



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 |
|-----------------------|------------|

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 |
|-------------------|---|

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 |
|-----------------------------------|---|

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 |
|-----------------|------------|

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%) | 15 / 298 (5.03%) | |
| | 8 | 18 | |
| Gastrointestinal disorders Gastrointestinal subjects affected / exposed occurrences (all) | Additional description: All combined, see non-SAE chart for details | | |
| | 119 / 297 (40.07%) | 123 / 298 (41.28%) | |
| | 222 | 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%) | 59 / 298 (19.80%) | |
| | 98 | 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 / 298 (6.38%) | |
| | 19 | 23 | |
| Endocrine disorders Endocrine subjects affected / exposed occurrences (all) Hepatobiliary/pancreas subjects affected / exposed occurrences (all) | Additional description: All combined, see non-SAE chart for details | | |
| | 10 / 297 (3.37%) | 10 / 298 (3.36%) | |
| | 10 | 12 | |
| | Additional description: All combined, see non-SAE chart for details | | |
| | 0 / 297 (0.00%) | 1 / 298 (0.34%) | |
| | 0 | 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%) | 25 / 298 (8.39%) | |
| | 21 | 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%) | 39 / 298 (13.09%) | |
| | 78 | 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