



Clinical trial results:

Targeted BEACOPP variants in patients with newly diagnosed advanced classical Hodgkin Lymphoma

Summary

| | |
|--------------------------|-----------------|
| EudraCT number | 2011-005082-21 |
| Trial protocol | DE |
| Global end of trial date | 15 October 2016 |

Results information

| | |
|--------------------------------|---------------|
| Result version number | v1 (current) |
| This version publication date | 08 April 2020 |
| First version publication date | 08 April 2020 |

Trial information

Trial identification

| | |
|-----------------------|----------------|
| Sponsor protocol code | Uni-Koeln-1491 |
|-----------------------|----------------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT01569204 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | University of Cologne |
| Sponsor organisation address | Albertus Magnus-Platz, Köln, Germany, 50923 |
| Public contact | Trial Coordination Center of the German Hodgkin Study Group (GHSG), German Hodgkin Study Group (GHSG), 0049 22147888200, ghsg@uk-koeln.de |
| Scientific contact | Trial Coordination Center of the German Hodgkin Study Group (GHSG), German Hodgkin Study Group (GHSG), 0049 22147888200, ghsg@uk-koeln.de |

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 | 03 August 2017 |
| Is this the analysis of the primary completion data? | No |

| | |
|----------------------------------|-----------------|
| Global end of trial reached? | Yes |
| Global end of trial date | 15 October 2016 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

The aim of the trial was to implement the antibody-drug conjugate brentuximab vedotin into the first-line treatment of patients with advanced classical Hodgkin lymphoma. The combination of targeted drugs such as brentuximab vedotin with conventional chemotherapy might allow reducing the doses of classical chemotherapeutic substances without compromising treatment efficacy. One major goal of this trial is to generate a novel BEACOPP-based treatment protocol to serve as comparator in the next GHSG treatment optimization trial for patients with newly diagnosed advanced classical Hodgkin lymphoma (HD21).

Protection of trial subjects:

Written informed consent before study entry, frequent DMC monitoring, hospitalization during first cycle recommended, mandatory prophylaxis during chemotherapy, dose reduction strategy in case of adverse events

Background therapy: -

Evidence for comparator: -

| | |
|---|-----------------|
| Actual start date of recruitment | 26 October 2012 |
| Long term follow-up planned | Yes |
| Long term follow-up rationale | Efficacy |
| Long term follow-up duration | 2 Years |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|--------------|
| Country: Number of subjects enrolled | Germany: 104 |
| Worldwide total number of subjects | 104 |
| EEA total number of subjects | 104 |

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) | 104 |
| From 65 to 84 years | 0 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

Between 26 October 2012 and 15 May 2014, a total of 104 patients with newly diagnosed advanced-stage Hodgkin lymphoma were recruited in 20 trial sites in Germany.

Pre-assignment

Screening details:

Main inclusion criteria: previously untreated classical Hodgkin lymphoma in advanced stages, normal organ function, life expectancy >3 months. Main exclusion criteria: severe pulmonary or cardiac disease, HIV positivity, WBC count <3x10⁹/L, platelet count <100x10⁹/L, bilirubin >2 mg/dL, AST or ALT >100 U/L, pregnancy or lactation, ECOG >2.

Period 1

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

Arms

| | |
|------------------------------|---------|
| Are arms mutually exclusive? | Yes |
| Arm title | BrECAPP |

Arm description:

Six 21-day cycles of BrECAPP

| | |
|--|--|
| Arm type | Experimental |
| Investigational medicinal product name | Brentuximab vedotin |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Powder for concentrate for solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

1.8 mg/kg body weight on day 1 of each 21-day cycle, calculated with the patient's actual weight up to 100 kg.

Patients with a weight of more than 100 kg receive the maximum dose of 180 mg of brentuximab vedotin.

| | |
|--|---------------------------------------|
| Investigational medicinal product name | Etoposide |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Concentrate for solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

200 mg/m² body surface area on days 2-4 of each 21-day cycle. The maximum upper limit for the calculation of chemotherapy is fixed at a body surface of 2.1 m², even if the calculated body surface exceeds this.

Etoposide phosphate may be applied as etoposide-equivalent dose: 113 mg etoposide phosphate is equivalent to 100 mg etoposide. This difference is due to different molecular weights.

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

Dosage and administration details:

1250 mg/m² body surface area on day 2 of each 21-day cycle. The maximum upper limit for the calculation of chemotherapy is fixed at a body surface of 2.1 m², even if the calculated body surface exceeds this.

Uromitexan according to current standards is obligatory. The patient should ingest 2.5 liters of fluid on the day of administration.

| | |
|--|---------------------------------------|
| Investigational medicinal product name | Doxorubicin |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Concentrate for solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

35 mg/m² body surface area on day 2 of each 21-day cycle. The maximum upper limit for the calculation of chemotherapy is fixed at a body surface of 2.1 m², even if the calculated body surface exceeds this.

| | |
|--|---------------|
| Investigational medicinal product name | Procarbazine |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Capsule, hard |
| Routes of administration | Oral use |

Dosage and administration details:

100 mg/m² body surface area on days 2-8 of each 21-day cycle. The maximum upper limit for the calculation of chemotherapy is fixed at a body surface of 2.1 m², even if the calculated body surface exceeds this.

| | |
|--|------------|
| Investigational medicinal product name | Prednisone |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

40 mg/m² body surface area on days 2-15 of each 21-day cycle. The maximum upper limit for the calculation of chemotherapy is fixed at a body surface of 2.1 m², even if the calculated body surface exceeds this.

| | |
|------------------|---------|
| Arm title | BrECADD |
|------------------|---------|

Arm description:

Six 21-day cycles of BrECADD

| | |
|--|--|
| Arm type | Experimental |
| Investigational medicinal product name | Brentuximab vedotin |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Powder for concentrate for solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

1.8 mg/kg body weight on day 1 of each 21-day cycle, calculated with the patient's actual weight up to 100 kg.
Patients with a weight of more than 100 kg receive the maximum dose of 180 mg of brentuximab vedotin.

| | |
|--|---------------------------------------|
| Investigational medicinal product name | Etoposide |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Concentrate for solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

150 mg/m² body surface area on days 2-4 of each 21-day cycle. The maximum upper limit for the calculation of chemotherapy is fixed at a body surface of 2.1 m², even if the calculated body surface exceeds this.

Etoposide phosphate may be applied as etoposide-equivalent dose: 113 mg etoposide phosphate is equivalent to 100 mg etoposide. This difference is due to different molecular weights.

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

Dosage and administration details:

1250 mg/m² body surface area on day 2 of each 21-day cycle. The maximum upper limit for the calculation of chemotherapy is fixed at a body surface of 2.1 m², even if the calculated body surface exceeds this.

Uromitexan according to current standards is obligatory. The patient should ingest 2.5 liters of fluid on the day of administration.

| | |
|--|---------------------------------------|
| Investigational medicinal product name | Doxorubicin |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Concentrate for solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

40 mg/m² body surface area on day 2 of each 21-day cycle. The maximum upper limit for the calculation of chemotherapy is fixed at a body surface of 2.1 m², even if the calculated body surface exceeds this.

| | |
|--|---|
| Investigational medicinal product name | Dacarbazine |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Powder for solution for infusion, Powder for solution for injection |
| Routes of administration | Intravenous use |

Dosage and administration details:

250 mg/m² body surface area on days 3-4 of each 21-day cycle. The maximum upper limit for the calculation of chemotherapy is fixed at a body surface of 2.1 m², even if the calculated body surface exceeds this.

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

Dosage and administration details:

40 mg/m² body surface area on days 2-5 of each 21-day cycle. The maximum upper limit for the calculation of chemotherapy is fixed at a body surface of 2.1 m², even if the calculated body surface exceeds this.

| Number of subjects in period 1 | BrECAPP | BrECADD |
|--------------------------------|---------|---------|
| Started | 52 | 52 |
| Started randomized treatment | 50 | 52 |
| Completed | 48 | 52 |
| Not completed | 4 | 0 |
| Consent withdrawn by subject | 1 | - |
| Physician decision | 1 | - |
| Adverse event, non-fatal | 1 | - |
| Violation of I/E criteria | 1 | - |

Baseline characteristics

Reporting groups

| | |
|-----------------------|---------|
| Reporting group title | BrECAPP |
|-----------------------|---------|

Reporting group description:

Six 21-day cycles of BrECAPP

| | |
|-----------------------|---------|
| Reporting group title | BrECADD |
|-----------------------|---------|

Reporting group description:

Six 21-day cycles of BrECADD

| Reporting group values | BrECAPP | BrECADD | Total |
|--|----------|----------|-------|
| Number of subjects | 52 | 52 | 104 |
| Age categorical | | | |
| Units: Subjects | | | |
| In utero | 0 | 0 | 0 |
| Preterm newborn infants (gestational age < 37 wks) | 0 | 0 | 0 |
| Newborns (0-27 days) | 0 | 0 | 0 |
| Infants and toddlers (28 days-23 months) | 0 | 0 | 0 |
| Children (2-11 years) | 0 | 0 | 0 |
| Adolescents (12-17 years) | 0 | 0 | 0 |
| Adults (18-64 years) | 52 | 52 | 104 |
| From 65-84 years | 0 | 0 | 0 |
| 85 years and over | 0 | 0 | 0 |
| Age continuous | | | |
| Units: years | | | |
| median | 29.5 | 28.5 | |
| full range (min-max) | 18 to 60 | 18 to 59 | - |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 21 | 20 | 41 |
| Male | 31 | 32 | 63 |
| Ann Arbor stage | | | |
| Units: Subjects | | | |
| IIB | 10 | 8 | 18 |
| IIIA | 15 | 9 | 24 |
| IIIB | 8 | 12 | 20 |
| IVA | 5 | 5 | 10 |
| IVB | 14 | 18 | 32 |
| Large mediastinal mass | | | |
| Units: Subjects | | | |
| No | 31 | 31 | 62 |
| Yes | 21 | 21 | 42 |
| Extranodal disease | | | |
| Units: Subjects | | | |
| No | 41 | 37 | 78 |
| Yes | 11 | 15 | 26 |
| At least 3 nodal areas involved | | | |

| | | | |
|--------------------------------|----|----|----|
| Units: Subjects | | | |
| No | 8 | 10 | 18 |
| Yes | 44 | 42 | 86 |
| Elevated ESR | | | |
| Units: Subjects | | | |
| No | 21 | 13 | 34 |
| Yes | 31 | 39 | 70 |
| International prognostic score | | | |
| Units: Subjects | | | |
| 0-2 | 35 | 33 | 68 |
| 3-7 | 17 | 19 | 36 |
| WHO activity index | | | |
| Units: Subjects | | | |
| 0 (fully active) | 23 | 18 | 41 |
| 1 (able to do light work) | 27 | 34 | 61 |
| 2 (unable to do light work) | 2 | 0 | 2 |

End points

End points reporting groups

| | |
|--|---------|
| Reporting group title | BrECAPP |
| Reporting group description: Six 21-day cycles of BrECAPP | |
| Reporting group title | BrECADD |
| Reporting group description: Six 21-day cycles of BrECADD | |

Primary: Complete response to chemotherapy

| | |
|---|--|
| End point title | Complete response to chemotherapy ^[1] |
| End point description: We defined complete response as the achievement of either complete remission, partial remission with residual lymphoma less than 2.5 cm, or PET negativity (Deauville score 1-3) after chemotherapy, according to central review. Both arms were analyzed separately. Assuming a complete response in 90% in each arm, we would be able to test the null hypothesis "complete response rate is 70% or lower" with a one-sided significance level of 2.5% and a power of 90% per arm. We calculated one-sided 97.5% Clopper-Pearson exact binominal CIs for observed responses in order to exclude the benchmark of 70%. | |
| End point type | Primary |
| End point timeframe: The CT-based restaging was scheduled within the last week of the last chemotherapy cycle. In patients with residual lymphoma of 2.5 cm or larger, a PET scan was to be performed at least 3 weeks after the end of the last chemotherapy cycle. | |

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: This is a phase-2 study with 2 regimens to be evaluated independently. There is no arm comparison but 2 single-arm analyses, which cannot be entered in the system.

Analyses were as follows:

The null hypothesis H0 "Complete response rate ≤ 70%" was tested versus a one-sided alternative via a one-sided 97.5% CI per arm.

The lower confidence limits were 73% and 77%, respectively, and thus both above the efficacy benchmark.

In conclusion, both null hypotheses could be rejected.

| End point values | BrECAPP | BrECADD | | |
|-----------------------------|-------------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 49 ^[2] | 52 | | |
| Units: subjects | | | | |
| Yes | 42 | 46 | | |
| No | 7 | 6 | | |

Notes:

[2] - 3/52 patients excluded: 2 did not receive any study treatment, 1 violated I/E criteria

Statistical analyses

No statistical analyses for this end point

Primary: Complete remission

| | |
|-----------------|-----------------------------------|
| End point title | Complete remission ^[3] |
|-----------------|-----------------------------------|

End point description:

We defined complete remission as complete remission after completion of study treatment or, in case of residual lymphoma after completion of study treatment, freedom from progression without additional treatment for at least 6 months.

Both arms were analyzed separately.

The co-primary efficacy endpoint was only to be tested if the null hypothesis for complete response could not be rejected.

Assuming a complete remission rate of 95% for each arm, we would be able to test the null hypothesis "complete remission rate is 80% or lower" with a one-sided significance level of 2.5% and a power of 90% per arm. To this end, one-sided 97.5% Clopper-Pearson exact binominal CIs for observed remissions would be calculated in order to exclude the benchmark of 80%.

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Within 6 months after end of study treatment

Notes:

[3] - 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: The co-primary efficacy endpoint "complete remission" was only to be tested if the null hypothesis for the primary endpoint "complete response" could not be rejected. As the null hypothesis for "complete response" could be rejected for both regimens, a confirmative test of "complete remission" was not done.

| End point values | BrECAPP | BrECADD | | |
|-----------------------------|-------------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 49 ^[4] | 52 | | |
| Units: patients | | | | |
| Yes | 46 | 46 | | |
| No | 3 | 6 | | |

Notes:

[4] - 3/52 patients excluded: 2 did not receive any study treatment, 1 violated I/E criteria

Statistical analyses

No statistical analyses for this end point

Secondary: Progression-free survival

| | |
|-----------------|---------------------------|
| End point title | Progression-free survival |
|-----------------|---------------------------|

End point description:

Progression-free survival is defined as time from randomization to disease progression or death from any cause and censored at the date of last tumor assessment for patients alive without progressive disease.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

18-months progression-free survival will be reported.

| End point values | BrECAPP | BrECADD | | |
|----------------------------------|-------------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 49 ^[5] | 52 | | |
| Units: percent | | | | |
| number (confidence interval 95%) | 95 (85 to 100) | 89 (77 to 100) | | |

Notes:

[5] - 3/52 patients excluded: 2 did not receive any study treatment, 1 violated I/E criteria

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All events up to 30 days after end of treatment had to be reported. Events that occurred later than 30 days after the end of treatment had to be reported if causality was rated at least as "possible".

Adverse event reporting additional description:

AEs were assessed on the therapy administration CRFs. SAEs were additionally assessed on specific forms. SAEs may thus be reported twice; non-serious and SAEs might include duplicate events and do not add up to a total number of AEs.

Hospitalization in connection with therapeutic measures of the trial and deaths from HL were no SAEs in this trial.

| | |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

Dictionary used

| | |
|--------------------|--------|
| Dictionary name | MedDRA |
| Dictionary version | 10.1 |

Reporting groups

| | |
|-----------------------|---------|
| Reporting group title | BrECAPP |
|-----------------------|---------|

Reporting group description:

Six 21-day cycles of BrECAPP

| | |
|-----------------------|---------|
| Reporting group title | BrECADD |
|-----------------------|---------|

Reporting group description:

Six 21-day cycles of BrECADD

| Serious adverse events | BrECAPP | BrECADD | |
|---|------------------|------------------|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 21 / 50 (42.00%) | 18 / 52 (34.62%) | |
| number of deaths (all causes) | 0 | 2 | |
| number of deaths resulting from adverse events | 0 | 0 | |
| Investigations | | | |
| Investigations | | | |
| subjects affected / exposed | 5 / 50 (10.00%) | 0 / 52 (0.00%) | |
| occurrences causally related to treatment / all | 4 / 5 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vascular disorders | | | |
| Vascular disorders | | | |
| subjects affected / exposed | 0 / 50 (0.00%) | 2 / 52 (3.85%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Surgical and medical procedures | | | |
| Surgical and medical procedures | | | |

| | | | |
|--|-----------------|-----------------|--|
| subjects affected / exposed | 1 / 50 (2.00%) | 0 / 52 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nervous system disorders | | | |
| Nervous system disorders | | | |
| subjects affected / exposed | 1 / 50 (2.00%) | 0 / 52 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Blood and lymphatic system disorders | | | |
| Blood and lymphatic system disorders | | | |
| subjects affected / exposed | 7 / 50 (14.00%) | 9 / 52 (17.31%) | |
| occurrences causally related to treatment / all | 9 / 9 | 11 / 11 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| General disorders and administration site conditions | | | |
| General disorders and administration site conditions | | | |
| subjects affected / exposed | 4 / 50 (8.00%) | 3 / 52 (5.77%) | |
| occurrences causally related to treatment / all | 4 / 4 | 4 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Immune system disorders | | | |
| Immune system disorders | | | |
| subjects affected / exposed | 1 / 50 (2.00%) | 0 / 52 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal disorders | | | |
| Gastrointestinal disorders | | | |
| subjects affected / exposed | 3 / 50 (6.00%) | 0 / 52 (0.00%) | |
| occurrences causally related to treatment / all | 3 / 3 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Psychiatric disorders | | | |
| Psychiatric disorders | | | |
| subjects affected / exposed | 1 / 50 (2.00%) | 0 / 52 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Musculoskeletal and connective tissue disorders | | | |
| Musculoskeletal and connective tissue disorders | | | |

| | | | |
|---|-----------------|-----------------|--|
| Musculoskeletal and connective tissue disorders | | | |
| subjects affected / exposed | 1 / 50 (2.00%) | 1 / 52 (1.92%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infections and infestations | | | |
| Infections and infestations | | | |
| subjects affected / exposed | 6 / 50 (12.00%) | 7 / 52 (13.46%) | |
| occurrences causally related to treatment / all | 6 / 6 | 7 / 7 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Metabolism and nutrition disorders | | | |
| Metabolism and nutrition disorders | | | |
| subjects affected / exposed | 1 / 50 (2.00%) | 0 / 52 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 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 | BrECAPP | BrECADD | |
|---|-------------------|------------------|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 50 / 50 (100.00%) | 51 / 52 (98.08%) | |
| Nervous system disorders | | | |
| Nervous system disorders, sensory | | | |
| alternative dictionary used: NCI CTCAE 4.0 | | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 16 / 50 (32.00%) | 18 / 52 (34.62%) | |
| occurrences (all) | 37 | 41 | |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| alternative dictionary used: NCI CTCAE 4.0 | | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 47 / 50 (94.00%) | 50 / 52 (96.15%) | |
| occurrences (all) | 234 | 251 | |
| Thrombocytopenia | | | |
| alternative dictionary used: NCI CTCAE 4.0 | | | |
| alternative assessment type: Non-systematic | | | |

| | | | |
|--|---|--|--|
| <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Leukopenia</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>45 / 50 (90.00%)</p> <p>190</p> <p>48 / 50 (96.00%)</p> <p>232</p> | <p>43 / 52 (82.69%)</p> <p>180</p> <p>46 / 52 (88.46%)</p> <p>222</p> | |
| <p>General disorders and administration site conditions</p> <p>Drug fever</p> <p>alternative dictionary used: NCI CTCAE 4.0</p> <p>alternative assessment type: Non-systematic</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>5 / 50 (10.00%)</p> <p>7</p> | <p>2 / 52 (3.85%)</p> <p>3</p> | |
| <p>Gastrointestinal disorders</p> <p>Nausea or vomiting</p> <p>alternative dictionary used: NCI CTCAE 4.0</p> <p>alternative assessment type: Non-systematic</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Mucositis</p> <p>alternative dictionary used: NCI CTCAE 4.0</p> <p>alternative assessment type: Non-systematic</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Gastrointestinal tract disorder</p> <p>alternative dictionary used: NCI CTCAE 4.0</p> <p>alternative assessment type: Non-systematic</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>22 / 50 (44.00%)</p> <p>46</p> <p>12 / 50 (24.00%)</p> <p>14</p> <p>14 / 50 (28.00%)</p> <p>18</p> | <p>19 / 52 (36.54%)</p> <p>32</p> <p>9 / 52 (17.31%)</p> <p>11</p> <p>16 / 52 (30.77%)</p> <p>18</p> | |
| <p>Respiratory, thoracic and mediastinal disorders</p> <p>Respiratory tract disorders</p> <p>alternative dictionary used: NCI CTCAE 4.0</p> <p>alternative assessment type: Non-systematic</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>5 / 50 (10.00%)</p> <p>6</p> | <p>8 / 52 (15.38%)</p> <p>13</p> | |
| Hepatobiliary disorders | | | |

| | | | |
|--|------------------------|------------------------|--|
| Hepatobiliary disorders alternative dictionary used: NCI CTCAE 4.0 alternative assessment type: Non-systematic subjects affected / exposed ^[1] occurrences (all) | 8 / 48 (16.67%) 26 | 7 / 44 (15.91%) 26 | |
| Skin and subcutaneous tissue disorders Skin disorders alternative dictionary used: NCI CTCAE 4.0 alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) | 5 / 50 (10.00%) 5 | 2 / 52 (3.85%) 2 | |
| Infections and infestations Infection alternative dictionary used: NCI CTCAE 4.0 alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) | 11 / 50 (22.00%) 14 | 13 / 52 (25.00%) 21 | |

Notes:

[1] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: Documentation of hepatobiliary disorders was introduced with an amendment of the case report form concerning acute AEs 3 months after start of recruitment. Thus, a small number of patients have no documented information about these AEs.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|-------------------|---|
| 18 December 2012 | Updated procedures for cases of peripheral neuropathy and PML, updated contact information for reporting of SAEs and pregnancies, added information on product complaints, reduction of obligatory pause between prephase and start of treatment from 7 to 2 days |
| 16 September 2013 | Addition of adverse reaction "acute pancreatitis" to the ICF following important drug warning for brentuximab vedotin, updated IB |
| 04 February 2014 | Adaption of the reference level for the evaluation of PET for radiotherapy recommendation |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

<http://www.ncbi.nlm.nih.gov/pubmed/29133014>