



Clinical trial results:

Phase II Study Evaluating the Efficacy and Tolerance of Bevacizumab (AVASTIN®) in HER2- Inflammatory Breast Cancer

Summary

| | |
|--------------------------|-------------------|
| EudraCT number | 2008-001807-53 |
| Trial protocol | FR |
| Global end of trial date | 26 September 2019 |

Results information

| | |
|--------------------------------|------------------|
| Result version number | v1 (current) |
| This version publication date | 05 November 2021 |
| First version publication date | 05 November 2021 |

Trial information

Trial identification

| | |
|-----------------------|----------------|
| Sponsor protocol code | PACS 09 / 0802 |
|-----------------------|----------------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT00820547 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | UNICANCER |
| Sponsor organisation address | 101 rue de Tolbiac, Paris, France, 75013 |
| Public contact | Nourredine AIT-RAHMOUNE, UNICANCER, 33 1 71 93 67 04 , n.ait-rahmoune@unicancer.fr |
| Scientific contact | Nourredine AIT-RAHMOUNE, UNICANCER, 33 1 71 93 67 04 , n.ait-rahmoune@unicancer.fr |

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 | 13 March 2020 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 26 September 2019 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

To evaluate the impact of concomitantly administering bevacizumab and neo-adjuvant chemotherapy, based on anthracyclines and taxanes, on the complete pathological response rate using mastectomy in patients with inflammatory breast cancer not overexpressing HER2.

Protection of trial subjects:

In order to ensure the protection of the rights, safety and well-being of trial subjects, this clinical trial was conducted in accordance with the Declaration of Helsinki (1964) and subsequent amendments, ICH Good Clinical Practice Guidelines (CPMP/ICH/135/95), the European Directive (2001/20/CE) and the applicable local regulatory requirements and laws.

Background therapy: -

Evidence for comparator: -

| | |
|---|------------------|
| Actual start date of recruitment | 19 January 2009 |
| Long term follow-up planned | Yes |
| Long term follow-up rationale | Safety, Efficacy |
| Long term follow-up duration | 8 Years |
| Independent data monitoring committee (IDMC) involvement? | No |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|-------------|
| Country: Number of subjects enrolled | France: 100 |
| Worldwide total number of subjects | 100 |
| EEA total number of subjects | 100 |

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) | 88 |

| | |
|---------------------|----|
| From 65 to 84 years | 12 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

This was national, multicentric phase II, open-label, non randomized, non controlled study, evaluating bevacizumab in the treatment of women >18 years old with HER2-negative inflammatory breast cancer. Patients were recruited in the study from 19-Jan-2009 to 08-Sep-2010.

Pre-assignment

Screening details:

The study consisted of a screening phase of up to 30 days before treatment initiation to establish eligibility and document baseline measurements, a treatment phase (28-day treatment cycles; 52 weeks), a long-term follow-up to monitor progression-free survival, relapse-free survival, overall survival, and safety.

Period 1

| | |
|------------------------------|--------------------------------|
| Period 1 title | Overall Trial (overall period) |
| Is this the baseline period? | Yes |
| Allocation method | Not applicable |
| Blinding used | Not blinded |

Arms

| | |
|-----------|-------------|
| Arm title | Bevacizumab |
|-----------|-------------|

Arm description:

patients received 15 mg/kg bevacizumab every 3 weeks for 54 weeks (in 2 phases) or until disease progression, unacceptable toxicity, or patient refusal.

| | |
|--|---|
| Arm type | Experimental |
| Investigational medicinal product name | Bevacizumab |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Concentrate and solvent for solution for infusion |
| Routes of administration | Infusion |

Dosage and administration details:

Bevacizumab was administered at the dose of 15 mg/kg (IV infusion over 90 minutes [+/- 15 minutes] for the first administration and over 60 minutes [+/- 10 minutes] for the second administration if good tolerance, over 30 minutes [+/- 10 minutes] thereafter for the next administrations if good tolerance) every 3 weeks. Bevacizumab was administered during 8 cycles in neoadjuvant treatment (concomitant of FEC100 then docetaxel before surgery) then 10 cycles in adjuvant cycles (concomitant of radiotherapy and hormone therapy). The average treatment duration with bevacizumab was 54 weeks (18 injections).

| | |
|---------------------------------------|-------------|
| Number of subjects in period 1 | Bevacizumab |
| Started | 100 |
| Completed | 100 |

Baseline characteristics

Reporting groups

| | |
|--------------------------------|---------------|
| Reporting group title | Overall Trial |
| Reporting group description: - | |

| Reporting group values | Overall Trial | Total | |
|---|---------------|-------|--|
| Number of subjects | 100 | 100 | |
| 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) | 88 | 88 | |
| From 65-84 years | 12 | 12 | |
| 85 years and over | 0 | 0 | |
| Age continuous | | | |
| Units: years | | | |
| median | 49 | | |
| full range (min-max) | 21 to 75 | - | |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 100 | 100 | |
| Male | 0 | 0 | |
| ECOG | | | |
| Units: Subjects | | | |
| ECOG 0 | 88 | 88 | |
| ECOG 1 | 12 | 12 | |
| Weight | | | |
| Units: kilogram(s) | | | |
| median | 70 | | |
| full range (min-max) | 45 to 117 | - | |
| size | | | |
| Units: meter | | | |
| median | 1.62 | | |
| full range (min-max) | 1.45 to 1.84 | - | |

Subject analysis sets

| | |
|---|--------------------|
| Subject analysis set title | ITT population |
| Subject analysis set type | Intention-to-treat |
| Subject analysis set description: | |
| All patients included in the study, whether or not they may have received one treatment dose. | |

| | | | |
|---|----------------|--|--|
| Reporting group values | ITT population | | |
| Number of subjects | 100 | | |
| 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) | 88 | | |
| From 65-84 years | 12 | | |
| 85 years and over | 0 | | |
| Age continuous Units: years | | | |
| median | 49 | | |
| full range (min-max) | 21 to 75 | | |
| Gender categorical Units: Subjects | | | |
| Female | 100 | | |
| Male | 0 | | |
| ECOG Units: Subjects | | | |
| ECOG 0 | 88 | | |
| ECOG 1 | 12 | | |
| Weight Units: kilogram(s) | | | |
| median | 70 | | |
| full range (min-max) | 45 to 117 | | |
| size Units: meter | | | |
| median | 1.62 | | |
| full range (min-max) | 1.45 to 1.84 | | |

End points

End points reporting groups

| | |
|--|--------------------|
| Reporting group title | Bevacizumab |
| Reporting group description: patients received 15 mg/kg bevacizumab every 3 weeks for 54 weeks (in 2 phases) or until disease progression, unacceptable toxicity, or patient refusal. | |
| Subject analysis set title | ITT population |
| Subject analysis set type | Intention-to-treat |
| Subject analysis set description: All patients included in the study, whether or not they may have received one treatment dose. | |

Primary: Complete pathological response

| | |
|--|---|
| End point title | Complete pathological response ^[1] |
| End point description: The primary endpoint was the complete pathological response on the operative specimen, after mastectomy, according to Sataloff criteria. | |
| End point type | Primary |
| End point timeframe: After mastectomy | |
| 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: The primary endpoint was pathological complete response in breast and axillary lymph nodes after neoadjuvant treatment. The decision rule was that if fewer than 22 (22%) pathological complete responses were seen, the regimen would be regarded as insufficiently active. | |

| End point values | Bevacizumab | | | |
|----------------------------------|-------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 100 | | | |
| Units: percent | | | | |
| number (confidence interval 95%) | 19 (11.8 to 28.1) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Progression-free survival rate

| | |
|--|--------------------------------|
| End point title | Progression-free survival rate |
| End point description: Progression-free survival at 3 and 5 years. Progression is defined as any local or regional relapse or any distant metastatic relapse, or any contralateral relapse, or any second cancer (except baso-cellular carcinoma, melanoma, in situ carcinoma of the cervix, in situ colon carcinoma, or in situ lobular carcinoma of the breast), or death of any cause. | |
| End point type | Secondary |
| End point timeframe: 3 and 5 years | |

| | | | | |
|----------------------------------|-----------------|--|--|--|
| End point values | Bevacizumab | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 100 | | | |
| Units: percent | | | | |
| number (confidence interval 95%) | | | | |
| 3-year | 56 (46 to 65) | | | |
| 5-year | 45 (35 to 55) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Relapse-free interval

| | |
|---|-----------------------|
| End point title | Relapse-free interval |
| End point description: The Relapse-free interval (RFI) at 3 and 5 years was calculated based on the date of patient inclusion until the date of relapse. Relapse is defined as any local, regional, or distant metastasis disease recurrence | |
| End point type | Secondary |
| End point timeframe: 3 and 5 years | |

| | | | | |
|----------------------------------|-----------------|--|--|--|
| End point values | Bevacizumab | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 100 | | | |
| Units: percent | | | | |
| number (confidence interval 95%) | | | | |
| 3-year | 98 (92 to 99) | | | |
| 5-year | 93 (84 to 97) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Overall survival

| | |
|--|------------------|
| End point title | Overall survival |
| End point description: Overall survival rate at 3 and 5 years. The time interval to death was calculated from the date of patient inclusion until the date of death | |
| End point type | Secondary |

End point timeframe:

3 and 5 years

| | | | | |
|----------------------------------|-----------------|--|--|--|
| End point values | Bevacizumab | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 100 | | | |
| Units: percent | | | | |
| number (confidence interval 95%) | | | | |
| 3-year | 75 (66 to 83) | | | |
| 5-year | 59 (48 to 68) | | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Overall period of the study (up to 8 years after first study intake)

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

Dictionary used

| | |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

| | |
|--------------------|------|
| Dictionary version | 22.1 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|-------------|
| Reporting group title | Bevacizumab |
|-----------------------|-------------|

Reporting group description:

Patients received 15 mg/kg bevacizumab every 3 weeks for 54 weeks (in 2 phases) or until disease progression, unacceptable toxicity, or patient refusal.

| Serious adverse events | Bevacizumab | | |
|---|-------------------|--|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 51 / 100 (51.00%) | | |
| number of deaths (all causes) | 25 | | |
| number of deaths resulting from adverse events | 0 | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Liver metastases | | | |
| subjects affected / exposed | 1 / 100 (1.00%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Neoplasm of uncertain behaviour of meninges | | | |
| subjects affected / exposed | 1 / 100 (1.00%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Vascular disorders | | | |
| Thrombosis venous | | | |
| subjects affected / exposed | 1 / 100 (1.00%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Catheter thrombosis | | | |

| | | | |
|--|-----------------|--|--|
| subjects affected / exposed | 1 / 100 (1.00%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Thrombosis cerebral vein | | | |
| subjects affected / exposed | 1 / 100 (1.00%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Surgical and medical procedures | | | |
| Abscess breast drainage | | | |
| subjects affected / exposed | 1 / 100 (1.00%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Abscess management | | | |
| subjects affected / exposed | 1 / 100 (1.00%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| General disorders and administration site conditions | | | |
| Asthenia | | | |
| subjects affected / exposed | 1 / 100 (1.00%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Fever | | | |
| subjects affected / exposed | 2 / 100 (2.00%) | | |
| occurrences causally related to treatment / all | 1 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Malaise | | | |
| subjects affected / exposed | 1 / 100 (1.00%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Malaise and Fatigue | | | |
| subjects affected / exposed | 1 / 100 (1.00%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

| | | | |
|---|-----------------|--|--|
| Wound healing delayed subjects affected / exposed | 1 / 100 (1.00%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Wound healing disturbance of subjects affected / exposed | 1 / 100 (1.00%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Immune system disorders | | | |
| Allergy to chemicals subjects affected / exposed | 1 / 100 (1.00%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Drug hypersensitivity subjects affected / exposed | 1 / 100 (1.00%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Dyspnea exacerbated subjects affected / exposed | 1 / 100 (1.00%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Respiratory insufficiency subjects affected / exposed | 1 / 100 (1.00%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Psychiatric disorders | | | |
| Depression subjects affected / exposed | 1 / 100 (1.00%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Melancholia | | | |

| | | | |
|---|-----------------|--|--|
| subjects affected / exposed | 1 / 100 (1.00%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Investigations | | | |
| Colonoscopy | | | |
| subjects affected / exposed | 1 / 100 (1.00%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Injury, poisoning and procedural complications | | | |
| Bone fracture (not spontaneous) | | | |
| subjects affected / exposed | 1 / 100 (1.00%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Device related infection | | | |
| subjects affected / exposed | 1 / 100 (1.00%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Skin injury | | | |
| subjects affected / exposed | 1 / 100 (1.00%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Wound surface unfolded | | | |
| subjects affected / exposed | 1 / 100 (1.00%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cardiac disorders | | | |
| Ventricular dysfunction | | | |
| subjects affected / exposed | 1 / 100 (1.00%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Heart failure NYHA class IV | | | |
| subjects affected / exposed | 1 / 100 (1.00%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

| | | | |
|---|-------------------|--|--|
| Blood and lymphatic system disorders | | | |
| Anemia | | | |
| subjects affected / exposed | 2 / 100 (2.00%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Febrile aplasia | | | |
| subjects affected / exposed | 9 / 100 (9.00%) | | |
| occurrences causally related to treatment / all | 1 / 11 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Febrile neutropenia | | | |
| subjects affected / exposed | 18 / 100 (18.00%) | | |
| occurrences causally related to treatment / all | 9 / 22 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Lymphocele | | | |
| subjects affected / exposed | 1 / 100 (1.00%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Neutropenia | | | |
| subjects affected / exposed | 2 / 100 (2.00%) | | |
| occurrences causally related to treatment / all | 2 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gastrointestinal disorders | | | |
| Anal fistula | | | |
| subjects affected / exposed | 1 / 100 (1.00%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Anal ulcer | | | |
| subjects affected / exposed | 1 / 100 (1.00%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Appendicitis perforated | | | |
| subjects affected / exposed | 1 / 100 (1.00%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

| | | | |
|---|-----------------|--|--|
| Colitis | | | |
| subjects affected / exposed | 1 / 100 (1.00%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Mucositis oral | | | |
| subjects affected / exposed | 7 / 100 (7.00%) | | |
| occurrences causally related to treatment / all | 5 / 7 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Tooth fracture | | | |
| subjects affected / exposed | 1 / 100 (1.00%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Skin and subcutaneous tissue disorders | | | |
| Cellulitis staphylococcal | | | |
| subjects affected / exposed | 1 / 100 (1.00%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Renal and urinary disorders | | | |
| Infection urinary tract | | | |
| subjects affected / exposed | 1 / 100 (1.00%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Proteinuria | | | |
| subjects affected / exposed | 1 / 100 (1.00%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Infections and infestations | | | |
| Anal abscess | | | |
| subjects affected / exposed | 2 / 100 (2.00%) | | |
| occurrences causally related to treatment / all | 2 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| axillary abscess | | | |

| | | | |
|--|-----------------|--|--|
| subjects affected / exposed | 1 / 100 (1.00%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Infection | | | |
| subjects affected / exposed | 1 / 100 (1.00%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| infection urinary tract | | | |
| subjects affected / exposed | 1 / 100 (1.00%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| local infection of skin and subcutaneous tissue, other | | | |
| subjects affected / exposed | 1 / 100 (1.00%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Wound infection | | | |
| subjects affected / exposed | 1 / 100 (1.00%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| infection wound bacterial | | | |
| subjects affected / exposed | 1 / 100 (1.00%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Metabolism and nutrition disorders | | | |
| Potassium deficiency | | | |
| subjects affected / exposed | 1 / 100 (1.00%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

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

| Non-serious adverse events | Bevacizumab | | |
|---|------------------------|--|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 100 / 100 (100.00%) | | |
| Vascular disorders | | | |
| Hot flush | | | |
| subjects affected / exposed | 29 / 100 (29.00%) | | |
| occurrences (all) | 71 | | |
| Hypertension | | | |
| subjects affected / exposed | 42 / 100 (42.00%) | | |
| occurrences (all) | 131 | | |
| Lymphocele | | | |
| subjects affected / exposed | 12 / 100 (12.00%) | | |
| occurrences (all) | 20 | | |
| Surgical and medical procedures | | | |
| Radioepidermitis | | | |
| subjects affected / exposed | 14 / 100 (14.00%) | | |
| occurrences (all) | 18 | | |
| General disorders and administration site conditions | | | |
| Wound healing | | | |
| subjects affected / exposed | 24 / 100 (24.00%) | | |
| occurrences (all) | 39 | | |
| Asthenia | | | |
| subjects affected / exposed | 100 / 100 (100.00%) | | |
| occurrences (all) | 401 | | |
| Fever | | | |
| subjects affected / exposed | 67 / 100 (67.00%) | | |
| occurrences (all) | 87 | | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Cough | | | |
| subjects affected / exposed | 14 / 100 (14.00%) | | |
| occurrences (all) | 20 | | |
| Dyspnoea | | | |
| subjects affected / exposed | 16 / 100 (16.00%) | | |
| occurrences (all) | 24 | | |
| Rhinitis | | | |

| | | | |
|--|--|--|--|
| subjects affected / exposed occurrences (all) | 36 / 100 (36.00%) 65 | | |
| Psychiatric disorders Insomnia subjects affected / exposed occurrences (all) | 6 / 100 (6.00%) 16 | | |
| Investigations Abnormal liver function test subjects affected / exposed occurrences (all) | 18 / 100 (18.00%) 52 | | |
| Cardiac disorders Cardiovascular toxicity subjects affected / exposed occurrences (all) | 9 / 100 (9.00%) 13 | | |
| Nervous system disorders Dysgeusia subjects affected / exposed occurrences (all) Headache subjects affected / exposed occurrences (all) Peripheral neuropathy subjects affected / exposed occurrences (all) | 25 / 100 (25.00%) 59 53 / 100 (53.00%) 113 65 / 100 (65.00%) 137 | | |
| Blood and lymphatic system disorders Febrile neutropenia subjects affected / exposed occurrences (all) Anemia subjects affected / exposed occurrences (all) Neutropenia subjects affected / exposed occurrences (all) Thrombocytopenia subjects affected / exposed occurrences (all) | 36 / 100 (36.00%) 52 92 / 100 (92.00%) 329 98 / 100 (98.00%) 288 35 / 100 (35.00%) 50 | | |

| | | | |
|--|------------------------|--|--|
| Eye disorders | | | |
| Conjunctivitis | | | |
| subjects affected / exposed | 45 / 100 (45.00%) | | |
| occurrences (all) | 100 | | |
| Gastrointestinal disorders | | | |
| Constipation | | | |
| subjects affected / exposed | 24 / 100 (24.00%) | | |
| occurrences (all) | 48 | | |
| Diarrhea | | | |
| subjects affected / exposed | 43 / 100 (43.00%) | | |
| occurrences (all) | 59 | | |
| Dysphagia | | | |
| subjects affected / exposed | 12 / 100 (12.00%) | | |
| occurrences (all) | 16 | | |
| Haemorrhoids | | | |
| subjects affected / exposed | 23 / 100 (23.00%) | | |
| occurrences (all) | 37 | | |
| Mucositis | | | |
| subjects affected / exposed | 100 / 100 (100.00%) | | |
| occurrences (all) | 352 | | |
| Nausea | | | |
| subjects affected / exposed | 97 / 100 (97.00%) | | |
| occurrences (all) | 272 | | |
| Pyrosis | | | |
| subjects affected / exposed | 9 / 100 (9.00%) | | |
| occurrences (all) | 10 | | |
| Xerostomia | | | |
| subjects affected / exposed | 7 / 100 (7.00%) | | |
| occurrences (all) | 13 | | |
| Skin and subcutaneous tissue disorders | | | |
| Alopecia | | | |
| subjects affected / exposed | 100 / 100 (100.00%) | | |
| occurrences (all) | 642 | | |
| Hand-foot syndrome | | | |
| subjects affected / exposed | 11 / 100 (11.00%) | | |
| occurrences (all) | 15 | | |

| | | | |
|--|--|--|--|
| Nail toxicity subjects affected / exposed occurrences (all) | 32 / 100 (32.00%) 67 | | |
| Skin toxicity subjects affected / exposed occurrences (all) | 93 / 100 (93.00%) 182 | | |
| Renal and urinary disorders Proteinuria subjects affected / exposed occurrences (all) | 59 / 100 (59.00%) 159 | | |
| Musculoskeletal and connective tissue disorders Musculoskeletal pain subjects affected / exposed occurrences (all) | 100 / 100 (100.00%) 277 | | |
| Infections and infestations Infection subjects affected / exposed occurrences (all) Mycosis subjects affected / exposed occurrences (all) | 74 / 100 (74.00%) 96 14 / 100 (14.00%) 20 | | |
| Metabolism and nutrition disorders Anorexia subjects affected / exposed occurrences (all) Oedema subjects affected / exposed occurrences (all) | 15 / 100 (15.00%) 23 23 / 100 (23.00%) 29 | | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|------------------|---|
| 10 December 2008 | In the first version of the protocol, post surgery bevacizumab was reintroduced concomittant with the radiotherapy. It was then decided to reintroduced bevacizumab at the same time of radiotherapy or at the latest during the week following the last radiotherapy session. Collection of a new blood sample was added before the initiation of cycle 5 to assess the correlation of CTC/CEC and proteomic with chemotherapy treatments (anthracycline and taxane). |
| 29 March 2010 | Modification of the procedure for the reporting of SAE grade 4 neutropenia without fever. A new paragraph was added to the protocol to specify that these particular SAE do not necessitate a declaration within the time delay specified by the article R.1123-47 of the Public Health Code. Due to their expected character they were reported to the Sponsor via toxicity report forms collected in the study CRF. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported