# Clinical trial results:
# Phase I/II study of Taxotere® (docetaxel), Eloxatin® (oxaliplatin) and Xeloda® (capecitabine) as first line treatment to patients with non-resectable ventricular cancer and/or distal esophageal cancer

## Summary

| | |
|---|---|
| EudraCT number | 2006-002270-21 |
| Trial protocol | DK |
| Global end of trial date | 10 September 2013 |

**Results information**

| | |
|---|---|
| Result version number | v1 (current) |
| This version publication date | 10 March 2021 |
| First version publication date | 10 March 2021 |

## Trial information

**Trial identification**

| | |
|---|---|
| Sponsor protocol code | 05.09 |

**Additional study identifiers**

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

Notes:

**Sponsors**

| | |
|---|---|
| Sponsor organisation name | Odense University Hospital |
| Sponsor organisation address | J.B. Winsløws Vej 2, entrance 140, basement, Odense C, Denmark, 5000 |
| Public contact | Ida Coordt Elle, Odense University Hospital, +45 29335922, ida.coordt.elle@rsyd.dk |
| Scientific contact | Per Pfeiffer, Odense University Hospital, +45 26283844, per.pfeiffer@rsyd.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 | 26 January 2010 |
| Is this the analysis of the primary completion data? | No |

| | |
|---|---|
| Global end of trial reached? | Yes |
| Global end of trial date | 10 September 2013 |
| Was the trial ended prematurely? | No |

Notes:

## General information about the trial

Main objective of the trial:

Phase I: To determine max. tolerable dose (MTD) for the combination regime docetaxel, oxaliplatin and capecitabine (TEX) as first line treatment to patients with primary or recurrent non-resectable cancer of the stomach

Phase II: To estimate response rate for treatment with TEX as first line treatment to patients with primary or recurrent non-resectable cancer of the stomach

Protection of trial subjects:

Pre-medication administered to minimize nausea.
Blood tests before start and before each treatment cycle.

Background therapy: -

Evidence for comparator: -

| | |
|---|---|
| Actual start date of recruitment | 03 September 2007 |
| 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 | Denmark: 23 |
| Worldwide total number of subjects | 23 |
| EEA total number of subjects | 23 |

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) | 18 |
| From 65 to 84 years | 5 |

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

## Subject disposition

### Recruitment

Recruitment details:

Patients were required to have histologically confirmed adenocarcinoma of the lower oesophagus, gastro-oesophageal junction or stomach not amenable to surgical resection.

### Pre-assignment

Screening details:

From June 2007 to April 2009 23 consecutive patients from two Danish oncology centres were enrolled in this phase I trial. Data was updated December 2009.

### Period 1

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

### Arms

| | |
|---|---|
| Are arms mutually exclusive? | Yes |
| **Arm title** | Dose level 1 |

Arm description:

Docetaxel (T) mg/m2: 60
Oxaliplatin (E) mg/m2: 85
Capecitabine (X): mg/m2/day: 500 x 2

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Docetaxel |
| Investigational medicinal product code | |
| Other name | Taxotere |
| Pharmaceutical forms | Solution and suspension for suspension for injection in pre-filled syringe |
| Routes of administration | Intravenous use |

Dosage and administration details:

Dose level 1-3: 60 mg/m2
Dose level 4-5: 75 mg/m2

| | |
|---|---|
| Investigational medicinal product name | Oxaliplatin |
| Investigational medicinal product code | |
| Other name | Eloxatin |
| Pharmaceutical forms | Solution for solution for infusion |
| Routes of administration | Intravenous drip use |

Dosage and administration details:

Dose level 1: 85 mg/m2
Dose level 2: 100 mg/m2
Dose level 3: 115 mg/m2
Dose level 4: 115 mg/m2
Dose level 5: 130 mg/m2

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

Dosage and administration details:

Dose level 1: 500 mg/m2/day
Dose level 2: 625 mg/m2/day
Dose level 3-5: 625 mg/m2/day

| **Arm title** | Dose level 2 |
|---|---|
| Arm description:<br>Docetaxel (T) mg/m2: 60<br>Oxaliplatin (E) mg/m2: 100<br>Capecitabine (X): mg/m2/day: 625 x 2 | |
| Arm type | Experimental |
| Investigational medicinal product name | Docetaxel |
| Investigational medicinal product code | |
| Other name | Taxotere |
| Pharmaceutical forms | Solution and suspension for suspension for injection in pre-filled syringe |
| Routes of administration | Intravenous use |
| Dosage and administration details:<br>Dose level 1-3: 60 mg/m2<br>Dose level 4-5: 75 mg/m2 | |
| Investigational medicinal product name | Oxaliplatin |
| Investigational medicinal product code | |
| Other name | Eloxatin |
| Pharmaceutical forms | Solution for solution for infusion |
| Routes of administration | Intravenous drip use |
| Dosage and administration details:<br>Dose level 1: 85 mg/m2<br>Dose level 2: 100 mg/m2<br>Dose level 3: 115 mg/m2<br>Dose level 4: 115 mg/m2<br>Dose level 5: 130 mg/m2 | |
| Investigational medicinal product name | Capecitabine |
| Investigational medicinal product code | |
| Other name | Xeloda |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |
| Dosage and administration details:<br>Dose level 1: 500 mg/m2/day<br>Dose level 2: 625 mg/m2/day<br>Dose level 3-5: 625 mg/m2/day | |
| **Arm title** | Dose level 3 |
| Arm description:<br>Docetaxel (T) mg/m2: 60<br>Oxaliplatin (E) mg/m2: 115<br>Capecitabine (X): mg/m2/day: 625 x 2 | |
| Arm type | Experimental |
| Investigational medicinal product name | Docetaxel |
| Investigational medicinal product code | |
| Other name | Taxotere |
| Pharmaceutical forms | Solution and suspension for suspension for injection in pre-filled syringe |
| Routes of administration | Intravenous use |
| Dosage and administration details:<br>Dose level 1-3: 60 mg/m2<br>Dose level 4-5: 75 mg/m2 | |
| Investigational medicinal product name | Oxaliplatin |
| Investigational medicinal product code | |
| Other name | Eloxatin |
| Pharmaceutical forms | Solution for solution for infusion |
| Routes of administration | Intravenous drip use |

| | |
|---|---|
| Dosage and administration details:<br>Dose level 1: 85 mg/m2<br>Dose level 2: 100 mg/m2<br>Dose level 3: 115 mg/m2<br>Dose level 4: 115 mg/m2<br>Dose level 5: 130 mg/m2 | |
| Investigational medicinal product name | Capecitabine |
| Investigational medicinal product code | |
| Other name | Xeloda |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |
| Dosage and administration details:<br>Dose level 1: 500 mg/m2/day<br>Dose level 2: 625 mg/m2/day<br>Dose level 3-5: 625 mg/m2/day | |
| **Arm title** | Dose level 4 |
| Arm description:<br>Docetaxel (T) mg/m2: 75<br>Oxaliplatin (E) mg/m2: 115<br>Capecitabine (X): mg/m2/day: 625 x 2 | |
| Arm type | Experimental |
| Investigational medicinal product name | Docetaxel |
| Investigational medicinal product code | |
| Other name | Taxotere |
| Pharmaceutical forms | Solution and suspension for suspension for injection in pre-filled syringe |
| Routes of administration | Intravenous use |
| Dosage and administration details:<br>Dose level 1-3: 60 mg/m2<br>Dose level 4-5: 75 mg/m2 | |
| Investigational medicinal product name | Oxaliplatin |
| Investigational medicinal product code | |
| Other name | Eloxatin |
| Pharmaceutical forms | Solution for solution for infusion |
| Routes of administration | Intravenous drip use |
| Dosage and administration details:<br>Dose level 1: 85 mg/m2<br>Dose level 2: 100 mg/m2<br>Dose level 3: 115 mg/m2<br>Dose level 4: 115 mg/m2<br>Dose level 5: 130 mg/m2 | |
| Investigational medicinal product name | Capecitabine |
| Investigational medicinal product code | |
| Other name | Xeloda |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |
| Dosage and administration details:<br>Dose level 1: 500 mg/m2/day<br>Dose level 2: 625 mg/m2/day<br>Dose level 3-5: 625 mg/m2/day | |
| **Arm title** | Dose level 5 |
| Arm description:<br>Docetaxel (T) mg/m2: 75<br>Oxaliplatin (E) mg/m2: 130<br>Capecitabine (X): mg/m2/day: 625 x 2 | |
| Arm type | Experimental |

| | |
|---|---|
| Investigational medicinal product name | Docetaxel |
| Investigational medicinal product code | |
| Other name | Taxotere |
| Pharmaceutical forms | Solution and suspension for suspension for injection in pre-filled syringe |
| Routes of administration | Intravenous use |

Dosage and administration details:

Dose level 1-3: 60 mg/m2
Dose level 4-5: 75 mg/m2

| | |
|---|---|
| Investigational medicinal product name | Oxaliplatin |
| Investigational medicinal product code | |
| Other name | Eloxatin |
| Pharmaceutical forms | Solution for solution for infusion |
| Routes of administration | Intravenous drip use |

Dosage and administration details:

Dose level 1: 85 mg/m2
Dose level 2: 100 mg/m2
Dose level 3: 115 mg/m2
Dose level 4: 115 mg/m2
Dose level 5: 130 mg/m2

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

Dosage and administration details:

Dose level 1: 500 mg/m2/day
Dose level 2: 625 mg/m2/day
Dose level 3-5: 625 mg/m2/day

| **Number of subjects in period 1** | Dose level 1 | Dose level 2 | Dose level 3 |
|---|---|---|---|
| Started | 3 | 3 | 3 |
| Completed | 3 | 3 | 3 |
| Not completed | 0 | 0 | 0 |
| Physician decision | - | - | - |
| Adverse event, non-fatal | - | - | - |
| deterioation of health | - | - | - |

| **Number of subjects in period 1** | Dose level 4 | Dose level 5 |
|---|---|---|
| Started | 10 | 4 |
| Completed | 3 | 1 |
| Not completed | 7 | 3 |
| Physician decision | 1 | - |
| Adverse event, non-fatal | 4 | 2 |
| deterioation of health | 2 | 1 |

## Baseline characteristics

| Reporting groups | |
|---|---|
| Reporting group title | Phase 1 |

Reporting group description: -

| Reporting group values | Phase 1 | Total | |
|---|---|---|---|
| Number of subjects | 23 | 23 | |
| Age categorical<br>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) | 18 | 18 | |
| From 65-84 years | 5 | 5 | |
| 85 years and over | 0 | 0 | |
| Gender categorical<br>Units: Subjects | | | |
| Female | 2 | 2 | |
| Male | 21 | 21 | |

## End points

### End points reporting groups

| Reporting group title | Dose level 1 |
|---|---|
| Reporting group description: | |
| Docetaxel (T) mg/m2: 60<br>Oxaliplatin (E) mg/m2: 85<br>Capecitabine (X): mg/m2/day: 500 x 2 | |
| Reporting group title | Dose level 2 |
| Reporting group description: | |
| Docetaxel (T) mg/m2: 60<br>Oxaliplatin (E) mg/m2: 100<br>Capecitabine (X): mg/m2/day: 625 x 2 | |
| Reporting group title | Dose level 3 |
| Reporting group description: | |
| Docetaxel (T) mg/m2: 60<br>Oxaliplatin (E) mg/m2: 115<br>Capecitabine (X): mg/m2/day: 625 x 2 | |
| Reporting group title | Dose level 4 |
| Reporting group description: | |
| Docetaxel (T) mg/m2: 75<br>Oxaliplatin (E) mg/m2: 115<br>Capecitabine (X): mg/m2/day: 625 x 2 | |
| Reporting group title | Dose level 5 |
| Reporting group description: | |
| Docetaxel (T) mg/m2: 75<br>Oxaliplatin (E) mg/m2: 130<br>Capecitabine (X): mg/m2/day: 625 x 2 | |

### Primary: Patients without DLT

| End point title | Patients without DLT[1] |
|---|---|
| End point description: | |
| | |
| End point type | Primary |
| End point timeframe: | |
| 24 weeks | |

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 end point of the trial was to establish recommended doses for the TEX regimen. This is done by counting the number of patients that experience dose limiting toxicities at various dose levels.
Dose levels and number of patients, who did not experience DLTs have been noted.

See also publication.

| End point values | Dose level 1 | Dose level 2 | Dose level 3 | Dose level 4 |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 3 | 3 | 3 | 10 |
| Units: patients | 3 | 3 | 3 | 9 |

| End point values | Dose level 5 | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 4 | | | |
| Units: patients | 2 | | | |

## Statistical analyses

No statistical analyses for this end point

## Adverse events

| Adverse events information | |
|---|---|
| Timeframe for reporting adverse events: Three months. | |
| Assessment type | Systematic |
| **Dictionary used** | |
| Dictionary name | MedDRA |
| Dictionary version | 23.1 |
| **Reporting groups** | |
| Reporting group title | Patients |

Reporting group description: -

| Serious adverse events | Patients | | |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 1 / 23 (4.35%) | | |
| number of deaths (all causes) | 0 | | |
| number of deaths resulting from adverse events | 0 | | |
| Blood and lymphatic system disorders | | | |
| Febrile neutropenia | | | |
| subjects affected / exposed | 1 / 23 (4.35%) | | |
| 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 | Patients | | |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 23 / 23 (100.00%) | | |
| Nervous system disorders | | | |
| Neuropathy peripheral | | | |
| subjects affected / exposed | 12 / 23 (52.17%) | | |
| occurrences (all) | 12 | | |
| Blood and lymphatic system disorders | | | |
| Neutropenia | | | |
| subjects affected / exposed | 19 / 23 (82.61%) | | |
| occurrences (all) | 19 | | |
| Thrombocytopenia | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 3 / 23 (13.04%) | | |
| occurrences (all) | 3 | | |
| General disorders and administration site conditions | | | |
| Fatigue | | | |
| subjects affected / exposed | 14 / 23 (60.87%) | | |
| occurrences (all) | 14 | | |
| Nail toxicity | | | |
| subjects affected / exposed | 14 / 23 (60.87%) | | |
| occurrences (all) | 14 | | |
| Gastrointestinal disorders | | | |
| Nausea | | | |
| subjects affected / exposed | 9 / 23 (39.13%) | | |
| occurrences (all) | 9 | | |
| Diarrhoea | | | |
| subjects affected / exposed | 12 / 23 (52.17%) | | |
| occurrences (all) | 12 | | |
| Vomiting | | | |
| subjects affected / exposed | 9 / 23 (39.13%) | | |
| occurrences (all) | 9 | | |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|---|---|
| 09 October 2008 | 3 patients have been treated at dose level I-IV (total 12 patients) and 4 patients have been treated at dose level V. 2 patients experienced DLT and additional 2 patients had a symptomatic neutrophenia which required dose reduction in subsequent courses. MTD was reached at dose level V.<br>To ensure tolerability of dose level IV we will include additional 6 patients at dose level IV as this is standard practice in most fase I studies. If 2 or more of the 6 new patients experience DLT, 6 additional patients will be treated at dose level III. Unfortunately this was not written in the original protocol. |
| 28 May 2010 | A small dose reduction to:<br><br>Taxotere 51 mg/m2 day 1 (reduced from 60 mg)<br>Oxaliplatin 100 mg/m2 day 1 (reduced from 115 mg)<br>Capecitabin 625 mg/m2 twice a day continuously |

Notes:

### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported

### Online references

http://www.ncbi.nlm.nih.gov/pubmed/20843172

http://www.ncbi.nlm.nih.gov/pubmed/20429725