# Clinical trial results:
# A Randomised Phase II trial of Epirubicin, Oxaliplatin and Capecitebine (EOX) versus Docetaxel and Oxaliplatin (ElTax) 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 |

### 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 (ElTax) 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 | Safety, Efficacy, Scientific research |
| 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<br>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<br>Units: years | | | |
| median | 62 | 64 | |
| full range (min-max) | 33 to 77 | 42 to 73 | - |
| Gender categorical<br>Units: Subjects | | | |
| Female | 6 | 3 | 9 |
| Male | 12 | 14 | 26 |
| Race<br>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.<br>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.<br>2=Ambulatory and capable of self-care but unable to carry out any work activities up and about more than 50% of waking hours.<br>3=Capable of only limited self-care, confined to bed or chair more than 50 waking hours.<br>4=Completely disabled. Cannot carry out any self-care. Totally confined to bed or chair.<br>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 | 14 | 22 | |
| full range (min-max) | 5 to 47 | 11 to 73 | - |
| Baseline Lab Result - Absolute neurophil count | | | |
| Units: (10to9/L) | | | |
| median | 5.110 | 5.400 | |
| full range (min-max) | 3.35 to 10.80 | 3.00 to 9.60 | - |
| Baseline Characteristic - Aspartate transaminase | | | |
| Units: U/L | | | |
| median | 19 | 29 | |
| full range (min-max) | 14 to 50 | 17 to 59 | - |
| Baseline Lab Result - Bilirubin | | | |
| Units: (umol/L) | | | |
| median | 6.50 | 9.00 | |
| full range (min-max) | 3.0 to 16.0 | 4.0 to 22.0 | - |
| Baseline Lab Result - Creatinine | | | |
| Units: (umol/L) | | | |
| median | 75.50 | 82.00 | |
| full range (min-max) | 37.0 to 112.0 | 55.0 to 114.0 | - |
| Baseline Lab Result - Haemoglobin | | | |
| Units: g/dl | | | |
| median | 12.450 | 12.500 | |
| full range (min-max) | 8.70 to 15.60 | 10.60 to 14.3 | - |
| Baseline Lab Results - Platelets | | | |
| Units: (10to9/L) | | | |
| median | 301.00 | 266.00 | |
| full range (min-max) | 173.0 to 550.0 | 160.00 to 676.00 | - |
| Baseline Vital Signs - Body Surface Area | | | |
| Units: (m^2) | | | |
| median | 1.770 | 1.890 | |
| full range (min-max) | 1.34 to 2.23 | 1.54 to 2.10 | - |
| Baseline Vital Sign - Diastolic blood pressure | | | |
| Units: (mmHg) | | | |
| median | 73.0 | 76.0 | |
| full range (min-max) | 59 to 90 | 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 |
|---|---|

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 |
|---|---|

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 |
| **Dictionary used** | |
| Dictionary name | MedDRA |
| Dictionary version | 21.0 |
| **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 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. | |

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

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|---|---|---|---|---|
| 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 | | |

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

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|---|---|---|---|
| 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 | |
| Diarrhoaea | | | |
| 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 | 1 / 18 (5.56%) | 0 / 15 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Skin and subcutaneous tissue disorders | | | |
| Alopecia | | | |
| subjects affected / exposed | 3 / 18 (16.67%) | 1 / 15 (6.67%) | |
| occurrences (all) | 3 | 1 | |
| Dry Skin | | | |
| subjects affected / exposed | 3 / 18 (16.67%) | 1 / 15 (6.67%) | |
| occurrences (all) | 3 | 1 | |
| Palmar-plantar erythrodysaesthesia syndrome | | | |
| subjects affected / exposed | 4 / 18 (22.22%) | 0 / 15 (0.00%) | |
| occurrences (all) | 4 | 0 | |
| Rash | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 2 / 15 (13.33%) | |
| occurrences (all) | 1 | 2 | |
| Erythema | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 15 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Nail Disorder | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 15 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Skin Reaction | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 1 / 15 (6.67%) | |
| occurrences (all) | 0 | 1 | |
| Musculoskeletal and connective tissue disorders | | | |
| Back Pain | | | |
| subjects affected / exposed | 2 / 18 (11.11%) | 3 / 15 (20.00%) | |
| occurrences (all) | 2 | 3 | |
| Pain in extremity | | | |
| subjects affected / exposed | 3 / 18 (16.67%) | 1 / 15 (6.67%) | |
| occurrences (all) | 3 | 1 | |
| Arthralgia | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 2 / 15 (13.33%) | |
| occurrences (all) | 0 | 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<br>Administrative and typographic corrections to the protocol |
| 24 January 2011 | Amended to Protocol Version 5.0 dated 19 Oct 2010<br>Was updated to new ICORG SOP format layout changes.<br>Change of CI and site<br>Also included updated, Conmed Information, Contraception Information in Inclusion Criteria and updated PIL to Version 2, dated 21 Aug 2009<br>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).

Notes: