



Clinical trial results:

Assessment of histopathological response to combination chemotherapy with Oxaliplatin, Irinotecan, Fluorouracil and Bevacizumab in patients with peritoneal metastasis from colorectal cancer (CARCINOSIS).

Summary

| | |
|--------------------------|------------------|
| EudraCT number | 2015-002917-30 |
| Trial protocol | AT |
| Global end of trial date | 16 December 2019 |

Results information

| | |
|--------------------------------|-------------------|
| Result version number | v1 (current) |
| This version publication date | 05 September 2020 |
| First version publication date | 05 September 2020 |

Trial information

Trial identification

| | |
|-----------------------|------------|
| Sponsor protocol code | CARCINOSIS |
|-----------------------|------------|

Additional study identifiers

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

Notes:

Sponsors

| | |
|------------------------------|--|
| Sponsor organisation name | Medical University of Vienna |
| Sponsor organisation address | Währinger Gürtel 18-20, Vienn, Austria, 1090 |
| Public contact | Department of Surgery, Medical University of Vienna, 0043 14040056210, thomas.bachleitner-hofmann@meduniwien.ac.at |
| Scientific contact | Department of Surgery, Medical University of Vienna, 0043 14040056210, thomas.bachleitner-hofmann@meduniwien.ac.at |

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 | 10 January 2019 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 10 January 2019 |
| Global end of trial reached? | Yes |
| Global end of trial date | 16 December 2019 |
| Was the trial ended prematurely? | Yes |

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the study is to prospectively assess the histopathological response to neoadjuvant chemotherapy with FOLFOXIRI + bevacizumab in peritoneal tumor deposits of 30 patients with pCCRC by determining the % of viable tumor cells (vtc) in the resected specimen after neoadjuvant chemotherapy using standard pathology.

Protection of trial subjects:

For reasons of comprehensive view, in the following section a list of adverse events from a clinical trial investigating the FOLFOXIRI + Bevacizumab treatment regimen in patients with metastatic colorectal cancer is provided. The complete listings are included in the Summary of Product Characteristics of Fluorouracil Accord, rev. 02/2014, the Summary of Product Characteristics of Calciumfolinat "Ebewe", rev. 01/2015, the Summary of Product Characteristics of Irinotecan Fresenius, rev. 11/2013, the Summary of Product Characteristics of Oxaliplatin Accord, rev. 04/2012 and the Summary of Product Characteristics of Avastin, rev. 03/2015.

Background therapy: -

Evidence for comparator: -

| | |
|---|-----------------|
| Actual start date of recruitment | 01 October 2015 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|------------|
| Country: Number of subjects enrolled | Austria: 8 |
| Worldwide total number of subjects | 8 |
| EEA total number of subjects | 8 |

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) | 3 |
| From 65 to 84 years | 5 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

After signing the informed consent form all patients will be screened and baseline procedures performed from 28 days to 1 day prior to surgical exploration, Signed informed consent, Demographics and medical history, Concomitant medications, Physical examination, Vital signs, ECOG performance status, 12 lead ECG, Laboratory tests, Urinalysis, Tumor marker

Pre-assignment period milestones

| | |
|------------------------------|---|
| Number of subjects started | 8 |
| Number of subjects completed | 8 |

Period 1

| | |
|------------------------------|-------------------------------|
| Period 1 title | Study period (overall period) |
| Is this the baseline period? | Yes |
| Allocation method | Non-randomised - controlled |
| Blinding used | Not blinded |

Arms

| | |
|--|--|
| Arm title | Assessment of histopathological response to combination chemot |
| Arm description: - | |
| Arm type | Experimental |
| Investigational medicinal product name | Fluorouracil Accord |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Infusion, Injection |
| Routes of administration | Intravenous use |

Dosage and administration details:

Fluorouracil is supplied as a clear, colourless liquid. The pH ranges from 8.6 -9.4. The formulation contains 50 mg Fluorouracil/1ml, sodium hydroxide, hydrochloric acid and water for injection (WFI).

| | |
|--|------------------------|
| Investigational medicinal product name | Calciumfolinat "Ebewe" |
| Investigational medicinal product code | |
| Other name | LEUCOVORIN CALCIUM |
| Pharmaceutical forms | Infusion, Injection |
| Routes of administration | Intravenous use |

Dosage and administration details:

Leucovorin is supplied as a clear, colourless to slightly yellow liquid. The pH ranges from 6.5 – 8.5. The formulation contains 12.71 mg Calciumfolinat .5 H₂O (corresponding to 10 mg folinic acid) and water for injection (WFI).

| | |
|--|----------------------|
| Investigational medicinal product name | Irinotecan Fresenius |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Irinotecan is supplied as a clear, slightly yellow liquid. The formulation contains 20 mg Irinotecanhydrochloride-Trihydrate/1ml, sorbitol (E 420), lactic acid, sodium hydroxide, hydrochloric acid and water for injection (WFI).

| | |
|--|--------------------|
| Investigational medicinal product name | Oxaliplatin Accord |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Infusion |
| Routes of administration | Intracavernous use |

Dosage and administration details:

Oxaliplatin is supplied as a clear, colourless sterile liquid. The pH ranges from 3.5-6.5. The formulation contains 5mg Oxaliplatin/1ml, lactose-monohydrate and water for injection (WFI).

| | |
|--|-----------------|
| Investigational medicinal product name | AVASTIN |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Bevacizumab is supplied as a clear to slightly opalescent, colourless to pale brown, sterile liquid for intravenous infusion in single-use vials which are preservative-free. Bevacizumab will be supplied either in 5 mL (100 mg, 25 mg/ml) glass vials with a 4 ml fill, or in 20 ml (400 mg, 25 mg/ml) glass vials with a 16 ml fill. The formulation contains sodium phosphate, trehalose, polysorbate 20, and sterile water for injection (SWFI), USP.

| Number of subjects in period 1 | Assessment of histopathological response to combination chemot |
|---------------------------------------|--|
| Started | 8 |
| Completed | 6 |
| Not completed | 2 |
| Death | 2 |

Baseline characteristics

Reporting groups

| | |
|--------------------------------|--|
| Reporting group title | Assessment of histopathological response to combination chemot |
| Reporting group description: - | |

| Reporting group values | Assessment of histopathological response to combination chemot | Total | |
|---------------------------------------|--|-------|--|
| Number of subjects | 8 | 8 | |
| Age categorical Units: Subjects | | | |
| Adults (18-64 years) | 3 | 3 | |
| From 65-84 years | 5 | 5 | |
| Gender categorical Units: Subjects | | | |
| Female | 3 | 3 | |
| Male | 5 | 5 | |

Subject analysis sets

| | |
|----------------------------|---------------|
| Subject analysis set title | Overall trial |
| Subject analysis set type | Full analysis |

Subject analysis set description:

The primary objective of the study is to prospectively assess the histopathological response to neoadjuvant chemotherapy with FOLFOXIRI + bevacizumab in peritoneal tumor deposits of 30 patients with pCRC by determining the percentage of viable tumor cells in the resected specimen after neoadjuvant chemotherapy. For patients with multiple peritoneal specimens, the median percentage of viable cells in all specimens will be used. Patients with 0-49% of viable cells will be considered as responders. The timepoint of the assessment of the primary objective will be during re-exploratory surgery/surgical cytoreduction between days 78 and 106 of the treatment phase of the study. We hypothesize that there will be >30% responders after neoadjuvant chemotherapy with FOLFOXIRI + bevacizumab.

| Reporting group values | Overall trial | | |
|---------------------------------------|---------------|--|--|
| Number of subjects | 8 | | |
| Age categorical Units: Subjects | | | |
| Adults (18-64 years) | 3 | | |
| From 65-84 years | 5 | | |
| Gender categorical Units: Subjects | | | |
| Female | 3 | | |
| Male | 5 | | |

End points

End points reporting groups

| | |
|--------------------------------|--|
| Reporting group title | Assessment of histopathological response to combination chemot |
| Reporting group description: - | |
| Subject analysis set title | Overall trial |
| Subject analysis set type | Full analysis |

Subject analysis set description:

The primary objective of the study is to prospectively assess the histopathological response to neoadjuvant chemotherapy with FOLFOXIRI + bevacizumab in peritoneal tumor deposits of 30 patients with pCRC by determining the percentage of viable tumor cells in the resected specimen after neoadjuvant chemotherapy. For patients with multiple peritoneal specimens, the median percentage of viable cells in all specimens will be used. Patients with 0-49% of viable cells will be considered as responders. The timepoint of the assessment of the primary objective will be during re-exploratory surgery/surgical cytoreduction between days 78 and 106 of the treatment phase of the study. We hypothesize that there will be >30% responders after neoadjuvant chemotherapy with FOLFOXIRI + bevacizumab.

Primary: Histopathological response to chemotherapy with FOLFOXIRI + bevacizumab

| | |
|-----------------|--|
| End point title | Histopathological response to chemotherapy with FOLFOXIRI + bevacizumab ^[1] |
|-----------------|--|

End point description:

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

End point timeframe:

During Re-exploratory/surgical cytoreduction (3 to 5 weeks after completion of chemotherapy (days 78 to 106))

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: no comparison between arms. no statistical analysis performed due to premature termination.

| End point values | Assessment of histopathological response to combination chemot | | | |
|-----------------------------|--|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 8 | | | |
| Units: whole | | | | |
| responder | 5 | | | |
| non-responder | 3 | | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

31.3.2016 until 10.1.2019

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

Dictionary used

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

| | |
|--------------------|------|
| Dictionary version | 10.0 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|---------------|
| Reporting group title | Overall trial |
|-----------------------|---------------|

Reporting group description: -

| Serious adverse events | Overall trial | | |
|--|----------------|--|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 6 / 8 (75.00%) | | |
| number of deaths (all causes) | 2 | | |
| number of deaths resulting from adverse events | 1 | | |
| Injury, poisoning and procedural complications | | | |
| Abdominal wound dehiscence | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cardiac disorders | | | |
| Cardiac arrest | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 1 | | |
| Blood and lymphatic system disorders | | | |
| Anemia | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| General disorders and administration site conditions | | | |
| General physical health deterioration | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 1 / 8 (12.50%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gastrointestinal disorders | | | |
| Gastrointestinal necrosis | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Subileus | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Ileus | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Small intestinal obstruction | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Lower gastrointestinal haemorrhage | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | | |
| occurrences causally related to treatment / all | 0 / 3 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Infections and infestations | | | |
| Infection | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Urogenital infection bacterial | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Metabolism and nutrition disorders | | | |

| | | | |
|---|----------------|--|--|
| Hyponatraemia | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

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

| Non-serious adverse events | Overall trial | | |
|---|-----------------|--|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 8 / 8 (100.00%) | | |
| Injury, poisoning and procedural complications | | | |
| Heat exhaustion | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | | |
| occurrences (all) | 1 | | |
| Vascular disorders | | | |
| Hypertension | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | | |
| occurrences (all) | 1 | | |
| Deep vein thrombosis | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | | |
| occurrences (all) | 1 | | |
| Cardiac disorders | | | |
| Tachycardia | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | | |
| occurrences (all) | 1 | | |
| Nervous system disorders | | | |
| Speech disorder | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | | |
| occurrences (all) | 1 | | |
| Paraesthesia | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | | |
| occurrences (all) | 1 | | |
| Syncope | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | | |
| occurrences (all) | 1 | | |
| Polyneuropathy | | | |

| | | | |
|--|--|--|--|
| subjects affected / exposed occurrences (all) | 2 / 8 (25.00%) 2 | | |
| Blood and lymphatic system disorders Leukopenia subjects affected / exposed occurrences (all) | 1 / 8 (12.50%) 1 | | |
| General disorders and administration site conditions Malaise subjects affected / exposed occurrences (all) Fatigue subjects affected / exposed occurrences (all) Fever subjects affected / exposed occurrences (all) | 1 / 8 (12.50%) 1 1 / 8 (12.50%) 1 1 / 8 (12.50%) 1 | | |
| Eye disorders Ocular hypertension subjects affected / exposed occurrences (all) | 1 / 8 (12.50%) 1 | | |
| Gastrointestinal disorders Constipation subjects affected / exposed occurrences (all) Nausea subjects affected / exposed occurrences (all) Stomatitis subjects affected / exposed occurrences (all) Diarrhea subjects affected / exposed occurrences (all) | 1 / 8 (12.50%) 1 1 / 8 (12.50%) 2 1 / 8 (12.50%) 1 2 / 8 (25.00%) 2 | | |
| Skin and subcutaneous tissue disorders Photosensitivity reaction | | | |

| | | | |
|--|---------------------|--|--|
| subjects affected / exposed occurrences (all) | 1 / 8 (12.50%) 1 | | |
| Musculoskeletal and connective tissue disorders Muscle spasms subjects affected / exposed occurrences (all) | 1 / 8 (12.50%) 1 | | |
| Infections and infestations Nasopharyngitis subjects affected / exposed occurrences (all) | 1 / 8 (12.50%) 1 | | |

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