



## Clinical trial results:

### Phase II Study of Oxaliplatin / Irinotecan / Bevacizumab Followed by Docetaxel / Bevacizumab in Inoperable Locally Advanced or Metastatic Gastric Cancer Patients

#### Summary

EudraCT number	2008-006128-79
Trial protocol	AT
Global end of trial date	09 June 2020

#### Results information

Result version number	v1 (current)
This version publication date	02 January 2021
First version publication date	02 January 2021

#### Trial information

##### Trial identification

Sponsor protocol code	AGMT_GASTRIC-3
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##### Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00952003
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, +43 662640 4411, d.wolkersdorfer@agmt.at
Scientific contact	Richard Greil, AGMT, +43 5 725525800, r.greil@salk.at

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	09 June 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	19 August 2016
Global end of trial reached?	Yes
Global end of trial date	09 June 2020
Was the trial ended prematurely?	No

Notes:

## General information about the trial

Main objective of the trial:

The primary objective of this study is to determine the efficacy of an Oxaliplatin / Irinotecan / Bevacizumab therapy followed by Docetaxel / Bevacizumab therapy followed by Bevacizumab until progression in the treatment of locally advanced metastatic gastric cancer, in terms of response rates (complete or partial response, determined by radiologic evaluation according to Response Evaluation Criteria in Solid Tumors (RECIST)).

Protection of trial subjects:

Toxicities were monitored beginning with the first dosing of study medication, throughout the course of the study and until completion of the last treatment cycle and for 28 days thereafter. Recommendations for dose modifications were given. Patients received full supportive care including transfusions of blood and blood products, antibiotics, anti-emetics etc., where applicable. Inclusion and exclusion criteria were defined.

Background therapy:

For the initial chemotherapy Oxaliplatin was dosed at 85 mg/m<sup>2</sup> every two weeks in combination with Irinotecan dosed at 125 mg/m<sup>2</sup> every two weeks for a maximum total of 3 cycles (1 cycle equals 28 days) in treatment cycles 1-3.

Docetaxel was dosed at 50 mg/m<sup>2</sup> every 2 weeks for 3 cycles (1 cycle = 4 weeks) for a maximum of 3 months, following completion of 3 cycles of Oxaliplatin / Irinotecan combination therapy.

Evidence for comparator:

Not applicable

Actual start date of recruitment	04 September 2009
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: 40
Worldwide total number of subjects	40
EEA total number of subjects	40

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)	22
From 65 to 84 years	18
85 years and over	0

## Subject disposition

### Recruitment

Recruitment details:

Between Sep 2009 and Mar 2012, 42 patients were screened for eligibility and 40 patients have been enrolled at 8 sites in Austria. Two patients did not meet inclusion criteria.

### Pre-assignment

Screening details:

Patients with inoperable, histologically confirmed locally advanced or metastatic gastric cancer were recruited into this study. Neo/Adjuvant treatment with Bevacizumab was prohibited. No previous palliative chemotherapy and/or immunotherapy was allowed.

### Period 1

Period 1 title	Overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

### Arms

Arm title	Overall trial
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Arm description:

Sequential first-line chemoimmunotherapy combination regime: Oxaliplatin, Irinotecan and Bevacizumab for 3 cycles followed by Docetaxel and Bevacizumab for a further 3 cycles followed by Bevacizumab maintenance until progression.

Arm type	Experimental
Investigational medicinal product name	Bevacizumab
Investigational medicinal product code	
Other name	Avastin
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Bevacizumab was administered at a fixed dose of 5 mg/kg every 2 weeks.

Number of subjects in period 1	Overall trial
Started	40
3 cycles of induction	29
6 cycles of induction	14
Completed	8
Not completed	32
Adverse event, serious fatal	1
Physician decision	1
Disease progression	15
Adverse event, non-fatal	12
Sponsor decision (compassionate use)	1
Patient wish	2



## Baseline characteristics

### Reporting groups

Reporting group title	Overall trial
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Reporting group description: -

Reporting group values	Overall trial	Total	
Number of subjects	40	40	
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	63		
full range (min-max)	26 to 83	-	
Gender categorical			
Units: Subjects			
Female	10	10	
Male	30	30	
ECOG performance status			
Units: Subjects			
ECOG 0	26	26	
ECOG 1	12	12	
Missing	2	2	
Metastatic disease			
Units: Subjects			
Single	26	26	
Multiple	14	14	
Body weight			
Units: kilogram(s)			
median	52		
full range (min-max)	38 to 122	-	
Disease duration			
Units: day			
median	31		
inter-quartile range (Q1-Q3)	9 to 239	-	

## End points

### End points reporting groups

Reporting group title	Overall trial
Reporting group description: Sequential first-line chemoimmunotherapy combination regime: Oxaliplatin, Irinotecan and Bevacizumab for 3 cycles followed by Docetaxel and Bevacizumab for a further 3 cycles followed by Bevacizumab maintenance until progression.	

### Primary: Objective response rate

End point title	Objective response rate <sup>[1]</sup>
End point description: Evaluation of best response. Objective response rate was available in 33 of 40 patients, 7 patients discontinued before first response assessment for other reasons than progression. Two patients were still receiving Bevacizumab in continuing CR after more than 5 years of treatment.	
End point type	Primary
End point timeframe: Sep 2009 to Aug 2016	
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 is provided as this is an one armed, open label, non-comperative study.	

End point values	Overall trial			
Subject group type	Reporting group			
Number of subjects analysed	33			
Units: Subjects				
Complete remission (CR)	4			
Partial remission (PR)	13			
Stable disease (SD)	9			
Progressive disease (PD)	7			

### Statistical analyses

No statistical analyses for this end point

### Secondary: Overall survival

End point title	Overall survival
End point description:	
End point type	Secondary
End point timeframe: Sep 2009 - Aug 2016	

<b>End point values</b>	Overall trial			
Subject group type	Reporting group			
Number of subjects analysed	40			
Units: months				
median (confidence interval 95%)	11 (9.0 to 15.0)			

### Statistical analyses

No statistical analyses for this end point

### Secondary: Time to progression

End point title	Time to progression
End point description:	
End point type	Secondary
End point timeframe:	
Sep 2009 - Aug 2016	

<b>End point values</b>	Overall trial			
Subject group type	Reporting group			
Number of subjects analysed	40			
Units: months				
median (confidence interval 95%)	7.0 (5.0 to 11.0)			

### Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Sep 2009 - Jun 2020

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

Adverse event reporting additional description:

Progression or objective / clinical progression of the malignancy under study were part of the efficacy assessment and should not have been reported as an AE or SAE.

Assessment type	Systematic
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### Dictionary used

Dictionary name	MedDRA
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Dictionary version	13.1
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### Reporting groups

Reporting group title	Overall trial
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Reporting group description:

All enrolled patients having received at least one dose of IMP.

Serious adverse events	Overall trial		
Total subjects affected by serious adverse events			
subjects affected / exposed	27 / 40 (67.50%)		
number of deaths (all causes)	38		
number of deaths resulting from adverse events	4		
Investigations			
Weight decreased			
subjects affected / exposed	2 / 40 (5.00%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Metastases to meninges			
subjects affected / exposed	2 / 40 (5.00%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 2		
Injury, poisoning and procedural complications			
Lumbar vertebral fracture			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Splenic rupture			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Stoma site reaction			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Circulatory collapse			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Angina pectoris			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Subarachnoid haemorrhage			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Febrile neutropenia			

subjects affected / exposed	3 / 40 (7.50%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
<b>Neutropenia</b>			
subjects affected / exposed	3 / 40 (7.50%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
<b>General disorders and administration site conditions</b>			
<b>Chest pain</b>			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>General physical health deterioration</b>			
subjects affected / exposed	2 / 40 (5.00%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
<b>Pyrexia</b>			
subjects affected / exposed	4 / 40 (10.00%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
<b>Stent malfunction</b>			
subjects affected / exposed	2 / 40 (5.00%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
<b>Ulcer</b>			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Gastrointestinal disorders</b>			
<b>Abdominal pain</b>			
subjects affected / exposed	2 / 40 (5.00%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		

Abdominal pain lower				
subjects affected / exposed	1 / 40 (2.50%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Abdominal pain upper				
subjects affected / exposed	1 / 40 (2.50%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Colitis				
subjects affected / exposed	1 / 40 (2.50%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Diaphragmatic hernia				
subjects affected / exposed	1 / 40 (2.50%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Diarrhoea				
subjects affected / exposed	6 / 40 (15.00%)			
occurrences causally related to treatment / all	1 / 6			
deaths causally related to treatment / all	0 / 0			
Duodenitis				
subjects affected / exposed	1 / 40 (2.50%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Dysphagia				
subjects affected / exposed	1 / 40 (2.50%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gastric perforation				
subjects affected / exposed	1 / 40 (2.50%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal haemorrhage				

subjects affected / exposed	1 / 40 (2.50%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Gastroesophageal reflux disease			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Haematemesis			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Haematochezia			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Ileus			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 1		
Inguinal hernia			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Jejunal ulcer			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Mechanical ileus			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nausea			

subjects affected / exposed	3 / 40 (7.50%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
<b>Oesophageal stenosis</b>			
subjects affected / exposed	2 / 40 (5.00%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
<b>Subileus</b>			
subjects affected / exposed	2 / 40 (5.00%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
<b>Vomiting</b>			
subjects affected / exposed	4 / 40 (10.00%)		
occurrences causally related to treatment / all	0 / 5		
deaths causally related to treatment / all	0 / 0		
<b>Renal and urinary disorders</b>			
<b>Hydronephrosis</b>			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Renal failure acute</b>			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Ureteric stenosis</b>			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Infections and infestations</b>			
<b>Anal abscess</b>			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Candida infection</b>			

subjects affected / exposed	1 / 40 (2.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Device related infection			
subjects affected / exposed	2 / 40 (5.00%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Gastroenteritis			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infection			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Oesophageal candidiasis			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Staphylococcal bacteraemia			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Urinary tract infection			
subjects affected / exposed	2 / 40 (5.00%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		

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

<b>Non-serious adverse events</b>	Overall trial		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	39 / 40 (97.50%)		
Vascular disorders			
Hypertension			
subjects affected / exposed	10 / 40 (25.00%)		
occurrences (all)	16		
Circulatory collapse			
subjects affected / exposed	2 / 40 (5.00%)		
occurrences (all)	2		
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	18 / 40 (45.00%)		
occurrences (all)	24		
Pain			
subjects affected / exposed	6 / 40 (15.00%)		
occurrences (all)	8		
Asthenia			
subjects affected / exposed	5 / 40 (12.50%)		
occurrences (all)	5		
Pyrexia			
subjects affected / exposed	4 / 40 (10.00%)		
occurrences (all)	4		
Chest pain			
subjects affected / exposed	4 / 40 (10.00%)		
occurrences (all)	5		
Mucosal inflammation			
subjects affected / exposed	4 / 40 (10.00%)		
occurrences (all)	4		
Oedema peripheral			
subjects affected / exposed	3 / 40 (7.50%)		
occurrences (all)	4		
General physical health deterioration			
subjects affected / exposed	2 / 40 (5.00%)		
occurrences (all)	2		
Respiratory, thoracic and mediastinal disorders			

Epistaxis			
subjects affected / exposed	6 / 40 (15.00%)		
occurrences (all)	11		
Dysphonia			
subjects affected / exposed	5 / 40 (12.50%)		
occurrences (all)	5		
Cough			
subjects affected / exposed	3 / 40 (7.50%)		
occurrences (all)	3		
Dyspnoea			
subjects affected / exposed	3 / 40 (7.50%)		
occurrences (all)	4		
Oropharyngeal pain			
subjects affected / exposed	2 / 40 (5.00%)		
occurrences (all)	2		
Productive cough			
subjects affected / exposed	2 / 40 (5.00%)		
occurrences (all)	3		
Psychiatric disorders			
Depression			
subjects affected / exposed	4 / 40 (10.00%)		
occurrences (all)	4		
Insomnia			
subjects affected / exposed	3 / 40 (7.50%)		
occurrences (all)	3		
Investigations			
C-reactive protein increased			
subjects affected / exposed	3 / 40 (7.50%)		
occurrences (all)	4		
Injury, poisoning and procedural complications			
Rib fracture			
subjects affected / exposed	2 / 40 (5.00%)		
occurrences (all)	2		
Nervous system disorders			
Polyneuropathy			

<p>subjects affected / exposed occurrences (all)</p> <p>Headache</p> <p>subjects affected / exposed occurrences (all)</p> <p>Dysgeusia</p> <p>subjects affected / exposed occurrences (all)</p> <p>Dysaesthesia</p> <p>subjects affected / exposed occurrences (all)</p> <p>Ageusia</p> <p>subjects affected / exposed occurrences (all)</p>	<p>21 / 40 (52.50%) 30</p> <p>5 / 40 (12.50%) 6</p> <p>2 / 40 (5.00%) 2</p> <p>2 / 40 (5.00%) 2</p> <p>2 / 40 (5.00%) 2</p>		
<p>Blood and lymphatic system disorders</p> <p>Neutropenia</p> <p>subjects affected / exposed occurrences (all)</p> <p>Leukopenia</p> <p>subjects affected / exposed occurrences (all)</p> <p>Anaemia</p> <p>subjects affected / exposed occurrences (all)</p>	<p>12 / 40 (30.00%) 20</p> <p>4 / 40 (10.00%) 9</p> <p>2 / 40 (5.00%) 3</p>		
<p>Ear and labyrinth disorders</p> <p>Vertigo</p> <p>subjects affected / exposed occurrences (all)</p>	<p>3 / 40 (7.50%) 3</p>		
<p>Eye disorders</p> <p>Lacrimation increased</p> <p>subjects affected / exposed occurrences (all)</p>	<p>2 / 40 (5.00%) 2</p>		
<p>Gastrointestinal disorders</p> <p>Diarrhoea</p> <p>subjects affected / exposed occurrences (all)</p> <p>Nausea</p>	<p>25 / 40 (62.50%) 37</p>		

subjects affected / exposed	23 / 40 (57.50%)		
occurrences (all)	43		
Vomiting			
subjects affected / exposed	16 / 40 (40.00%)		
occurrences (all)	23		
Abdominal pain			
subjects affected / exposed	9 / 40 (22.50%)		
occurrences (all)	16		
Abdominal pain upper			
subjects affected / exposed	7 / 40 (17.50%)		
occurrences (all)	11		
Constipation			
subjects affected / exposed	6 / 40 (15.00%)		
occurrences (all)	6		
Abdominal distension			
subjects affected / exposed	3 / 40 (7.50%)		
occurrences (all)	3		
Stomatitis			
subjects affected / exposed	3 / 40 (7.50%)		
occurrences (all)	4		
Gastrooesophageal reflux disease			
subjects affected / exposed	3 / 40 (7.50%)		
occurrences (all)	3		
Glossodynia			
subjects affected / exposed	2 / 40 (5.00%)		
occurrences (all)	2		
Dysphagia			
subjects affected / exposed	2 / 40 (5.00%)		
occurrences (all)	2		
Flatulence			
subjects affected / exposed	2 / 40 (5.00%)		
occurrences (all)	2		
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	4 / 40 (10.00%)		
occurrences (all)	5		

Alopecia subjects affected / exposed occurrences (all)	3 / 40 (7.50%) 3		
Dry skin subjects affected / exposed occurrences (all)	2 / 40 (5.00%) 2		
Psoriasis subjects affected / exposed occurrences (all)	2 / 40 (5.00%) 2		
Renal and urinary disorders Proteinuria subjects affected / exposed occurrences (all)	3 / 40 (7.50%) 9		
Musculoskeletal and connective tissue disorders Back pain subjects affected / exposed occurrences (all)	4 / 40 (10.00%) 5		
Arthralgia subjects affected / exposed occurrences (all)	2 / 40 (5.00%) 3		
Infections and infestations Nasopharyngitis subjects affected / exposed occurrences (all)	4 / 40 (10.00%) 5		
Rhinitis subjects affected / exposed occurrences (all)	4 / 40 (10.00%) 4		
Urinary tract infection subjects affected / exposed occurrences (all)	3 / 40 (7.50%) 9		
Bronchitis subjects affected / exposed occurrences (all)	2 / 40 (5.00%) 2		
Pneumonia subjects affected / exposed occurrences (all)	2 / 40 (5.00%) 2		

Upper respiratory tract infection subjects affected / exposed occurrences (all)	2 / 40 (5.00%) 3		
Febrile infection subjects affected / exposed occurrences (all)	2 / 40 (5.00%) 2		
Metabolism and nutrition disorders			
Hypokalaemia subjects affected / exposed occurrences (all)	10 / 40 (25.00%) 13		
Decreased appetite subjects affected / exposed occurrences (all)	8 / 40 (20.00%) 9		
Hyperglycaemia subjects affected / exposed occurrences (all)	3 / 40 (7.50%) 3		
Hypocalcaemia subjects affected / exposed occurrences (all)	2 / 40 (5.00%) 2		

## **More information**

### **Substantial protocol amendments (globally)**

Were there any global substantial amendments to the protocol? No

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### **Interruptions (globally)**

Were there any global interruptions to the trial? No

### **Limitations and caveats**

None reported

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### **Online references**

<http://www.ncbi.nlm.nih.gov/pubmed/28982869>