Clinical trial results:
A randomised phase III trial to assess response adapted therapy using FDG-PET imaging in patients with newly diagnosed, advanced Hodgkin Lymphoma

Summary

EudraCT number	2007-006064-30
Trial protocol	GB IT IE SE DK
Global end of trial date	01 May 2024

Results information

Result version number	v1 (current)
This version publication date	27 May 2026
First version publication date	27 May 2026

Trial information

Trial identification

Sponsor protocol code	UCL/07/146

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00678327
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Cancer Research UK & UCL Cancer Trials Centre
Sponsor organisation address	90 Tottenham Court Road, London, United Kingdom, W1T 4TJ
Public contact	RATHL Trial Manager, Cancer Research UK & UCL Cancer Trials Centre, 0044 020 7670 4696, rathl@ctc.ucl.ac.uk
Scientific contact	RATHL Trial Statistician, Cancer Research UK & UCL Cancer Trials Centre, 0044 0207 679 9231, rathl@ctc.ucl.ac.uk

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	02 November 2015
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	01 May 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The aim of this study is to evaluate prospectively the role of FDG-PET imaging after 2 cycles of ABVD chemotherapy in determining response assessment and subsequent management decisions for patients receiving first-line treatment for advanced Hodgkin lymphoma.

Protection of trial subjects:

At the time of the RATHL study, six cycles of ABVD was considered the standard of care for patients with advanced Hodgkin's lymphoma within the countries taking part in the RATHL trial. BEACOPP14 or escalated BEACOPP represented a safe and effective alternative adopted as standard of care in other European countries based on trials conducted by the German Hodgkin Study Group.

The RATHL study tested both the efficacy of two cycles of ABVD followed by up to six cycles of BEACOPP14 or four cycles of escalated BEACOPP in patients with interval PET-positive disease; as well as testing the comparative efficacy and toxicity of six cycles of ABVD compared to two cycles of ABVD followed by four cycles of AVD in patients with interval PET-negative disease, in a 1:1 randomisation. PET-CT scans after 2 cycles of ABVD were centrally reviewed with this review used to decide whether a patient was eligible for the dose de-escalation randomisation or should be escalated to BEACOPP14/escalated BEACOPP.

Patients were closely monitored for toxicity and the protocol continuation criterion for therapy and dose modification. G-CSF was mandated during BEACOPP cycles and could be given at the investigator's discretion within the ABVD/AVD arms. There was no data available for PET negative patients treated with AVD; however an independent data monitoring committee reviewed the trial data at least yearly and could halt the trial if there were any safety or efficacy concerns.

Background therapy:

Supportive care was given as per local practise, specifically.

Patients in need of urgent treatment are permitted to receive steroids up to a dose of 50mg of prednisolone or the equivalent for up to 7 days prior to their baseline trial PET-CT scan.

Granulocyte colony stimulating factors are not indicated as a matter of routine for ABVD/AVD, but can be used at the discretion of the treating clinician, in accordance with local policy.

Evidence for comparator:

Evidence for PET as a prognostic factor

Several studies have assessed the role of PET imaging in response assessment in HL: the largest being collective data from the Italian and Danish groups which prospectively evaluated and compared the prognostic role of FDG-PET and the International Prognostic Score (IPS) in 260 newly diagnosed patients with advanced HL, treated with conventional ABVD and consolidation radiotherapy if indicated. FDG-PET scan was performed at baseline and after two courses of ABVD, with no treatment change allowed on the basis of the PET-2 results. After a median follow-up of 2.19 years (range, 0.32 to 5.18 years), 205 patients were in continued complete remission, 2 patients were in partial remission, 43 patients progressed during therapy or immediately after and 10 patients had relapsed. The 2-year PFS for patients with positive PET-2 results was 12.8% and for patients with negative PET-2 results was 95% ($P < .0001$). In multivariate analyses, only PET-2 results were significant ($P < .0001$). Based on this data it was felt that it was safe to de-escalate treatment (to AVD) for patients who were PET2 negative and that patients who were PE2 positive so switch to a more intensive regimen.
Evidence for BEACOPP.

The BEACOPP regimen devised by the German Hodgkin Lymphoma Study Group substitutes etoposide

for dacarbazine and vinblastine and encompasses two main intensification principles: dose escalation of the putative most important drugs (cyclophosphamide, etoposide, and doxorubicin) and time intensification accomplished by shortening the respective chemotherapy cycles from 4 to 3 weeks. Within the randomized multicentre HD9 trial, it was demonstrated that the BEACOPP led to a significantly lower progression rate and an improved failure-free and overall survival as compared with standard COPP/ABVD. At 34 months, freedom from treatment failure (FFTF) rates were 90% and 81% for BEACOPP-escalated and BEACOPP-21 respectively.

Actual start date of recruitment	29 August 2008
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Norway: 75
Country: Number of subjects enrolled	Sweden: 51
Country: Number of subjects enrolled	United Kingdom: 854
Country: Number of subjects enrolled	Denmark: 11
Country: Number of subjects enrolled	Italy: 128
Country: Number of subjects enrolled	Australia: 70
Country: Number of subjects enrolled	New Zealand: 14
Worldwide total number of subjects	1203
EEA total number of subjects	265

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	1152
From 65 to 84 years	51
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

29/08/2008 - 21/12/2012 from 7 countries and 138 recruiting centres.

Pre-assignment

Screening details:

Previously untreated patients 18 years of age or older with advanced classic Hodgkin's lymphoma that was confirmed by histologic analysis were eligible if they were fit to receive a full course of combination chemotherapy.

Period 1

Period 1 title	Registration
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Blinding implementation details:

N/A, registration has no arms.

Arms

Arm title	ABVD (Cycle 1 and Cycle 2)

Arm description:

All patients treated with 2 cycles of ABVD chemotherapy after registration, as per standard of care.

Arm type	See description
Investigational medicinal product name	ABVD
Investigational medicinal product code	
Other name	Doxorubicin, Bleomycin, Vinblastine and Dacarbazine
Pharmaceutical forms	Powder for solution for infusion, Powder for solution for injection, Powder for solution for injection/infusion, Solution for infusion, Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

All patients will receive 2 cycles of ABVD according to the following schedule which should be repeated every 28 days:

Doxorubicin 25 mg/m2 IV Days 1 & 15
Bleomycin 10,000 IU/m2 IV Days 1 & 15
Vinblastine 6 mg/m2 IV Days 1 & 15
Dacarbazine 375 mg/m2 IV Days 1 & 15

Number of subjects in period 1	ABVD (Cycle 1 and Cycle 2)
Started	1203
Completed	1135
Not completed	68
Physician decision	2
Consent withdrawn by subject	3
PET CT scan error	53
Adverse event, non-fatal	6

Death	1
Treatment delays	1
Moved	1
Larceny and drug abuse	1

Period 2

Period 2 title	PET-negative randomisation
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Not blinded

Blinding implementation details:

N/A

Arms

Are arms mutually exclusive?	Yes
Arm title	PET negative ABVD

Arm description:

4 further cycles of ABVD chemotherapy.

Arm type	Active comparator
Investigational medicinal product name	ABVD
Investigational medicinal product code	
Other name	Doxorubicin, Bleomycin, Vinblastine and Dacarbazine
Pharmaceutical forms	Powder for solution for infusion, Powder for solution for injection, Powder for solution for injection/infusion, Solution for infusion, Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

ABVD (repeated every 28 days for 4 cycles)

Doxorubicin 25 mg/m2 IV Days 1 & 15

Bleomycin 10,000 IU/m2 IV Days 1 & 15

Vinblastine 6 mg/m2 IV Days 1 & 15

Dacarbazine 375 mg/m2 IV Days 1 & 15

Arm title	PET negative AVD

Arm description:

4 cycles of AVD chemotherapy.

Arm type	Experimental
Investigational medicinal product name	ABVD
Investigational medicinal product code	
Other name	Doxorubicin, Bleomycin, Vinblastine and Dacarbazine
Pharmaceutical forms	Powder for solution for infusion, Powder for solution for injection/infusion, Solution for infusion, Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

ABVD (repeated every 28 days for 4 cycles)

Doxorubicin 25 mg/m2 IV Days 1 & 15

Bleomycin 10,000 IU/m2 IV Days 1 & 15

Vinblastine 6 mg/m2 IV Days 1 & 15

Dacarbazine 375 mg/m2 IV Days 1 & 15

Number of subjects in period 2[1]	PET negative ABVD	PET negative AVD
Started	468	457
Completed	458	446
Not completed	10	11
Consent withdrawn by subject	2	1
Physician decision	-	1
Adverse event, non-fatal	3	7
Death	1	-
was treated at center with vinblastine shortage	-	1
Other medical conditions	2	-
Could not get to hospital	1	-
Moved	-	1
Was withdrawn owing to patient anxiety	1	-

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.
Justification: It is justified.

Period 3

Period 3 title	PET-positive BEACOPP escalation
Is this the baseline period?	No
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Blinding implementation details:

N/A

Arms

Are arms mutually exclusive?	Yes
Arm title	BEACOPP-14

Arm description:

BEACOPP-14 chemotherapy.

Arm type	Experimental

Investigational medicinal product name	BEACOPP-14
Investigational medicinal product code	
Other name	Doxorubicin, Cyclophosphamide, Etoposide, Procarbazine, Prednisolone, Bleomycin, Vincristine and G-CSF
Pharmaceutical forms	Concentrate for solution for infusion, Powder for solution for injection, Powder for solution for injection/infusion, Solution for infusion, Solution for injection, Tablet
Routes of administration	Intravenous use, Oral use

Dosage and administration details:

BEACOPP-14 (repeated every 14 days for 4 to 6 cycles – see section 1.2 of RATHL protocol v6.0 21.06.2022)

Doxorubicin 25mg/m2 iv Day 1

Cyclophosphamide 650mg/m2 iv Day 1

Etoposide 100mg/m2 iv Days 1-3

Procarbazine (or Natulan) 100mg/m2 po Days 1-7

Prednisolone 80mg/m2 po Days 1-7

Bleomycin 10,000units/m2 iv Day 8

Vincristine* 1.4mg/m2 iv Day 8

G-CSF 263/300mcg or equivalent PEG-Filgrastim single dose Day 9-13

Arm title	esc-BEACOPP

Arm description:

escalated BEACOPP

Arm type	Experimental
Investigational medicinal product name	BEACOPP-escalated
Investigational medicinal product code	
Other name	Doxorubicin, Cyclophosphamide, Etoposide, Procarbazine, Prednisolone, Bleomycin, Vincristine and G-CSF
Pharmaceutical forms	Capsule, Concentrate for solution for infusion, Powder for solution for injection, Solution for infusion, Solution for injection, Tablet
Routes of administration	Intravenous use, Oral use

Dosage and administration details:

Level 1- escalated dose Cyclophosphamide -1250mg/m2
Level 2- escalated dose Cyclophosphamide -1100mg/m2
Level 3- escalated dose Cyclophosphamide -950mg/m2
Level 4- escalated dose Cyclophosphamide -800mg/m2
Level 5- escalated dose Cyclophosphamide -650mg/m2

Level 1- escalated dose Etoposide -200mg/m2
Level 2- escalated dose Etoposide -175mg/m2
Level 3- escalated dose Etoposide -150mg/m2
Level 4- escalated dose Etoposide -125mg/m2
Level 5- escalated dose Etoposide -100mg/m2

Number of subjects in period 3[2]	BEACOPP-14	esc-BEACOPP
Started	94	78
Completed	76	66
Not completed	18	12
Physician decision	1	-
Consent withdrawn by subject	3	2
Disease progression	1	1
Transferred Hospital	1	-
Adverse event, non-fatal	5	2
Death	1	2
Unknown	-	3
Other medical conditions	-	2
Medical conditions	2	-
Lack of efficacy	3	-
Protocol deviation	1	-

Notes:

[2] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.
Justification: It is justified.

Baseline characteristics

Reporting groups

Reporting group title	Registration

Reporting group description: -

Reporting group values	Registration	Total	
Number of subjects	1203	1203	
Age categorical Units: Subjects			
18-24	299	299	
25-44	576	576	
45-59	213	213	
60 years and over	115	115	
Age continuous Units: years			
median	33		
full range (min-max)	18 to 79	-	
Gender categorical Units: Subjects			
Female	547	547	
Male	656	656	
ECOG Units: Subjects			
Zero	889	889	
One	271	271	
Two	28	28	
Three	14	14	
Missing	1	1	
Ann Arbor stage Units: Subjects			
II	500	500	
III	363	363	
IV	340	340	
International prognostic score Units: Subjects			
0 or 1	404	404	
2 or 3	579	579	
≥4	209	209	
Missing	11	11	

Subject analysis sets

Subject analysis set title	PET2 negative ABVD randomised patients
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

All eligible patients randomised to ABVD.

Subject analysis set title	PET2 negative AVD randomised patients

Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

All eligible AVD randomised patients.

Subject analysis set title	PET2 positive patients
Subject analysis set type	Per protocol

Subject analysis set description:

PET2 positive patients who were treated with BEACOPP.

Reporting group values	PET2 negative ABVD randomised patients	PET2 negative AVD randomised patients	PET2 positive patients
Number of subjects	470	465	172
Age categorical Units: Subjects			
18-24	121	117	47
25-44	231	223	75
45-59	80	81	32
60 years and over	38	44	18
Age continuous Units: years			
median	32	33	32
full range (min-max)	18 to 79	18 to 76	18 to 70
Gender categorical Units: Subjects			
Female	209	213	80
Male	261	252	92
ECOG Units: Subjects			
Zero	340	354	123
One	113	96	40
Two	11	9	6
Three	6	6	2
Missing	0	0	1
Ann Arbor stage Units: Subjects			
II	195	197	73
III	157	140	34
IV	118	128	65
International prognostic score Units: Subjects			
0 or 1	170	172	34
2 or 3	219	224	84
≥4	75	67	52
Missing	6	2	2

End points

End points reporting groups

Reporting group title	ABVD (Cycle 1 and Cycle 2)
Reporting group description:	
All patients treated with 2 cycles of ABVD chemotherapy after registration, as per standard of care.	
Reporting group title	PET negative ABVD
Reporting group description:	
4 further cycles of ABVD chemotherapy.	
Reporting group title	PET negative AVD
Reporting group description:	
4 cycles of AVD chemotherapy.	
Reporting group title	BEACOPP-14
Reporting group description:	
BEACOPP-14 chemotherapy.	
Reporting group title	esc-BEACOPP
Reporting group description:	
escalated BEACOPP	
Subject analysis set title	PET2 negative ABVD randomised patients
Subject analysis set type	Modified intention-to-treat
Subject analysis set description:	
All eligible patients randomised to ABVD.	
Subject analysis set title	PET2 negative AVD randomised patients
Subject analysis set type	Modified intention-to-treat
Subject analysis set description:	
All eligible AVD randomised patients.	
Subject analysis set title	PET2 positive patients
Subject analysis set type	Per protocol
Subject analysis set description:	
PET2 positive patients who were treated with BEACOPP.	

Primary: Progression Free Survival

End point title	Progression Free Survival
End point description:	
End point type	Primary
End point timeframe:	
3 years after registration.	

End point values	ABVD (Cycle 1 and Cycle 2)	PET2 negative ABVD randomised patients	PET2 negative AVD randomised patients	PET2 positive patients
Subject group type	Reporting group	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	1203	470	465	172
Units: percentage				
number (confidence interval 95%)	82.6 (80.2 to 84.7)	85.7 (82.1 to 88.6)	84.4 (80.7 to 87.5)	67.5 (59.7 to 74.2)

Attachments (see zip file)	RATHL_KM_plot_PFS_ALL.tif RATHL_KM_plot_PFS_BEACOPP.tif RATHL_KM_plot_PFS_randomisedITT.tif

Statistical analyses

Statistical analysis title	PFS at 3 yrs in PET2 negative randomised patients

Statistical analysis description:

This is the primary endpoint for the randomised comparison and is based on the 3 year rates in the 2 arms and the hazard ratio.
ABVD: 85.7% (95% CI: 82.1 - 88.6)
AVD: 84.4% (95% CI: 80.7 - 87.5)
Hazard Ratio: 1.13 (95%CI : 0.81 - 1.57)

Comparison groups	PET2 negative ABVD randomised patients v PET2 negative AVD randomised patients
Number of subjects included in analysis	935
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	Risk difference (RD)
Point estimate	1.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.2
upper limit	5.3
Variability estimate	Standard error of the mean

Statistical analysis title	Hazard ratio for PFS in PET2 randomised patients
Comparison groups	PET2 negative AVD randomised patients v PET2 negative ABVD randomised patients
Number of subjects included in analysis	935
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.48 [1]
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	1.13
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.81
upper limit	1.57

Variability estimate	Standard error of the mean

Notes:

[1] - Two-tailed P = 0.48 for the null hypothesis of
a hazard ratio of 1.00; one-tailed P = 0.11 for the null hypothesis of a hazard ratio of ≥1.39 [i.e., a difference of 5 percentage points from 80.7%
to 85.7%] vs. the alternative hazard ratio of <1.39)

Secondary: Overall Survival

End point title	Overall Survival

End point description:

End point type	Secondary

End point timeframe:

3 years after registration.

End point values	ABVD (Cycle 1 and Cycle 2)	PET2 negative ABVD randomised patients	PET2 negative AVD randomised patients	PET2 positive patients
Subject group type	Reporting group	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	1203	470	465	172
Units: percentage				
number (confidence interval 95%)	95.8 (94.4 to 96.8)	97.2 (95.1 to 98.4)	97.6 (95.6 to 98.7)	87.8 (81.5 to 92.1)

Attachments (see zip file)	RATHL_KM_plot_OS_randomisedITT.tif RATHL_KM_plot_OS_BEACOPP.tif RATHL_KM_plot_OS_ALL.tif

Statistical analyses

Statistical analysis title	OS comparing PET2 randomised arms
Comparison groups	PET2 negative AVD randomised patients v PET2 negative ABVD randomised patients
Number of subjects included in analysis	935
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.76
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.47
upper limit	1.74
Variability estimate	Standard error of the mean

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All adverse events that occur between informed consent and 30 days post last trial treatment administration.

Adverse event reporting additional description:

Severity of each adverse event will be determined by using the Common Terminology Criteria for Adverse Events (CTCAE) v3.0 as a guideline, wherever possible.

Assessment type	Systematic

Dictionary used

Dictionary name	CTCAE
Dictionary version	3.0

Reporting groups

Reporting group title	ABVD (Cycle 1 and Cycle 2)

Reporting group description:

All patients treated with 2 cycles of ABVD chemotherapy after registration.

Reporting group title	Cycles 3 - 6 ABVD

Reporting group description:

All PET 2 negative eligible patients who started ABVD cycles 3 to 6. For non-serious adverse events only patients with an AE form returned are included and only grades 3-5 reported. SAEs are also are also included within the AE reporting numbers i.e. these are the total number of all grade 3-5 events.

Reporting group title	Cycles 3 - 6 AVD

Reporting group description:

All PET 2 negative eligible patients who started AVD cycles 3 to 6. For non-serious adverse events only patients with an AE form returned are included and only grades 3-5 reported. SAEs are also are also included within the AE reporting numbers i.e. these are the total number of all grade 3-5 events.

Reporting group title	Cycles 1 - 6 BEACOPP-14

Reporting group description:

All PET 2 positive eligible patients who started BEACOPP-14 who started cycles 1 to 6. For non-serious adverse events only patients with an AE form returned are included and only grades 3-5 reported. SAEs are also are also included within the AE reporting numbers i.e. these are the total number of all grade 3-5 events.

Reporting group title	Cycles 1 - 4 BEACOPP-ESC

Reporting group description:

All PET 2 positive eligible patients who started BEACOPP-ESC cycles 1 to 4. For non-serious adverse events only patients with an AE form returned are included and only grades 3-5 reported. SAEs are also are also included within the AE reporting numbers i.e. these are the total number of all grade 3-5 events.

Serious adverse events	ABVD (Cycle 1 and Cycle 2)	Cycles 3 - 6 ABVD	Cycles 3 - 6 AVD
Total subjects affected by serious adverse events			
subjects affected / exposed	90 / 1203 (7.48%)	70 / 468 (14.96%)	53 / 457 (11.60%)
number of deaths (all causes)	1	1	0
number of deaths resulting from adverse events			
Vascular disorders			
Thrombosis			

subjects affected / exposed	6 / 1203 (0.50%)	7 / 468 (1.50%)	4 / 457 (0.88%)
occurrences causally related to treatment / all	0 / 6	0 / 7	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Embolism			
subjects affected / exposed	0 / 1203 (0.00%)	3 / 468 (0.64%)	0 / 457 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pregnancy, puerperium and perinatal conditions			
Other - pregnancy with multiple dysmorphic features and congenital abnormalities			
subjects affected / exposed	0 / 1203 (0.00%)	1 / 468 (0.21%)	0 / 457 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	0 / 1203 (0.00%)	0 / 468 (0.00%)	2 / 457 (0.44%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fever			
subjects affected / exposed	2 / 1203 (0.17%)	0 / 468 (0.00%)	4 / 457 (0.88%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Insomnia			
subjects affected / exposed	1 / 1203 (0.08%)	0 / 468 (0.00%)	0 / 457 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chest pain			
subjects affected / exposed	1 / 1203 (0.08%)	0 / 468 (0.00%)	0 / 457 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pain			

subjects affected / exposed	3 / 1203 (0.25%)	0 / 468 (0.00%)	0 / 457 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Death			
subjects affected / exposed	1 / 1203 (0.08%)	0 / 468 (0.00%)	0 / 457 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oedema			
subjects affected / exposed	0 / 1203 (0.00%)	1 / 468 (0.21%)	1 / 457 (0.22%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Allergic reaction			
subjects affected / exposed	0 / 1203 (0.00%)	1 / 468 (0.21%)	0 / 457 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Infertility			
subjects affected / exposed	0 / 1203 (0.00%)	0 / 468 (0.00%)	0 / 457 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Pulmonary fibrosis			
subjects affected / exposed	0 / 1203 (0.00%)	1 / 468 (0.21%)	0 / 457 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonitis			
subjects affected / exposed	0 / 1203 (0.00%)	3 / 468 (0.64%)	1 / 457 (0.22%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoxia			

subjects affected / exposed	1 / 1203 (0.08%)	0 / 468 (0.00%)	0 / 457 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea			
subjects affected / exposed	2 / 1203 (0.17%)	4 / 468 (0.85%)	0 / 457 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cough			
subjects affected / exposed	0 / 1203 (0.00%)	0 / 468 (0.00%)	0 / 457 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
upper respiratory pain			
subjects affected / exposed	0 / 1203 (0.00%)	1 / 468 (0.21%)	0 / 457 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
chest wall pain			
subjects affected / exposed	0 / 1203 (0.00%)	1 / 468 (0.21%)	0 / 457 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 1203 (0.00%)	0 / 468 (0.00%)	1 / 457 (0.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper respiratory tract infection			
subjects affected / exposed	0 / 1203 (0.00%)	1 / 468 (0.21%)	2 / 457 (0.44%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Depression			
subjects affected / exposed	1 / 1203 (0.08%)	0 / 468 (0.00%)	1 / 457 (0.22%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anxiety			

subjects affected / exposed	1 / 1203 (0.08%)	0 / 468 (0.00%)	0 / 457 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Agitation			
subjects affected / exposed	1 / 1203 (0.08%)	0 / 468 (0.00%)	0 / 457 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	1 / 1203 (0.08%)	0 / 468 (0.00%)	0 / 457 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac Troponin I			
subjects affected / exposed	0 / 1203 (0.00%)	1 / 468 (0.21%)	1 / 457 (0.22%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac troponin T			
subjects affected / exposed	0 / 1203 (0.00%)	0 / 468 (0.00%)	0 / 457 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pericardial effusion			
subjects affected / exposed	3 / 1203 (0.25%)	0 / 468 (0.00%)	0 / 457 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
vasovagal episode			
subjects affected / exposed	0 / 1203 (0.00%)	1 / 468 (0.21%)	0 / 457 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac ischemia/infarction			
subjects affected / exposed	2 / 1203 (0.17%)	0 / 468 (0.00%)	0 / 457 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac Arrhythmia - Other - left ventricular systolic dysfunction			

subjects affected / exposed	0 / 1203 (0.00%)	1 / 468 (0.21%)	0 / 457 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Supraventricular arrhythmia NOS			
subjects affected / exposed	1 / 1203 (0.08%)	0 / 468 (0.00%)	0 / 457 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 1203 (0.00%)	0 / 468 (0.00%)	0 / 457 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dizziness			
subjects affected / exposed	0 / 1203 (0.00%)	0 / 468 (0.00%)	1 / 457 (0.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebrovascular ischemia			
subjects affected / exposed	2 / 1203 (0.17%)	0 / 468 (0.00%)	0 / 457 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Seizure			
subjects affected / exposed	1 / 1203 (0.08%)	0 / 468 (0.00%)	0 / 457 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	2 / 1203 (0.17%)	0 / 468 (0.00%)	0 / 457 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sensory neuropathy			
subjects affected / exposed	0 / 1203 (0.00%)	1 / 468 (0.21%)	0 / 457 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Motor neuropathy			

subjects affected / exposed	0 / 1203 (0.00%)	0 / 468 (0.00%)	1 / 457 (0.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CSF leak			
subjects affected / exposed	0 / 1203 (0.00%)	0 / 468 (0.00%)	1 / 457 (0.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 1203 (0.00%)	0 / 468 (0.00%)	1 / 457 (0.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Leucopenia			
subjects affected / exposed	0 / 1203 (0.00%)	1 / 468 (0.21%)	4 / 457 (0.88%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutropenia			
subjects affected / exposed	14 / 1203 (1.16%)	6 / 468 (1.28%)	17 / 457 (3.72%)
occurrences causally related to treatment / all	0 / 14	0 / 6	0 / 17
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombocytopenia			
subjects affected / exposed	16 / 1203 (1.33%)	6 / 468 (1.28%)	15 / 457 (3.28%)
occurrences causally related to treatment / all	0 / 16	0 / 6	0 / 15
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Colitis			
subjects affected / exposed	0 / 1203 (0.00%)	1 / 468 (0.21%)	0 / 457 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Constipation			
subjects affected / exposed	1 / 1203 (0.08%)	1 / 468 (0.21%)	0 / 457 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dehydration			

subjects affected / exposed	1 / 1203 (0.08%)	0 / 468 (0.00%)	0 / 457 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	1 / 1203 (0.08%)	0 / 468 (0.00%)	0 / 457 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ileus			
subjects affected / exposed	0 / 1203 (0.00%)	0 / 468 (0.00%)	1 / 457 (0.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nausea			
subjects affected / exposed	1 / 1203 (0.08%)	1 / 468 (0.21%)	0 / 457 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Obstruction, GI - Rectum			
subjects affected / exposed	1 / 1203 (0.08%)	0 / 468 (0.00%)	0 / 457 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	3 / 1203 (0.25%)	2 / 468 (0.43%)	1 / 457 (0.22%)
occurrences causally related to treatment / all	0 / 3	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal haemorrhage			
subjects affected / exposed	0 / 1203 (0.00%)	0 / 468 (0.00%)	0 / 457 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower gastrointestinal haemorrhage			
subjects affected / exposed	0 / 1203 (0.00%)	0 / 468 (0.00%)	0 / 457 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
rectal pain			

subjects affected / exposed	1 / 1203 (0.08%)	0 / 468 (0.00%)	0 / 457 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
AST increased			
subjects affected / exposed	1 / 1203 (0.08%)	0 / 468 (0.00%)	0 / 457 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	2 / 1203 (0.17%)	0 / 468 (0.00%)	0 / 457 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 1203 (0.08%)	0 / 468 (0.00%)	0 / 457 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bone pain			
subjects affected / exposed	0 / 1203 (0.00%)	0 / 468 (0.00%)	0 / 457 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Back pain			
subjects affected / exposed	0 / 1203 (0.00%)	0 / 468 (0.00%)	0 / 457 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myalgia			
subjects affected / exposed	1 / 1203 (0.08%)	0 / 468 (0.00%)	1 / 457 (0.22%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Muscle weakness			
subjects affected / exposed	1 / 1203 (0.08%)	0 / 468 (0.00%)	0 / 457 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Soft tissue injury			
subjects affected / exposed	1 / 1203 (0.08%)	0 / 468 (0.00%)	0 / 457 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Ear infection			
subjects affected / exposed	0 / 1203 (0.00%)	0 / 468 (0.00%)	1 / 457 (0.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colitis			
subjects affected / exposed	0 / 1203 (0.00%)	0 / 468 (0.00%)	0 / 457 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Febrile neutropenia			
subjects affected / exposed	16 / 1203 (1.33%)	16 / 468 (3.42%)	8 / 457 (1.75%)
occurrences causally related to treatment / all	0 / 16	0 / 16	0 / 8
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	0 / 1203 (0.00%)	3 / 468 (0.64%)	0 / 457 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Clostridium difficile colitis			
subjects affected / exposed	0 / 1203 (0.00%)	0 / 468 (0.00%)	0 / 457 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	0 / 1203 (0.00%)	1 / 468 (0.21%)	0 / 457 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Perianal infection			
subjects affected / exposed	0 / 1203 (0.00%)	1 / 468 (0.21%)	0 / 457 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lymphatic infection			

subjects affected / exposed	0 / 1203 (0.00%)	0 / 468 (0.00%)	1 / 457 (0.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal infection			
subjects affected / exposed	0 / 1203 (0.00%)	1 / 468 (0.21%)	0 / 457 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Soft tissue infection			
subjects affected / exposed	0 / 1203 (0.00%)	0 / 468 (0.00%)	0 / 457 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
not specified			
subjects affected / exposed	13 / 1203 (1.08%)	11 / 468 (2.35%)	6 / 457 (1.31%)
occurrences causally related to treatment / all	0 / 13	0 / 11	0 / 6
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chest infection			
subjects affected / exposed	1 / 1203 (0.08%)	0 / 468 (0.00%)	0 / 457 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper respiratory infection			
subjects affected / exposed	1 / 1203 (0.08%)	3 / 468 (0.64%)	1 / 457 (0.22%)
occurrences causally related to treatment / all	0 / 1	0 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infection NOS			
subjects affected / exposed	17 / 1203 (1.41%)	6 / 468 (1.28%)	8 / 457 (1.75%)
occurrences causally related to treatment / all	0 / 17	0 / 6	0 / 8
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutropenic infection G3-G4			
subjects affected / exposed	7 / 1203 (0.58%)	6 / 468 (1.28%)	6 / 457 (1.31%)
occurrences causally related to treatment / all	0 / 7	0 / 6	0 / 6
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Hyperglycaemia			

subjects affected / exposed	1 / 1203 (0.08%)	0 / 468 (0.00%)	0 / 457 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypokalaemia			
subjects affected / exposed	1 / 1203 (0.08%)	0 / 468 (0.00%)	0 / 457 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyponatraemia			
subjects affected / exposed	1 / 1203 (0.08%)	0 / 468 (0.00%)	0 / 457 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Cycles 1 - 6 BEACOPP-14	Cycles 1 - 4 BEACOPP-ESC	
Total subjects affected by serious adverse events			
subjects affected / exposed	40 / 94 (42.55%)	36 / 78 (46.15%)	
number of deaths (all causes)	0	1	
number of deaths resulting from adverse events		0	
Vascular disorders			
Thrombosis			
subjects affected / exposed	5 / 94 (5.32%)	1 / 78 (1.28%)	
occurrences causally related to treatment / all	0 / 5	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Embolism			
subjects affected / exposed	0 / 94 (0.00%)	0 / 78 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pregnancy, puerperium and perinatal conditions			
Other - pregnancy with multiple dysmorphic features and congenital abnormalities			
subjects affected / exposed	0 / 94 (0.00%)	0 / 78 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Fatigue			

subjects affected / exposed	0 / 94 (0.00%)	0 / 78 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fever			
subjects affected / exposed	0 / 94 (0.00%)	2 / 78 (2.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Insomnia			
subjects affected / exposed	0 / 94 (0.00%)	0 / 78 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chest pain			
subjects affected / exposed	0 / 94 (0.00%)	0 / 78 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pain			
subjects affected / exposed	1 / 94 (1.06%)	1 / 78 (1.28%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Death			
subjects affected / exposed	0 / 94 (0.00%)	0 / 78 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oedema			
subjects affected / exposed	0 / 94 (0.00%)	0 / 78 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Allergic reaction			
subjects affected / exposed	0 / 94 (0.00%)	0 / 78 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			

Infertility			
subjects affected / exposed	1 / 94 (1.06%)	0 / 78 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Pulmonary fibrosis			
subjects affected / exposed	0 / 94 (0.00%)	0 / 78 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonitis			
subjects affected / exposed	0 / 94 (0.00%)	2 / 78 (2.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoxia			
subjects affected / exposed	0 / 94 (0.00%)	0 / 78 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea			
subjects affected / exposed	1 / 94 (1.06%)	0 / 78 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cough			
subjects affected / exposed	1 / 94 (1.06%)	0 / 78 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
upper respiratory pain			
subjects affected / exposed	0 / 94 (0.00%)	0 / 78 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
chest wall pain			
subjects affected / exposed	0 / 94 (0.00%)	0 / 78 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Pneumonia			
subjects affected / exposed	2 / 94 (2.13%)	1 / 78 (1.28%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper respiratory tract infection			
subjects affected / exposed	1 / 94 (1.06%)	0 / 78 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Depression			
subjects affected / exposed	0 / 94 (0.00%)	0 / 78 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anxiety			
subjects affected / exposed	0 / 94 (0.00%)	0 / 78 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Agitation			
subjects affected / exposed	0 / 94 (0.00%)	0 / 78 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 94 (0.00%)	0 / 78 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac Troponin I			
subjects affected / exposed	0 / 94 (0.00%)	0 / 78 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac troponin T			
subjects affected / exposed	1 / 94 (1.06%)	0 / 78 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Pericardial effusion			
subjects affected / exposed	0 / 94 (0.00%)	0 / 78 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
vasovagal episode			
subjects affected / exposed	0 / 94 (0.00%)	0 / 78 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac ischemia/infarction			
subjects affected / exposed	0 / 94 (0.00%)	0 / 78 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac Arrhythmia - Other - left ventricular systolic dysfunction			
subjects affected / exposed	0 / 94 (0.00%)	0 / 78 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Supraventricular arrhythmia NOS			
subjects affected / exposed	0 / 94 (0.00%)	0 / 78 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 94 (0.00%)	1 / 78 (1.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dizziness			
subjects affected / exposed	0 / 94 (0.00%)	0 / 78 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebrovascular ischemia			
subjects affected / exposed	1 / 94 (1.06%)	1 / 78 (1.28%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Seizure			
subjects affected / exposed	0 / 94 (0.00%)	0 / 78 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope			
subjects affected / exposed	0 / 94 (0.00%)	0 / 78 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sensory neuropathy			
subjects affected / exposed	0 / 94 (0.00%)	0 / 78 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Motor neuropathy			
subjects affected / exposed	0 / 94 (0.00%)	0 / 78 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
CSF leak			
subjects affected / exposed	0 / 94 (0.00%)	0 / 78 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	4 / 94 (4.26%)	2 / 78 (2.56%)	
occurrences causally related to treatment / all	0 / 4	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Leucopenia			
subjects affected / exposed	0 / 94 (0.00%)	3 / 78 (3.85%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenia			
subjects affected / exposed	9 / 94 (9.57%)	11 / 78 (14.10%)	
occurrences causally related to treatment / all	0 / 9	0 / 11	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombocytopenia			

subjects affected / exposed	18 / 94 (19.15%)	33 / 78 (42.31%)	
occurrences causally related to treatment / all	0 / 18	0 / 33	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Colitis			
subjects affected / exposed	1 / 94 (1.06%)	0 / 78 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Constipation			
subjects affected / exposed	0 / 94 (0.00%)	0 / 78 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dehydration			
subjects affected / exposed	0 / 94 (0.00%)	0 / 78 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	2 / 94 (2.13%)	1 / 78 (1.28%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ileus			
subjects affected / exposed	0 / 94 (0.00%)	0 / 78 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nausea			
subjects affected / exposed	1 / 94 (1.06%)	1 / 78 (1.28%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Obstruction, GI - Rectum			
subjects affected / exposed	0 / 94 (0.00%)	0 / 78 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			

subjects affected / exposed	2 / 94 (2.13%)	1 / 78 (1.28%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal haemorrhage			
subjects affected / exposed	1 / 94 (1.06%)	0 / 78 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower gastrointestinal haemorrhage			
subjects affected / exposed	1 / 94 (1.06%)	0 / 78 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
rectal pain			
subjects affected / exposed	1 / 94 (1.06%)	0 / 78 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
AST increased			
subjects affected / exposed	0 / 94 (0.00%)	0 / 78 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	0 / 94 (0.00%)	0 / 78 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 94 (0.00%)	1 / 78 (1.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bone pain			
subjects affected / exposed	2 / 94 (2.13%)	1 / 78 (1.28%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Back pain			
subjects affected / exposed	0 / 94 (0.00%)	4 / 78 (5.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myalgia			
subjects affected / exposed	0 / 94 (0.00%)	2 / 78 (2.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Muscle weakness			
subjects affected / exposed	0 / 94 (0.00%)	0 / 78 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Soft tissue injury			
subjects affected / exposed	1 / 94 (1.06%)	0 / 78 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Ear infection			
subjects affected / exposed	0 / 94 (0.00%)	0 / 78 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis			
subjects affected / exposed	1 / 94 (1.06%)	1 / 78 (1.28%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile neutropenia			
subjects affected / exposed	8 / 94 (8.51%)	16 / 78 (20.51%)	
occurrences causally related to treatment / all	0 / 8	0 / 16	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis			
subjects affected / exposed	0 / 94 (0.00%)	0 / 78 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clostridium difficile colitis			

subjects affected / exposed	1 / 94 (1.06%)	0 / 78 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	1 / 94 (1.06%)	0 / 78 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Perianal infection			
subjects affected / exposed	1 / 94 (1.06%)	0 / 78 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lymphatic infection			
subjects affected / exposed	0 / 94 (0.00%)	0 / 78 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal infection			
subjects affected / exposed	0 / 94 (0.00%)	0 / 78 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Soft tissue infection			
subjects affected / exposed	0 / 94 (0.00%)	1 / 78 (1.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
not specified			
subjects affected / exposed	5 / 94 (5.32%)	6 / 78 (7.69%)	
occurrences causally related to treatment / all	0 / 5	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chest infection			
subjects affected / exposed	1 / 94 (1.06%)	0 / 78 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper respiratory infection			

subjects affected / exposed	1 / 94 (1.06%)	0 / 78 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infection NOS			
subjects affected / exposed	5 / 94 (5.32%)	4 / 78 (5.13%)	
occurrences causally related to treatment / all	0 / 5	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenic infection G3-G4			
subjects affected / exposed	9 / 94 (9.57%)	5 / 78 (6.41%)	
occurrences causally related to treatment / all	0 / 9	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Hyperglycaemia			
subjects affected / exposed	0 / 94 (0.00%)	0 / 78 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypokalaemia			
subjects affected / exposed	1 / 94 (1.06%)	0 / 78 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyponatraemia			
subjects affected / exposed	1 / 94 (1.06%)	0 / 78 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	ABVD (Cycle 1 and Cycle 2)	Cycles 3 - 6 ABVD	Cycles 3 - 6 AVD
Total subjects affected by non-serious adverse events			
subjects affected / exposed	771 / 1203 (64.09%)	322 / 468 (68.80%)	299 / 457 (65.43%)
Vascular disorders			
Thrombosis/Thrombus/embolism			
subjects affected / exposed	14 / 1203 (1.16%)	20 / 468 (4.27%)	11 / 457 (2.41%)
occurrences (all)	14	20	11

Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	8 / 1203 (0.67%)	7 / 468 (1.50%)	4 / 457 (0.88%)
occurrences (all)	8	7	4
Leucopenia			
subjects affected / exposed	162 / 1203 (13.47%)	107 / 468 (22.86%)	100 / 457 (21.88%)
occurrences (all)	162	107	100
Neutropenia			
subjects affected / exposed	694 / 1203 (57.69%)	275 / 468 (58.76%)	269 / 457 (58.86%)
occurrences (all)	694	275	269
Thrombocytopenia			
subjects affected / exposed	16 / 1203 (1.33%)	6 / 468 (1.28%)	15 / 457 (3.28%)
occurrences (all)	16	6	15
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	14 / 1203 (1.16%)	14 / 468 (2.99%)	5 / 457 (1.09%)
occurrences (all)	14	14	5
Fever			
subjects affected / exposed	16 / 1203 (1.33%)	4 / 468 (0.85%)	7 / 457 (1.53%)
occurrences (all)	16	4	7
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	4 / 1203 (0.33%)	0 / 468 (0.00%)	3 / 457 (0.66%)
occurrences (all)	4	0	3
Infections and infestations			
Febrile neutropenia			
subjects affected / exposed	24 / 1203 (2.00%)	22 / 468 (4.70%)	10 / 457 (2.19%)
occurrences (all)	24	22	10
Infection - Not specified			
subjects affected / exposed	57 / 1203 (4.74%)	47 / 468 (10.04%)	34 / 457 (7.44%)
occurrences (all)	57	47	34
Infection with G34 ANC	Additional description: Infection with G34 ANC under infections and infestations.		
subjects affected / exposed	7 / 1203 (0.58%)	6 / 468 (1.28%)	6 / 457 (1.31%)
occurrences (all)	7	6	6
Infection with normal ANC	Additional description: under Infections and infestations.		

subjects affected / exposed	17 / 1203 (1.41%)	6 / 468 (1.28%)	8 / 457 (1.75%)
occurrences (all)	17	6	8

Non-serious adverse events	Cycles 1 - 6 BEACOPP-14	Cycles 1 - 4 BEACOPP-ESC	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	75 / 94 (79.79%)	65 / 78 (83.33%)	
Vascular disorders			
Thrombosis/Thrombus/embolism			
subjects affected / exposed	8 / 94 (8.51%)	2 / 78 (2.56%)	
occurrences (all)	8	2	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	32 / 94 (34.04%)	18 / 78 (23.08%)	
occurrences (all)	32	18	
Leucopenia			
subjects affected / exposed	25 / 94 (26.60%)	6 / 78 (7.69%)	
occurrences (all)	25	6	
Neutropenia			
subjects affected / exposed	59 / 94 (62.77%)	52 / 78 (66.67%)	
occurrences (all)	59	52	
Thrombocytopenia			
subjects affected / exposed	18 / 94 (19.15%)	33 / 78 (42.31%)	
occurrences (all)	18	33	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	8 / 94 (8.51%)	3 / 78 (3.85%)	
occurrences (all)	8	3	
Fever			
subjects affected / exposed	2 / 94 (2.13%)	9 / 78 (11.54%)	
occurrences (all)	2	9	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	4 / 94 (4.26%)	5 / 78 (6.41%)	
occurrences (all)	4	5	
Infections and infestations			
Febrile neutropenia			

subjects affected / exposed	10 / 94 (10.64%)	20 / 78 (25.64%)	
occurrences (all)	10	20	
Infection - Not specified			
subjects affected / exposed	19 / 94 (20.21%)	17 / 78 (21.79%)	
occurrences (all)	19	17	
Infection with G34 ANC	Additional description: Infection with G34 ANC under infections and infestations.		
subjects affected / exposed	10 / 94 (10.64%)	5 / 78 (6.41%)	
occurrences (all)	10	5	
Infection with normal ANC	Additional description: under Infections and infestations.		
subjects affected / exposed	5 / 94 (5.32%)	5 / 78 (6.41%)	
occurrences (all)	5	5	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
16 May 2008	First Approved Protocol
18 September 2008	Timing of PET scanning changed, timing of the response assessment clarified and a number of other administrative changes.
10 October 2008	PIS, GP Letter and consent form removed from protocol. Number of other minor changes.
30 November 2009	Inclusion criterion number 9 relating to pulmonary function test removed, Assessment times changed for bloods and other investigations. A number of other changes.

10 February 2012	Protocol restructured in line with current UCL CTC template. Key changes include: Updated trial contacts to include TMG details. Expanded study synopsis (section 1.1). More detailed site selection criteria (section 3). New section on informed consent (section 4). Pregnancy testing for women of childbearing potential added to baseline investigations (section 5.1). Inclusion criterion 12 updated to specify "approved PET-CT scanning facility" (section 5.3.1). Exclusion criterion 8 revised: now allows previous malignancies if disease-free ≥5 years; concurrent active malignancy remains exclusionary (section 5.3.2). Pathology specimens now sent directly to HMDS instead of UCL CTC (section 5.4). Guidance on contraception and fertility added (section 5.5). Additional detail on registration procedures (section 6). Clarified dose adjustments and capping; added info on Natulan use when UK-licensed procarbazine unavailable; updated pharmacy responsibilities (section 7). Clarified requirement for 3-month post-treatment CT scan (section 8.3). PV section (section 11) amended: now collecting all AEs, not just grade 3/4; expanded SAE exemptions; added overdose guidance; updated SAE/SUSAR processing and DSUR submission. Information added on incident reporting, serious breaches (section 12), and monitoring/oversight (section 13). Sponsorship and Indemnity section updated (section 18). Expanded publication policy (section 20), added references (section 21), and list of abbreviations (appendix 1). Expected AEs updated for ABVD, AVD, and BEACOPP regimens (appendix 3). Pregnancy test added to schedule of investigations (appendix 4). Change to PET scan uptake time (appendix 5). Minor typographical corrections made.
22 June 2022	• Section 8.4 has been updated to state annual follow-up will be collected via CRF and that annual follow-up will cease from sites if approval to collect data from a national registry is granted. • Section 15.1 has been updated to state the End of Trial will be declared once final data items for the trial are received. • A section has been added to the exploratory objectives which includes additional analyses of the PET scans.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

AEs: occurrences all number can't be provided as only highest grade are collected. Subjects affected is entered instead (only grade 3-4 reported). Treatment related death/relatedness to SAEs not available (0 entered). N = 11 ineligible pts excluded.

Notes:

Online references

http://www.ncbi.nlm.nih.gov/pubmed/30220622

http://www.ncbi.nlm.nih.gov/pubmed/33641019

http://www.ncbi.nlm.nih.gov/pubmed/26747247

http://www.ncbi.nlm.nih.gov/pubmed/38824206

http://www.ncbi.nlm.nih.gov/pubmed/27332902

http://www.ncbi.nlm.nih.gov/pubmed/41102172