



Clinical trial results:

A Randomised Phase II trial of Epirubicin, Oxaliplatin and Capecitabine (EOX) versus Docetaxel and Oxaliplatin (EITax) in the treatment of Advanced Gastro-oesophageal cancer - The ELECT trial

Summary

EudraCT number	2006-003332-29
Trial protocol	IE GB
Global end of trial date	08 September 2015

Results information

Result version number	v1 (current)
This version publication date	07 April 2021
First version publication date	07 April 2021

Trial information

Trial identification

Sponsor protocol code	ICORG 06-05
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01710592
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Cancer Trials Ireland
Sponsor organisation address	Innovation House, Old Finglas Road, Dublin 11, Ireland, D11 KXN4
Public contact	Clinical Project Manager, Cancer Trials Ireland, 353 016677211, info@cancertrials.ie
Scientific contact	Clinical Project Manager, Cancer Trials Ireland, 353 016677211, info@cancertrials.ie

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	27 November 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	08 September 2015
Global end of trial reached?	Yes
Global end of trial date	08 September 2015
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The primary objective is to determine in a randomised study if the response rate to docetaxel and oxaliplatin (EITax) is comparable to epirubicin, oxaliplatin and capecitabine (EOX) and warrants further evaluation in advanced gastro-oesophageal cancer.

Protection of trial subjects:

This clinical study was designed, implemented, and reported in accordance with the International Conference on Harmonization (ICH) Harmonized Tripartite Guidelines for Good Clinical Practice (GCP), with applicable local regulations SI 190 of 2004 as amend and European Directive 2001/20/EC. The study was approved by the HPRA and SJH/AMNCH Research Ethics Committee.

Background therapy: -

Evidence for comparator:

The comparator used in the trial was standard chemotherapy combination of epirubicin, oxaliplatin, and capecitabine (EOX) in the treatment of advanced gastro-oesophageal cancer.

The study was to determine if the study research treatment, a combination of docetaxel and oxaliplatin (EITax), had a comparable response rate to the comparator (EOX), and to determine if it (EITax) warrants further evaluation in advanced gastro-oesophageal cancer.

Actual start date of recruitment	11 September 2007
Long term follow-up planned	Yes
Long term follow-up rationale	Scientific research, Efficacy, Safety
Long term follow-up duration	3 Years
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Ireland: 35
Worldwide total number of subjects	35
EEA total number of subjects	35

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	0

months)	
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	20
From 65 to 84 years	15
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

There were 35 patients recruited in this study. The first patient was enrolled in 2007 and accrual continued until March 2009, when the last patient was recruited.

Pre-assignment

Screening details:

The target population were patients with unresectable or metastatic, histologically confirmed adenocarcinoma of the stomach, gastro-oesophageal junction or lower third of the oesophagus with measurable disease on CT scanning who had no previous treatment for the advanced disease and who met all of the inclusion and none of the exclusion criteria.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	EOX (Standard Arm)

Arm description:

Participants on this arm will receive Epirubicin, Oxaliplatin and Capecitabine (EOX) . This will be the comparator/standard arm for this study.

Arm type	Active comparator
Investigational medicinal product name	Epirubicin
Investigational medicinal product code	
Other name	Ellence, Pharmorubicin, Epirubicin Ebewe
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intravenous bolus use

Dosage and administration details:

Epirubicin 50 mg/m² bolus injection day 1.

Cycle repeated every 3 weeks for a maximum of 8 cycles (= 24 weeks).

Commercial stock of all of the study drugs will be used.

Investigational medicinal product name	Oxaliplatin
Investigational medicinal product code	
Other name	Eloxatin
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Oxaliplatin 130 mg/m² in 250mls of 5% dextrose. i.v. over 2 hours day 1.

Cycle repeated every 3 weeks for a maximum of 8 cycles (= 24 weeks).

Commercial stock of all of the study drugs will be used.

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

Dosage and administration details:

Capecitabine 625 mg/m² b.d. orally days 1 – 21.

Cycle repeated every 3 weeks for a maximum of 8 cycles (= 24 weeks).

Commercial stock of all of the study drugs will be used.

Arm title	EITax (research arm of the trial)
Arm description:	
Participants on this arm will receive Oxaliplatin and Taxotere (EITax) – research arm of the study.	
Arm type	Experimental
Investigational medicinal product name	Docetaxel
Investigational medicinal product code	
Other name	Taxotere
Pharmaceutical forms	Concentrate and solvent for solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

Docetaxel 20 mg/m² in 250mls of 5% dextrose. i.v. over 30 minutes days 1, 8 and 15

Cycle repeated every 4 weeks for a maximum of 6 cycles (= 24 weeks).

Commercial stock of all of the study drugs will be used.

Investigational medicinal product name	Oxaliplatin
Investigational medicinal product code	
Other name	Eloxatin
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Oxaliplatin 85 mg/ m² in 250mls of 5% dextrose. i.v. over 2 hours days 1 and 15.

Cycle repeated every 4 weeks for a maximum of 6 cycles (= 24 weeks).

Commercial stock of all of the study drugs will be used

Investigational medicinal product name	Dexamethasone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

Dexamethasone 8mg i.v. 30 minutes prior to Docetaxel

Investigational medicinal product name	Chlorpheniramine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

Chlorpheniramine 10mg i.v. 30 minutes prior to Docetaxel

Cycle repeated every 4 weeks for a maximum of 6 cycles (= 24 weeks).

Commercial stock of all of the study drugs will be used.

Investigational medicinal product name	Ranitidine
Investigational medicinal product code	
Other name	Zantac
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

Ranitidine 50mg i.v. 30 minutes prior to Docetaxel

Cycle repeated every 4 weeks for a maximum of 6 cycles (= 24 weeks).

Commercial stock of all of the study drugs will be used.

Number of subjects in period 1	EOX (Standard Arm)	EITax (research arm of the trial)
Started	18	17
Completed	2	1
Not completed	16	16
Patient is for chemo break as per PI	1	-
Good response & Frail hense desired chemo holiday	-	1
Interstitial Lung Disease	-	1
Disease Progression	4	5
Patient choice due to toxicites experienced	1	-
Consent withdrawn by subject	1	-
Bloods out of range day 1 cycle 1	-	1
Adverse event, non-fatal	1	1
W/d after 6 cycles-due for surgery to resect mets	1	-
Death	5	3
Neurpathy >= Grade 2	-	3
Unknown	-	1
More than 3 weeks delay of treatment	1	-
Protocol deviation	1	-

Baseline characteristics

Reporting groups

Reporting group title	EOX (Standard Arm)
Reporting group description:	
Participants on this arm will receive Epirubicin, Oxaliplatin and Capecitabine (EOX) . This will be the comparator/standard arm for this study.	
Reporting group title	EITax (research arm of the trial)
Reporting group description:	
Participants on this arm will receive Oxaliplatin and Taxotere (EITax) – research arm of the study.	

Reporting group values	EOX (Standard Arm)	EITax (research arm of the trial)	Total
Number of subjects	18	17	35
Age categorical			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	11	9	20
From 65-84 years	7	8	15
85 years and over	0	0	0
Age continuous			
Units: years			
median	62	64	
full range (min-max)	33 to 77	42 to 73	-
Gender categorical			
Units: Subjects			
Female	6	3	9
Male	12	14	26
Race			
Units: Subjects			
Caucasian	17	17	34
North African	1	0	1
ECOG Performance Status			
0=Fully active, able to carry on all pre-disease performance without restriction. 1=Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature e.g. light house work, office work. 2=Ambulatory and capable of self-care but unable to carry out any work activities up and about more than 50% of waking hours. 3=Capable of only limited self-care, confined to bed or chair more than 50 waking hours. 4=Completely disabled. Cannot carry out any self-care. Totally confined to bed or chair. 5=Dead			
Units: Subjects			
0.	7	5	12
1.	10	11	21
2.	1	1	2

3.	0	0	0
4.	0	0	0
5.	0	0	0
Tumor Stage			
Sites of metastasis are Bone, Liver, Lung, Lymph Nodes, Peritoneum, GI, Pancreas, Ovarian Metastases & Periumbilical Soft Tissue			
Units: Subjects			
Distal Metastatic	16	15	31
Locally Advanced Unresectable	2	2	4
Baseline Lab Result - Alanine transaminase Units: (U/L) median full range (min-max)	14 5 to 47	22 11 to 73	-
Baseline Lab Result - Absolute neutrophil count Units: (10to9/L) median full range (min-max)	5.110 3.35 to 10.80	5.400 3.00 to 9.60	-
Baseline Characteristic - Aspartate transaminase Units: U/L median full range (min-max)	19 14 to 50	29 17 to 59	-
Baseline Lab Result - Bilirubin Units: (umol/L) median full range (min-max)	6.50 3.0 to 16.0	9.00 4.0 to 22.0	-
Baseline Lab Result - Creatinine Units: (umol/L) median full range (min-max)	75.50 37.0 to 112.0	82.00 55.0 to 114.0	-
Baseline Lab Result - Haemoglobin Units: g/dl median full range (min-max)	12.450 8.70 to 15.60	12.500 10.60 to 14.3	-
Baseline Lab Results - Platelets Units: (10to9/L) median full range (min-max)	301.00 173.0 to 550.0	266.00 160.00 to 676.00	-
Baseline Vital Signs - Body Surface Area Units: (m^2) median full range (min-max)	1.770 1.34 to 2.23	1.890 1.54 to 2.10	-
Baseline Vital Sign - Diastolic blood pressure Units: (mmHg) median full range (min-max)	73.0 59 to 90	76.0 54 to 91	-
Baseline Vital Sign - Heart Rate Units: Per minute median	72.5	74.0	

full range (min-max)	55 to 100	62 to 96	-
Baseline Vital Sign - Height			
Units: cm			
median	169.35	170.00	
full range (min-max)	149.8 to 185	158.6 to 182.00	-
Baseline Vital Sign - Systolic Blood Pressure			
Units: (mmHg)			
median	126.0	127.0	
full range (min-max)	97 to 162	98 to 153	-
Baseline Vital Signs - Weight			
Units: kg			
median	65.80	76.60	
full range (min-max)	41.5 to 105.1	53.6 to 94.8	-

End points

End points reporting groups

Reporting group title	EOX (Standard Arm)
Reporting group description: Participants on this arm will receive Epirubicin, Oxaliplatin and Capecitabine (EOX) . This will be the comparator/standard arm for this study.	
Reporting group title	EITax (research arm of the trial)
Reporting group description: Participants on this arm will receive Oxaliplatin and Taxotere (EITax) – research arm of the study.	

Primary: Tumor Response Rate

End point title	Tumor Response Rate ^[1]
End point description: The primary objective in this study was to determine and compare the tumour response rate for each treatment. The response is defined as: • Yes = CR or PR sustained for ≥ 4 weeks using the RECIST criteria. • No = Otherwise • Not done = There were 2 individuals who did not receive any treatment and 7 other participants who did not have any RECIST assessments. The Fisher's exact test was used to compare differences between treatment arms. * otherwise falls into one of the following categories: 1) stable disease, 2) progressive disease, 3) early death from malignant disease, 4) early death from toxicity, 5) early death because of other cause, or 6) unknown (not assessable, insufficient data).	
End point type	Primary
End point timeframe: Tumor response to treatment will be measured radiologically using CT scanning every 12 weeks from the beginning of both treatment arms.	

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 statistical analysis carried out. Using the Fisher's Exact Test for Count Data it was determined there was no significant differences between the groups ($p= 0.3913$)

End point values	EOX (Standard Arm)	EITax (research arm of the trial)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	18	17		
Units: No of Subjects				
Not Done	4	5		
Yes (CR or PR)	5	2		
No	9	10		

Statistical analyses

No statistical analyses for this end point

Secondary: Progression Free Survival

End point title	Progression Free Survival
End point description:	
End point type	Secondary
End point timeframe:	
Progression free survival was assessed as the time from first treatment to disease progression or death, whichever is reported first (in months). Patients who were lost to follow-up, or who did not progress or die at the time of the data export, were ce	

End point values	EOX (Standard Arm)	EITax (research arm of the trial)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	18	17		
Units: Months				
median (confidence interval 95%)	8.4 (4.3 to 10.1)	5.3 (2.8 to 8.1)		

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival (OS)

End point title	Overall Survival (OS)
End point description:	
End point type	Secondary
End point timeframe:	
Overall survival was assessed as the time from first treatment to death from any cause (in months). Patients who were lost to follow-up, or who were still alive at the time of the data export, were censored at the time they were last known to be alive.	

End point values	EOX (Standard Arm)	EITax (research arm of the trial)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	18	17 ^[2]		
Units: Months				
median (confidence interval 95%)	12.3 (9.2 to 23.6)	17.9 (5.8 to 99999)		

Notes:

[2] - The upper bound confidence interval was undetermined for the EITax group (trial treatment).

Statistical analyses

No statistical analyses for this end point

Secondary: Quality of Life

End point title	Quality of Life
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End point description:

Due to the much-reduced sample size and the early termination of the study, repeated measures analysis was not carried out.

End point type	Secondary
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End point timeframe:

Quality of life was assessed at registration, every 4 weeks during treatment for EITax and every 3 weeks during treatment for EOX, end of treatment, and every 8 weeks thereafter using the EORTC QLQ-OES18 questionnaire.

End point values	EOX (Standard Arm)	EITax (research arm of the trial)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0 ^[3]	0 ^[4]		
Units: QOL Score				

Notes:

[3] - Due to the much-reduced sample size and the early termination of the study, analysis not carried out

[4] - Due to the much-reduced sample size and the early termination of the study, analysis not carried out

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Oct 2007 - Sept 2015 (8 years)

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	21.0
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Reporting groups

Reporting group title	EOX (Standard Arm)
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Reporting group description:

Participants on this arm will receive Epirubicin, Oxaliplatin and Capecitabine (EOX) . This will be the comparator arm for this study.

Reporting group title	EITax (research arm of the trial)
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Reporting group description:

Participants on this arm will receive Oxaliplatin and Taxotere (EITax) – research arm of the study.

Serious adverse events	EOX (Standard Arm)	EITax (research arm of the trial)	
Total subjects affected by serious adverse events			
subjects affected / exposed	12 / 18 (66.67%)	11 / 15 (73.33%)	
number of deaths (all causes)	10	8	
number of deaths resulting from adverse events			
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	1 / 18 (5.56%)	0 / 15 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fatigue			
subjects affected / exposed	0 / 18 (0.00%)	1 / 15 (6.67%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mucosal inflammation			
subjects affected / exposed	0 / 18 (0.00%)	1 / 15 (6.67%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pain			

subjects affected / exposed	1 / 18 (5.56%)	0 / 15 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			
subjects affected / exposed	1 / 18 (5.56%)	0 / 15 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Pneumothorax			
subjects affected / exposed	2 / 18 (11.11%)	0 / 15 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			
subjects affected / exposed	1 / 18 (5.56%)	1 / 15 (6.67%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Apnoea			
subjects affected / exposed	0 / 18 (0.00%)	1 / 15 (6.67%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hiccups			
subjects affected / exposed	0 / 18 (0.00%)	1 / 15 (6.67%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory tract infection			
subjects affected / exposed	0 / 18 (0.00%)	1 / 15 (6.67%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Blood potassium decreased			
subjects affected / exposed	1 / 18 (5.56%)	0 / 15 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Haemoglobin decreased			
subjects affected / exposed	1 / 18 (5.56%)	0 / 15 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Foot fracture			
subjects affected / exposed	0 / 18 (0.00%)	1 / 15 (6.67%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Laryngeal nerve dysfunction			
subjects affected / exposed	1 / 18 (5.56%)	0 / 15 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	1 / 18 (5.56%)	0 / 15 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Palpitations			
subjects affected / exposed	1 / 18 (5.56%)	0 / 15 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Headache			
subjects affected / exposed	2 / 18 (11.11%)	0 / 15 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ataxia			
subjects affected / exposed	0 / 18 (0.00%)	1 / 15 (6.67%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral ischaemia			

subjects affected / exposed	0 / 18 (0.00%)	1 / 15 (6.67%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral motor neuropathy			
subjects affected / exposed	1 / 18 (5.56%)	0 / 15 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral sensory neuropathy			
subjects affected / exposed	1 / 18 (5.56%)	0 / 15 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	2 / 18 (11.11%)	0 / 15 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile neutropenia			
subjects affected / exposed	1 / 18 (5.56%)	0 / 15 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	3 / 18 (16.67%)	4 / 15 (26.67%)	
occurrences causally related to treatment / all	3 / 5	2 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	4 / 18 (22.22%)	4 / 15 (26.67%)	
occurrences causally related to treatment / all	4 / 5	3 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	3 / 18 (16.67%)	2 / 15 (13.33%)	
occurrences causally related to treatment / all	3 / 4	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain			

subjects affected / exposed	2 / 18 (11.11%)	2 / 15 (13.33%)	
occurrences causally related to treatment / all	2 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Constipation			
subjects affected / exposed	0 / 18 (0.00%)	2 / 15 (13.33%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematemesis			
subjects affected / exposed	0 / 18 (0.00%)	2 / 15 (13.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ascites			
subjects affected / exposed	1 / 18 (5.56%)	0 / 15 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dysphagia			
subjects affected / exposed	1 / 18 (5.56%)	0 / 15 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Bile duct obstruction			
subjects affected / exposed	0 / 18 (0.00%)	1 / 15 (6.67%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	0 / 18 (0.00%)	1 / 15 (6.67%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 18 (0.00%)	1 / 15 (6.67%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Musculoskeletal and connective tissue disorders			
Back Pain			
subjects affected / exposed	1 / 18 (5.56%)	0 / 15 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neck Pain			
subjects affected / exposed	1 / 18 (5.56%)	0 / 15 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Lower respiratory tract infection			
subjects affected / exposed	0 / 18 (0.00%)	1 / 15 (6.67%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	2 / 18 (11.11%)	2 / 15 (13.33%)	
occurrences causally related to treatment / all	1 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Decreased appetite			
subjects affected / exposed	1 / 18 (5.56%)	2 / 15 (13.33%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	EOX (Standard Arm)	EITax (research arm of the trial)	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	18 / 18 (100.00%)	15 / 15 (100.00%)	
Vascular disorders			
Hypotension			
subjects affected / exposed	1 / 18 (5.56%)	1 / 15 (6.67%)	
occurrences (all)	1	1	
Orthostatic Hypotension			

subjects affected / exposed	1 / 18 (5.56%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Phlebitis			
subjects affected / exposed	1 / 18 (5.56%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	12 / 18 (66.67%)	11 / 15 (73.33%)	
occurrences (all)	21	22	
Pain			
subjects affected / exposed	1 / 18 (5.56%)	2 / 15 (13.33%)	
occurrences (all)	1	2	
Chest discomfort			
subjects affected / exposed	2 / 18 (11.11%)	1 / 15 (6.67%)	
occurrences (all)	2	1	
Chest Pain			
subjects affected / exposed	0 / 18 (0.00%)	2 / 15 (13.33%)	
occurrences (all)	0	2	
Mucosal inflammation			
subjects affected / exposed	1 / 18 (5.56%)	1 / 15 (6.67%)	
occurrences (all)	1	1	
Oedema Peripheral			
subjects affected / exposed	1 / 18 (5.56%)	2 / 15 (13.33%)	
occurrences (all)	1	2	
Early Satiety			
subjects affected / exposed	1 / 18 (5.56%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Injection site inflammation			
subjects affected / exposed	1 / 18 (5.56%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Mucositis			
subjects affected / exposed	1 / 18 (5.56%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Oedema			

subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0	1 / 15 (6.67%) 1	
Reproductive system and breast disorders Vaginal haemorrhage subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1	1 / 15 (6.67%) 2	
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all)	4 / 18 (22.22%) 4	6 / 15 (40.00%) 8	
Dyspnoea subjects affected / exposed occurrences (all)	5 / 18 (27.78%) 5	1 / 15 (6.67%) 1	
Hiccups subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 3	1 / 15 (6.67%) 2	
Laryngospasm subjects affected / exposed occurrences (all)	3 / 18 (16.67%) 3	0 / 15 (0.00%) 0	
Dysphonia subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0	2 / 15 (13.33%) 2	
Epistaxis subjects affected / exposed occurrences (all)	2 / 18 (11.11%) 2	0 / 15 (0.00%) 0	
Dyspnoea exertional subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0	1 / 15 (6.67%) 1	
Hypoxia subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0	1 / 15 (6.67%) 1	
Oropharyngeal pain subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0	1 / 15 (6.67%) 1	
Rhinorrhoea			

subjects affected / exposed	1 / 18 (5.56%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Infection			
subjects affected / exposed	1 / 18 (5.56%)	1 / 15 (6.67%)	
occurrences (all)	1	1	
Dysaesthesia pharynx			
subjects affected / exposed	1 / 18 (5.56%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Psychiatric disorders			
Insomnia			
subjects affected / exposed	0 / 18 (0.00%)	3 / 15 (20.00%)	
occurrences (all)	0	4	
Mood Altered			
subjects affected / exposed	2 / 18 (11.11%)	0 / 15 (0.00%)	
occurrences (all)	2	0	
Depression			
subjects affected / exposed	1 / 18 (5.56%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Investigations			
Haemoglobin decreased			
subjects affected / exposed	8 / 18 (44.44%)	6 / 15 (40.00%)	
occurrences (all)	14	9	
Aspartate aminotransferase decreased			
subjects affected / exposed	5 / 18 (27.78%)	8 / 15 (53.33%)	
occurrences (all)	6	11	
Platelet count decreased			
subjects affected / exposed	4 / 18 (22.22%)	4 / 15 (26.67%)	
occurrences (all)	6	9	
Neutrophil count decrease			
subjects affected / exposed	6 / 18 (33.33%)	0 / 15 (0.00%)	
occurrences (all)	12	0	
Alanine aminotransferase increased			
subjects affected / exposed	3 / 18 (16.67%)	5 / 15 (33.33%)	
occurrences (all)	3	8	
Blood Albumin decreased			

subjects affected / exposed	3 / 18 (16.67%)	5 / 15 (33.33%)
occurrences (all)	3	7
Blood Alkaline phosphatase increased		
subjects affected / exposed	3 / 18 (16.67%)	4 / 15 (26.67%)
occurrences (all)	3	7
Gamma glutamyltransferase increased		
subjects affected / exposed	4 / 18 (22.22%)	5 / 15 (33.33%)
occurrences (all)	4	5
Weight Decrease		
subjects affected / exposed	5 / 18 (27.78%)	4 / 15 (26.67%)
occurrences (all)	5	4
Blood bilirubin increase		
subjects affected / exposed	1 / 18 (5.56%)	5 / 15 (33.33%)
occurrences (all)	1	7
White Blood Cell Count Decreased		
subjects affected / exposed	4 / 18 (22.22%)	2 / 15 (13.33%)
occurrences (all)	6	2
White Blood Cell Count Increased		
subjects affected / exposed	0 / 18 (0.00%)	4 / 15 (26.67%)
occurrences (all)	0	6
Blood potassium decreased		
subjects affected / exposed	1 / 18 (5.56%)	1 / 15 (6.67%)
occurrences (all)	2	1
Protein Total Decreased		
subjects affected / exposed	1 / 18 (5.56%)	3 / 15 (20.00%)
occurrences (all)	1	3
Blood Calcium Decreased		
subjects affected / exposed	2 / 18 (11.11%)	1 / 15 (6.67%)
occurrences (all)	2	1
Blood Creatinine Decreased		
subjects affected / exposed	3 / 18 (16.67%)	0 / 15 (0.00%)
occurrences (all)	3	0
Blood glucose increased		

subjects affected / exposed	0 / 18 (0.00%)	2 / 15 (13.33%)
occurrences (all)	0	3
Blood Magnesium decreased		
subjects affected / exposed	1 / 18 (5.56%)	1 / 15 (6.67%)
occurrences (all)	1	2
Blood Sodium Decreased		
subjects affected / exposed	1 / 18 (5.56%)	2 / 15 (13.33%)
occurrences (all)	1	2
Neutrophil count increased		
subjects affected / exposed	0 / 18 (0.00%)	3 / 15 (20.00%)
occurrences (all)	0	3
Blood urea increased		
subjects affected / exposed	0 / 18 (0.00%)	2 / 15 (13.33%)
occurrences (all)	0	2
Blood alkaline phosphatase		
subjects affected / exposed	0 / 18 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	1
Blood bicarbonate decreased		
subjects affected / exposed	0 / 18 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	1
Blood creatinine increased		
subjects affected / exposed	0 / 18 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	1
Blood iron decreased		
subjects affected / exposed	0 / 18 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	1
Blood lactate dehydrogenase increase		
subjects affected / exposed	0 / 18 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	1
Blood phosphorus		
subjects affected / exposed	0 / 18 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	1
Blood phosphorus decreased		
subjects affected / exposed	0 / 18 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	1

Blood sodium increased subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1	0 / 15 (0.00%) 0	
Injury, poisoning and procedural complications			
Infusion Related Reactions subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0	1 / 15 (6.67%) 2	
Contusion subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1	0 / 15 (0.00%) 0	
Stoma Site Infection subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1	0 / 15 (0.00%) 0	
Stoma site Pain subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1	0 / 15 (0.00%) 0	
Nervous system disorders			
Peripheral sensory neuropathy subjects affected / exposed occurrences (all)	4 / 18 (22.22%) 13	8 / 15 (53.33%) 17	
Neuropathy peripheral subjects affected / exposed occurrences (all)	8 / 18 (44.44%) 8	4 / 15 (26.67%) 7	
Paraesthesia subjects affected / exposed occurrences (all)	4 / 18 (22.22%) 9	0 / 15 (0.00%) 0	
Dysgeusia subjects affected / exposed occurrences (all)	3 / 18 (16.67%) 6	0 / 15 (0.00%) 0	
Headache subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1	0 / 15 (0.00%) 0	
Peripheral motor neuropathy subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0	2 / 15 (13.33%) 2	
Dizziness			

subjects affected / exposed	1 / 18 (5.56%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Dysarthria			
subjects affected / exposed	1 / 18 (5.56%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Hypoaesthesia			
subjects affected / exposed	0 / 18 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Muscle contractions involuntary			
subjects affected / exposed	1 / 18 (5.56%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	5 / 18 (27.78%)	1 / 15 (6.67%)	
occurrences (all)	17	1	
Anaemia			
subjects affected / exposed	5 / 18 (27.78%)	3 / 15 (20.00%)	
occurrences (all)	8	4	
Leukopenia			
subjects affected / exposed	1 / 18 (5.56%)	0 / 15 (0.00%)	
occurrences (all)	8	0	
Thrombocytopenia			
subjects affected / exposed	3 / 18 (16.67%)	2 / 15 (13.33%)	
occurrences (all)	5	2	
Ear and labyrinth disorders			
Deafness			
subjects affected / exposed	0 / 18 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Otorrhoea			
subjects affected / exposed	1 / 18 (5.56%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Eye disorders			
Ocular hyperaemia			
subjects affected / exposed	1 / 18 (5.56%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal disorders			

Nausea		
subjects affected / exposed	9 / 18 (50.00%)	6 / 15 (40.00%)
occurrences (all)	25	14
Diarrhoea		
subjects affected / exposed	8 / 18 (44.44%)	6 / 15 (40.00%)
occurrences (all)	20	10
Vomiting		
subjects affected / exposed	4 / 18 (22.22%)	5 / 15 (33.33%)
occurrences (all)	7	9
Abdominal Pain		
subjects affected / exposed	5 / 18 (27.78%)	2 / 15 (13.33%)
occurrences (all)	8	5
Constipation		
subjects affected / exposed	8 / 18 (44.44%)	6 / 15 (40.00%)
occurrences (all)	10	12
Dysphagia		
subjects affected / exposed	2 / 18 (11.11%)	4 / 15 (26.67%)
occurrences (all)	2	6
Dry Mouth		
subjects affected / exposed	4 / 18 (22.22%)	2 / 15 (13.33%)
occurrences (all)	5	3
Abdominal Pain Upper		
subjects affected / exposed	0 / 18 (0.00%)	2 / 15 (13.33%)
occurrences (all)	0	3
Epigastric discomfort		
subjects affected / exposed	3 / 18 (16.67%)	0 / 15 (0.00%)
occurrences (all)	3	0
Gastrointestinal pain		
subjects affected / exposed	1 / 18 (5.56%)	0 / 15 (0.00%)
occurrences (all)	3	0
Abdominal Distension		
subjects affected / exposed	2 / 18 (11.11%)	0 / 15 (0.00%)
occurrences (all)	2	0
Flatulence		
subjects affected / exposed	2 / 18 (11.11%)	0 / 15 (0.00%)
occurrences (all)	2	0

Gastrooesophageal reflux disease		
subjects affected / exposed	2 / 18 (11.11%)	0 / 15 (0.00%)
occurrences (all)	2	0
Mouth Haemorrhage		
subjects affected / exposed	1 / 18 (5.56%)	0 / 15 (0.00%)
occurrences (all)	2	0
Odynophagia		
subjects affected / exposed	0 / 18 (0.00%)	2 / 15 (13.33%)
occurrences (all)	0	2
Abdominal Discomfort		
subjects affected / exposed	1 / 18 (5.56%)	0 / 15 (0.00%)
occurrences (all)	1	0
Colitis		
subjects affected / exposed	1 / 18 (5.56%)	0 / 15 (0.00%)
occurrences (all)	1	0
Defaecation urgency		
subjects affected / exposed	1 / 18 (5.56%)	0 / 15 (0.00%)
occurrences (all)	1	0
Dyspepsia		
subjects affected / exposed	1 / 18 (5.56%)	0 / 15 (0.00%)
occurrences (all)	1	0
Eructation		
subjects affected / exposed	1 / 18 (5.56%)	0 / 15 (0.00%)
occurrences (all)	1	0
Frequent Bowel Movements		
subjects affected / exposed	1 / 18 (5.56%)	0 / 15 (0.00%)
occurrences (all)	1	0
Haematochezia		
subjects affected / exposed	1 / 18 (5.56%)	0 / 15 (0.00%)
occurrences (all)	1	0
Retching		
subjects affected / exposed	1 / 18 (5.56%)	0 / 15 (0.00%)
occurrences (all)	1	0
Stomatitis		
subjects affected / exposed	0 / 18 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	1

Toothache subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1	0 / 15 (0.00%) 0	
Skin and subcutaneous tissue disorders Alopecia subjects affected / exposed occurrences (all)	3 / 18 (16.67%) 3	1 / 15 (6.67%) 1	
Dry Skin subjects affected / exposed occurrences (all)	3 / 18 (16.67%) 3	1 / 15 (6.67%) 1	
Palmar-plantar erythrodysesthesia syndrome subjects affected / exposed occurrences (all)	4 / 18 (22.22%) 4	0 / 15 (0.00%) 0	
Rash subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1	2 / 15 (13.33%) 2	
Erythema subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1	0 / 15 (0.00%) 0	
Nail Disorder subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1	0 / 15 (0.00%) 0	
Skin Reaction subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0	1 / 15 (6.67%) 1	
Musculoskeletal and connective tissue disorders Back Pain subjects affected / exposed occurrences (all)	2 / 18 (11.11%) 2	3 / 15 (20.00%) 3	
Pain in extremity subjects affected / exposed occurrences (all)	3 / 18 (16.67%) 3	1 / 15 (6.67%) 1	
Arthralgia subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0	2 / 15 (13.33%) 2	
Flank Pain			

subjects affected / exposed	0 / 18 (0.00%)	2 / 15 (13.33%)	
occurrences (all)	0	2	
Muscle Spasms			
subjects affected / exposed	1 / 18 (5.56%)	0 / 15 (0.00%)	
occurrences (all)	2	0	
trismus			
subjects affected / exposed	1 / 18 (5.56%)	0 / 15 (0.00%)	
occurrences (all)	2	0	
Joint Stiffness			
subjects affected / exposed	1 / 18 (5.56%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Infections and infestations			
Oral Herpes			
subjects affected / exposed	1 / 18 (5.56%)	2 / 15 (13.33%)	
occurrences (all)	1	2	
Cellulitis			
subjects affected / exposed	1 / 18 (5.56%)	1 / 15 (6.67%)	
occurrences (all)	1	1	
Nasopharyngitis			
subjects affected / exposed	0 / 18 (0.00%)	2 / 15 (13.33%)	
occurrences (all)	0	2	
Respiratory Tract Infection			
subjects affected / exposed	0 / 18 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Clostridium difficile infection			
subjects affected / exposed	1 / 18 (5.56%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Influenza			
subjects affected / exposed	0 / 18 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Kidney Infection			
subjects affected / exposed	1 / 18 (5.56%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Nail Infection			
subjects affected / exposed	1 / 18 (5.56%)	0 / 15 (0.00%)	
occurrences (all)	1	0	

Neutropenic Infection			
subjects affected / exposed	1 / 18 (5.56%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Neutropenic sepsis			
subjects affected / exposed	0 / 18 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Onychomycosis			
subjects affected / exposed	1 / 18 (5.56%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Pharyngitis			
subjects affected / exposed	0 / 18 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Sweating fever			
subjects affected / exposed	1 / 18 (5.56%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Tooth Infection			
subjects affected / exposed	1 / 18 (5.56%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	8 / 18 (44.44%)	5 / 15 (33.33%)	
occurrences (all)	11	8	
Hyponatraemia			
subjects affected / exposed	3 / 18 (16.67%)	1 / 15 (6.67%)	
occurrences (all)	5	3	
Hypocalcaemia			
subjects affected / exposed	3 / 18 (16.67%)	1 / 15 (6.67%)	
occurrences (all)	5	2	
Dehydration			
subjects affected / exposed	0 / 18 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Hypokalaemia			
subjects affected / exposed	3 / 18 (16.67%)	1 / 15 (6.67%)	
occurrences (all)	5	1	
Hyperglycaemia			

subjects affected / exposed	1 / 18 (5.56%)	1 / 15 (6.67%)	
occurrences (all)	1	2	
Hypomagnesaemia			
subjects affected / exposed	1 / 18 (5.56%)	1 / 15 (6.67%)	
occurrences (all)	2	1	
Hypoalbuminaemia			
subjects affected / exposed	0 / 18 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
30 March 2007	Revised Protocol Version 3.1 dated 01Mar2007 - contains additional exclusion criteria requested by the IBM
08 May 2009	Amended to version 4.0 dated 29 April 2008 Administrative and typographic corrections to the protocol
24 January 2011	Amended to Protocol Version 5.0 dated 19 Oct 2010 Was updated to new ICORG SOP format layout changes. Change of CI and site Also included updated, Conmed Information, Contraception Information in Inclusion Criteria and updated PIL to Version 2, dated 21 Aug 2009 Administrative changes throughout the protocol.

Notes:

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.

140 patients were originally planned to be recruited, the study was terminated early due to poor accrual rate, and only 35 patients participated in the study (17 in the EITax group and 18 in the EOX group).
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Notes: