



## 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
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##### 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. Winsløvs Vej 2, entrance 140, basement, Odense C, Denmark, 5000
Public contact	Ida Coordt Elle, Odense University Hospital, +45 29335922, ida.coordt.elle@rsyd.dk
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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



## 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
<b>Arm title</b>	Dose level 1

Arm description:

Docetaxel (T) mg/m<sup>2</sup>: 60  
Oxaliplatin (E) mg/m<sup>2</sup>: 85  
Capecitabine (X): mg/m<sup>2</sup>/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/m<sup>2</sup>  
Dose level 4-5: 75 mg/m<sup>2</sup>

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/m<sup>2</sup>  
Dose level 2: 100 mg/m<sup>2</sup>  
Dose level 3: 115 mg/m<sup>2</sup>  
Dose level 4: 115 mg/m<sup>2</sup>  
Dose level 5: 130 mg/m<sup>2</sup>

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/m<sup>2</sup>/day  
Dose level 2: 625 mg/m<sup>2</sup>/day  
Dose level 3-5: 625 mg/m<sup>2</sup>/day

<b>Arm title</b>	Dose level 2
Arm description: Docetaxel (T) mg/m2: 60 Oxaliplatin (E) mg/m2: 100 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	
<b>Arm title</b>	Dose level 3
Arm description: Docetaxel (T) mg/m2: 60 Oxaliplatin (E) mg/m2: 115 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/m <sup>2</sup> Dose level 2: 100 mg/m <sup>2</sup> Dose level 3: 115 mg/m <sup>2</sup> Dose level 4: 115 mg/m <sup>2</sup> Dose level 5: 130 mg/m <sup>2</sup>	
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/m <sup>2</sup> /day Dose level 2: 625 mg/m <sup>2</sup> /day Dose level 3-5: 625 mg/m <sup>2</sup> /day	
<b>Arm title</b>	Dose level 4
Arm description: Docetaxel (T) mg/m <sup>2</sup> : 75 Oxaliplatin (E) mg/m <sup>2</sup> : 115 Capecitabine (X): mg/m <sup>2</sup> /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/m <sup>2</sup> Dose level 4-5: 75 mg/m <sup>2</sup>	
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/m <sup>2</sup> Dose level 2: 100 mg/m <sup>2</sup> Dose level 3: 115 mg/m <sup>2</sup> Dose level 4: 115 mg/m <sup>2</sup> Dose level 5: 130 mg/m <sup>2</sup>	
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/m <sup>2</sup> /day Dose level 2: 625 mg/m <sup>2</sup> /day Dose level 3-5: 625 mg/m <sup>2</sup> /day	
<b>Arm title</b>	Dose level 5
Arm description: Docetaxel (T) mg/m <sup>2</sup> : 75 Oxaliplatin (E) mg/m <sup>2</sup> : 130 Capecitabine (X): mg/m <sup>2</sup> /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/m<sup>2</sup>

Dose level 4-5: 75 mg/m<sup>2</sup>

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/m<sup>2</sup>

Dose level 2: 100 mg/m<sup>2</sup>

Dose level 3: 115 mg/m<sup>2</sup>

Dose level 4: 115 mg/m<sup>2</sup>

Dose level 5: 130 mg/m<sup>2</sup>

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/m<sup>2</sup>/day

Dose level 2: 625 mg/m<sup>2</sup>/day

Dose level 3-5: 625 mg/m<sup>2</sup>/day

<b>Number of subjects in period 1</b>	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	-	-	-

<b>Number of subjects in period 1</b>	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
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Reporting group description: -

Reporting group values	Phase 1	Total	
Number of subjects	23	23	
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)	18	18	
From 65-84 years	5	5	
85 years and over	0	0	
Gender categorical			
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 Oxaliplatin (E) mg/m2: 85 Capecitabine (X): mg/m2/day: 500 x 2	
Reporting group title	Dose level 2
Reporting group description: Docetaxel (T) mg/m2: 60 Oxaliplatin (E) mg/m2: 100 Capecitabine (X): mg/m2/day: 625 x 2	
Reporting group title	Dose level 3
Reporting group description: Docetaxel (T) mg/m2: 60 Oxaliplatin (E) mg/m2: 115 Capecitabine (X): mg/m2/day: 625 x 2	
Reporting group title	Dose level 4
Reporting group description: Docetaxel (T) mg/m2: 75 Oxaliplatin (E) mg/m2: 115 Capecitabine (X): mg/m2/day: 625 x 2	
Reporting group title	Dose level 5
Reporting group description: Docetaxel (T) mg/m2: 75 Oxaliplatin (E) mg/m2: 130 Capecitabine (X): mg/m2/day: 625 x 2	

### Primary: Patients without DLT

End point title	Patients without DLT <sup>[1]</sup>
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

<b>End point values</b>	Dose level 5			
Subject group type	Reporting group			
Number of subjects analysed	4			
Units: patients	2			

### Statistical analyses

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No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Three months.

Assessment type	Systematic
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### Dictionary used

Dictionary name	MedDRA
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Dictionary version	23.1
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### Reporting groups

Reporting group title	Patients
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Reporting group description: -

<b>Serious adverse events</b>	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 %

<b>Non-serious adverse events</b>	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 occurrences (all)	3 / 23 (13.04%) 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. 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: Taxotere 51 mg/m <sup>2</sup> day 1 (reduced from 60 mg) Oxaliplatin 100 mg/m <sup>2</sup> day 1 (reduced from 115 mg) Capecitabin 625 mg/m <sup>2</sup> twice a day continuously

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported

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### Online references

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

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