



Clinical trial results:

Randomized phase III study on the effect of early intensification of rituximab in combination with 2-weekly CHOP chemotherapy followed by rituximab maintenance in patients with diffuse large B-cell lymphoma Summary

EudraCT number	2006-005174-42
Trial protocol	NL DK BE
Global end of trial date	03 March 2021

Results information

Result version number	v1 (current)
This version publication date	15 December 2022
First version publication date	15 December 2022

Trial information

Trial identification

Sponsor protocol code	HOVON84NHL
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Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	HOVON
Sponsor organisation address	De Boelelaan 1117, Amsterdam, Netherlands,
Public contact	HOVON Data Center, HOVON, 31 107041560, hdc@erasmusmc.nl
Scientific contact	HOVON Data Center, HOVON, 31 107041560, hdc@erasmusmc.nl

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	21 April 2021
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	03 March 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess in a prospective, multicenter, randomized phase III study in patients with DLBCL the effect of early intensification of rituximab combined with 2-weekly CHOP +G-CSF (CHOP14) in comparison to no intensification of rituximab on the response rate (complete remission and FDG-PET negative partial remission/unconfirmed complete remission) and time to reach response

Protection of trial subjects:

Monitoring and Insurance

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	23 May 2007
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	Netherlands: 461
Country: Number of subjects enrolled	Belgium: 26
Country: Number of subjects enrolled	Denmark: 113
Worldwide total number of subjects	600
EEA total number of subjects	600

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)	301
From 65 to 84 years	299

85 years and over	0
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Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

All subjects gave written informed consent and were screened according to the inclusion- and exclusion criteria.

Period 1

Period 1 title	Overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Arm A

Arm description:

For young patients 18-65 (inclusive) years:

Arm A: 8 cycles of R-CHOP14 plus G-CSF: pegfilgrastim (Neulasta). Rituximab (MabThera) will be administered at day 1 of each cycle

For elderly patients 66-80 (inclusive) years:

Arm A: 6 cycles of R-CHOP14 plus G-CSF: pegfilgrastim (Neulasta). Rituximab (MabThera) will be administered at day 1 of cycle I-V, and at day 1, 15 and 29 of cycle VI

Arm type	Active comparator
Investigational medicinal product name	Prednisone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

18-65 years: 100mg on day -4, -3, -2, -1, 0

66-80 years: 100mg on day -4, -3, -2, -1, 0

Investigational medicinal product name	Cyclophosphamide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solvent for solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

18-65 years: 750mg/m² on day 1

66-80 years: 750mg/m² on day 1

Investigational medicinal product name	Doxorubicin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

18-65 years: 50mg/m² on day 1

66-80 years: 50 mg/m² on day 1

Investigational medicinal product name	Vincristine
Investigational medicinal product code	
Other name	

Pharmaceutical forms	Powder for solution for injection
Routes of administration	Intravenous use
Dosage and administration details:	
18-65 years: 1.4 mg/m ² (max 2mg) on day 1	
66-80 years: 1.4 mg/m ² (max 2mg) on day 1	
Investigational medicinal product name	Prednisone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
18-65 years: 100mg on day 1, 2, 3, 4, 5	
66-80 years: 100mg on day 1, 2, 3, 4, 5	
Investigational medicinal product name	G-CSF
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use
Dosage and administration details:	
18-65 years: 6mg on day 2	
66-80 years: 6mg on day 2	
Investigational medicinal product name	Rituximab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Infusion
Dosage and administration details:	
18-65 years: 375 mg/m ² (max 750mg) on day 1	
66-80 years: 375 mg/m ² (max 750mg) on day 1 (cycle I-V) and on day 1, 15, 29 (cycle VI)	
Arm title	Arm B
Arm description:	
For young patients 18-65 (inclusive) years:	
Arm B: 8 cycles of R-CHOP14 plus G-CSF: pegfilgrastim (Neulasta) with intensification of rituximab (MabThera) during the first 4 cycles. Rituximab will be administered at day 1 and 8 of cycle I-IV and at day 1 of cycle V-VIII	
For elderly patients 66-80 (inclusive) years:	
Arm B: 6 cycles of R-CHOP14 plus G-CSF: pegfilgrastim (Neulasta) with intensification of rituximab (MabThera) during the first 4 cycles. Rituximab will be administered at day 1 and 8 of cycle I-IV, at day 1 of cycle V, and at day 1, 15 and 29 of cycle VI	
Arm type	Experimental
Investigational medicinal product name	Prednisone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
18-65 years: 100mg on day -4, -3, -2, -1, 0	
66-80 years: 100mg on day -4, -3, -2, -1, 0	
Investigational medicinal product name	Cyclophosphamide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solvent for solution for injection
Routes of administration	Intravenous use

Dosage and administration details: 18-65 years: 750mg/m ² on day 1 66-80 years: 750mg/m ² on day 1	
Investigational medicinal product name	Doxorubicin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use
Dosage and administration details: 18-65 years: 50mg/m ² on day 1 66-80 years: 50 mg/m ² on day 1	
Investigational medicinal product name	Vincristine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for injection
Routes of administration	Intravenous use
Dosage and administration details: 18-65 years: 1.4 mg/m ² (max 2mg) on day 1 66-80 years: 1.4 mg/m ² (max 2mg) on day 1	
Investigational medicinal product name	Prednisone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details: 18-65 years: 100mg on day 1, 2, 3, 4, 5 66-80 years: 100mg on day 1, 2, 3, 4, 5	
Investigational medicinal product name	G-CSF
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use
Dosage and administration details: 18-65 years: 6mg on day 2 66-80 years: 6mg on day 2	
Investigational medicinal product name	Rituximab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Infusion
Dosage and administration details: 18-65 years: 375 mg/m ² (max 750mg) on day 1, 8 (cycle I-IV) and on day 1 (cycle V-VIII) 66-80 years: 375 mg/m ² (max 750mg) on day 1, 8 (cycle I-IV) and on day 1, (cycle V) and on day 1, 15, 29 (cycle VI)	

Number of subjects in period 1	Arm A	Arm B
Started	300	300
Completed	176	177
Not completed	124	123
Adverse events, all combined	27	21
Other	38	39
Lost to follow-up	-	1
Lack of efficacy	59	62

Baseline characteristics

Reporting groups

Reporting group title	Overall trial
Reporting group description: -	

Reporting group values	Overall trial	Total	
Number of subjects	600	600	
Age categorical			
Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	301	301	
From 65-84 years	299	299	
85 years and over	0	0	
Age continuous			
Units: years			
median	65		
full range (min-max)	18 to 80	-	
Gender categorical			
Units: Subjects			
Female	291	291	
Male	309	309	

End points

End points reporting groups

Reporting group title	Arm A
Reporting group description:	
For young patients 18-65 (inclusive) years:	
Arm A: 8 cycles of R-CHOP14 plus G-CSF: pegfilgrastim (Neulasta). Rituximab (MabThera) will be administered at day 1 of each cycle	
For elderly patients 66-80 (inclusive) years:	
Arm A: 6 cycles of R-CHOP14 plus G-CSF: pegfilgrastim (Neulasta). Rituximab (MabThera) will be administered at day 1 of cycle I-V, and at day 1, 15 and 29 of cycle VI	
Reporting group title	Arm B
Reporting group description:	
For young patients 18-65 (inclusive) years:	
Arm B: 8 cycles of R-CHOP14 plus G-CSF: pegfilgrastim (Neulasta) with intensification of rituximab (MabThera) during the first 4 cycles. Rituximab will be administered at day 1 and 8 of cycle I-IV and at day 1 of cycle V-VIII	
For elderly patients 66-80 (inclusive) years:	
Arm B: 6 cycles of R-CHOP14 plus G-CSF: pegfilgrastim (Neulasta) with intensification of rituximab (MabThera) during the first 4 cycles. Rituximab will be administered at day 1 and 8 of cycle I-IV, at day 1 of cycle V, and at day 1, 15 and 29 of cycle VI	

Primary: Primary Endpoint

End point title	Primary Endpoint ^[1]
End point description:	
End point type	Primary
End point timeframe:	
See publication	
Notes:	
[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.	
Justification: Statistical analysis has been uploaded in the chart section.	

End point values	Arm A	Arm B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	286	288		
Units: Whole	286	288		

Attachments (see zip file)	List of reported SAE's/saedata84-21Oct2022.pdf List of reported non-SAE's/nonsaedata84-21Oct2022.pdf Statistical data section from publication/HO84 Methods and
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Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All adverse events of Grade 2 or higher, with the exception of progression of disease, occurring during the protocol treatment period will be reported. Adverse events occurring after that period should also be reported if considered related to protocol.

Assessment type	Systematic
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Dictionary used

Dictionary name	CTCAE
Dictionary version	3

Reporting groups

Reporting group title	Arm A
Reporting group description: -	
Reporting group title	Arm B
Reporting group description: -	

Serious adverse events	Arm A	Arm B	
Total subjects affected by serious adverse events			
subjects affected / exposed	151 / 297 (50.84%)	144 / 298 (48.32%)	
number of deaths (all causes)	106	128	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Neoplasms benign, malignant and unspecified	Additional description: All combined, see SAE chart for details		
subjects affected / exposed	6 / 297 (2.02%)	5 / 298 (1.68%)	
occurrences causally related to treatment / all	1 / 7	1 / 5	
deaths causally related to treatment / all	1 / 3	0 / 2	
Vascular disorders			
Vascular disorders	Additional description: All combined, see SAE chart for details		
subjects affected / exposed	9 / 297 (3.03%)	6 / 298 (2.01%)	
occurrences causally related to treatment / all	5 / 9	1 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Surgical and medical procedures			
Surgical and medical procedures	Additional description: All combined, see SAE chart for details		
subjects affected / exposed	2 / 297 (0.67%)	1 / 298 (0.34%)	
occurrences causally related to treatment / all	1 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			

General disorders and administration site conditions	Additional description: All combined, see SAE chart for details		
subjects affected / exposed	24 / 297 (8.08%)	31 / 298 (10.40%)	
occurrences causally related to treatment / all	20 / 27	26 / 34	
deaths causally related to treatment / all	0 / 2	1 / 1	
Immune system disorders	Additional description: All combined, see SAE chart for details		
Immune system disorders	Additional description: All combined, see SAE chart for details		
subjects affected / exposed	2 / 297 (0.67%)	0 / 298 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders	Additional description: All combined, see SAE chart for details		
Reproductive system and breast disorders	Additional description: All combined, see SAE chart for details		
subjects affected / exposed	0 / 297 (0.00%)	1 / 298 (0.34%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders	Additional description: All combined, see SAE chart for details		
Respiratory, thoracic and mediastinal disorders	Additional description: All combined, see SAE chart for details		
subjects affected / exposed	20 / 297 (6.73%)	20 / 298 (6.71%)	
occurrences causally related to treatment / all	8 / 21	14 / 21	
deaths causally related to treatment / all	0 / 1	1 / 1	
Psychiatric disorders	Additional description: All combined, see SAE chart for details		
Psychiatric disorders	Additional description: All combined, see SAE chart for details		
subjects affected / exposed	4 / 297 (1.35%)	4 / 298 (1.34%)	
occurrences causally related to treatment / all	3 / 4	3 / 5	
deaths causally related to treatment / all	0 / 0	1 / 1	
Investigations	Additional description: All combined, see SAE chart for details		
Investigations	Additional description: All combined, see SAE chart for details		
subjects affected / exposed	5 / 297 (1.68%)	6 / 298 (2.01%)	
occurrences causally related to treatment / all	5 / 5	2 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications	Additional description: All combined, see SAE chart for details		
Injury, poisoning and procedural complications	Additional description: All combined, see SAE chart for details		

subjects affected / exposed	0 / 297 (0.00%)	4 / 298 (1.34%)	
occurrences causally related to treatment / all	0 / 0	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Cardiac disorders	Additional description: All combined, see SAE chart for details		
subjects affected / exposed	14 / 297 (4.71%)	15 / 298 (5.03%)	
occurrences causally related to treatment / all	8 / 17	12 / 18	
deaths causally related to treatment / all	1 / 1	3 / 3	
Nervous system disorders			
Nervous system disorders	Additional description: All combined, see SAE chart for details		
subjects affected / exposed	7 / 297 (2.36%)	13 / 298 (4.36%)	
occurrences causally related to treatment / all	4 / 9	8 / 15	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Blood and lymphatic disorders	Additional description: All combined, see SAE chart for details		
subjects affected / exposed	40 / 297 (13.47%)	40 / 298 (13.42%)	
occurrences causally related to treatment / all	57 / 62	51 / 52	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Gastrointestinal disorders	Additional description: All combined, see SAE chart for details		
subjects affected / exposed	36 / 297 (12.12%)	30 / 298 (10.07%)	
occurrences causally related to treatment / all	27 / 45	26 / 39	
deaths causally related to treatment / all	2 / 2	3 / 3	
Hepatobiliary disorders			
Hepatobiliary disorder	Additional description: All combined, see SAE chart for details		
subjects affected / exposed	1 / 297 (0.34%)	0 / 298 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Skin and subcutaneous tissue disorders	Additional description: All combined, see SAE chart for details		
subjects affected / exposed	1 / 297 (0.34%)	0 / 298 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Renal and urinary disorders	Additional description: All combined, see SAE chart for details		

subjects affected / exposed	3 / 297 (1.01%)	0 / 298 (0.00%)	
occurrences causally related to treatment / all	1 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocrine disorders			
Endocrine disorders	Additional description: All combined, see SAE chart for details		
subjects affected / exposed	0 / 297 (0.00%)	1 / 298 (0.34%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Musculoskeletal and connective tissue disorders	Additional description: All combined, see SAE chart for details		
subjects affected / exposed	9 / 297 (3.03%)	2 / 298 (0.67%)	
occurrences causally related to treatment / all	3 / 9	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Infections and infestations	Additional description: All combined, see SAE chart for details		
subjects affected / exposed	52 / 297 (17.51%)	39 / 298 (13.09%)	
occurrences causally related to treatment / all	55 / 66	44 / 51	
deaths causally related to treatment / all	4 / 5	3 / 4	
Metabolism and nutrition disorders			
Metabolism and nutrition disorders	Additional description: All combined, see SAE chart for details		
subjects affected / exposed	7 / 297 (2.36%)	9 / 298 (3.02%)	
occurrences causally related to treatment / all	6 / 9	2 / 9	
deaths causally related to treatment / all	1 / 1	0 / 0	

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Arm A	Arm B	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	286 / 297 (96.30%)	285 / 298 (95.64%)	
Surgical and medical procedures			
Surgery/intra-operative injury	Additional description: All combined, see non-SAE chart for details		
subjects affected / exposed	1 / 297 (0.34%)	1 / 298 (0.34%)	
occurrences (all)	1	1	
General disorders and administration site conditions			

Growth and development subjects affected / exposed occurrences (all)	Additional description: All combined, see non-SAE chart for details		
	2 / 297 (0.67%)	0 / 298 (0.00%)	
	3	0	
Secondary malignancy subjects affected / exposed occurrences (all)	Additional description: All combined, see non-SAE chart for details		
	2 / 297 (0.67%)	2 / 298 (0.67%)	
	2	2	
Syndroms subjects affected / exposed occurrences (all)	Additional description: All combined, see non-SAE chart for details		
	6 / 297 (2.02%)	4 / 298 (1.34%)	
	6	4	
Immune system disorders Allergy/immunology subjects affected / exposed occurrences (all)	Additional description: All combined, see non-SAE chart for details		
	5 / 297 (1.68%)	9 / 298 (3.02%)	
	5	10	
	Additional description: All combined, see non-SAE chart for details		
	107 / 297 (36.03%)	130 / 298 (43.62%)	
	168	191	
Infection subjects affected / exposed occurrences (all)	Additional description: All combined, see non-SAE chart for details		
	96 / 297 (32.32%)	92 / 298 (30.87%)	
	143	139	
Reproductive system and breast disorders Sexual/reproductive function subjects affected / exposed occurrences (all)	Additional description: All combined, see non-SAE chart for details		
	1 / 297 (0.34%)	4 / 298 (1.34%)	
	1	4	
Respiratory, thoracic and mediastinal disorders Pulmonary/upper respiratory subjects affected / exposed occurrences (all)	Additional description: All combined, see non-SAE chart for details		
	34 / 297 (11.45%)	47 / 298 (15.77%)	
	41	69	
Cardiac disorders Cardiac arrhythmia subjects affected / exposed occurrences (all)	Additional description: All combined, see non-SAE chart for details		
	17 / 297 (5.72%)	16 / 298 (5.37%)	
	19	16	
	Additional description: All combined, see non-SAE chart for details		
	7 / 297 (2.36%)	22 / 298 (7.38%)	
	7	27	
Nervous system disorders			

Neurology subjects affected / exposed occurrences (all)	Additional description: All combined, see non-SAE chart for details		
	154 / 297 (51.85%)	174 / 298 (58.39%)	
	208	251	
Pain subjects affected / exposed occurrences (all)	Additional description: All combined, see non-SAE chart for details		
	49 / 297 (16.50%)	47 / 298 (15.77%)	
	73	66	
Blood and lymphatic system disorders			
ANC subjects affected / exposed occurrences (all)	Additional description: All combined, see non-SAE chart for details		
	134 / 297 (45.12%)	155 / 298 (52.01%)	
	329	397	
Anemia subjects affected / exposed occurrences (all)	Additional description: All combined, see non-SAE chart for details		
	217 / 297 (73.06%)	214 / 298 (71.81%)	
	766	742	
Coagulation subjects affected / exposed occurrences (all)	Additional description: All combined, see non-SAE chart for details		
	3 / 297 (1.01%)	4 / 298 (1.34%)	
	3	4	
Hemorrhage/bleeding subjects affected / exposed occurrences (all)	Additional description: All combined, see non-SAE chart for details		
	2 / 297 (0.67%)	4 / 298 (1.34%)	
	2	4	
Lymphatics subjects affected / exposed occurrences (all)	Additional description: All combined, see non-SAE chart for details		
	11 / 297 (3.70%)	13 / 298 (4.36%)	
	11	16	
Platelets subjects affected / exposed occurrences (all)	Additional description: All combined, see non-SAE chart for details		
	64 / 297 (21.55%)	71 / 298 (23.83%)	
	154	133	
Vascular subjects affected / exposed occurrences (all)	Additional description: All combined, see non-SAE chart for details		
	28 / 297 (9.43%)	21 / 298 (7.05%)	
	28	23	
WBC subjects affected / exposed occurrences (all)	Additional description: All combined, see non-SAE chart for details		
	170 / 297 (57.24%)	194 / 298 (65.10%)	
	456	592	
Ear and labyrinth disorders			
Auditory/ear subjects affected / exposed occurrences (all)	Additional description: All combined, see non-SAE chart for details		
	3 / 297 (1.01%)	6 / 298 (2.01%)	
	3	6	
Eye disorders			

Ocular/visual subjects affected / exposed occurrences (all)	Additional description: All combined, see non-SAE chart for details		
	8 / 297 (2.69%) 8	15 / 298 (5.03%) 18	
Gastrointestinal disorders Gastrointestinal subjects affected / exposed occurrences (all)	Additional description: All combined, see non-SAE chart for details		
	119 / 297 (40.07%) 222	123 / 298 (41.28%) 220	
Skin and subcutaneous tissue disorders Dermatology/Skin subjects affected / exposed occurrences (all)	Additional description: All combined, see non-SAE chart for details		
	74 / 297 (24.92%) 98	59 / 298 (19.80%) 73	
Renal and urinary disorders Renal/genitourinary subjects affected / exposed occurrences (all)	Additional description: All combined, see non-SAE chart for details		
	16 / 297 (5.39%) 19	19 / 298 (6.38%) 23	
Endocrine disorders Endocrine subjects affected / exposed occurrences (all)	Additional description: All combined, see non-SAE chart for details		
	10 / 297 (3.37%) 10	10 / 298 (3.36%) 12	
	Additional description: All combined, see non-SAE chart for details		
	Hepatobiliary/pancreas subjects affected / exposed occurrences (all)	0 / 297 (0.00%) 0	1 / 298 (0.34%) 1
Musculoskeletal and connective tissue disorders Musculoskeletal/soft tissue subjects affected / exposed occurrences (all)	Additional description: All combined, see non-SAE chart for details		
	18 / 297 (6.06%) 21	25 / 298 (8.39%) 32	
Metabolism and nutrition disorders Metabolic/laboratory subjects affected / exposed occurrences (all)	Additional description: All combined, see non-SAE chart for details		
	38 / 297 (12.79%) 78	39 / 298 (13.09%) 86	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
16 July 2009	Change in the number of R-CHOP14 cycles for the elderly patient group aged 66-80 years from 8 cycles to 6 cycles. The number of rituximab administrations will remain the same; the rituximab administrations at cycle 6 will be given at days 1, 15 and 29. This change is based on the publication of the RICOVER-60 trial by the German High Grade Lymphoma Study Group. Inclusion of young patients aged 18-65 years with an age-adjusted IPI score of 1-3. Changes and clarification of PET scan (review) procedures Administrative corrections (i.e. new phone and fax numbers Erasmus MC, change of statistician)

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported