. This amendment was based on the sponsor's analysis of blinded pooled data from the study, the final PFS data from the preceding phase 1 study to ECHELON-2,[1] and was conducted in collaboration with regulatory authorities.

The scheduled Independent Data Monitoring Committee data reviews included a futility analysis, safety reviews, and a review for serious adverse events and overall survival. For the futility analysis, an Independent Data Monitoring Committee was to determine whether the CR rate per IRF was lower in the A+CHP arm compared to the CHOP arm with non-overlapping exact 95% CIs, and whether the observed hazard ratio for PFS was in the direction of superior efficacy in the CHOP arm. A pre-specified formal interim analysis for futility focused on CR rate per BICR was performed after 50% of subjects had completed end-of-treatment assessments; treatment assignment remained blinded to the sponsor. Following the analysis, an independent data monitoring committee Independent Data Monitoring Committee recommended that the trial continue per protocol. Seven safety review meetings were planned to occur approximately every six months after the initiation of enrolment through the date the last subject completed treatment. Approximately one year after the last subject completed treatment, the Independent Data Monitoring Committee was to conduct a serious adverse events and overall survival review. The Independent Data Monitoring Committee was to review a report of the available SAE and OS data and notify the Independent Data Monitoring Committee chair if they felt an Independent Data Monitoring Committee meeting was warranted.

The estimated duration of the study through final analysis of the primary objective was approximately four to seven years from randomisation of the first subject. The estimated duration to a final descriptive analysis of OS is approximately two years from the completion of primary analysis.

Text S3. Data Sharing Statement

Seattle Genetics policy on data sharing can be found here: http://www.seattlegenetics.com/patients-healthcare-professionals/clinical-data-requests

Part III - Supplementary Tables S1-S10

Table S1: Recommended dose modifications for study treatment-associated neuropathy

Grade of Treatment-Associated Neuropathy	Recommended Dose Modification	
	Sensory Neuropathy	**Motor Neuropathy**
1	Continue study treatment at same dose level.	Continue study treatment at same dose level.
2	Continue study treatment at the same dose level.	Reduce dose levels of brentuximab vedotin/vincristine*.
3	Reduce dose levels of brentuximab vedotin/vincristine*.	Discontinue treatment with brentuximab vedotin/vincristine.
4	Discontinue treatment with brentuximab vedotin/vincristine.	Discontinue treatment with brentuximab vedotin/vincristine.

*To maintain the study blind, dose levels of both blinded study treatments must have been reduced as follows: 1·2 mg/kg brentuximab vedotin and 1 mg vincristine. No further dose reductions were permitted.

Table S2: Baseline characteristics (not shown in body)

Characteristic	A+CHP (N=226)	CHOP (N=226)
Time from diagnosis to first dose of study treatment (months)		
n	222	224
Mean (standard deviation)	1·1 (1·5)	1·1 (0·9)
Median	0·8	0·9
Min, Max	0, 19	0, 10
Initial diagnosis of cutaneous ALCL (for subjects with sALCL)	13 (6%)	4 (2%)
Time from cutaneous ALCL diagnosis to sALCL diagnosis (months)		
n	11	4
Mean (standard deviation)	16·0 (20·6)	9·8 (12·8)
Median	4·8	4·7
Min, Max	1, 69	1, 29
Serum LDH per local laboratory,		
≤1 × upper limit of normal	113 (50%)	97 (43%)
>1 × upper limit of normal	113 (50%)	129 (57%)
Extranodal disease involvement		
≤1 site	142 (63%)	146 (65%)
>1 site	84 (37%)	80 (35%)
HTLV-1 status		
Positive	5 (2%)	4 (2%)
Negative	216 (96%)	219 (97%)
Intended number of cycles		
6	185 (82%)	182 (81%)
8	41 (18%)	44 (19%)
Intention of stem cell transplant following completion of study regimen		
Yes	89 (39%)	81 (36%)
No	136 (60%)	144 (64%)
Baseline bone marrow biopsy-lymphoma involvement		
Yes	30 (13%)	34 (15%)
No	196 (87%)	192 (85%)
Percent CD30 positive cells, per local assessment		
n	224	226
Mean (standard deviation)	76·5 (32·7)	77·0 (30·7)
Median	90·5	90·0
Min, Max	10, 100	10, 100
Percent CD30 positive cells, per central review		
n	222	220
Mean (standard deviation)	81·1 (28·4)	77·6 (30·6)
Median	95·0	90·0
Min, Max	0, 100	0, 100

Data are n (%), unless stated otherwise. Data shown are for the intention-to-treat population. Percentages may not total 100 because of rounding. A+CHP=brentuximab vedotin, cyclophosphamide, doxorubicin, and prednisone; ALCL=anaplastic large cell lymphoma; CHOP=cyclophosphamide, doxorubicin, vincristine, and prednisone; sALCL=systemic anaplastic large cell lymphoma.

Table S3: Consolidative therapies

	A+CHP (N=226)	CHOP (N=226)
Subjects who received consolidative treatment*	61 (27%)	44 (19%)
Consolidative radiotherapy	14 (6%)	6 (3%)
Consolidative stem cell transplant	50 (22%)	39 (17%)
Autologous	49 (22%)	39 (17%)
Allogeneic	1 (0%)	0

Data are n (%). Data shown are for the intention-to-treat population.*Subjects may have received more than one type of therapy. A+CHP=brentuximab vedotin, cyclophosphamide, doxorubicin, and prednisone; CHOP=cyclophosphamide, doxorubicin, vincristine, and prednisone.

Table S4: Summary of progression-free survival per Blinded Independent Central Review

	A+CHP (N=226)		CHOP (N=226)
Number of subjects with a PFS event, n (%)	95 (42%)		124 (55%)
Disease progression per Cheson	71 (31%)		86 (38%)
Death	13 (6%)		17 (8%)
New therapy*	11 (5%)		21 (9%)
Stratified hazard ratio (95% CI) (A+CHP to CHOP)		0·71 (0·54, 0·93)	
Stratified log-rank p-value†		0·0110	
Median PFS (months) (95% CI) ‡	48·2 (35·2, -)		20·8 (12·7, 47·6)
75th, 25th percentile	8·87, -		4·70, -
Estimated progression-free rate (95% CI) ‡ at:			
6 months	82·1% (76·4%, 86·6%)		70·8% (64·3%, 76·3%)
12 months	71·7% (65·1%, 77·2%)		58·2% (51·4%, 64·3%)
24 months	61·4% (54·4%, 67·6%)		47·4% (40·6%, 53·8%)
36 months	57·1% (49·9%, 63·7%)		44·4% (37·6%, 50·9%)

Data shown are for the intention-to-treat population. A+CHP=brentuximab vedotin, cyclophosphamide, doxorubicin, and prednisone; ALK=anaplastic lymphoma kinase; CHOP=cyclophosphamide, doxorubicin, vincristine, and prednisone; CI=confidence interval; PFS=progression-free survival; sALCL=systemic anaplastic large cell lymphoma. *New systemic chemotherapy to treat residual or progressive disease initiated prior to Blinded Independent Central Review-documented progression per Cheson,[2] including palliative radiotherapy. †From stratified log-rank test with stratification factors (ALK-positive sALCL: Yes/No and International Prognostic Index score: 0-1/2-3/4-5) at randomisation. ‡PFS rate is estimated using Kaplan-Meier methods and 95% CI is calculated using the complementary log-log transformation method.[3]

Table S5: Summary of overall survival

	A+CHP (N=226)		CHOP (N=226)
Number of deaths, n (%)	51 (23%)		73 (32%)
Stratified hazard ratio (95% CI) (A+CHP to CHOP)		0·66 (0·46, 0·95)	
Stratified log-rank P value*		0·0244	
Median overall survival (months) (95% CI) †	- (-, -)		- (54·2, -)
75th, 25th percentile	-, -		17.5, -
Estimated survival rate (95% CI)† at:			
6 months	93·7% (89·6%, 96·2%)		89·2% (84·4%, 92·7%)
12 months	87·8% (82·8%, 91·5%)		82·4% (76·7%, 86·8%)
24 months	80·8% (75·0%, 85·5%)		72·6% (66·2%, 78·0%)
36 months	76·8% (70·4%, 82·0%)		69·1% (62·3%, 74·9%)

Data shown are for the intention-to-treat population. A+CHP=brentuximab vedotin, cyclophosphamide, doxorubicin, and prednisone; ALK=anaplastic lymphoma kinase; CHOP=cyclophosphamide, doxorubicin, vincristine, and prednisone; CI=confidence interval; PFS=progression-free survival; sALCL=systemic anaplastic large cell lymphoma. *From stratified log-rank test with stratification factors (ALK-positive sALCL: Yes/No and IPI score: 0-1/2-3/4-5) at randomisation. †Overall survival rate is estimated using Kaplan-Meier methods and 95% CI is calculated using the complementary log-log transformation method.

Table S6: Subsequent anti-cancer therapies

	A+CHP (N=226)	CHOP (N=226)
Subjects who received subsequent anti-cancer therapy*	65 (29%)	96 (42%)
Systemic therapy for residual or progressive disease	59 (25%)	94 (40%)
Brentuximab vedotin-containing	23 (10%)	49 (22%)
Palliative radiation	10 (4%)	8 (3%)
Systemic therapy for other malignancies	7 (3%)	3 (1%)

Data are n (%). Data shown are for the intention-to-treat population. A+CHP=brentuximab vedotin, cyclophosphamide, doxorubicin, and prednisone; CHOP=cyclophosphamide, doxorubicin, vincristine, and prednisone. *Subjects may have received more than one type of therapy.

Table S7: Summary of exposure: duration of treatment

	A+CHP (N=223)	CHOP (N=226)
Duration of treatment (weeks)		
n	223	226
Median	18·1	18·0
Min, Max	3, 34	3, 31
Number of treatment cycles intended per subject at baseline		
6 cycles	182 (82%)	182 (81%)
8 cycles	41 (18%)	44 (19%)
Number of treatment cycles received per subject		
n	223	226
Median	6·0	6·0
Min, Max	1, 8	1, 8
Number of subjects treated by cycle		
1	6 (3%)	6 (3%)
2	6 (3%)	10 (4%)
3	5 (2%)	8 (4%)
4	7 (3%)	13 (6%)
5	1 (0%)	5 (2%)
6	156 (70%)	140 (62%)
7	2 (1%)	0
8	40 (18%)	44 (19%)

Data are n (%), unless stated otherwise. Data shown are for the safety population. A+CHP=brentuximab vedotin, cyclophosphamide, doxorubicin, and prednisone; CHOP=cyclophosphamide, doxorubicin, vincristine, and prednisone; Max=maximum; Min=minimum.

Table S8: Summary of cause of death due to adverse events

Subjects	A+CHP (N=223)	CHOP (N=226)
Overall Grade 5 adverse events	7 (3%)	9 (4%)
Acute kidney injury	1 (0%)	0
Arrhythmia	0	1 (0%)
Cardiac arrest	1 (0%)	1 (0%)
Death†	0	1 (0%)
Febrile neutropenia	0	1 (0%)
Hydrocephalus	0	1 (0%)
Multiple organ dysfunction syndrome*	0	2 (1%)
Pneumonia	1 (0%)	0
Pneumonia aspiration	1 (0%)	0
Pulmonary cavitation	1 (0%)	0
Sepsis*	1 (0%)	2 (1%)
Septic shock	0	1 (0%)
Ventricular fibrillation	1 (0%)	0

Data are n (%). Data shown are for the safety population. A+CHP=brentuximab vedotin, cyclophosphamide, doxorubicin, and prednisone; CHOP=cyclophosphamide, doxorubicin, vincristine, and prednisone. *Two fatal adverse events were reported for one subject on the CHOP arm. †The cause of death was unknown.

Table S9: Summary of neutropenia by primary prophylaxis with G-CSF

	A+CHP (N=223)		CHOP (N=226)	
Subjects	**No G-CSF Primary Prophylaxis (N=148) n (%)**	**G-CSF Primary Prophylaxis* (N=75) n (%)**	**No G-CSF Primary Prophylaxis (N=165) n (%)**	**G-CSF Primary Prophylaxis* (N=61) n (%)**
Febrile neutropenia in Cycle 1	17 (11%)	9 (12%)	16 (10%)	4 (7%)
Febrile neutropenia on study	29 (20%)	12 (16%)	26 (16%)	7 (11%)
Incidence of Grade 3 or higher neutropenia†	67 (45%)	10 (13%)	69 (42%)	8 (13%)
Incidence of Grade 4 or higher neutropenia†,	39 (26%)	7 (9%)	43 (26%)	6 (10%)
Incidence of Grade 3 or higher infections and infestations	30 (20%)	12 (16%)	23 (14%)	8 (13%)
Incidence of serious adverse events of febrile neutropenia, neutropenia, sepsis, neutropenic sepsis, pyrexia, or infections and infestations	41 (28%)	23 (31%)	37 (22%)	15 (25%)

Data are n (%). Data shown are for the safety population. Treatment-emergent adverse events are presented and defined as newly occurring (not present at baseline) or worsening after first dose of brentuximab vedotin or any component of multiagent chemotherapy. A+CHP=brentuximab vedotin, cyclophosphamide, doxorubicin, and prednisone; CHOP=cyclophosphamide, doxorubicin, vincristine, and prednisone; G-CSF=granulocyte-colony stimulating factor. *Receipt of primary prophylaxis with G-CSF is defined as use by Day 8 of Cycle 1 of treatment. †Neutropenia includes preferred terms of 'Neutropenia' and 'Neutrophil count decreased'.

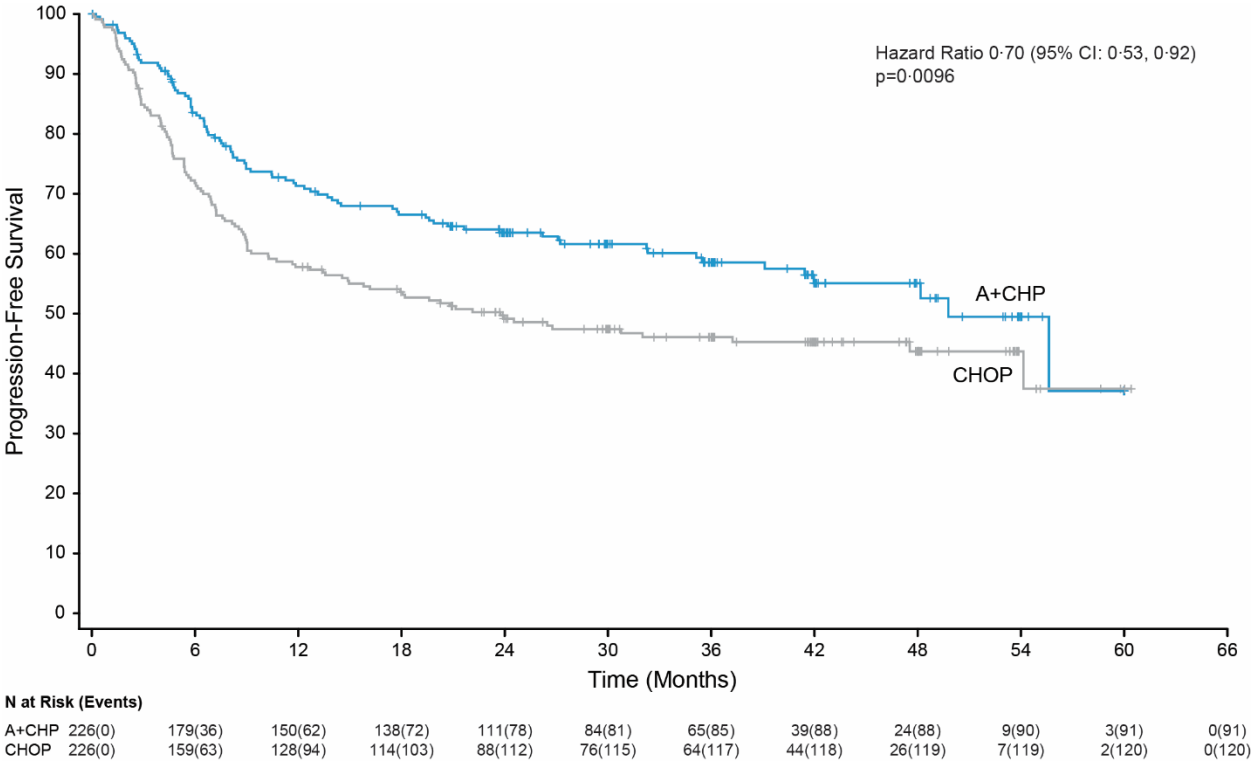
Table S10: Summary of peripheral neuropathy

Subjects	A+CHP (N=223)	CHOP (N=226)
Peripheral neuropathy (SMQ*)		
Pre-existing peripheral neuropathy	24 (11%)	25 (11%)
Any treatment-emergent peripheral neuropathy (SMQ*) event	117 (52%)	124 (55%)
Worst severity Grade 2	33 (15%)	26 (12%)
Worst severity Grade 3	8 (4%)	10 (4%)
Worst severity Grade 4	1 (0%)	0
Dose modification due to peripheral neuropathy†	16 (7%)	16 (7%)
Resolution of all treatment-emergent peripheral neuropathy events‡	58 (50%)	79 (64%)
Improvement of treatment-emergent peripheral neuropathy adverse events§	14 (12%)	15 (12%)
No improvement or resolution of treatment-emergent peripheral neuropathy events	45 (38%)	30 (24%)
Peripheral neuropathy (SMQ*) events		
Peripheral sensory neuropathy	100 (45%)	92 (41%)
Paraesthesia	10 (4%)	18 (8%)
Peripheral motor neuropathy	8 (4%)	17 (8%)
Muscular weakness	6 (3%)	8 (4%)
Peripheral sensorimotor neuropathy	6 (3%)	2 (1%)
Hypoaesthesia	3 (1%)	3 (1%)
Dysaesthesia	2 (1%)	1 (0%)
Areflexia	1 (0%)	0
Burning sensation	1 (0%)	1 (0%)
Peroneal nerve palsy	1 (0%)	0
Polyneuropathy	1 (0%)	1 (0%)
Autonomic neuropathy	0	2 (1%)
Gait disturbance	0	1 (0%)
Muscle atrophy	0	1 (0%)
Neuralgia	0	2 (1%)

Data are n (%). Data shown are for the safety population. A+CHP=brentuximab vedotin, cyclophosphamide, doxorubicin, and prednisone; CHOP=cyclophosphamide, doxorubicin, vincristine, and prednisone; SMQ=standardized MedDRA query. *The SMQ includes the preferred terms of peripheral sensory neuropathy, paraesthesia, peripheral motor neuropathy, muscular weakness, peripheral sensorimotor neuropathy, hypoaesthesia, dysaesthesia, areflexia, burning sensation, peroneal nerve palsy, polyneuropathy, autonomic neuropathy, gait disturbance, muscle atrophy, and neuralgia. †Dose reduction or dose delay attributed to an adverse event of peripheral neuropathy. ‡Resolution is defined as event status of resolved/recovered or resolved/recovered with sequelae; or return to baseline or lower severity as of the latest assessment for pre-existing events. §Resolution implies improvement. In addition, for events that are not resolved, improvement is defined as decrease by at least one grade from the worst grade without any subsequent grades(s) equal to the worst grade. Subjects with improvement in any event at last follow up are those with at least one improved event and date of improvement is before last follow up date. Subjects with all events resolved will be excluded.

Part IV - Supplementary Figure S1

Figure S1A: Prespecified analyses of progression-free survival - as assessed by investigators



N at Risk (Events)

A+CHP	226(0)	179(36)	150(62)	138(72)	111(78)	84(81)	65(85)	39(88)	24(88)	9(90)	3(91)	0(91)
CHOP	226(0)	159(63)	128(94)	114(103)	88(112)	76(115)	64(117)	44(118)	26(119)	7(119)	2(120)	0(120)

Figure S1A: Kaplan–Meier estimates of progression-free survival, by treatment arm, according to study investigators. The hazard ratio for treatment with A+CHP versus CHOP and the 95% confidence intervals (CIs) were computed from log-rank test using stratification factors (ALK-positive sALCL: yes/no and IPI score: 0-1/2-3/4-5) at randomisation. Hash marks indicate censored data. A+CHP=brentuximab vedotin, cyclophosphamide, doxorubicin, and prednisone; ALK=anaplastic lymphoma kinase; CHOP=cyclophosphamide, doxorubicin, vincristine, and prednisone; CI=confidence interval; IPI=international prognostic index; sALCL=systemic anaplastic large cell lymphoma.

Figure S1B: Prespecified analyses of progression-free survival - events limited to progression and death as assessed by Blinded Independent Central Review

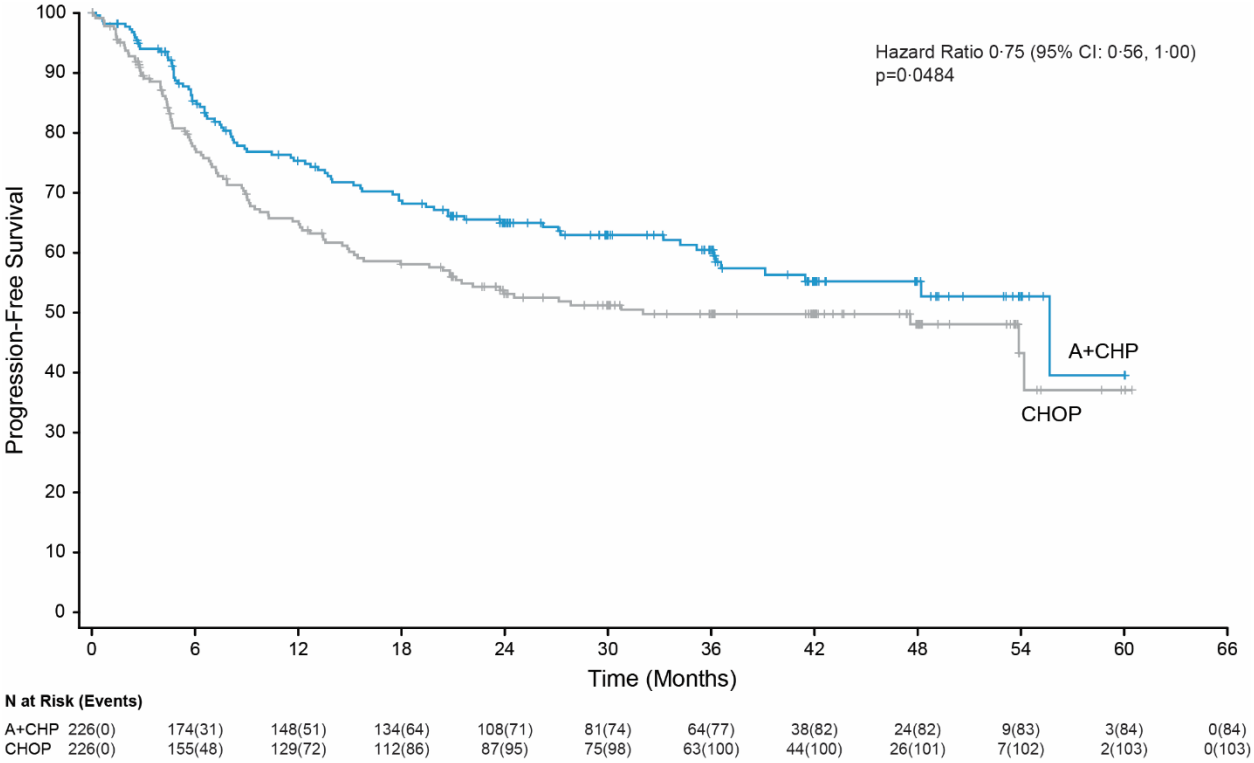


Figure S1B: Kaplan–Meier estimates of progression-free survival with events limited to progression and death, by treatment arm, according to the BICR for the ITT population. Subjects with new anticancer therapy prior to progression or death are censored at their last adequate tumour assessment before the therapy. The hazard ratio for treatment with A+CHP versus CHOP and the 95% confidence intervals (CIs) were computed from log-rank test using stratification factors (ALK-positive sALCL: yes/no and IPI score: 0-1/2-3/4-5) at randomisation. Hash marks indicate censored data. A+CHP=brentuximab vedotin, cyclophosphamide, doxorubicin, and prednisone; ALK=anaplastic lymphoma kinase; CHOP=cyclophosphamide, doxorubicin, vincristine, and prednisone; CI=confidence interval; IPI=international prognostic index; sALCL=systemic anaplastic large cell lymphoma.

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