



Clinical trial results:

Etude de phase II randomisée chez des patients porteurs d'un cancer épidermoïde métastatique de l'œsophage évaluant l'intérêt de la poursuite ou non d'un traitement cytotoxique chez des patients non progressifs après 6 semaines de chimiothérapie

Summary

EudraCT number	2010-021439-16
Trial protocol	FR
Global end of trial date	12 January 2016

Results information

Result version number	v1 (current)
This version publication date	25 June 2022
First version publication date	25 June 2022

Trial information

Trial identification

Sponsor protocol code	E-DIS-1006
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01248299
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Centre Oscar Lambret
Sponsor organisation address	3 Rue Frédéric Combemale, Lille, France, 59000
Public contact	Marie VANSEYMORTIER, Centre Oscar Lambret, 33 320295918, promotion@o-lambret.fr
Scientific contact	Antoine Adenis, Centre Oscar Lambret, 33 467612442, antoine.Adenis@icm.unicancer.fr
Sponsor organisation name	Centre Oscar Lambret
Sponsor organisation address	3 Rue Frédéric Combemale, Lille, France, 59000
Public contact	Marie VANSEYMORTIER, Centre Oscar Lambret, 33 320295918, promotion@o-lambret.fr
Scientific contact	Antoine ADENIS, Centre Oscar Lambret, 33 467612442, Antoine.Adenis@icm.unicancer.fr

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	12 January 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	12 January 2016
Global end of trial reached?	Yes
Global end of trial date	12 January 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To estimate overall survival

Protection of trial subjects:

This clinical trial will be conducted in accordance with the protocol, the ethical principles laid down by the 18th World Medical Assembly (Helsinki, 1964) and all applicable amendments laid down by the World Medical Assemblies, the International Conference on Harmonization (ICH) consolidated Guideline E6 for Good Clinical Practice (CPMP/ICH/135/95), and all applicable laws and regulations.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	03 January 2011
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	France: 105
Worldwide total number of subjects	105
EEA total number of subjects	105

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	61
From 65 to 84 years	44

85 years and over	0
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Subject disposition

Recruitment

Recruitment details:

105 patients were included in the initial part between 03/01/2011 and 09/02/2015 in 13 french centers. 67 patients were randomised between 07/03/2011 and 24/03/2015: 34 in arm A (continue CT) and 33 in arm B (stop CT).

Pre-assignment

Screening details:

A total of 106 patients are needed to allow the randomisation of 31 patients in each treatment arm.

Period 1

Period 1 title	Initial phase
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Initial part
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Arm description:

Study chemotherapy during the initial part was at the choice of the investigator: FU-CDDP (2 cures expected), or LV5FU2-CDDP (3 cures expected), or FOLFOX (3 cures expected), or TFP 4b (2 cures expected). During the initial part, chemotherapy lasts 6 weeks

Arm type	Experimental
Investigational medicinal product name	Cisplatin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Protocole FU-CDDP

J1 à J5 Fluoro-uracile 800 mg/m²
J1 ou J2 CisPlatine 75 mg/m²
Tous les 21 jours

Protocole LV5FU2-CDDP

J1 et J2 Elvorine 200 mg/m² sur 2h
J1 et J2 Fluoro-uracile 400 mg/m² bolus
J1 et J2 Fluoro-uracile 600 mg/m² continu sur 22h
J2 CisPlatine 50 mg/m²
Tous les 14 jours

Protocole FOLFOX

J1 Oxaliplatine 85 mg/m² sur 2h
J1 et J2 Fluoro-uracile 400 mg/m² bolus
J1 et J2 Fluoro-uracile 600 mg/m² continu sur 22h
J1 et J2 Elvorine 500 mg/m²
Tous les 14 jours

Protocole TPF

J1 et J8 Docetaxel 30 mg/m²
J1 CisPlatine 60 mg/m²
En continu Fluoro-uracile 200 mg/m² /j
Tous les 21 jours

Ou

J1 Docetaxel 50 mg/m²

J1 CisPlatine 70 mg/m²
 J1 à J5 Fluoro-uracile 700 mg/m² /j

Investigational medicinal product name	Calcium Levofolinate
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Protocole FU-CDDP

J1 à J5 Fluoro-uracile 800 mg/m²
 J1 ou J2 CisPlatine 75 mg/m²
 Tous les 21 jours

Protocole LV5FU2-CDDP

J1 et J2 Elvorine 200 mg/m² sur 2h
 J1 et J2 Fluoro-uracile 400 mg/m² bolus
 J1 et J2 Fluoro-uracile 600 mg/m² continu sur 22h
 J2 CisPlatine 50 mg/m²
 Tous les 14 jours

Protocole FOLFOX

J1 Oxaliplatine 85 mg/m² sur 2h
 J1 et J2 Fluoro-uracile 400 mg/m² bolus
 J1 et J2 Fluoro-uracile 600 mg/m² continu sur 22h
 J1 et J2 Elvorine 500 mg/m²
 Tous les 14 jours

Protocole TPF

J1 et J8 Docetaxel 30 mg/m²
 J1 CisPlatine 60 mg/m²
 En continu Fluoro-uracile 200 mg/m² /j
 Tous les 21 jours

Ou

J1 Docetaxel 50 mg/m²
 J1 CisPlatine 70 mg/m²
 J1 à J5 Fluoro-uracile 700 mg/m² /j

Investigational medicinal product name	Fluoro-uracile
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Protocole FU-CDDP

J1 à J5 Fluoro-uracile 800 mg/m²
 J1 ou J2 CisPlatine 75 mg/m²
 Tous les 21 jours

Protocole LV5FU2-CDDP

J1 et J2 Elvorine 200 mg/m² sur 2h
 J1 et J2 Fluoro-uracile 400 mg/m² bolus
 J1 et J2 Fluoro-uracile 600 mg/m² continu sur 22h
 J2 CisPlatine 50 mg/m²
 Tous les 14 jours

Protocole FOLFOX

J1 Oxaliplatine 85 mg/m² sur 2h
 J1 et J2 Fluoro-uracile 400 mg/m² bolus
 J1 et J2 Fluoro-uracile 600 mg/m² continu sur 22h
 J1 et J2 Elvorine 500 mg/m²
 Tous les 14 jours

Protocole TPF

J1 et J8 Docetaxel 30 mg/m²
 J1 CisPlatine 60 mg/m²
 En continu Fluoro-uracile 200 mg/m² /j
 Tous les 21 jours

Ou

J1 Docetaxel 50 mg/m²
 J1 CisPlatine 70 mg/m²
 J1 à J5 Fluoro-uracile 700 mg/m² /j

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

Dosage and administration details:

Protocole FU-CDDP

J1 à J5 Fluoro-uracile 800 mg/m²
 J1 ou J2 CisPlatine 75 mg/m²
 Tous les 21 jours

Protocole LV5FU2-CDDP

J1 et J2 Elvorine 200 mg/m² sur 2h
 J1 et J2 Fluoro-uracile 400 mg/m² bolus
 J1 et J2 Fluoro-uracile 600 mg/m² continu sur 22h
 J2 CisPlatine 50 mg/m²
 Tous les 14 jours

Protocole FOLFOX

J1 Oxaliplatine 85 mg/m² sur 2h
 J1 et J2 Fluoro-uracile 400 mg/m² bolus
 J1 et J2 Fluoro-uracile 600 mg/m² continu sur 22h
 J1 et J2 Elvorine 500 mg/m²
 Tous les 14 jours

Protocole TPF

J1 et J8 Docetaxel 30 mg/m²
 J1 CisPlatine 60 mg/m²
 En continu Fluoro-uracile 200 mg/m² /j
 Tous les 21 jours

Ou

J1 Docetaxel 50 mg/m²
 J1 CisPlatine 70 mg/m²
 J1 à J5 Fluoro-uracile 700 mg/m² /j

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

Dosage and administration details:

Protocole FU-CDDP

J1 à J5 Fluoro-uracile 800 mg/m²
 J1 ou J2 CisPlatine 75 mg/m²
 Tous les 21 jours

Protocole LV5FU2-CDDP

J1 et J2 Elvorine 200 mg/m² sur 2h
 J1 et J2 Fluoro-uracile 400 mg/m² bolus
 J1 et J2 Fluoro-uracile 600 mg/m² continu sur 22h
 J2 CisPlatine 50 mg/m²
 Tous les 14 jours

Protocole FOLFOX

J1	Oxaliplatine	85 mg/m ² sur 2h
J1 et J2	Fluoro-uracile	400 mg/m ² bolus
J1 et J2	Fluoro-uracile	600 mg/m ² continu sur 22h
J1 et J2	Elvorine	500 mg/m ²

Tous les 14 jours

Protocole TPF

J1 et J8	Docetaxel	30 mg/m ²
J1	CisPlatine	60 mg/m ²
En continu	Fluoro-uracile	200 mg/m ² /j

Tous les 21 jours

Ou

J1	Docetaxel	50 mg/m ²
J1	CisPlatine	70 mg/m ²
J1 à J5	Fluoro-uracile	700 mg/m ² /j

Number of subjects in period 1	Initial part
Started	105
Completed	101
Not completed	4
Protocol deviation	4

Period 2

Period 2 title	Randomisation phase
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	CT-CONT

Arm description:

Patients randomised in this CT-CONT arm continue the same chemotherapy as the chemotherapy received in the initial arm

Arm type	Experimental
Investigational medicinal product name	Cisplatin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Protocole FU-CDDP

J1 à J5	Fluoro-uracile	800 mg/m ²
J1 ou J2	CisPlatine	75 mg/m ²

Tous les 21 jours

Protocole LV5FU2-CDDP
 J1 et J2 Elvorine 200 mg/m² sur 2h
 J1 et J2 Fluoro-uracile 400 mg/m² bolus
 J1 et J2 Fluoro-uracile 600 mg/m² continu sur 22h
 J2 CisPlatine 50 mg/m²
 Tous les 14 jours

Protocole FOLFOX
 J1 Oxaliplatine 85 mg/m² sur 2h
 J1 et J2 Fluoro-uracile 400 mg/m² bolus
 J1 et J2 Fluoro-uracile 600 mg/m² continu sur 22h
 J1 et J2 Elvorine 500 mg/m²
 Tous les 14 jours

Protocole TPF
 J1 et J8 Docetaxel 30 mg/m²
 J1 CisPlatine 60 mg/m²
 En continu Fluoro-uracile 200 mg/m² /j
 Tous les 21 jours

Ou

J1 Docetaxel 50 mg/m²
 J1 CisPlatine 70 mg/m²
 J1 à J5 Fluoro-uracile 700 mg/m² /j

Investigational medicinal product name	Calcium Levofolinate
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Protocole FU-CDDP
 J1 à J5 Fluoro-uracile 800 mg/m²
 J1 ou J2 CisPlatine 75 mg/m²
 Tous les 21 jours

Protocole LV5FU2-CDDP
 J1 et J2 Elvorine 200 mg/m² sur 2h
 J1 et J2 Fluoro-uracile 400 mg/m² bolus
 J1 et J2 Fluoro-uracile 600 mg/m² continu sur 22h
 J2 CisPlatine 50 mg/m²
 Tous les 14 jours

Protocole FOLFOX
 J1 Oxaliplatine 85 mg/m² sur 2h
 J1 et J2 Fluoro-uracile 400 mg/m² bolus
 J1 et J2 Fluoro-uracile 600 mg/m² continu sur 22h
 J1 et J2 Elvorine 500 mg/m²
 Tous les 14 jours

Protocole TPF
 J1 et J8 Docetaxel 30 mg/m²
 J1 CisPlatine 60 mg/m²
 En continu Fluoro-uracile 200 mg/m² /j
 Tous les 21 jours

Ou

J1 Docetaxel 50 mg/m²
 J1 CisPlatine 70 mg/m²
 J1 à J5 Fluoro-uracile 700 mg/m² /j

Investigational medicinal product name	Fluoro-uracile
Investigational medicinal product code	
Other name	

Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Protocole FU-CDDP

J1 à J5 Fluoro-uracile 800 mg/m²
J1 ou J2 CisPlatine 75 mg/m²
Tous les 21 jours

Protocole LV5FU2-CDDP

J1 et J2 Elvorine 200 mg/m² sur 2h
J1 et J2 Fluoro-uracile 400 mg/m² bolus
J1 et J2 Fluoro-uracile 600 mg/m² continu sur 22h
J2 CisPlatine 50 mg/m²
Tous les 14 jours

Protocole FOLFOX

J1 Oxaliplatine 85 mg/m² sur 2h
J1 et J2 Fluoro-uracile 400 mg/m² bolus
J1 et J2 Fluoro-uracile 600 mg/m² continu sur 22h
J1 et J2 Elvorine 500 mg/m²
Tous les 14 jours

Protocole TPF

J1 et J8 Docetaxel 30 mg/m²
J1 CisPlatine 60 mg/m²
En continu Fluoro-uracile 200 mg/m² /j
Tous les 21 jours

Ou

J1 Docetaxel 50 mg/m²
J1 CisPlatine 70 mg/m²
J1 à J5 Fluoro-uracile 700 mg/m² /j

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

Dosage and administration details:

Protocole FU-CDDP

J1 à J5 Fluoro-uracile 800 mg/m²
J1 ou J2 CisPlatine 75 mg/m²
Tous les 21 jours

Protocole LV5FU2-CDDP

J1 et J2 Elvorine 200 mg/m² sur 2h
J1 et J2 Fluoro-uracile 400 mg/m² bolus
J1 et J2 Fluoro-uracile 600 mg/m² continu sur 22h
J2 CisPlatine 50 mg/m²
Tous les 14 jours

Protocole FOLFOX

J1 Oxaliplatine 85 mg/m² sur 2h
J1 et J2 Fluoro-uracile 400 mg/m² bolus
J1 et J2 Fluoro-uracile 600 mg/m² continu sur 22h
J1 et J2 Elvorine 500 mg/m²
Tous les 14 jours

Protocole TPF

J1 et J8 Docetaxel 30 mg/m²
J1 CisPlatine 60 mg/m²
En continu Fluoro-uracile 200 mg/m² /j
Tous les 21 jours

Ou

J1 Docetaxel 50 mg/m²
 J1 CisPlatine 70 mg/m²
 J1 à J5 Fluoro-uracile 700 mg/m² /j

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

Dosage and administration details:

Protocole FU-CDDP

J1 à J5 Fluoro-uracile 800 mg/m²
 J1 ou J2 CisPlatine 75 mg/m²
 Tous les 21 jours

Protocole LV5FU2-CDDP

J1 et J2 Elvorine 200 mg/m² sur 2h
 J1 et J2 Fluoro-uracile 400 mg/m² bolus
 J1 et J2 Fluoro-uracile 600 mg/m² continu sur 22h
 J2 CisPlatine 50 mg/m²
 Tous les 14 jours

Protocole FOLFOX

J1 Oxaliplatine 85 mg/m² sur 2h
 J1 et J2 Fluoro-uracile 400 mg/m² bolus
 J1 et J2 Fluoro-uracile 600 mg/m² continu sur 22h
 J1 et J2 Elvorine 500 mg/m²
 Tous les 14 jours

Protocole TPF

J1 et J8 Docetaxel 30 mg/m²
 J1 CisPlatine 60 mg/m²
 En continu Fluoro-uracile 200 mg/m² /j
 Tous les 21 jours

Ou

J1 Docetaxel 50 mg/m²
 J1 CisPlatine 70 mg/m²
 J1 à J5 Fluoro-uracile 700 mg/m² /j

Arm title	CT-DISC
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Arm description:

Patients randomised in this CT-DISC arm did not received any treatment

Arm type	No intervention
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No investigational medicinal product assigned in this arm

Arm title	Not randomised
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Arm description:

Some patients were not randomised due to progression during the initial part of the study

Arm type	No intervention
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No investigational medicinal product assigned in this arm

Number of subjects in period 2	CT-CONT	CT-DISC	Not randomised
Started	34	33	34
Completed	34	33	34

Baseline characteristics

Reporting groups

Reporting group title	Initial part
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Reporting group description:

Study chemotherapy during the initial part was at the choice of the investigator: FU-CDDP (2 cures expected), or LV5FU2-CDDP (3 cures expected), or FOLFOX (3 cures expected), or TFP 4b (2 cures expected). During the initial part, chemotherapy lasts 6 weeks

Reporting group values	Initial part	Total	
Number of subjects	105	105	
Age categorical			
Units: Subjects			
In utero		0	
Preterm newborn infants (gestational age < 37 wks)		0	
Newborns (0-27 days)		0	
Infants and toddlers (28 days-23 months)		0	
Children (2-11 years)		0	
Adolescents (12-17 years)		0	
Adults (18-64 years)		0	
From 65-84 years		0	
85 years and over		0	
Age continuous			
Units: years			
median	62		
full range (min-max)	43 to 81	-	
Gender categorical			
Units: Subjects			
Female	16	16	
Male	89	89	

End points

End points reporting groups

Reporting group title	Initial part
Reporting group description: Study chemotherapy during the initial part was at the choice of the investigator: FU-CDDP (2 cures expected), or LV5FU2-CDDP (3 cures expected), or FOLFOX (3 cures expected), or TFP 4b (2 cures expected). During the initial part, chemotherapy lasts 6 weeks	
Reporting group title	CT-CONT
Reporting group description: Patients randomised in this CT-CONT arm continue the same chemotherapy as the chemotherapy received in the initial arm	
Reporting group title	CT-DISC
Reporting group description: Patients randomised in this CT-DISC arm did not received any treatment	
Reporting group title	Not randomised
Reporting group description: Some patients were not randomised due to progression during the initial part of the study	
Subject analysis set title	ITT randomised
Subject analysis set type	Intention-to-treat
Subject analysis set description: All patients randomised are analyzed (67 patients: 34 in CT-CONT arm and 33 patient in CT-DISC arm)	

Primary: Overall survival

End point title	Overall survival
End point description:	
End point type	Primary
End point timeframe: median overall survival in months	

End point values	CT-CONT	CT-DISC	ITT randomised	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	34	33	67	
Units: months				
number (confidence interval 95%)	8.5 (6.6 to 12)	8.8 (5.9 to 13.4)	8.5 (6.2 to 9.9)	

Statistical analyses

Statistical analysis title	Overall survival randomised part
Statistical analysis description: No treatment arm comparison was planned	
Comparison groups	CT-CONT v CT-DISC

Number of subjects included in analysis	67
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	o treatment arm comparison was planned
Parameter estimate	No treatment arm comparison was planned

Secondary: Progression-free survival

End point title	Progression-free survival
End point description:	
End point type	Secondary
End point timeframe:	
median progression-free survival	

End point values	CT-CONT	CT-DISC	ITT randomised	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	34	33	67	
Units: months				
number (confidence interval 95%)	4 (2.8 to 5.8)	1.4 (1.4 to 2.7)	3 (2.7 to 4.1)	

Statistical analyses

No statistical analyses for this end point

Secondary: Quality of life

End point title	Quality of life
End point description:	
<p>For functional scales, QLQ-C30 and QLQ-OES18 scores were considered as a definitive deterioration if the score decreased by more than 10 points compared with the score at randomisation and without later improvement superior to 10 points compared with the baseline. For symptom scales, a definitive deterioration was defined as an increase of 10 points or more without subsequent decrease. For each dimension of the QoL questionnaires, the time until definitive deterioration (TUDD) was defined as the time from randomisation to the first observation of a definitive deterioration of the corresponding score or death. Patients alive without reported definitive deterioration were censored at the date of the last follow-up visit. Patients without any QoL questionnaires were censored at randomisation. TUDD was estimated using the Kaplan Meier method. The impact of treatments on the different dimensions of the QoL was estimated by hazard ratios of QoL deterioration using Cox models.</p>	
End point type	Secondary
End point timeframe:	
<p>QoL was assessed using the EORTC quality of life score questionnaire (QLQ-C30) and with the oesophagus-specific questionnaire (QLQ-OES18) at the baseline and every 6 weeks thereafter until 42 weeks after randomisation.</p>	

End point values	CT-CONT	CT-DISC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	34	33		
Units: median				
number (confidence interval 95%)				
QLQ-C30 Physical	7.3 (5.6 to 9.4)	5.4 (2.9 to 8.5)		
QLQ-C30 Global health status	6.6 (3.3 to 12.4)	4.2 (2.9 to 8.5)		
QLQ-C30 Role	5.6 (3.1 to 8.1)	4.5 (3.2 to 8.3)		
QLQ-C30 Emotional	7.1 (4.2 to 11.9)	5.6 (3.2 to 7.8)		
QLQ-C30 Cognitive	7.8 (3.3 to 12)	4.1 (2.8 to 8.5)		
QLQ-C30 Social	5.6 (3.0 to 8.1)	6.2 (4.2 to 8.8)		
QLQ-C30 Fatigue	5.6 (2.8 to 9.6)	4.4 (2.9 to 6.4)		
QLQ-C30 Nausea	7.8 (3.3 to 9.8)	5.4 (2.0 to 7.8)		
QLQ-C30 Pain	5.6 (2.8 to 7.0)	2.9 (2.1 to 6.3)		
QLQ-C30 Dyspnoea	7.3 (4.2 to 11.9)	4.4 (2.8 to 7.8)		
QLQ-C30 Insomnia	7.3 (3.3 to 11.9)	5.4 (2.0 to 7.8)		
QLQ-C30 Appetite loss	7.1 (5.2 to 12)	4.5 (2.9 to 7.8)		
QLQ-C30 Constipation	7.3 (5.2 to 11.9)	5.7 (2.8 to 9.9)		
QLQ-C30 Diarrhoea	6.6 (3.3 to 9.9)	4.5 (2.9 to 8.5)		
QLQ-C30 Financial difficulties	8.1 (5.6 to 12.4)	6.3 (3.2 to 9.9)		
QLQ-C30 Pain alone	5.6 (3.0 to 7.3)	5.4 (2.8 to 8.3)		
QLQ-OES18 Dysphagia	7.3 (4.2 to 12)	2.9 (1.4 to 4.4)		
QLQ-OES18 Eating	7.7 (5.6 to 9.5)	2.9 (2.0 to 5.9)		
QLQ-OES18 Reflux	7.8 (4.7 to 11.9)	3.2 (1.4 to 7.8)		
QLQ-OES18 Pain	8.1 (5.6 to 12.0)	2.4 (1.4 to 3.2)		
QLQ-OES18 Trouble swallowing	7.8 (5.2 to 11.9)	6.3 (3.2 to 9.1)		
QLQ-OES18 Choked when swallowing	7.1 (4.2 to 9.9)	5.4 (3.0 to 6.9)		
QLQ-OES18 Dry mouth	6.8 (3.3 to 9.8)	5.9 (3.1 to 9.9)		
QLQ-OES18 Taste	7.3 (5.2 to 9.5)	4.4 (2.9 to 7.8)		
QLQ-OES18 Coughing	8.1 (5.6 to 9.9)	6.3 (3.2 to 8.8)		

Statistical analyses

Statistical analysis title	TUDD Global health status
Statistical analysis description:	
TUDD was estimated using the KaplanMeier method. The impact of treatments on the different dimensions of the QoL was estimated by hazard ratios (HRCT-DISC/CTCONT of QoL deterioration using Cox models.	
Comparison groups	CT-CONT v CT-DISC

Number of subjects included in analysis	67
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	1.44
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.82
upper limit	2.53

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Patients were observed until death or until 48 months after study entry.

Assessment type	Non-systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	2
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Reporting groups

Reporting group title	All adverse events
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Reporting group description: -

Serious adverse events	All adverse events		
Total subjects affected by serious adverse events			
subjects affected / exposed	19 / 64 (29.69%)		
number of deaths (all causes)	54		
number of deaths resulting from adverse events	1		
Investigations			
WEIGHT DECREASED			
subjects affected / exposed	1 / 64 (1.56%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Tongue neoplasm malignant stage unspecified			
subjects affected / exposed	1 / 64 (1.56%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
SHOCK			
subjects affected / exposed	1 / 64 (1.56%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
HEPATIC ENCEPHALOPATHY			

subjects affected / exposed	1 / 64 (1.56%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
ALTERED STATE OF CONSCIOUSNESS			
subjects affected / exposed	1 / 64 (1.56%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
EPILEPSY			
subjects affected / exposed	1 / 64 (1.56%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
FEBRILE NEUTROPENIA			
subjects affected / exposed	1 / 64 (1.56%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
General physical health deterioration			
subjects affected / exposed	1 / 64 (1.56%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
PYREXIA			
subjects affected / exposed	1 / 64 (1.56%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
ANAL FISSURE			
subjects affected / exposed	1 / 64 (1.56%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
DYSPHAGIA			

subjects affected / exposed	7 / 64 (10.94%)		
occurrences causally related to treatment / all	1 / 9		
deaths causally related to treatment / all	0 / 0		
PANCREATITIS			
subjects affected / exposed	1 / 64 (1.56%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
LUNG DISORDER			
subjects affected / exposed	1 / 64 (1.56%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
DYSPNOEA			
subjects affected / exposed	1 / 64 (1.56%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
PULMONARY EMBOLISM			
subjects affected / exposed	1 / 64 (1.56%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
DIVERTICULITIS			
subjects affected / exposed	1 / 64 (1.56%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
INFECTION			
subjects affected / exposed	1 / 64 (1.56%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	All adverse events		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	49 / 64 (76.56%)		
Nervous system disorders			
PARAESTHESIA			
subjects affected / exposed	20 / 64 (31.25%)		
occurrences (all)	65		
Blood and lymphatic system disorders			
ANAEMIA			
subjects affected / exposed	8 / 64 (12.50%)		
occurrences (all)	22		
NEUTROPENIA			
subjects affected / exposed	12 / 64 (18.75%)		
occurrences (all)	24		
LYMPHOPENIA			
subjects affected / exposed	4 / 64 (6.25%)		
occurrences (all)	8		
Thrombocytopenia			
subjects affected / exposed	6 / 64 (9.38%)		
occurrences (all)	15		
General disorders and administration site conditions			
ASTHENIA			
subjects affected / exposed	17 / 64 (26.56%)		
occurrences (all)	39		
FATIGUE			
subjects affected / exposed	10 / 64 (15.63%)		
occurrences (all)	20		
Gastrointestinal disorders			
CONSTIPATION			
subjects affected / exposed	7 / 64 (10.94%)		
occurrences (all)	9		
DYSPHAGIA			
subjects affected / exposed	6 / 64 (9.38%)		
occurrences (all)	9		
MUCOSAL INFLAMMATION			
subjects affected / exposed	8 / 64 (12.50%)		
occurrences (all)	8		

NAUSEA subjects affected / exposed occurrences (all)	8 / 64 (12.50%) 15		
VOMITING subjects affected / exposed occurrences (all)	6 / 64 (9.38%) 7		
Metabolism and nutrition disorders DECREASED APPETITE subjects affected / exposed occurrences (all)	8 / 64 (12.50%) 8		
Weight decreased subjects affected / exposed occurrences (all)	4 / 64 (6.25%) 7		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
25 November 2010	Addition of investigators
07 February 2011	Addition of an investigator and addition of trial site
07 July 2011	Addition of a center
08 August 2011	Addition of an investigator
17 October 2011	Protocol amendement (pharmaco-vigilance and update of the investigator list)
03 June 2013	Addition of a center Modification of study duration and number of patients Addition of investigators
31 July 2013	Addition of a center

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

<http://www.ncbi.nlm.nih.gov/pubmed/30798084>