

## Supplementary Appendix

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

Supplement to: Johnson P, Federico M, Kirkwood A, et al. Adapted treatment guided by interim PET-CT scan in advanced Hodgkin's lymphoma. *N Engl J Med* 2016;374:2419-29. DOI: 10.1056/NEJMoa1510093

## **Supplementary appendix:**

Supplement to Johnson P, Federico M, Kirkwood A. et al., Treatment adaptation guided by interim PET scanning in advanced Hodgkin lymphoma.

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**BEACOPP-14** (repeated every 14 days)

Doxorubicin	25mg/m <sup>2</sup> iv	Day 1
Cyclophosphamide	650mg/m <sup>2</sup> iv	Day 1
Etoposide	100mg/m <sup>2</sup> iv	Days 1-3
Procarbazine (or Natulan)	100mg/m <sup>2</sup> po	Days 1-7
Prednisolone	80mg/m <sup>2</sup> po	Days 1-7
Bleomycin	10,000units/m <sup>2</sup> iv	Day 8
Vincristine*	1.4mg/m <sup>2</sup> iv	Day 8
G-CSF	263/300mcg or equivalent PEG-Filgrastim single dose	Day 9-13

**BEACOPP-escalated** (repeated every 21 days)

Doxorubicin	35mg/m <sup>2</sup> iv	Day 1
Cyclophosphamide	1250mg/m <sup>2</sup> iv	Day 1
Etoposide	200mg/m <sup>2</sup> iv	Days 1-3
Procarbazine (or Natulan)	100mg/m <sup>2</sup> po	Days 1-7
Prednisolone	40mg/m <sup>2</sup> po	Days 1-14
Bleomycin	10,000units/m <sup>2</sup> iv	Day 8
Vincristine*	1.4mg/m <sup>2</sup> iv	Day 8
G-CSF	263/300mcg or equivalent PEG-Filgrastim single dose	Day 9 until count recovered

Addendum to sample size calculation:

The original sample size was calculated using a STATA add-on module called ARTSURV. After RATHL completed recruitment, it was discovered that there was an error in this program which under-estimates sample size for non-inferiority trials.

Original calculation:

101 events required; sample size 950 randomized patients.

Revised calculation (calculated using NQuery):

91 events required; sample size 1238 randomized patients.

Figure S1: Trial schema

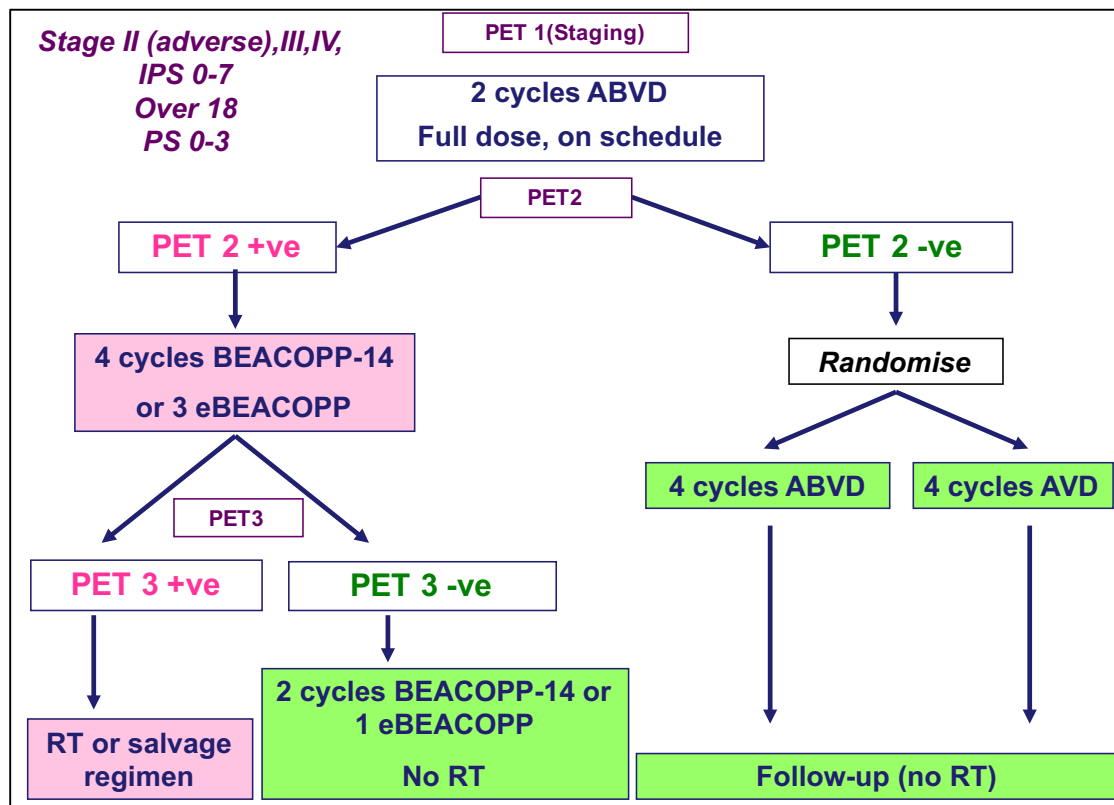


Figure S2: Progression-free and overall survival for all patients

Fig S2a: Progression free survival for all eligible patients.

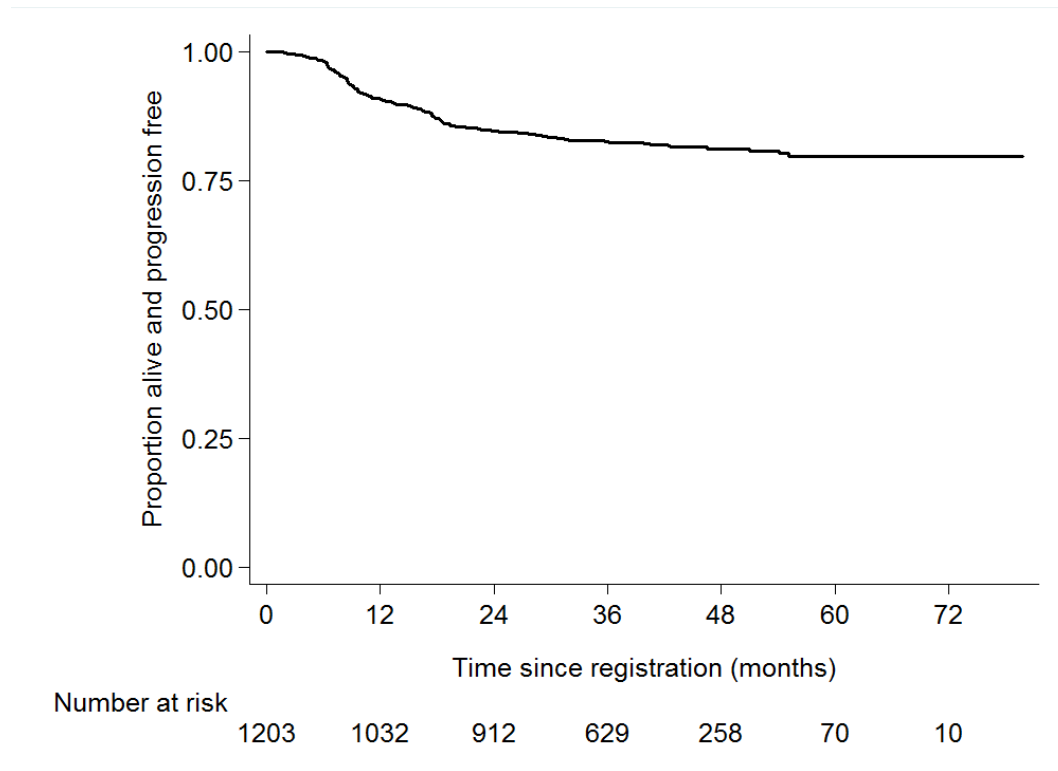


Fig S2b: Overall survival for all eligible patients.

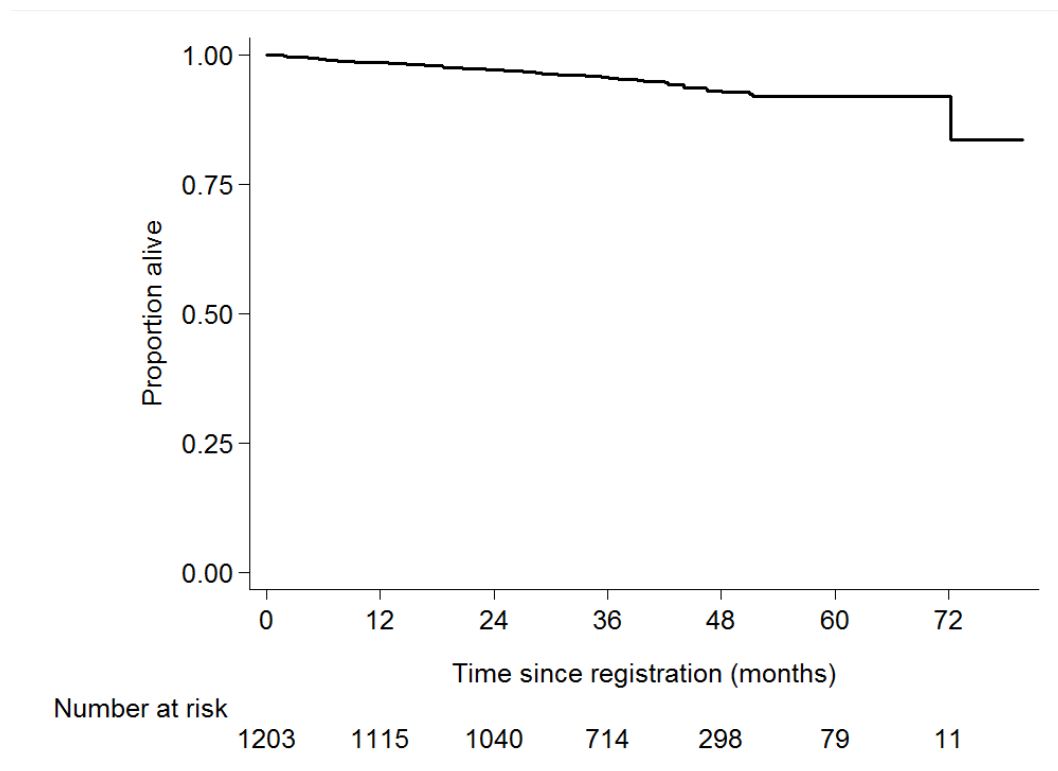


Figure S3: Subgroup analysis of the effects on progression-free survival of the omission of bleomycin following negative interim PET

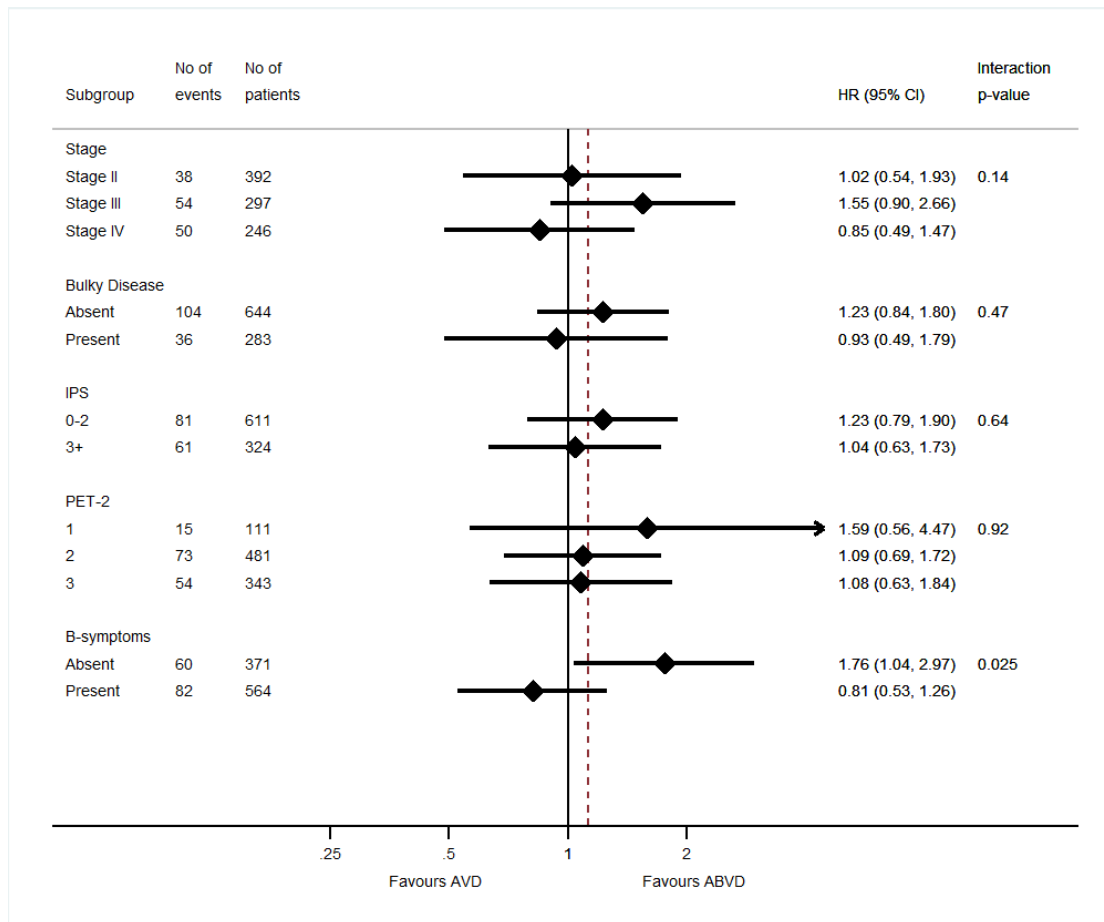


Table S1: Association of prognostic factors and progression-free survival following negative interim PET.

		Events/n	Hazard ratio (95% CI)	p	3 year PFS %
Stage	II	38/392	1.00	<0.001	90.0 (86.4 - 92.6)
	III	54/297	1.98(1.31-2.99)		83.1 (78.2 - 87.0)
	IV	50/246	2.18 (1.43-3.32)		79.6 (73.8 - 84.2)
IPS	0-2	81/611	1.00	0.029	86.9 (83.8 - 89.4)
	≥3	61/324	1.44 (1.04-2.01)		81.7 (76.9 - 85.6)
Bulk	Absent	104/644	1.00	0.20	84.0 (80.9 - 86.7)
	Present	36/283	0.78 (0.54-1.14)		87.6 (83.1 - 91.0)
PET-2 score	1	15/111	1.00	0.77	88.1 (80.3 - 92.9)
	2	73/481	1.11 (0.64-1.94)		84.9 (81.3 - 87.9)
	3	54/343	1.21 (0.68-2.15)		84.4 (80.0 - 87.9)
B Symptoms	Absent	60/372	1.00	0.47	84.2 (80.0 - 87.6)
	Present	82/564	0.89 (0.63 - 1.24)		85.6 (82.3 - 88.3)
Age (for 10 year increase )		142/935	1.15 (1.03 - 1.29)	0.012	-



Table S2: Progression-free survival among 348 patients with stage II disease with a negative interim PET-CT scan and who did not receive consolidation radiotherapy, according to risk categories:

Risk factor		Number	%	Events	3 year PFS
Bulk	Present	119	34.7	10	91.5 (84.8 – 95.3)
	Absent	224	65.3	18	91.7 (87.1 - 94.7)
B symptoms	Present	206	59.4	16	92.0 (87.3 – 95.0)
	Absent	141	40.6	13	90.6 (84.4 – 94.4)
B symptoms or bulk	Present	257	74.5	23	90.9 (86.6 – 93.8)
	Absent	88	25.6	5	94.1 (86.3 – 97.5)
Chemotherapy outcome	CR/CRu	258	74.4	20	92.0 (87.8 – 94.7)
	PR	89	25.7	9	89.8 (81.3 – 94.6)

Table S3: recruitment by country

Country	N (%)
UK	854 (71.0)
Italy	128 (10.6)
Norway	75 (6.2)
Australia/NZ	84 (7.0)
Sweden	51 (4.2)
Denmark	11 (0.9)

Full list of sites and investigators:

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