



Clinical trial results:

Intra-hepatic chemotherapy with oxaliplatin every second week in combination with systemic capecitabine and in patients with a HER2-positive tumour in combination with trastuzumab (Herceptin®) in patient with non-resectable liver metastases from breast cancer.

A phase II trial in patients with limited extrahepatic disease.

Summary

| | |
|--------------------------|----------------|
| EudraCT number | 2009-014821-17 |
| Trial protocol | DK |
| Global end of trial date | 01 May 2017 |

Results information

| | |
|--------------------------------|-----------------|
| Result version number | v1 (current) |
| This version publication date | 05 October 2019 |
| First version publication date | 05 October 2019 |

Trial information

Trial identification

| | |
|-----------------------|--------|
| Sponsor protocol code | MA0918 |
|-----------------------|--------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT01387295 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | Herlev Hospital |
| Sponsor organisation address | Herlev Ringvej 75, Herlev, Denmark, 2730 |
| Public contact | Dorte Nielsen, Department of Oncology Herlev Hospital, +45 38682344, dorte.nielsen.01@regionh.dk |
| Scientific contact | Dorte Nielsen, Department of Oncology Herlev Hospital, +45 38682344, dorte.nielsen.01@regionh.dk |

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 | 01 September 2017 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 01 May 2017 |
| Global end of trial reached? | Yes |
| Global end of trial date | 01 May 2017 |
| Was the trial ended prematurely? | Yes |

Notes:

General information about the trial

Main objective of the trial:

Response rate

Number of patients with complete or partial response in the liver (RECIST version 1.1)

Protection of trial subjects:

Eligibility criteria, Dose modification
no additional measures

Background therapy:

NA

Evidence for comparator:

NA

| | |
|---|-----------------|
| Actual start date of recruitment | 01 October 2009 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | No |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|-------------|
| Country: Number of subjects enrolled | Denmark: 38 |
| Worldwide total number of subjects | 38 |
| EEA total number of subjects | 38 |

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) | 30 |
| From 65 to 84 years | 8 |

| | |
|-------------------|---|
| 85 years and over | 0 |
|-------------------|---|

Subject disposition

Recruitment

Recruitment details:

Patients recruited at single site at Herlev Hospital, Department of Oncology, Denmark, Recruitment was open from October 2009 to September 2016

Pre-assignment

Screening details:

Patients with histologically confirmed adenocarcinoma of the breast with main metastases in liver and limited extrahepatic disease were allowed. Liver metastases evaluated not suitable for local ablation by RFA, SBRT, or surgery and had <70% of the liver affected. Extra-hepatic metastasis without progression within past 6 months.

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 | Protocol treatment |
|-----------|--------------------|

Arm description:

Single Arm study

| | |
|--|---------------------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Oxaliplatin |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Concentrate for solution for infusion |
| Routes of administration | Intrahepatic use , Intravenous use |

Dosage and administration details:

Patients received oxaliplatin every two weeks alternating between hepatic arterial and systemic administration. Dose was at 85 mg/m².

| | |
|--|--------------------|
| Investigational medicinal product name | Capecitabine |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Film-coated tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Capecitabine was given at a daily dose of 1300 mg/m² on a continuous schedule

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

Dosage and administration details:

Patients with HER-2 positive tumors received additional trastuzumab 8 mg/kg on day 1 followed by 6 mg/kg every third week.

| Number of subjects in period 1 | Protocol treatment |
|---------------------------------------|--------------------|
| Started | 38 |
| Completed | 38 |

Baseline characteristics

Reporting groups

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

| Reporting group values | Overall trial | Total | |
|---|---------------|-------|--|
| Number of subjects | 38 | 38 | |
| 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 | | | |
| median | 54.5 | | |
| full range (min-max) | 31 to 72 | - | |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 38 | 38 | |
| Male | 0 | 0 | |

End points

End points reporting groups

| | |
|------------------------------|--------------------|
| Reporting group title | Protocol treatment |
| Reporting group description: | |
| Single Arm study | |

Primary: Response rate (hepatic)

| | |
|------------------------|--|
| End point title | Response rate (hepatic) ^[1] |
| End point description: | |

| | |
|--|---------|
| End point type | Primary |
| End point timeframe: | |
| treatment start to progression of disease or death | |

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: single arm trial

| End point values | Protocol treatment | | | |
|-----------------------------|--------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 38 | | | |
| Units: number of patients | | | | |
| CR | 2 | | | |
| PR | 13 | | | |
| SD | 21 | | | |
| PD | 1 | | | |
| Not evaluable | 1 | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Overall reponse rate

| | |
|------------------------|----------------------|
| End point title | Overall reponse rate |
| End point description: | |

| | |
|--|-----------|
| End point type | Secondary |
| End point timeframe: | |
| treatment start to progression of disease or death | |

| End point values | Protocol treatment | | | |
|-----------------------------|--------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 38 | | | |
| Units: number of patients | | | | |
| CR | 0 | | | |
| PR | 15 | | | |
| SD | 21 | | | |
| PD | 2 | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: PFS

| | |
|-----------------|-----|
| End point title | PFS |
|-----------------|-----|

End point description:

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

End point timeframe:

PFS was calculated as the period from the first treatment to disease progression or death of any cause.

| End point values | Protocol treatment | | | |
|-------------------------------|--------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 38 | | | |
| Units: months | | | | |
| median (full range (min-max)) | 12.8 (6.9 to 18.6) | | | |

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:

OS was calculated as the time from the first treatment to death from any cause or until May 1st 2017

| | | | | |
|-------------------------------|---------------------|--|--|--|
| End point values | Protocol treatment | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 38 | | | |
| Units: months | | | | |
| median (full range (min-max)) | 24.0 (17.2 to 30.8) | | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Informed consent to 30 days after last treatment

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

Dictionary used

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|-----------------|-----------|
| Dictionary name | NCI-CTCAE |
|-----------------|-----------|

| | |
|--------------------|-----|
| Dictionary version | 3.0 |
|--------------------|-----|

Reporting groups

| | |
|-----------------------|--------------------|
| Reporting group title | Protocol treatment |
|-----------------------|--------------------|

Reporting group description:

Single Arm study

| Serious adverse events | Protocol treatment | | |
|--|--------------------|--|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 8 / 38 (21.05%) | | |
| number of deaths (all causes) | 33 | | |
| number of deaths resulting from adverse events | 0 | | |
| Injury, poisoning and procedural complications | | | |
| Morphine toxication | | | |
| subjects affected / exposed | 1 / 38 (2.63%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Vascular disorders | | | |
| Pulmonary embolism | | | |
| subjects affected / exposed | 2 / 38 (5.26%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| General disorders and administration site conditions | | | |
| Fever | | | |
| subjects affected / exposed | 1 / 38 (2.63%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hepatobiliary disorders | | | |
| gallbladder stone | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 1 / 38 (2.63%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Infections and infestations | | | |
| Infection | | | |
| subjects affected / exposed | 3 / 38 (7.89%) | | |
| occurrences causally related to treatment / all | 0 / 3 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Metabolism and nutrition disorders | | | |
| Diabetes mellitus | | | |
| subjects affected / exposed | 1 / 38 (2.63%) | | |
| 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 | Protocol treatment | | |
|---|--------------------|--|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 38 / 38 (100.00%) | | |
| Investigations | | | |
| Alanine aminotransferase increased | | | |
| subjects affected / exposed | 15 / 38 (39.47%) | | |
| occurrences (all) | 54 | | |
| Aspartate aminotransferase increased | | | |
| subjects affected / exposed | 19 / 38 (50.00%) | | |
| occurrences (all) | 77 | | |
| Alkaline phosphatase increased | | | |
| subjects affected / exposed | 17 / 38 (44.74%) | | |
| occurrences (all) | 46 | | |
| Amylase increased | | | |
| subjects affected / exposed | 14 / 38 (36.84%) | | |
| occurrences (all) | 35 | | |
| Hyperbilirubinaemia | | | |
| subjects affected / exposed | 3 / 38 (7.89%) | | |
| occurrences (all) | 8 | | |

| | | | |
|---|-------------------------|--|--|
| Thrombocytopenia subjects affected / exposed occurrences (all) | 17 / 38 (44.74%) 82 | | |
| Neutropenia subjects affected / exposed occurrences (all) | 15 / 38 (39.47%) 25 | | |
| Nervous system disorders | | | |
| Dysaesthesia subjects affected / exposed occurrences (all) | 35 / 38 (92.11%) 304 | | |
| Peripheral motor neuropathy subjects affected / exposed occurrences (all) | 11 / 38 (28.95%) 41 | | |
| Peripheral sensory neuropathy subjects affected / exposed occurrences (all) | 29 / 38 (76.32%) 179 | | |
| General disorders and administration site conditions | | | |
| Allergic reaction subjects affected / exposed occurrences (all) | 3 / 38 (7.89%) 6 | | |
| Fatigue subjects affected / exposed occurrences (all) | 30 / 38 (78.95%) 159 | | |
| Fever subjects affected / exposed occurrences (all) | 9 / 38 (23.68%) 12 | | |
| pain subjects affected / exposed occurrences (all) | 23 / 38 (60.53%) 59 | | |
| Blood and lymphatic system disorders | | | |
| Anaemia subjects affected / exposed occurrences (all) | 9 / 38 (23.68%) 12 | | |
| Gastrointestinal disorders | | | |
| Diarrhoea | | | |

| | | | |
|---|------------------------------------|--|--|
| <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>21 / 38 (55.26%)</p> <p>55</p> | | |
| <p>Stomatitis</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>21 / 38 (55.26%)</p> <p>62</p> | | |
| <p>Nausea</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>34 / 38 (89.47%)</p> <p>119</p> | | |
| <p>Vomiting</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>20 / 38 (52.63%)</p> <p>36</p> | | |
| <p>Dyspepsia</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>5 / 38 (13.16%)</p> <p>12</p> | | |
| <p>Skin and subcutaneous tissue disorders</p> <p>Palmar-plantar erythrodysesthesia syndrome</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>33 / 38 (86.84%)</p> <p>184</p> | | |
| <p>Alopecia</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>6 / 38 (15.79%)</p> <p>6</p> | | |
| <p>Musculoskeletal and connective tissue disorders</p> <p>Myalgia</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>5 / 38 (13.16%)</p> <p>12</p> | | |
| <p>Arthralgia</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>4 / 38 (10.53%)</p> <p>8</p> | | |
| <p>Infections and infestations</p> <p>infection</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>2 / 38 (5.26%)</p> <p>3</p> | | |
| <p>Metabolism and nutrition disorders</p> <p>Anorexia</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>24 / 38 (63.16%)</p> <p>91</p> | | |

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

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

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|------------------------------|
| recruitment goal not reached |
|------------------------------|

Notes:

Online references

<http://www.ncbi.nlm.nih.gov/pubmed/30544058>