



Clinical trial results:

Phase-IIb-Study to Evaluate the Effect of a Neoadjuvant Chemotherapy with Docetaxel, Epirubicine and Cyclophosphamide (TEC) in Patients with primary HER-2 neu Negative Mammacarcinoma

Summary

| | |
|--------------------------|----------------|
| EudraCT number | 2008-003064-19 |
| Trial protocol | DE |
| Global end of trial date | 07 July 2016 |

Results information

| | |
|-----------------------------------|--|
| Result version number | v1 (current) |
| This version publication date | 02 August 2020 |
| First version publication date | 02 August 2020 |
| Summary attachment (see zip file) | Study report (NeoTEC_Ergebnisbericht_Behörde_final_2.0_2020-03- |

Trial information

Trial identification

| | |
|-----------------------|--------|
| Sponsor protocol code | NeoTEC |
|-----------------------|--------|

Additional study identifiers

| | |
|------------------------------------|--------------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | - |
| WHO universal trial number (UTN) | - |
| Other trial identifiers | DRKS: DRKS00000162 |

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | University of Leipzig |
| Sponsor organisation address | Ritterstr. 26, Leipzig, Germany, 04109 |
| Public contact | Coordinating Investigator, Coordinating Investigator, St. Elisabeth-Krankenhaus Leipzig, Brustzentrum, Leipzig, 0049 341 39 59 493, Dagmar.Langanke@ek-leipzig.de |
| Scientific contact | Coordinating Investigator, St. Elisabeth-Krankenhaus Leipzig, Brustzentrum, Leipzig, 0049 341 39 59 493, Dagmar.Langanke@ek-leipzig.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 | 30 December 2016 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 07 July 2016 |
| Global end of trial reached? | Yes |
| Global end of trial date | 07 July 2016 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

Estimation of the complete remission rate of invasive tumor cells in the breast confirmed by histological examinations, at surgery.

The treatment of the mammacarcinoma consists in this study normally on 6 chemotherapy cycles of the combination Docetaxel, Epirubicine and Cyclophosphamide (TEC-therapy). Followed by the surgery of the carcinoma, which takes place on day 28 after the last chemotherapy application, at the latest. An evaluation of the response of the treatment is performed after 2 and 4 cycles by use of palpation and mamma sonography. In case of complete remission, partial remission and no change the patient receives further two TEC cycles. In case of progress under therapy the surgery is immediately performed.

Protection of trial subjects:

During the course of the trial, every patient was monitored closely concerning the described safety parameters. Besides the documentation of adverse events , this encompasses the following parameters:

- physical examinations
- Performancestatus (ECOG, Karnofsky Index)
- Labory parameters

Background therapy: -

Evidence for comparator: -

| | |
|---|---------------|
| Actual start date of recruitment | 19 March 2009 |
| Long term follow-up planned | Yes |
| Long term follow-up rationale | Efficacy |
| Long term follow-up duration | 5 Years |
| Independent data monitoring committee (IDMC) involvement? | No |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|--------------|
| Country: Number of subjects enrolled | Germany: 152 |
| Worldwide total number of subjects | 152 |
| EEA total number of subjects | 152 |

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) | 124 |
| From 65 to 84 years | 28 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

Between March 2009 and February 2011, 152 patients were recruited to the NeoTEC study in 15 Trial sites in Germany. The trial contained one arm only.

Pre-assignment

Screening details:

Eligibility for the study if:

- Women with histologically verified mamma carcinoma (assessment of estrogen and progesterone receptors, grading, negative HER-2/neu status)
- All receptor-negative mamma carcinoma starting from cT1c, all receptor-positive mamma carcinoma starting from cT3, cT4 includes inflammatory mamma carcinoma

Period 1

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

Arms

| | |
|-----------|-----------|
| Arm title | Study arm |
|-----------|-----------|

Arm description:

Chemotherapy combination of Docetaxel, Epirubicine and Cyclophosphamide with breast preserving surgery

| | |
|--|------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Docetaxel |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Intravenous use |

Dosage and administration details:

Docetaxel 75 mg/m² every 3 weeks for 6 cycles

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

Dosage and administration details:

Epirubicin 75 mg/m² every 3 weeks for 6 cycles

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

Dosage and administration details:

500 mg/m² every 3 weeks for 6 cycles

| Number of subjects in period 1 | Study arm |
|--------------------------------|-----------|
| Started | 152 |
| Completed | 148 |
| Not completed | 4 |
| Adverse event, serious fatal | 2 |
| Consent withdrawn by subject | 1 |
| Adverse event, non-fatal | 1 |

Period 2

| | |
|------------------------------|----------------|
| Period 2 title | Follow-up |
| Is this the baseline period? | No |
| Allocation method | Not applicable |
| Blinding used | Not blinded |

Arms

| | |
|---|-----------|
| Arm title | Follow-up |
| Arm description: | |
| 5 years Follow-up after study treatment | |
| Arm type | Follow-up |
| No investigational medicinal product assigned in this arm | |

| Number of subjects in period 2 | Follow-up |
|--|-----------|
| Started | 148 |
| Completed | 126 |
| Not completed | 22 |
| change to another treating institution | 4 |
| removal to another city/contry | 2 |
| Lost to follow-up | 15 |
| termination due to psychosocial problems | 1 |

Baseline characteristics

Reporting groups

| | |
|-----------------------|------------------|
| Reporting group title | treatment period |
|-----------------------|------------------|

Reporting group description: -

| Reporting group values | treatment period | Total | |
|---|------------------|-------|--|
| Number of subjects | 152 | 152 | |
| Age categorical | | | |
| Units: Subjects | | | |
| In utero | | 0 | |
| Preterm newborn infants (gestational age < 37 wks) | | 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) | | 0 | |
| From 65-84 years | | 0 | |
| 85 years and over | | 0 | |
| Age continuous | | | |
| Units: years | | | |
| arithmetic mean | 52.7 | | |
| standard deviation | ± 11.2 | - | |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 152 | 152 | |
| Male | 0 | 0 | |
| ECOG | | | |
| Units: Subjects | | | |
| full activity | 125 | 125 | |
| restricted activity | 23 | 23 | |
| self-supply possible | 3 | 3 | |
| no data | 1 | 1 | |
| concomitant disease/s | | | |
| Units: Subjects | | | |
| yes | 79 | 79 | |
| no | 73 | 73 | |
| type of tumor | | | |
| Units: Subjects | | | |
| invasive-ductal | 134 | 134 | |
| invasice-lobular | 12 | 12 | |
| other | 5 | 5 | |
| no data | 1 | 1 | |
| receptor status | | | |
| Units: Subjects | | | |
| ER and PR-positive | 55 | 55 | |
| one of both positive | 96 | 96 | |

| | | | |
|--------------------------|--------|----|--|
| no data | 1 | 1 | |
| TNM stage (sono) | | | |
| Units: Subjects | | | |
| T1N0M0 | 4 | 4 | |
| T1N1M0 | 9 | 9 | |
| T2N0M0 | 28 | 28 | |
| T2N1M0 | 68 | 68 | |
| T2N2M0 | 2 | 2 | |
| T2N3M0 | 2 | 2 | |
| T3N0M0 | 5 | 5 | |
| T3N1M0 | 9 | 9 | |
| T4N0M0 | 11 | 11 | |
| T4N1M0 | 12 | 12 | |
| T4N2M0 | 1 | 1 | |
| no data | 1 | 1 | |
| menopause | | | |
| Units: Subjects | | | |
| yes | 85 | 85 | |
| no | 66 | 66 | |
| not available | 1 | 1 | |
| Body Surface Area | | | |
| Units: m ² | | | |
| arithmetic mean | 1.81 | | |
| standard deviation | ± 0.19 | - | |
| BMI | | | |
| Units: kg/m ² | | | |
| arithmetic mean | 28.3 | | |
| standard deviation | ± 6.0 | - | |
| tumor size (sono) | | | |
| Units: mm ² | | | |
| arithmetic mean | 1459 | | |
| standard deviation | ± 6837 | - | |

Subject analysis sets

| | |
|----------------------------|---------------|
| Subject analysis set title | FAS |
| Subject analysis set type | Full analysis |

Subject analysis set description:

Since this study was one-armed, the overall description of all patients is the only useful information

| | | | |
|---|-----|--|--|
| Reporting group values | FAS | | |
| Number of subjects | 152 | | |
| Age categorical | | | |
| Units: Subjects | | | |
| In utero | | | |
| Preterm newborn infants (gestational age < 37 wks) | | | |
| Newborns (0-27 days) | | | |
| Infants and toddlers (28 days-23 months) | | | |
| Children (2-11 years) | | | |
| Adolescents (12-17 years) | | | |

| | | | |
|---|--|--|--|
| Adults (18-64 years) From 65-84 years 85 years and over | | | |
| Age continuous Units: years arithmetic mean standard deviation | 52.7 ± 11.2 | | |
| Gender categorical Units: Subjects | | | |
| Female Male | 152 0 | | |
| ECOG Units: Subjects | | | |
| full activity restricted activity self-supply possible no data | 125 23 3 1 | | |
| concomitant disease/s Units: Subjects | | | |
| yes no | 79 73 | | |
| type of tumor Units: Subjects | | | |
| invasive-ductal invasice-lobular other no data | 134 12 5 1 | | |
| receptor status Units: Subjects | | | |
| ER and PR-positive one of both positive no data | 55 96 1 | | |
| TNM stage (sono) Units: Subjects | | | |
| T1N0M0 T1N1M0 T2N0M0 T2N1M0 T2N2M0 T2N3M0 T3N0M0 T3N1M0 T4N0M0 T4N1M0 T4N2M0 no data | 4 9 28 68 2 2 5 9 11 12 1 1 | | |
| menopause Units: Subjects | | | |
| yes no not available | 85 66 1 | | |

| | | | |
|--|----------------|--|--|
| Body Surface Area Units: m ² arithmetic mean standard deviation | 1.81 ± 0.19 | | |
| BMI Units: kg/m ² arithmetic mean standard deviation | 28.3 ± 6.0 | | |
| tumor size (sono) Units: mm ² arithmetic mean standard deviation | 1459 ± 6837 | | |

End points

End points reporting groups

| | |
|---|---------------|
| Reporting group title | Study arm |
| Reporting group description: Chemotherapy combination of Docetaxel, Epirubicine and Cyclophosphamide with breast preserving surgery | |
| Reporting group title | Follow-up |
| Reporting group description: 5 years Follow-up after study treatment | |
| Subject analysis set title | FAS |
| Subject analysis set type | Full analysis |
| Subject analysis set description: Since this study was one-armed, the overall description of all patients is the only useful information | |

Primary: pCR b inv

| | |
|--|--------------------------|
| End point title | pCR b inv ^[1] |
| End point description: no microscopic findings of vital invasive tumor cells in resected tissues post surgery; in breast only, lymph nodes not considered | |
| End point type | Primary |
| End point timeframe: assessed after all cycles of TEC regimen applied and the following surgery | |
| 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: Due to the single-armed design no statistical analysis but the interval estimate of the end points (primary and secondary) are provided. | |

| End point values | FAS | | | |
|-----------------------------|----------------------|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 152 | | | |
| Units: subjects | | | | |
| complete remission | 49 | | | |
| incomplete remission | 103 | | | |

| | |
|-----------------------------------|------------------------------|
| Attachments (see zip file) | DRKS-Meldg_NeoTEC-1armig.pdf |
|-----------------------------------|------------------------------|

Statistical analyses

No statistical analyses for this end point

Secondary: pCR inv

| | |
|--|-----------|
| End point title | pCR inv |
| End point description: neither in breast nor in axillary lymphnodes invasive rests of tumor; results of pathology; patients with premature EoT did not reach CR | |
| End point type | Secondary |

End point timeframe:
after all cycles of TEC and surgery (if applicable) = end of treatment

| | | | | |
|-----------------------------|----------------------|--|--|--|
| End point values | FAS | | | |
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 152 | | | |
| Units: subjects | | | | |
| premature EoT | 4 | | | |
| no rests | 40 | | | |
| rests | 108 | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: pCR

| | |
|--|-----------|
| End point title | pCR |
| End point description: | |
| neither invasive nor noninvasive rests of tumor (results of pathology) | |
| End point type | Secondary |
| End point timeframe: | |
| after EoT | |

| | | | | |
|-----------------------------|----------------------|--|--|--|
| End point values | FAS | | | |
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 152 | | | |
| Units: subjects | | | | |
| premature EoT | 4 | | | |
| no rests | 34 | | | |
| rests | 114 | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: cCR

| | |
|------------------------|-----------|
| End point title | cCR |
| End point description: | |
| clinical response | |
| End point type | Secondary |

End point timeframe:
after EoT

| End point values | FAS | | | |
|-----------------------------|----------------------|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 150 ^[2] | | | |
| Units: subjects | | | | |
| complete remission | 25 | | | |
| partial remission | 99 | | | |
| minimal response | 9 | | | |
| no change | 7 | | | |
| progressive disease | 5 | | | |
| premature EoT | 5 | | | |

Notes:

[2] - no data in 2 patients

Statistical analyses

No statistical analyses for this end point

Secondary: Regression grade (Sinn 1994)

| | |
|---|------------------------------|
| End point title | Regression grade (Sinn 1994) |
| End point description: acc. to Sinn HP et al. Geburtshilfe und Frauenheilkunde 1994:54; 552-558. | |
| End point type | Secondary |
| End point timeframe: after EoT | |

| End point values | FAS | | | |
|-----------------------------|----------------------|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 148 | | | |
| Units: subjects | | | | |
| grade 3/4 | 43 | | | |
| grade<3 | 105 | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: EFS

| | |
|-----------------|-----|
| End point title | EFS |
|-----------------|-----|

End point description:

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

End point timeframe:

until the end of Study (60 months of FUP)

| End point values | FAS | | | |
|-----------------------------|----------------------|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 152 | | | |
| Units: subjects | | | | |
| no event | 110 | | | |
| relapse/ metastasis/ death | 42 | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: OS

| | |
|-----------------|----|
| End point title | OS |
|-----------------|----|

End point description:

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

End point timeframe:

until EoS (60 months of FUP)

| End point values | FAS | | | |
|-----------------------------|----------------------|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 152 | | | |
| Units: subjects | | | | |
| survived | 125 | | | |
| deceased | 27 | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: breast-preserving surgery

| | |
|-----------------|---------------------------|
| End point title | breast-preserving surgery |
|-----------------|---------------------------|

End point description:

| | |
|-----------------------------------|-----------|
| End point type | Secondary |
| End point timeframe: after EoT | |

| End point values | FAS | | | |
|-----------------------------|----------------------|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 152 | | | |
| Units: subjects | | | | |
| yes | 107 | | | |
| no | 41 | | | |
| premature EoT w/o surgery | 4 | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Treatment-associated toxicity of WHO grade >2

| | |
|---|---|
| End point title | Treatment-associated toxicity of WHO grade >2 |
| End point description: | |
| End point type | Secondary |
| End point timeframe: until the end of (S)AE reporting period | |

| End point values | FAS | | | |
|-----------------------------|----------------------|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 152 | | | |
| Units: subjects | | | | |
| Yes | 110 | | | |
| No | 42 | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: SAE occurred

| | |
|------------------------|--------------|
| End point title | SAE occurred |
| End point description: | |
| End point type | Secondary |

End point timeframe:
until the end of (S)AE reporting period

| | | | | |
|-----------------------------|----------------------|--|--|--|
| End point values | FAS | | | |
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 152 | | | |
| Units: subjects | | | | |
| yes | 28 | | | |
| no | 124 | | | |

Statistical analyses

No statistical analyses for this end point

Other pre-specified: tox-associated premature EoT

| | |
|-----------------|------------------------------|
| End point title | tox-associated premature EoT |
|-----------------|------------------------------|

End point description:

| | |
|----------------|---------------------|
| End point type | Other pre-specified |
|----------------|---------------------|

End point timeframe:
during chemotherapy (max. 6 cycles)

| | | | | |
|-----------------------------|----------------------|--|--|--|
| End point values | FAS | | | |
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 152 | | | |
| Units: subjects | | | | |
| Yes | 6 | | | |
| no | 146 | | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From first chemotherapy cycle up to 8 weeks after Administration of the last neoadjuvant chemotherapy cycle

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

Dictionary used

| | |
|--------------------|--------|
| Dictionary name | MedDRA |
| Dictionary version | 16.0 |

Reporting groups

| | |
|-----------------------|--------|
| Reporting group title | Safety |
|-----------------------|--------|

Reporting group description:

This set of patients is identical to the FAS.

The number of death refers to the entire period of observation (see sEP overall survival).

| Serious adverse events | Safety | | |
|--|-------------------|--|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 28 / 152 (18.42%) | | |
| number of deaths (all causes) | 27 | | |
| number of deaths resulting from adverse events | 2 | | |
| Vascular disorders | | | |
| Subclavian vein thrombosis | | | |
| subjects affected / exposed | 1 / 152 (0.66%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Venous thrombosis limb | | | |
| subjects affected / exposed | 1 / 152 (0.66%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Haematoma | | | |
| subjects affected / exposed | 1 / 152 (0.66%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| General disorders and administration site conditions | | | |
| Chest pain | | | |

| | | | |
|---|-----------------|--|--|
| subjects affected / exposed | 1 / 152 (0.66%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Device dislocation | | | |
| subjects affected / exposed | 1 / 152 (0.66%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Fatigue | | | |
| subjects affected / exposed | 1 / 152 (0.66%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| General physical health deterioration | | | |
| subjects affected / exposed | 1 / 152 (0.66%) | | |
| occurrences causally related to treatment / all | 5 / 5 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Mucosal inflammation | | | |
| subjects affected / exposed | 1 / 152 (0.66%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Multi-organ failure | | | |
| subjects affected / exposed | 1 / 152 (0.66%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 1 / 1 | | |
| Pyrexia | | | |
| subjects affected / exposed | 1 / 152 (0.66%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Immune system disorders | | | |
| Anaphylactic reaction | | | |
| subjects affected / exposed | 1 / 152 (0.66%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Respiratory, thoracic and mediastinal disorders | | | |

| | | | |
|---|-----------------|--|--|
| Cough | | | |
| subjects affected / exposed | 2 / 152 (1.32%) | | |
| occurrences causally related to treatment / all | 1 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Dyspnoea | | | |
| subjects affected / exposed | 2 / 152 (1.32%) | | |
| occurrences causally related to treatment / all | 2 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Investigations | | | |
| Haemoglobin decreased | | | |
| subjects affected / exposed | 1 / 152 (0.66%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Injury, poisoning and procedural complications | | | |
| Craniocerebral injury | | | |
| subjects affected / exposed | 1 / 152 (0.66%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cardiac disorders | | | |
| Cardiomyopathy | | | |
| subjects affected / exposed | 1 / 152 (0.66%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Blood and lymphatic system disorders | | | |
| Agranulocytosis | | | |
| subjects affected / exposed | 1 / 152 (0.66%) | | |
| occurrences causally related to treatment / all | 3 / 3 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Anaemia | | | |
| subjects affected / exposed | 5 / 152 (3.29%) | | |
| occurrences causally related to treatment / all | 6 / 6 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Febrile neutropenia | | | |

| | | | |
|---|------------------|--|--|
| subjects affected / exposed | 3 / 152 (1.97%) | | |
| occurrences causally related to treatment / all | 3 / 3 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Granulocytopenia | | | |
| subjects affected / exposed | 1 / 152 (0.66%) | | |
| occurrences causally related to treatment / all | 2 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Leukopenia | | | |
| subjects affected / exposed | 11 / 152 (7.24%) | | |
| occurrences causally related to treatment / all | 20 / 20 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Neutropenia | | | |
| subjects affected / exposed | 7 / 152 (4.61%) | | |
| occurrences causally related to treatment / all | 10 / 10 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pancytopenia | | | |
| subjects affected / exposed | 1 / 152 (0.66%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Thrombocytopenia | | | |
| subjects affected / exposed | 4 / 152 (2.63%) | | |
| occurrences causally related to treatment / all | 4 / 4 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gastrointestinal disorders | | | |
| Diarrhoea | | | |
| subjects affected / exposed | 4 / 152 (2.63%) | | |
| occurrences causally related to treatment / all | 4 / 4 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Enteritis | | | |
| subjects affected / exposed | 1 / 152 (0.66%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Nausea | | | |

| | | | |
|---|-----------------|--|--|
| subjects affected / exposed | 6 / 152 (3.95%) | | |
| occurrences causally related to treatment / all | 6 / 6 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Vomiting | | | |
| subjects affected / exposed | 4 / 152 (2.63%) | | |
| occurrences causally related to treatment / all | 4 / 4 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Renal and urinary disorders | | | |
| Renal failure | | | |
| subjects affected / exposed | 1 / 152 (0.66%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 1 / 152 (0.66%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Bone pain | | | |
| subjects affected / exposed | 1 / 152 (0.66%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Infections and infestations | | | |
| Abdominal wall abscess | | | |
| subjects affected / exposed | 1 / 152 (0.66%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Abscess | | | |
| subjects affected / exposed | 1 / 152 (0.66%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Infection | | | |
| subjects affected / exposed | 3 / 152 (1.97%) | | |
| occurrences causally related to treatment / all | 2 / 3 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

| | | | |
|---|-----------------|--|--|
| Influenza | | | |
| subjects affected / exposed | 1 / 152 (0.66%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Localised infection | | | |
| subjects affected / exposed | 1 / 152 (0.66%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Mastitis | | | |
| subjects affected / exposed | 1 / 152 (0.66%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pneumonia | | | |
| subjects affected / exposed | 1 / 152 (0.66%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Sepsis | | | |
| subjects affected / exposed | 2 / 152 (1.32%) | | |
| occurrences causally related to treatment / all | 2 / 2 | | |
| deaths causally related to treatment / all | 1 / 1 | | |
| Metabolism and nutrition disorders | | | |
| Dehydration | | | |
| subjects affected / exposed | 1 / 152 (0.66%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hypocalcaemia | | | |
| subjects affected / exposed | 1 / 152 (0.66%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hypokalaemia | | | |
| subjects affected / exposed | 1 / 152 (0.66%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

Frequency threshold for reporting non-serious adverse events: 4 %

| Non-serious adverse events | Safety | | |
|---|--------------------|--|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 110 / 152 (72.37%) | | |
| Vascular disorders | | | |
| Hot flush | | | |
| subjects affected / exposed | 6 / 152 (3.95%) | | |
| occurrences (all) | 12 | | |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 7 / 152 (4.61%) | | |
| occurrences (all) | 9 | | |
| Granulocytopenia | | | |
| subjects affected / exposed | 40 / 152 (26.32%) | | |
| occurrences (all) | 113 | | |
| Leukopenia | | | |
| subjects affected / exposed | 64 / 152 (42.11%) | | |
| occurrences (all) | 202 | | |
| Thrombocytopenia | | | |
| subjects affected / exposed | 8 / 152 (5.26%) | | |
| occurrences (all) | 15 | | |
| General disorders and administration site conditions | | | |
| Fatigue | | | |
| subjects affected / exposed | 11 / 152 (7.24%) | | |
| occurrences (all) | 20 | | |
| Mucosal inflammation | | | |
| subjects affected / exposed | 7 / 152 (4.61%) | | |
| occurrences (all) | 15 | | |
| Gastrointestinal disorders | | | |
| Intestinal obstruction | | | |
| subjects affected / exposed | 4 / 152 (2.63%) | | |
| occurrences (all) | 9 | | |
| Nausea | | | |
| subjects affected / exposed | 7 / 152 (4.61%) | | |
| occurrences (all) | 9 | | |

| | | | |
|--|-------------------|--|--|
| Skin and subcutaneous tissue disorders | | | |
| Alopecia | | | |
| subjects affected / exposed | 35 / 152 (23.03%) | | |
| occurrences (all) | 114 | | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported