Clinical trial results:
A Phase Ib/II, open-label, multicenter trial with oral cMET inhibitor INC280 alone and in combination with erlotinib versus platinum/pemetrexed in adult patients with EGFR mutated, cMET-amplified, locally advanced/metastatic non-small cell lung cancer (NSCLC) with acquired resistance to prior EGFR tyrosine kinase inhibitor (EGFR TKI)

Summary

EudraCT number	2015-001241-84
Trial protocol	ES HU NL BE FR GB PT IT
Global end of trial date	05 December 2018

Results information

Result version number	v1 (current)
This version publication date	20 December 2019
First version publication date	20 December 2019

Trial information

Trial identification

Sponsor protocol code	CINC280B2201

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02468661
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Novartis Pharma, AG
Sponsor organisation address	CH-4002, Basel, Switzerland,
Public contact	Clinical Disclosure Office, Novartis Pharma, AG, +41 6133241111, novartis.email@novartis.com
Scientific contact	Clinical Disclosure Office, Novartis Pharma, AG, +41 6133241111, novartis.email@novartis.com

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	05 December 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	15 November 2017
Global end of trial reached?	Yes
Global end of trial date	05 December 2018
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To determine MTD and/or RP2D of INC280 in combination with erlotinib

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and the International Conference on Harmonization (ICH) Good Clinical Practice (GCP) guidelines. All the local regulatory requirements pertinent to safety of trial subjects were also followed during the conduct of the trial.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	23 September 2015
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	Belgium: 1
Country: Number of subjects enrolled	France: 4
Country: Number of subjects enrolled	Germany: 2
Country: Number of subjects enrolled	Italy: 3
Country: Number of subjects enrolled	Korea, Republic of: 4
Country: Number of subjects enrolled	Netherlands: 2
Country: Number of subjects enrolled	Singapore: 4
Country: Number of subjects enrolled	Spain: 1
Country: Number of subjects enrolled	United States: 2
Worldwide total number of subjects	23
EEA total number of subjects	13

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)	18
From 65 to 84 years	5
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

23 subjects were enrolled in the phase I part of the study and the study was terminated prior to opening of the randomized phase.

Pre-assignment

Screening details:

23 subjects were enrolled in the phase I part of the study and the study was terminated prior to opening of the randomized phase.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	INC280 200mg BID + ERL 150mg QD

Arm description:

Subjects who received 200mg of INC280 twice daily (BID) and erlotinib 150mg once daily (QD)

Arm type	Experimental
Investigational medicinal product name	capmatinib
Investigational medicinal product code	INC280
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Capmatinib comes in 100 mg, 150mg, 200 mg dose taken twice daily (BID)

Investigational medicinal product name	erlotinib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Erlotinib comes in 25 mg, 100mg, 150 mg and is taken once daily.

Arm title	INC280 400mg BID + ERL 150mg QD

Arm description:

Subjects who received 400mg of INC280 twice daily (BID) and erlotinib 150mg once daily (QD)

Arm type	Experimental
Investigational medicinal product name	capmatinib
Investigational medicinal product code	INC280
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Capmatinib comes in 100 mg, 150mg, 200 mg dose taken twice daily (BID)

Investigational medicinal product name	erlotinib
Investigational medicinal product code	
Other name	

Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Erlotinib comes in 25 mg, 100mg, 150 mg and is taken once daily.

Number of subjects in period 1	INC280 200mg BID + ERL 150mg QD	INC280 400mg BID + ERL 150mg QD
Started	7	16
Completed	0	0
Not completed	7	16
Adverse event, serious fatal	-	2
Physician decision	-	1
Adverse event, non-fatal	-	3
Progressive disease	7	8
Subject/guardian decision	-	2

Baseline characteristics

Reporting groups	
Reporting group title	INC280 200mg BID + ERL 150mg QD
Reporting group description:	
Subjects who received 200mg of INC280 twice daily (BID) and erlotinib 150mg once daily (QD)	
Reporting group title	INC280 400mg BID + ERL 150mg QD
Reporting group description:	
Subjects who received 400mg of INC280 twice daily (BID) and erlotinib 150mg once daily (QD)	

Reporting group values	INC280 200mg BID + ERL 150mg QD	INC280 400mg BID + ERL 150mg QD	Total
Number of subjects	7	16	23
Age Categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	7	11	18
From 65-84 years	0	5	5
85 years and over	0	0	0
Age Continuous Units: years			
arithmetic mean	49.7	58.6	
standard deviation	± 8.50	± 11.38	-
Gender Categorical Units: Subjects			
Female	5	10	15
Male	2	6	8

End points

End points reporting groups

Reporting group title	INC280 200mg BID + ERL 150mg QD
Reporting group description: Subjects who received 200mg of INC280 twice daily (BID) and erlotinib 150mg once daily (QD)	
Reporting group title	INC280 400mg BID + ERL 150mg QD
Reporting group description: Subjects who received 400mg of INC280 twice daily (BID) and erlotinib 150mg once daily (QD)	
Subject analysis set title	DDS: INC280 200mg BID + ERL 150mg QD
Subject analysis set type	Sub-group analysis
Subject analysis set description: Dose determining set	
Subject analysis set title	DDS: INC280 400mg BID + ERL 150mg QD
Subject analysis set type	Sub-group analysis
Subject analysis set description: Dose Determining Set	

Primary: Dose Limiting Toxicities (DLTs)

End point title	Dose Limiting Toxicities (DLTs)[1]

End point description:

Dose limiting toxicity (DLT): an adverse event (AE) or abnorm. lab. val. assessed as unrelated to disease, disease prog., inter-current illness, or concom. meds that occurs within 1st 28 days of treatmnt with INC280 in comb. with erlotinib during dose escalation (DE) part of study & meets any of the National Cancer Institute Common Terminology Criteria for AEs ver. 4.03 used for all grading. For purpose of DE, DLTs were consid. & incl. in BLRM. *1 subject's AEs fatigue, peripheral oedema & abnorm. blood TSH (all grade 1), were not in line with DLT def. as documented in CSR & occurred after DLT period (cycle 1). **1 subj. wasn't incl. in DDS population. At time of DE BLRM analysis cutoff, subj. was considered not evaluable since they didn't start study treatmnt & therefore not includ. in analysis. On Day 15 subj. dev. grd 3 dry skin & didn't receive any concomit. med. for this toxicity. Subj. decided not to cont. clinical trial; Investig. considered this event clin. significant as DLT

End point type	Primary

End point timeframe:

28 days

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 was planned for this endpoint.

End point values	DDS: INC280 200mg BID + ERL 150mg QD	DDS: INC280 400mg BID + ERL 150mg QD		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	4	12		
Units: subjects				
Any primary system organ class**	0	4		
Gen. disorders & admin site conditns: fatigue	0	1		
Gen disorders& admin site conds:Oedema peripheral*	0	1		
Infections & infestations: Rash pustular	0	1		
Investigations: Alanine aminotransferase increased	0	1		
Investigatns: Aspartate aminotransferase increased	0	1		

Investigatns: Blood thyroid stim. hormone abnormal	0	1		
Resp. thoracic & mediastinal disorders:Pneumonitis	0	1		
Skin & subcutaneous tissue disorders: rash	0	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Response Rate (ORR)

End point title	Overall Response Rate (ORR)

End point description:

ORR is the percentage of subjects with a best overall response of complete response or partial response (CR+PR).
CR:
PR:

End point type	Secondary

End point timeframe:

Provide time frame

End point values	INC280 200mg BID + ERL 150mg QD	INC280 400mg BID + ERL 150mg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7	16		
Units: percentage of subjects				
number (confidence interval 95%)	42.9 (9.90 to 81.59)	18.8 (4.05 to 45.65)		

Statistical analyses

No statistical analyses for this end point

Secondary: Disease Control Rate (DCR)

End point title	Disease Control Rate (DCR)

End point description:

DCR is the percentage of subjects with best overall response of complete response, partial response of stable disease (CR, PR or SD).
CR:
PR:
SD:

End point type	Secondary

End point timeframe:

Provide time frame

End point values	INC280 200mg BID + ERL 150mg QD	INC280 400mg BID + ERL 150mg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7	16		
Units: percentage of subjects				
number (confidence interval 95%)	42.9 (9.90 to 81.59)	68.8 (41.34 to 88.98)		

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Response (DOR)

End point title	Duration of Response (DOR)

End point description:

DOR is defined as time from the first documented CR or PR to first documented progression or death due to any cause.

End point type	Secondary

End point timeframe:

provide time frame

End point values	INC280 200mg BID + ERL 150mg QD	INC280 400mg BID + ERL 150mg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7	16		
Units: days	136	304		

Statistical analyses

No statistical analyses for this end point

Secondary: INC280 Pharmacokinetics (PK) parameter: AUCinf, AUClast

End point title	INC280 Pharmacokinetics (PK) parameter: AUCinf, AUClast

End point description:

AUCinf: The area under the plasma concentration-time curve extrapolated to infinity(ng*hr/mL)
AUClast: The AUC from time zero to the last measurable concentration

End point type	Secondary

End point timeframe:

Cycle 1 Day 1, Cycle 1 Day 15

End point values	INC280 200mg BID + ERL 150mg QD	INC280 400mg BID + ERL 150mg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7	16		
Units: ng*hr/mL				
geometric mean (geometric coefficient of variation)				
AUCinf: D1C1 (n = 4, 7)	10200 (± 47.4)	21700 (± 50.8)		
AUCinf: D1C15 (n = 5, 6)	14700 (± 35.9)	35800 (± 20.7)		
AUClast: D1C1	10400 (± 40.0)	21400 (± 47.9)		
AUClast: D1C15 (n = 6, 12)	9450 (± 88.0)	28200 (± 37.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: INC280 PK parameter: Cmax

End point title	INC280 PK parameter: Cmax
End point description:	
Cmax: The observed maximum plasma concentration following administration (ng/mL)	
End point type	Secondary
End point timeframe:	
Cycle 1 Day 1, Cycle 1 Day 15	

End point values	INC280 200mg BID + ERL 150mg QD	INC280 400mg BID + ERL 150mg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7	16		
Units: ng/mL				
geometric mean (geometric coefficient of variation)				
C1D1	2590 (± 40.2)	5720 (± 47.3)		
C1D15 (7, 13)	3070 (± 108.3)	7760 (± 41.5)		

Statistical analyses

No statistical analyses for this end point

Secondary: INC280 PK parameter: Tmax, T1/2

End point title	INC280 PK parameter: Tmax, T1/2

End point description:
Tmax: The time to reach peak or maximum concentration (hr) T1/2: Elimination half-life determined as 0.693/lambda_z (hr)

End point type	Secondary

End point timeframe:
Cycle 1 Day 1, Cycle 1 Day 15

End point values	INC280 200mg BID + ERL 150mg QD	INC280 400mg BID + ERL 150mg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7	16		
Units: hour (hr)				
median (full range (min-max))				
Tmax: C1D1	1.00 (0.933 to 4.00)	1.08 (0.5 to 6.05)		
Tmax: C1D15 (n = 7, 13)	2.00 (1.00 to 4.00)	1.05 (0.5 to 2.12)		
T1/2: C1D1 n= (4, 7)	2.56 (2.26 to 2.71)	2.66 (2.46 to 3.06)		
T1/2: C1D15 (n= 5, 6)	2.65 (2.22 to 2.98)	2.73 (1.85 to 3.85)		

Statistical analyses

No statistical analyses for this end point

Secondary: INC280 PK parameter: CL/F:

End point title	INC280 PK parameter: CL/F:

End point description:
CL/F: The apparent total body clearance from plasma (L/hr)

End point type	Secondary

End point timeframe:
Cycle 1 Day 1

End point values	INC280 200mg BID + ERL 150mg QD	INC280 400mg BID + ERL 150mg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7	16		
Units: L/hr				
geometric mean (geometric coefficient of variation)				
C1D1 (n = 4, 7)	19.6 (± 47.4)	18.5 (± 50.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: INC280 PK parameter: Vz_F_obs

End point title	INC280 PK parameter: Vz_F_obs

End point description:

Vz/F: The apparent volume of distribution during the terminal elimination phase (L)

End point type	Secondary

End point timeframe:

Cycle 1 Day 1

End point values	INC280 200mg BID + ERL 150mg QD	INC280 400mg BID + ERL 150mg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7	16		
Units: Litres (L)				
geometric mean (geometric coefficient of variation)				
Vz_F_obs (n = 4, 7)	70.9 (± 47.7)	72.0 (± 48.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: INC280 PK parameter: AUCtau

End point title	INC280 PK parameter: AUCtau

End point description:

AUCtau: The AUC within the dosing interval (tau) (mass x time x volume-1)

End point type	Secondary

End point timeframe:

Cycle 1 Day 15

End point values	INC280 200mg BID + ERL 150mg QD	INC280 400mg BID + ERL 150mg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7	16		
Units: ng*hr/mL				
geometric mean (geometric coefficient of variation)				
C1D15 (n = 5, 6)	14000 (± 37.1)	33800 (± 19.6)		

Statistical analyses

No statistical analyses for this end point

Secondary: INC280 PK parameter: Vz/F

End point title	INC280 PK parameter: Vz/F
End point description:	
Vz/F: The apparent volume of distribution during the terminal elimination phase (L)	
End point type	Secondary
End point timeframe:	
Cycle 1 Day 15	

End point values	INC280 200mg BID + ERL 150mg QD	INC280 400mg BID + ERL 150mg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7	16		
Units: Litres (L)				
geometric mean (geometric coefficient of variation)				
C1D15 (n = 5, 6)	54.0 (± 48.8)	45.3 (± 38.5)		

Statistical analyses

No statistical analyses for this end point

Secondary: INC280 PK parameter: CLss/F

End point title	INC280 PK parameter: CLss/F
End point description:	
CL/F: The apparent total body clearance from plasma (L/hr)	
End point type	Secondary
End point timeframe:	
Cycle 1 Day 15	

End point values	INC280 200mg BID + ERL 150mg QD	INC280 400mg BID + ERL 150mg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7	16		
Units: L/hr				
geometric mean (geometric coefficient of variation)				
C1D15 (n = 5, 6)	14.3 (± 37.1)	11.3 (± 25.0)		

Statistical analyses

No statistical analyses for this end point

Secondary: INC280 PK parameter: Racc

End point title	INC280 PK parameter: Racc
End point description:	
Racc: Accumulation ratio	
End point type	Secondary
End point timeframe:	
Cycle 1 Day 15	

End point values	INC280 200mg BID + ERL 150mg QD	INC280 400mg BID + ERL 150mg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7	16		
Units: ratio				
geometric mean (geometric coefficient of variation)				
C1D15 (n = 6, 12)	0.979 (± 92.2)	1.58 (± 37.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: Erlotinib Pharmacokinetics (PK) parameter: AUClast

End point title	Erlotinib Pharmacokinetics (PK) parameter: AUClast
End point description:	
AUClast: The AUC from time zero to the last measurable concentration	
End point type	Secondary

End point timeframe:
Cycle 1 Day 1, Cycle 1 Day 15

End point values	INC280 200mg BID + ERL 150mg QD	INC280 400mg BID + ERL 150mg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7	16		
Units: ng*hr/mL				
geometric mean (geometric coefficient of variation)				
C1D1	18800 (± 43.5)	14700 (± 51.4)		
C1D15 (n = 5, 12)	20100 (± 59.6)	21700 (± 45.3)		

Statistical analyses

No statistical analyses for this end point

Secondary: Erlotinib PK parameter: Cmax

End point title	Erlotinib PK parameter: Cmax

End point description:
Cmax: The observed maximum plasma concentration following administration (ng/mL)

End point type	Secondary

End point timeframe:
Cycle 1 Day 1, Cycle 1 Day 15

End point values	INC280 200mg BID + ERL 150mg QD	INC280 400mg BID + ERL 150mg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7	16		
Units: ng/mL				
geometric mean (geometric coefficient of variation)				
C1D1	1140 (± 40.5)	984 (± 38.3)		
C1D15 (n = 6, 13)	1510 (± 52.4)	1460 (± 44.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: Erlotinib PK parameter: Tmax

End point title	Erlotinib PK parameter: Tmax

End point description: Tmax: The time to reach peak or maximum concentration (hr)	
End point type	Secondary
End point timeframe: Cycle 1 Day 1, Cycle 1 Day 15	

End point values	INC280 200mg BID + ERL 150mg QD	INC280 400mg BID + ERL 150mg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7	16		
Units: hour (hr)				
median (full range (min-max))				
C1D1 C1D1 (n = 6, 13)	2.15 (1.00 to 23.9) 4.07 (1.00 to 23.1)	2.24 (1.00 to 23.4) 2.00 (1.00 to 3.97)		

Statistical analyses

No statistical analyses for this end point

Secondary: Erlotinib PK parameter: Racc

End point title	Erlotinib PK parameter: Racc
End point description: Racc: Accumulation ratio	
End point type	Secondary
End point timeframe: Cycl1 1 Day 15	

End point values	INC280 200mg BID + ERL 150mg QD	INC280 400mg BID + ERL 150mg QD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7	16		
Units: ratio				
geometric mean (geometric coefficient of variation)				
C1D15 (n = 5, 12)	1.21 (± 115.5)	1.55 (± 47.1)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse Events are collected from First Patient First Visit (FPFV) until Last Patient Last Visit (LPLV). All Adverse events are reported in this record from First Patient First Treatment until Last Patient Last Visit.

Adverse event reporting additional description:

Consistent with EudraCT disclosure specifications, Novartis has reported under the Serious adverse events field "number of deaths resulting from adverse events" all those deaths, resulting from serious adverse events that are deemed to be causally related to treatment by the investigator.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	21.1

Reporting groups

Reporting group title	INC280 200mg BID + ERL 150mg QD

Reporting group description:

Subjects who received 200mg of INC280 twice daily (BID) and erlotinib 150mg once daily (QD)

Reporting group title	All subjects

Reporting group description:

Total number of subjects enrolled in the study

Reporting group title	INC280 400mg BID + ERL 150mg QD

Reporting group description:

Subjects who received 400mg of INC280 twice daily (BID) and erlotinib 150mg once daily (QD)

Serious adverse events	INC280 200mg BID + ERL 150mg QD	All subjects	INC280 400mg BID + ERL 150mg QD
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 7 (85.71%)	11 / 23 (47.83%)	5 / 16 (31.25%)
number of deaths (all causes)	0	2	2
number of deaths resulting from adverse events	0	1	1
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 7 (0.00%)	1 / 23 (4.35%)	1 / 16 (6.25%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 7 (0.00%)	1 / 23 (4.35%)	1 / 16 (6.25%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			

Metastases to central nervous system			
subjects affected / exposed	1 / 7 (14.29%)	1 / 23 (4.35%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	0 / 7 (0.00%)	1 / 23 (4.35%)	1 / 16 (6.25%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Cardiac failure			
subjects affected / exposed	0 / 7 (0.00%)	1 / 23 (4.35%)	1 / 16 (6.25%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Stress cardiomyopathy			
subjects affected / exposed	1 / 7 (14.29%)	1 / 23 (4.35%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Brain oedema			
subjects affected / exposed	1 / 7 (14.29%)	1 / 23 (4.35%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Food allergy			
subjects affected / exposed	1 / 7 (14.29%)	1 / 23 (4.35%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Pneumonitis			
subjects affected / exposed	0 / 7 (0.00%)	1 / 23 (4.35%)	1 / 16 (6.25%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	1 / 1	1 / 1
Pulmonary embolism			

subjects affected / exposed	1 / 7 (14.29%)	1 / 23 (4.35%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	0 / 7 (0.00%)	1 / 23 (4.35%)	1 / 16 (6.25%)
occurrences causally related to treatment / all	0 / 0	2 / 2	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Infectious pleural effusion			
subjects affected / exposed	1 / 7 (14.29%)	1 / 23 (4.35%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 7 (0.00%)	1 / 23 (4.35%)	1 / 16 (6.25%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 1
Streptococcal sepsis			
subjects affected / exposed	0 / 7 (0.00%)	1 / 23 (4.35%)	1 / 16 (6.25%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper respiratory tract infection			
subjects affected / exposed	1 / 7 (14.29%)	1 / 23 (4.35%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	INC280 200mg BID + ERL 150mg QD	All subjects	INC280 400mg BID + ERL 150mg QD
Total subjects affected by non-serious adverse events			
subjects affected / exposed	7 / 7 (100.00%)	23 / 23 (100.00%)	16 / 16 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			

subjects affected / exposed	0 / 7 (0.00%)	1 / 23 (4.35%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Tumour pain			
subjects affected / exposed	1 / 7 (14.29%)	1 / 23 (4.35%)	0 / 16 (0.00%)
occurrences (all)	1	1	0
Vascular disorders			
Hot flush			
subjects affected / exposed	0 / 7 (0.00%)	1 / 23 (4.35%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Hypertension			
subjects affected / exposed	0 / 7 (0.00%)	1 / 23 (4.35%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Hypotension			
subjects affected / exposed	0 / 7 (0.00%)	1 / 23 (4.35%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Venous thrombosis			
subjects affected / exposed	0 / 7 (0.00%)	1 / 23 (4.35%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 7 (0.00%)	4 / 23 (17.39%)	4 / 16 (25.00%)
occurrences (all)	0	5	5
Face oedema			
subjects affected / exposed	0 / 7 (0.00%)	1 / 23 (4.35%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Fatigue			
subjects affected / exposed	1 / 7 (14.29%)	4 / 23 (17.39%)	3 / 16 (18.75%)
occurrences (all)	1	7	6
Influenza like illness			
subjects affected / exposed	1 / 7 (14.29%)	1 / 23 (4.35%)	0 / 16 (0.00%)
occurrences (all)	1	1	0
Injection site reaction			
subjects affected / exposed	0 / 7 (0.00%)	1 / 23 (4.35%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Malaise			

subjects affected / exposed	0 / 7 (0.00%)	1 / 23 (4.35%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Non-cardiac chest pain			
subjects affected / exposed	0 / 7 (0.00%)	2 / 23 (8.70%)	2 / 16 (12.50%)
occurrences (all)	0	2	2
Oedema			
subjects affected / exposed	1 / 7 (14.29%)	1 / 23 (4.35%)	0 / 16 (0.00%)
occurrences (all)	1	1	0
Oedema peripheral			
subjects affected / exposed	2 / 7 (28.57%)	8 / 23 (34.78%)	6 / 16 (37.50%)
occurrences (all)	2	11	9
Pyrexia			
subjects affected / exposed	3 / 7 (42.86%)	6 / 23 (26.09%)	3 / 16 (18.75%)
occurrences (all)	3	7	4
Respiratory, thoracic and mediastinal disorders			
Catarrh			
subjects affected / exposed	0 / 7 (0.00%)	2 / 23 (8.70%)	2 / 16 (12.50%)
occurrences (all)	0	2	2
Cough			
subjects affected / exposed	2 / 7 (28.57%)	5 / 23 (21.74%)	3 / 16 (18.75%)
occurrences (all)	2	6	4
Dyspnoea			
subjects affected / exposed	3 / 7 (42.86%)	4 / 23 (17.39%)	1 / 16 (6.25%)
occurrences (all)	3	4	1
Epistaxis			
subjects affected / exposed	1 / 7 (14.29%)	2 / 23 (8.70%)	1 / 16 (6.25%)
occurrences (all)	1	2	1
Haemoptysis			
subjects affected / exposed	0 / 7 (0.00%)	1 / 23 (4.35%)	1 / 16 (6.25%)
occurrences (all)	0	2	2
Pleural effusion			
subjects affected / exposed	1 / 7 (14.29%)	1 / 23 (4.35%)	0 / 16 (0.00%)
occurrences (all)	1	1	0
Pneumonitis			

subjects affected / exposed	0 / 7 (0.00%)	1 / 23 (4.35%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Productive cough			
subjects affected / exposed	0 / 7 (0.00%)	1 / 23 (4.35%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Pulmonary embolism			
subjects affected / exposed	1 / 7 (14.29%)	2 / 23 (8.70%)	1 / 16 (6.25%)
occurrences (all)	1	2	1
Respiratory tract irritation			
subjects affected / exposed	0 / 7 (0.00%)	1 / 23 (4.35%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Rhinorrhoea			
subjects affected / exposed	0 / 7 (0.00%)	1 / 23 (4.35%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Sinus disorder			
subjects affected / exposed	1 / 7 (14.29%)	1 / 23 (4.35%)	0 / 16 (0.00%)
occurrences (all)	1	1	0
Upper-airway cough syndrome			
subjects affected / exposed	0 / 7 (0.00%)	1 / 23 (4.35%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Psychiatric disorders			
Agitation			
subjects affected / exposed	0 / 7 (0.00%)	2 / 23 (8.70%)	2 / 16 (12.50%)
occurrences (all)	0	2	2
Confusional state			
subjects affected / exposed	0 / 7 (0.00%)	1 / 23 (4.35%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Depression			
subjects affected / exposed	0 / 7 (0.00%)	2 / 23 (8.70%)	2 / 16 (12.50%)
occurrences (all)	0	2	2
Irritability			
subjects affected / exposed	0 / 7 (0.00%)	1 / 23 (4.35%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Investigations			
Alanine aminotransferase increased			

subjects affected / exposed	1 / 7 (14.29%)	3 / 23 (13.04%)	2 / 16 (12.50%)
occurrences (all)	1	3	2
Amylase increased			
subjects affected / exposed	1 / 7 (14.29%)	2 / 23 (8.70%)	1 / 16 (6.25%)
occurrences (all)	1	8	7
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 7 (14.29%)	2 / 23 (8.70%)	1 / 16 (6.25%)
occurrences (all)	1	2	1
Blood alkaline phosphatase increased			
subjects affected / exposed	1 / 7 (14.29%)	3 / 23 (13.04%)	2 / 16 (12.50%)
occurrences (all)	1	3	2
Blood bilirubin increased			
subjects affected / exposed	0 / 7 (0.00%)	3 / 23 (13.04%)	3 / 16 (18.75%)
occurrences (all)	0	3	3
Blood thyroid stimulating hormone abnormal			
subjects affected / exposed	0 / 7 (0.00%)	1 / 23 (4.35%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
C-reactive protein increased			
subjects affected / exposed	0 / 7 (0.00%)	1 / 23 (4.35%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Gamma-glutamyltransferase increased			
subjects affected / exposed	2 / 7 (28.57%)	4 / 23 (17.39%)	2 / 16 (12.50%)
occurrences (all)	2	5	3
Lipase increased			
subjects affected / exposed	0 / 7 (0.00%)	2 / 23 (8.70%)	2 / 16 (12.50%)
occurrences (all)	0	3	3
Lymphocyte count decreased			
subjects affected / exposed	1 / 7 (14.29%)	1 / 23 (4.35%)	0 / 16 (0.00%)
occurrences (all)	1	1	0
N-terminal prohormone brain natriuretic peptide increased			
subjects affected / exposed	0 / 7 (0.00%)	1 / 23 (4.35%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Neutrophil count decreased			

subjects affected / exposed	1 / 7 (14.29%)	2 / 23 (8.70%)	1 / 16 (6.25%)
occurrences (all)	2	3	1
Platelet count decreased			
subjects affected / exposed	0 / 7 (0.00%)	1 / 23 (4.35%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Weight decreased			
subjects affected / exposed	1 / 7 (14.29%)	3 / 23 (13.04%)	2 / 16 (12.50%)
occurrences (all)	1	3	2
Weight increased			
subjects affected / exposed	0 / 7 (0.00%)	1 / 23 (4.35%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
White blood cell count decreased			
subjects affected / exposed	1 / 7 (14.29%)	1 / 23 (4.35%)	0 / 16 (0.00%)
occurrences (all)	1	1	0
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 7 (0.00%)	1 / 23 (4.35%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Rib fracture			
subjects affected / exposed	0 / 7 (0.00%)	1 / 23 (4.35%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Cardiac disorders			
Bradycardia			
subjects affected / exposed	0 / 7 (0.00%)	1 / 23 (4.35%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Palpitations			
subjects affected / exposed	1 / 7 (14.29%)	1 / 23 (4.35%)	0 / 16 (0.00%)
occurrences (all)	1	1	0
Sinus tachycardia			
subjects affected / exposed	0 / 7 (0.00%)	1 / 23 (4.35%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Supraventricular tachycardia			
subjects affected / exposed	0 / 7 (0.00%)	1 / 23 (4.35%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Ventricular extrasystoles			

subjects affected / exposed	0 / 7 (0.00%)	1 / 23 (4.35%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Nervous system disorders			
Ageusia			
subjects affected / exposed	0 / 7 (0.00%)	1 / 23 (4.35%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Balance disorder			
subjects affected / exposed	0 / 7 (0.00%)	3 / 23 (13.04%)	3 / 16 (18.75%)
occurrences (all)	0	3	3
Dizziness			
subjects affected / exposed	0 / 7 (0.00%)	2 / 23 (8.70%)	2 / 16 (12.50%)
occurrences (all)	0	2	2
Head discomfort			
subjects affected / exposed	0 / 7 (0.00%)	1 / 23 (4.35%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Headache			
subjects affected / exposed	0 / 7 (0.00%)	4 / 23 (17.39%)	4 / 16 (25.00%)
occurrences (all)	0	5	5
Neuropathy peripheral			
subjects affected / exposed	0 / 7 (0.00%)	1 / 23 (4.35%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Paraesthesia			
subjects affected / exposed	0 / 7 (0.00%)	1 / 23 (4.35%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Somnolence			
subjects affected / exposed	0 / 7 (0.00%)	1 / 23 (4.35%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Tremor			
subjects affected / exposed	1 / 7 (14.29%)	1 / 23 (4.35%)	0 / 16 (0.00%)
occurrences (all)	1	1	0
Visual field defect			
subjects affected / exposed	0 / 7 (0.00%)	1 / 23 (4.35%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Blood and lymphatic system disorders			
Anaemia			

subjects affected / exposed	1 / 7 (14.29%)	2 / 23 (8.70%)	1 / 16 (6.25%)
occurrences (all)	1	2	1
Lymphopenia			
subjects affected / exposed	1 / 7 (14.29%)	2 / 23 (8.70%)	1 / 16 (6.25%)
occurrences (all)	1	2	1
Neutropenia			
subjects affected / exposed	0 / 7 (0.00%)	1 / 23 (4.35%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Ear and labyrinth disorders			
Deafness			
subjects affected / exposed	0 / 7 (0.00%)	1 / 23 (4.35%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Deafness neurosensory			
subjects affected / exposed	0 / 7 (0.00%)	1 / 23 (4.35%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Tinnitus			
subjects affected / exposed	0 / 7 (0.00%)	1 / 23 (4.35%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Vertigo			
subjects affected / exposed	0 / 7 (0.00%)	1 / 23 (4.35%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Eye disorders			
Cataract			
subjects affected / exposed	0 / 7 (0.00%)	1 / 23 (4.35%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Cataract nuclear			
subjects affected / exposed	0 / 7 (0.00%)	1 / 23 (4.35%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Dry eye			
subjects affected / exposed	2 / 7 (28.57%)	2 / 23 (8.70%)	0 / 16 (0.00%)
occurrences (all)	2	2	0
Eye irritation			
subjects affected / exposed	0 / 7 (0.00%)	1 / 23 (4.35%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Eye pain			

subjects affected / exposed	0 / 7 (0.00%)	1 / 23 (4.35%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Keratitis			
subjects affected / exposed	0 / 7 (0.00%)	1 / 23 (4.35%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Periorbital oedema			
subjects affected / exposed	0 / 7 (0.00%)	1 / 23 (4.35%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Vision blurred			
subjects affected / exposed	1 / 7 (14.29%)	2 / 23 (8.70%)	1 / 16 (6.25%)
occurrences (all)	1	2	1
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	2 / 7 (28.57%)	5 / 23 (21.74%)	3 / 16 (18.75%)
occurrences (all)	2	6	4
Abdominal pain upper			
subjects affected / exposed	0 / 7 (0.00%)	2 / 23 (8.70%)	2 / 16 (12.50%)
occurrences (all)	0	3	3
Abnormal faeces			
subjects affected / exposed	0 / 7 (0.00%)	1 / 23 (4.35%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Cheilitis			
subjects affected / exposed	1 / 7 (14.29%)	1 / 23 (4.35%)	0 / 16 (0.00%)
occurrences (all)	1	1	0
Constipation			
subjects affected / exposed	1 / 7 (14.29%)	3 / 23 (13.04%)	2 / 16 (12.50%)
occurrences (all)	1	3	2
Diarrhoea			
subjects affected / exposed	2 / 7 (28.57%)	13 / 23 (56.52%)	11 / 16 (68.75%)
occurrences (all)	2	15	13
Dry mouth			
subjects affected / exposed	1 / 7 (14.29%)	1 / 23 (4.35%)	0 / 16 (0.00%)
occurrences (all)	1	1	0
Dyspepsia			
subjects affected / exposed	0 / 7 (0.00%)	1 / 23 (4.35%)	1 / 16 (6.25%)
occurrences (all)	0	1	1

Dysphagia			
subjects affected / exposed	0 / 7 (0.00%)	1 / 23 (4.35%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Inguinal hernia			
subjects affected / exposed	0 / 7 (0.00%)	1 / 23 (4.35%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Mouth ulceration			
subjects affected / exposed	1 / 7 (14.29%)	1 / 23 (4.35%)	0 / 16 (0.00%)
occurrences (all)	1	1	0
Nausea			
subjects affected / exposed	5 / 7 (71.43%)	11 / 23 (47.83%)	6 / 16 (37.50%)
occurrences (all)	5	15	10
Stomatitis			
subjects affected / exposed	1 / 7 (14.29%)	3 / 23 (13.04%)	2 / 16 (12.50%)
occurrences (all)	1	3	2
Vomiting			
subjects affected / exposed	1 / 7 (14.29%)	3 / 23 (13.04%)	2 / 16 (12.50%)
occurrences (all)	1	3	2
Hepatobiliary disorders			
Hyperbilirubinaemia			
subjects affected / exposed	0 / 7 (0.00%)	1 / 23 (4.35%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Skin and subcutaneous tissue disorders			
Blister			
subjects affected / exposed	0 / 7 (0.00%)	1 / 23 (4.35%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Dermatitis			
subjects affected / exposed	0 / 7 (0.00%)	1 / 23 (4.35%)	1 / 16 (6.25%)
occurrences (all)	0	2	2
Dermatitis acneiform			
subjects affected / exposed	2 / 7 (28.57%)	6 / 23 (26.09%)	4 / 16 (25.00%)
occurrences (all)	3	7	4
Dry skin			
subjects affected / exposed	0 / 7 (0.00%)	2 / 23 (8.70%)	2 / 16 (12.50%)
occurrences (all)	0	2	2
Erythema			

subjects affected / exposed	0 / 7 (0.00%)	2 / 23 (8.70%)	2 / 16 (12.50%)
occurrences (all)	0	3	3
Hyperhidrosis			
subjects affected / exposed	0 / 7 (0.00%)	1 / 23 (4.35%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Night sweats			
subjects affected / exposed	0 / 7 (0.00%)	1 / 23 (4.35%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Onychalgia			
subjects affected / exposed	1 / 7 (14.29%)	1 / 23 (4.35%)	0 / 16 (0.00%)
occurrences (all)	1	1	0
Onychoclasis			
subjects affected / exposed	0 / 7 (0.00%)	1 / 23 (4.35%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Palmar-plantar erythrodysaesthesia syndrome			
subjects affected / exposed	1 / 7 (14.29%)	1 / 23 (4.35%)	0 / 16 (0.00%)
occurrences (all)	1	1	0
Pigmentation disorder			
subjects affected / exposed	0 / 7 (0.00%)	1 / 23 (4.35%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Pruritus			
subjects affected / exposed	0 / 7 (0.00%)	2 / 23 (8.70%)	2 / 16 (12.50%)
occurrences (all)	0	2	2
Rash			
subjects affected / exposed	2 / 7 (28.57%)	10 / 23 (43.48%)	8 / 16 (50.00%)
occurrences (all)	2	19	17
Rash follicular			
subjects affected / exposed	0 / 7 (0.00%)	1 / 23 (4.35%)	1 / 16 (6.25%)
occurrences (all)	0	2	2
Rash maculo-papular			
subjects affected / exposed	4 / 7 (57.14%)	5 / 23 (21.74%)	1 / 16 (6.25%)
occurrences (all)	4	5	1
Rash papular			
subjects affected / exposed	0 / 7 (0.00%)	1 / 23 (4.35%)	1 / 16 (6.25%)
occurrences (all)	0	1	1

Skin disorder			
subjects affected / exposed	1 / 7 (14.29%)	1 / 23 (4.35%)	0 / 16 (0.00%)
occurrences (all)	1	1	0
Skin lesion			
subjects affected / exposed	0 / 7 (0.00%)	1 / 23 (4.35%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Skin ulcer			
subjects affected / exposed	0 / 7 (0.00%)	2 / 23 (8.70%)	2 / 16 (12.50%)
occurrences (all)	0	2	2
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 7 (0.00%)	1 / 23 (4.35%)	1 / 16 (6.25%)
occurrences (all)	0	2	2
Renal pain			
subjects affected / exposed	0 / 7 (0.00%)	1 / 23 (4.35%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 7 (14.29%)	3 / 23 (13.04%)	2 / 16 (12.50%)
occurrences (all)	1	3	2
Flank pain			
subjects affected / exposed	1 / 7 (14.29%)	1 / 23 (4.35%)	0 / 16 (0.00%)
occurrences (all)	1	1	0
Joint range of motion decreased			
subjects affected / exposed	0 / 7 (0.00%)	1 / 23 (4.35%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Limb discomfort			
subjects affected / exposed	1 / 7 (14.29%)	1 / 23 (4.35%)	0 / 16 (0.00%)
occurrences (all)	1	1	0
Muscle fatigue			
subjects affected / exposed	0 / 7 (0.00%)	1 / 23 (4.35%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Muscle spasms			
subjects affected / exposed	0 / 7 (0.00%)	2 / 23 (8.70%)	2 / 16 (12.50%)
occurrences (all)	0	2	2
Muscular weakness			

subjects affected / exposed	0 / 7 (0.00%)	1 / 23 (4.35%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Musculoskeletal chest pain			
subjects affected / exposed	0 / 7 (0.00%)	1 / 23 (4.35%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Musculoskeletal pain			
subjects affected / exposed	0 / 7 (0.00%)	1 / 23 (4.35%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Neck pain			
subjects affected / exposed	0 / 7 (0.00%)	1 / 23 (4.35%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Pain in extremity			
subjects affected / exposed	1 / 7 (14.29%)	2 / 23 (8.70%)	1 / 16 (6.25%)
occurrences (all)	1	2	1
Tendon disorder			
subjects affected / exposed	1 / 7 (14.29%)	1 / 23 (4.35%)	0 / 16 (0.00%)
occurrences (all)	1	1	0
Vertebral lesion			
subjects affected / exposed	0 / 7 (0.00%)	1 / 23 (4.35%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Infections and infestations			
Conjunctivitis			
subjects affected / exposed	0 / 7 (0.00%)	2 / 23 (8.70%)	2 / 16 (12.50%)
occurrences (all)	0	2	2
Cystitis			
subjects affected / exposed	1 / 7 (14.29%)	1 / 23 (4.35%)	0 / 16 (0.00%)
occurrences (all)	1	1	0
Erysipelas			
subjects affected / exposed	0 / 7 (0.00%)	2 / 23 (8.70%)	2 / 16 (12.50%)
occurrences (all)	0	3	3
Folliculitis			
subjects affected / exposed	1 / 7 (14.29%)	2 / 23 (8.70%)	1 / 16 (6.25%)
occurrences (all)	1	4	3
Fungal skin infection			
subjects affected / exposed	0 / 7 (0.00%)	1 / 23 (4.35%)	1 / 16 (6.25%)
occurrences (all)	0	1	1

Groin infection			
subjects affected / exposed	0 / 7 (0.00%)	1 / 23 (4.35%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Influenza			
subjects affected / exposed	0 / 7 (0.00%)	1 / 23 (4.35%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Oral fungal infection			
subjects affected / exposed	0 / 7 (0.00%)	1 / 23 (4.35%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Paronychia			
subjects affected / exposed	2 / 7 (28.57%)	4 / 23 (17.39%)	2 / 16 (12.50%)
occurrences (all)	2	5	3
Pneumonia			
subjects affected / exposed	0 / 7 (0.00%)	1 / 23 (4.35%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Rash pustular			
subjects affected / exposed	0 / 7 (0.00%)	2 / 23 (8.70%)	2 / 16 (12.50%)
occurrences (all)	0	2	2
Rhinitis			
subjects affected / exposed	0 / 7 (0.00%)	1 / 23 (4.35%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Skin infection			
subjects affected / exposed	1 / 7 (14.29%)	1 / 23 (4.35%)	0 / 16 (0.00%)
occurrences (all)	1	1	0
Upper respiratory tract infection			
subjects affected / exposed	2 / 7 (28.57%)	2 / 23 (8.70%)	0 / 16 (0.00%)
occurrences (all)	2	2	0
Urinary tract infection			
subjects affected / exposed	1 / 7 (14.29%)	4 / 23 (17.39%)	3 / 16 (18.75%)
occurrences (all)	1	4	3
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	3 / 7 (42.86%)	10 / 23 (43.48%)	7 / 16 (43.75%)
occurrences (all)	3	10	7
Hyperuricaemia			

subjects affected / exposed	0 / 7 (0.00%)	1 / 23 (4.35%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Hypoalbuminaemia			
subjects affected / exposed	1 / 7 (14.29%)	3 / 23 (13.04%)	2 / 16 (12.50%)
occurrences (all)	1	3	2
Hypocalcaemia			
subjects affected / exposed	0 / 7 (0.00%)	1 / 23 (4.35%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Hypokalaemia			
subjects affected / exposed	1 / 7 (14.29%)	6 / 23 (26.09%)	5 / 16 (31.25%)
occurrences (all)	1	9	8
Hypomagnesaemia			
subjects affected / exposed	0 / 7 (0.00%)	1 / 23 (4.35%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Hyponatraemia			
subjects affected / exposed	1 / 7 (14.29%)	2 / 23 (8.70%)	1 / 16 (6.25%)
occurrences (all)	1	2	1
Hypophosphataemia			
subjects affected / exposed	2 / 7 (28.57%)	2 / 23 (8.70%)	0 / 16 (0.00%)
occurrences (all)	2	2	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
20 November 2015	The main purpose of this protocol amendment was to optimize the subject safety and toxicity monitoring and to align Novartis study protocols.
27 October 2017	The main purpose of this amendment was to introduce the new dosage strength of INC280 150mg oral tablets were used to administer doses of 300mg (150mg x2) INC280 to ensure continuity of treatment. The INC280 100mg oral tablets would no longer be manufactured to support a dose of 300mg required for dose reductions from the 400mg starting dose.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported