Clinical trial results:
Randomised Phase II Pilot Studiy: Induction Chemotherapy with Docetaxel, Cisplatin und Cetuximab versus Docetaxel, Cisplatin und 5 FU followed by Radiotherapy with Cetuximab for locally advanced or not resectable Carcinoma of the Head and Neck

Summary

EudraCT number	2011-005540-99
Trial protocol	AT
Global end of trial date	28 January 2021

Results information

Result version number	v1
This version publication date	29 January 2022
First version publication date	29 January 2022

Trial information

Trial identification

Sponsor protocol code	AGMT_HNO2

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01884259
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	AGMT
Sponsor organisation address	Gentzgasse 60/21, Vienna, Austria, 1180
Public contact	Daniela Wolkersdorfer, AGMT gemeinnützige GmbH, +43 6626404412, d.wolkersdorfer@agmt.at
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Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	08 December 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	08 June 2018
Global end of trial reached?	Yes
Global end of trial date	28 January 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Response Rate (CR, PR) 3 months after end of therapy (RECIST)

Protection of trial subjects:

Safety assessments were done on a regular basis. All patients having received at least one dose of the study medication have been followed for adverse events for 28 days after discontinuing study treatment or completion of study treatment. In general, concomitant medications and therapies necessary for supportive care and safety of the patient were allowed and recommended.

Background therapy:

Arm A: Docetaxel 75mg/m² day 1; Cisplatin 75mg/m² day 1; 5FU 750 mg/m² day 1 -5
Arm B: Docetaxel 75 mg/m² day 1; Cisplatin 75mg/m² day 1

Evidence for comparator: -

Actual start date of recruitment	31 May 2013
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	Austria: 100
Worldwide total number of subjects	100
EEA total number of subjects	100

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)	75
From 65 to 84 years	25
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

From March 2013 to January 2016, 102 patients were recruited in 8 sites in Austria.

Pre-assignment

Screening details:

2 patients were ineligible for study participation and had to be replaced to reach the planned number of 100 eligible patients: 1 patient did not meet inclusion criteria, and 1 patient withdrew consent before treatment was intiated.

Period 1

Period 1 title	Induction chemotherapy
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	TPF-arm

Arm description:

3 21-day cycles of induction chemotherapy consisting of docetaxel 75 mg/m2 given as a 1-h infusion and cisplatin 75 mg/m2 given as a 2-h infusion on day one, followed by 5FU 750 mg/m2 administered as a continuous infusion for five consecutive days.

Arm type	Experimental
Investigational medicinal product name	Docetaxel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Infusion

Dosage and administration details:

Docetaxel 75mg/m2 day 1

Investigational medicinal product name	Cisplatin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Infusion

Dosage and administration details:

Cisplatin 75 mg/m2 day 1

Investigational medicinal product name	5FU
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Infusion

Dosage and administration details:

5FU 750mg/m2 day 1-5

Arm title	TPC-arm

Arm description:

3 21-day cycles of induction chemotherapy consisting of docetaxel 75 mg/m2 given as a 1-h infusion and cisplatin 75 mg/m2 cetuximab 400 mg/m2 given as a 2-h infusion on day one as a loading dose, followed by cetuximab 250 mg/m2 given as a 1-h infusion weekly (thrice per cycle).

Arm type	Experimental

Investigational medicinal product name	Cetuximab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Infusion

Dosage and administration details:

Cetuximab 400 mg/m2 given as a 2-h infusion on day one as a loading dose, followed by cetuximab 250 mg/m2 given as a 1-h infusion weekly (thrice per cycle).

Investigational medicinal product name	Docetaxel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Infusion

Dosage and administration details:

Docetaxel 75mg/m2 day 1

Investigational medicinal product name	Cisplatin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Infusion

Dosage and administration details:

Cisplatin 75 mg/m2 day 1

Number of subjects in period 1	TPF-arm	TPC-arm
Started	49	51
Completed	46	46
Not completed	3	5
death	-	1
drop-out	3	4

Period 2

Period 2 title	Radiation therapy plus Cetuximab
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes

Arm title	TPF-arm

Arm description:

RT started maximum 6 weeks after the last administration of docetaxel and cisplatin. A loading dose of cetuximab 400 mg/m2 intravenously over 120 min was administered to the TPF arm one week before the start of concomitant boost RT. Followed by weekly infusions of cetuximab 250 mg/m2 during the whole course of RT (seven infusions in total).

Arm type	Experimental
Investigational medicinal product name	Cetuximab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Infusion

Dosage and administration details:

Loading dose 400mg/m2; followed by weekly infusions with 250 mg/m2

Arm title	TPC-arm

Arm description:

RT started maximum 6 weeks after the last administration of docetaxel and cisplatin. A dose of cetuximab 250mg/m2 intravenously over 120 min was administered to the TPC arm one week before the start of concomitant boost RT. Followed by weekly infusions of cetuximab 250 mg/m2 during the whole course of RT (seven infusions in total).

Arm type	Experimental
Investigational medicinal product name	Cetuximab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Infusion

Dosage and administration details:

250 mg/m2 one week before and during the whole course of RT (seven infusions in total).

Number of subjects in period 2[1]	TPF-arm	TPC-arm
Started	44	45
Completed	44	44
Not completed	0	1
death	-	1

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.
Justification: TPF-arm: 2 patients did not start Radiotherapy+C: 1 patient due to PD, 1 patient due to protocol violation;
TPC-arm: 1 patient did not start Radiotherapy+C due to PD

Baseline characteristics

Reporting groups	
Reporting group title	TPF-arm
Reporting group description:	
3 21-day cycles of induction chemotherapy consisting of docetaxel 75 mg/m2 given as a 1-h infusion and cisplatin 75 mg/m2 given as a 2-h infusion on day one, followed by 5FU 750 mg/m2 administered as a continuous infusion for five consecutive days.	
Reporting group title	TPC-arm
Reporting group description:	
3 21-day cycles of induction chemotherapy consisting of docetaxel 75 mg/m2 given as a 1-h infusion and cisplatin 75 mg/m2 cetuximab 400 mg/m2 given as a 2-h infusion on day one as a loading dose, followed by cetuximab 250 mg/m2 given as a 1-h infusion weekly (thrice per cycle).	

Reporting group values	TPF-arm	TPC-arm	Total
Number of subjects	49	51	100
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			
geometric mean	58.3	58.2	
full range (min-max)	40 to 72	35 to 78	-
Gender categorical Units: Subjects			
Female	7	6	13
Male	42	45	87

End points

End points reporting groups

Reporting group title	TPF-arm
Reporting group description:	
3 21-day cycles of induction chemotherapy consisting of docetaxel 75 mg/m2 given as a 1-h infusion and cisplatin 75 mg/m2 given as a 2-h infusion on day one, followed by 5FU 750 mg/m2 administered as a continuous infusion for five consecutive days.	
Reporting group title	TPC-arm
Reporting group description:	
3 21-day cycles of induction chemotherapy consisting of docetaxel 75 mg/m2 given as a 1-h infusion and cisplatin 75 mg/m2 cetuximab 400 mg/m2 given as a 2-h infusion on day one as a loading dose, followed by cetuximab 250 mg/m2 given as a 1-h infusion weekly (thrice per cycle).	
Reporting group title	TPF-arm
Reporting group description:	
RT started maximum 6 weeks after the last administration of docetaxel and cisplatin. A loading dose of cetuximab 400 mg/m2 intravenously over 120 min was administered to the TPF arm one week before the start of concomitant boost RT. Followed by weekly infusions of cetuximab 250 mg/m2 during the whole course of RT (seven infusions in total).	
Reporting group title	TPC-arm
Reporting group description:	
RT started maximum 6 weeks after the last administration of docetaxel and cisplatin. A dose of cetuximab 250mg/m2 intravenously over 120 min was administered to the TPC arm one week before the start of concomitant boost RT. Followed by weekly infusions of cetuximab 250 mg/m2 during the whole course of RT (seven infusions in total).	

Primary: Response three months after RT + C

End point title	Response three months after RT + C[1]
End point description:	
The primary end-point of the study was overall response rate (ORR: complete remission [CR] + partial remission [PR]) three months after RT + C was finished, assessed on the basis of CT or MRI performance as per the RECIST criteria.	
End point type	Primary
End point timeframe:	
Three months after radiotherapie plus cetuximab	
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: Although the ORR of TPC compared favourably with TPF (74.5% and 63.3%, respectively), the observed difference did not reach statistical significance.	

End point values	TPF-arm	TPC-arm		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	49	51		
Units: subjects				
Complete Remission (CR)	16	25		
Partial Remission (PR)	15	13		
Stable Disaease (SD)	3	2		
Overall Response Rate (ORR)	31	38		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All patients having received at least one dose of the study medication were followed for adverse events for at least 28 days after discontinuing study treatment or completion of study treatment.

Adverse event reporting additional description:

Acute chemotherapy toxicity was collected after each cycle of chemotherapy until the start of radiation. Acute radiation toxicity was recorded once at the end of radiation or at toxicity-related pauses or discontinuation of radiation therapy. Acute toxicity was recorded 30 days and 3 months after the end of cetuximab and radiation.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	21.0

Reporting groups

Reporting group title	Overall trial

Reporting group description:

Relation to IMP cetuximab is given.

Serious adverse events	Overall trial		
Total subjects affected by serious adverse events			
subjects affected / exposed	77 / 100 (77.00%)		
number of deaths (all causes)	41		
number of deaths resulting from adverse events	2		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenoma benign			
subjects affected / exposed	1 / 100 (1.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 100 (1.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Thrombosis			
subjects affected / exposed	1 / 100 (1.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Hypotension				
subjects affected / exposed	1 / 100 (1.00%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
General disorders and administration site conditions				
Mucosal inflammation				
subjects affected / exposed	18 / 100 (18.00%)			
occurrences causally related to treatment / all	0 / 27			
deaths causally related to treatment / all	0 / 0			
General physical health deterioration				
subjects affected / exposed	11 / 100 (11.00%)			
occurrences causally related to treatment / all	2 / 17			
deaths causally related to treatment / all	0 / 0			
Pyrexia				
subjects affected / exposed	1 / 100 (1.00%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Chest pain				
subjects affected / exposed	1 / 100 (1.00%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Impaired healing				
subjects affected / exposed	1 / 100 (1.00%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Extravasation				
subjects affected / exposed	1 / 100 (1.00%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Pain				
subjects affected / exposed	1 / 100 (1.00%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			

Facial pain				
subjects affected / exposed	1 / 100 (1.00%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Asthenia				
subjects affected / exposed	1 / 100 (1.00%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Fatigue				
subjects affected / exposed	1 / 100 (1.00%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Immune system disorders				
Anaphylactic reaction				
subjects affected / exposed	2 / 100 (2.00%)			
occurrences causally related to treatment / all	2 / 2			
deaths causally related to treatment / all	0 / 0			
Respiratory, thoracic and mediastinal disorders				
Dyspnoea				
subjects affected / exposed	1 / 100 (1.00%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Respiratory failure				
subjects affected / exposed	1 / 100 (1.00%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Epistaxis				
subjects affected / exposed	1 / 100 (1.00%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumothorax				
subjects affected / exposed	1 / 100 (1.00%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			

Pulmonary fibrosis			
subjects affected / exposed	1 / 100 (1.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Insomnia			
subjects affected / exposed	1 / 100 (1.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Delirium			
subjects affected / exposed	1 / 100 (1.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Investigations			
C-reactive protein increased			
subjects affected / exposed	9 / 100 (9.00%)		
occurrences causally related to treatment / all	0 / 9		
deaths causally related to treatment / all	0 / 0		
Blood creatine increased			
subjects affected / exposed	5 / 100 (5.00%)		
occurrences causally related to treatment / all	1 / 5		
deaths causally related to treatment / all	0 / 0		
Weight decreased			
subjects affected / exposed	2 / 100 (2.00%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
White blood cell count decreased			
subjects affected / exposed	1 / 100 (1.00%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Inflammatory marker increased			
subjects affected / exposed	1 / 100 (1.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Creatinine renal clearance decreased				
subjects affected / exposed	1 / 100 (1.00%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Injury, poisoning and procedural complications				
Radiation skin injury				
subjects affected / exposed	6 / 100 (6.00%)			
occurrences causally related to treatment / all	0 / 6			
deaths causally related to treatment / all	0 / 0			
Infusion related reaction				
subjects affected / exposed	2 / 100 (2.00%)			
occurrences causally related to treatment / all	2 / 2			
deaths causally related to treatment / all	0 / 0			
Laceration				
subjects affected / exposed	1 / 100 (1.00%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cardiac disorders				
Atrial fibrillation				
subjects affected / exposed	1 / 100 (1.00%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Arteriospasm coronary				
subjects affected / exposed	1 / 100 (1.00%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Acute myocardial infarction				
subjects affected / exposed	1 / 100 (1.00%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Acute right ventricular failure				
subjects affected / exposed	1 / 100 (1.00%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			

Nervous system disorders			
Orthostatic intolerance			
subjects affected / exposed	1 / 100 (1.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Transient ischaemic attack			
subjects affected / exposed	1 / 100 (1.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Peroneal nerve palsy			
subjects affected / exposed	1 / 100 (1.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Dizziness			
subjects affected / exposed	1 / 100 (1.00%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Aphasia			
subjects affected / exposed	1 / 100 (1.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Neuropathy peripheral			
subjects affected / exposed	1 / 100 (1.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Leukopenia			
subjects affected / exposed	7 / 100 (7.00%)		
occurrences causally related to treatment / all	0 / 9		
deaths causally related to treatment / all	0 / 0		
Neutropenia			
subjects affected / exposed	5 / 100 (5.00%)		
occurrences causally related to treatment / all	0 / 5		
deaths causally related to treatment / all	0 / 0		

Febrile neutropenia				
subjects affected / exposed	3 / 100 (3.00%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Thrombocytopenia				
subjects affected / exposed	1 / 100 (1.00%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Anaemia				
subjects affected / exposed	1 / 100 (1.00%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Ear and labyrinth disorders				
Vertigo				
subjects affected / exposed	1 / 100 (1.00%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal disorders				
Diarrhoea				
subjects affected / exposed	13 / 100 (13.00%)			
occurrences causally related to treatment / all	3 / 18			
deaths causally related to treatment / all	0 / 0			
Dysphagia				
subjects affected / exposed	13 / 100 (13.00%)			
occurrences causally related to treatment / all	0 / 13			
deaths causally related to treatment / all	0 / 0			
Vomiting				
subjects affected / exposed	3 / 100 (3.00%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Stomatitis				
subjects affected / exposed	3 / 100 (3.00%)			
occurrences causally related to treatment / all	1 / 4			
deaths causally related to treatment / all	0 / 0			

Gastrointestinal haemorrhage				
subjects affected / exposed	1 / 100 (1.00%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Abdominal pain upper				
subjects affected / exposed	1 / 100 (1.00%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cheilitis				
subjects affected / exposed	1 / 100 (1.00%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Abdominal pain				
subjects affected / exposed	1 / 100 (1.00%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Nausea				
subjects affected / exposed	1 / 100 (1.00%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Rectal haemorrhage				
subjects affected / exposed	1 / 100 (1.00%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Colitis				
subjects affected / exposed	1 / 100 (1.00%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gastritis				
subjects affected / exposed	1 / 100 (1.00%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hepatobiliary disorders				

Hepatic necrosis				
subjects affected / exposed	1 / 100 (1.00%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cholelithiasis				
subjects affected / exposed	1 / 100 (1.00%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Bile duct stone				
subjects affected / exposed	1 / 100 (1.00%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Biliary colic				
subjects affected / exposed	1 / 100 (1.00%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Skin and subcutaneous tissue disorders				
Dermatitis				
subjects affected / exposed	9 / 100 (9.00%)			
occurrences causally related to treatment / all	1 / 11			
deaths causally related to treatment / all	0 / 0			
Rash				
subjects affected / exposed	2 / 100 (2.00%)			
occurrences causally related to treatment / all	2 / 2			
deaths causally related to treatment / all	0 / 0			
Acne				
subjects affected / exposed	2 / 100 (2.00%)			
occurrences causally related to treatment / all	2 / 2			
deaths causally related to treatment / all	0 / 0			
Seborrhoeic dermatitis				
subjects affected / exposed	1 / 100 (1.00%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Skin lesion				

subjects affected / exposed	1 / 100 (1.00%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Dermatitis acneiform				
subjects affected / exposed	1 / 100 (1.00%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Renal and urinary disorders				
Renal failure				
subjects affected / exposed	4 / 100 (4.00%)			
occurrences causally related to treatment / all	0 / 4			
deaths causally related to treatment / all	0 / 0			
Acute kidney injury				
subjects affected / exposed	3 / 100 (3.00%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Renal impairment				
subjects affected / exposed	1 / 100 (1.00%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Musculoskeletal and connective tissue disorders				
Pain in extremity				
subjects affected / exposed	1 / 100 (1.00%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Back pain				
subjects affected / exposed	1 / 100 (1.00%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Infections and infestations				
Pneumonia				
subjects affected / exposed	8 / 100 (8.00%)			
occurrences causally related to treatment / all	1 / 11			
deaths causally related to treatment / all	0 / 1			

Infection			
subjects affected / exposed	6 / 100 (6.00%)		
occurrences causally related to treatment / all	0 / 7		
deaths causally related to treatment / all	0 / 0		
Device related infection			
subjects affected / exposed	3 / 100 (3.00%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Staphylococcal infection			
subjects affected / exposed	3 / 100 (3.00%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal infection			
subjects affected / exposed	2 / 100 (2.00%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Wound infection			
subjects affected / exposed	1 / 100 (1.00%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Pseudomonal sepsis			
subjects affected / exposed	1 / 100 (1.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Oral candidiasis			
subjects affected / exposed	1 / 100 (1.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Brain abscess			
subjects affected / exposed	1 / 100 (1.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory tract infection			

subjects affected / exposed	1 / 100 (1.00%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cystitis				
subjects affected / exposed	1 / 100 (1.00%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Sepsis				
subjects affected / exposed	1 / 100 (1.00%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Clostridial infection				
subjects affected / exposed	1 / 100 (1.00%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Tracheitis				
subjects affected / exposed	1 / 100 (1.00%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Tracheostomy infection				
subjects affected / exposed	1 / 100 (1.00%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Influenza				
subjects affected / exposed	1 / 100 (1.00%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Abscess				
subjects affected / exposed	1 / 100 (1.00%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Mastoiditis				

subjects affected / exposed	1 / 100 (1.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Hypokalaemia			
subjects affected / exposed	2 / 100 (2.00%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Hypophagia			
subjects affected / exposed	1 / 100 (1.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Electrolyte imbalance			
subjects affected / exposed	1 / 100 (1.00%)		
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	Overall trial		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	99 / 100 (99.00%)		
Investigations			
Weight decreased			
subjects affected / exposed	74 / 100 (74.00%)		
occurrences (all)	115		
C-reactive protein increased			
subjects affected / exposed	10 / 100 (10.00%)		
occurrences (all)	14		
Blood creatine increased			
subjects affected / exposed	6 / 100 (6.00%)		
occurrences (all)	7		
Injury, poisoning and procedural complications			

Radiation skin injury subjects affected / exposed occurrences (all)	24 / 100 (24.00%) 24		
Vascular disorders Lymphoedema subjects affected / exposed occurrences (all)	7 / 100 (7.00%) 7		
Nervous system disorders Dysgeusia subjects affected / exposed occurrences (all) Neuropathy peripheral subjects affected / exposed occurrences (all)	20 / 100 (20.00%) 23 6 / 100 (6.00%) 7		
Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all) Leukopenia subjects affected / exposed occurrences (all) Thrombocytopenia subjects affected / exposed occurrences (all) Neutropenia subjects affected / exposed occurrences (all)	50 / 100 (50.00%) 122 33 / 100 (33.00%) 61 29 / 100 (29.00%) 50 24 / 100 (24.00%) 33		
General disorders and administration site conditions Mucosal inflammation subjects affected / exposed occurrences (all) Fatigue subjects affected / exposed occurrences (all) Pain	71 / 100 (71.00%) 123 35 / 100 (35.00%) 42		

subjects affected / exposed	19 / 100 (19.00%)		
occurrences (all)	20		
Application site oedema			
subjects affected / exposed	10 / 100 (10.00%)		
occurrences (all)	11		
Pyrexia			
subjects affected / exposed	7 / 100 (7.00%)		
occurrences (all)	7		
Gastrointestinal disorders			
Dry mouth			
subjects affected / exposed	53 / 100 (53.00%)		
occurrences (all)	65		
Dysphagia			
subjects affected / exposed	49 / 100 (49.00%)		
occurrences (all)	52		
Diarrhoea			
subjects affected / exposed	24 / 100 (24.00%)		
occurrences (all)	26		
Nausea			
subjects affected / exposed	24 / 100 (24.00%)		
occurrences (all)	32		
Stomatitis			
subjects affected / exposed	14 / 100 (14.00%)		
occurrences (all)	17		
Skin and subcutaneous tissue disorders			
Dermatitis acneiform			
subjects affected / exposed	35 / 100 (35.00%)		
occurrences (all)	54		
Dermatitis			
subjects affected / exposed	31 / 100 (31.00%)		
occurrences (all)	39		
Rash			
subjects affected / exposed	15 / 100 (15.00%)		
occurrences (all)	18		
Acne			

subjects affected / exposed occurrences (all)	14 / 100 (14.00%) 18		
Infections and infestations Candida infection subjects affected / exposed occurrences (all) Urinary tract infection subjects affected / exposed occurrences (all)	 11 / 100 (11.00%) 11 6 / 100 (6.00%) 6		
Metabolism and nutrition disorders Hypokalaemia subjects affected / exposed occurrences (all) Hypomagnesaemia subjects affected / exposed occurrences (all) Hypocalcaemia subjects affected / exposed occurrences (all)	 33 / 100 (33.00%) 47 14 / 100 (14.00%) 21 7 / 100 (7.00%) 10		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

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.

None

Notes:

Online references

http://www.ncbi.nlm.nih.gov/pubmed/34022697