



Clinical trial results:

A phase I/II, multicenter, open-label dose finding study of oral CFG920 in patients with metastatic castration-resistant prostate cancer

Summary

EudraCT number	2012-001961-33
Trial protocol	ES BE
Global end of trial date	03 March 2016

Results information

Result version number	v1 (current)
This version publication date	15 February 2017
First version publication date	15 February 2017

Trial information

Trial identification

Sponsor protocol code	CFG920X2101
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01647789
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 613241111,
Scientific contact	Clinical Disclosure Office, Novartis Pharma, AG, 41 613241111,

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	03 March 2016
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	03 March 2016
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

Phase I/Dose escalation phase: To estimate the maximum tolerated dose (MTD) or recommended Phase II dose (RP2D) of oral CFG920 when co administered with prednisone to adult patients with CRPC.

Phase II: To assess preliminary antitumor activity of CFG920 across two CRPC groups:

Arm 1: Abiraterone acetate (ABI)-naïve

Arm 2: ABI resistant

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	04 December 2012
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	Spain: 6
Country: Number of subjects enrolled	Belgium: 6
Country: Number of subjects enrolled	Canada: 9
Country: Number of subjects enrolled	United States: 10
Worldwide total number of subjects	31
EEA total number of subjects	12

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)	9
From 65 to 84 years	22
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

The study planned to include approximately 24 patients during dose escalation part and at least 50 patients during dose expansion part (with a minimum of 20 patients in arm 1 and 30 in arm 2). Overall, 31 patients were enrolled and treated in dose escalation part (Phase I) of the study, and all of them were analyzed.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
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Arm title	CFG920 50mg bid + 5mg prednisone bid
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Arm description:

The initial dose of CFG920 was 50 mg bid co-administered with 5 mg bid of prednisone for 28 day cycles. Dose escalation continued until the MTD/RP2D was estimated.

Arm type	Experimental
Investigational medicinal product name	CFG920
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Capsules of CFG920 were supplied to the Investigators at dose strengths of 25 mg and 100 mg. Patients continuously received daily dosing of oral CFG920 capsule.

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

Dosage and administration details:

Commercially available prednisone tablets were supplied to the Investigators at dose strengths of 5 mg. Patients continuously received daily dosing of oral CFG920 capsule co-administered with prednisone twice daily for 28 day (4 week) cycles, with no breaks between cycles.

Arm title	CFG920 100mg bid + 5mg prednisone bid
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Arm description:

The dose of CFG920 was 100 mg bid co-administered with 5 mg bid of prednisone for 28 day cycles. Dose escalation continued until the MTD/RP2D was estimated.

Arm type	Experimental
Investigational medicinal product name	CFG920
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Capsules of CFG920 were supplied to the Investigators at dose strengths of 25 mg and 100 mg. Patients

continuously received daily dosing of oral CFG920 capsule.

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

Dosage and administration details:

Commercially available prednisone tablets were supplied to the Investigators at dose strengths of 5 mg. Patients continuously received daily dosing of oral CFG920 capsule co-administered with prednisone twice daily for 28 day (4 week) cycles, with no breaks between cycles.

Arm title	CFG920 150mg bid + 5mg prednisone bid
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Arm description:

The initial dose of CFG920 was 150 mg bid co-administered with 5 mg bid of prednisone for 28 day cycles. Dose escalation continued until the MTD/RP2D was estimated.

Arm type	Experimental
Investigational medicinal product name	CFG920
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Capsules of CFG920 were supplied to the Investigators at dose strengths of 25 mg and 100 mg. Patients continuously received daily dosing of oral CFG920 capsule.

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

Dosage and administration details:

Commercially available prednisone tablets were supplied to the Investigators at dose strengths of 5 mg. Patients continuously received daily dosing of oral CFG920 capsule co-administered with prednisone twice daily for 28 day (4 week) cycles, with no breaks between cycles.

Arm title	CFG920 200mg bid + 5mg prednisone bid
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Arm description:

The initial dose of CFG920 was 150 mg bid co-administered with 5 mg bid of prednisone for 28 day cycles. Dose escalation continued until the MTD/RP2D was estimated.

Arm type	Experimental
Investigational medicinal product name	CFG920
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Capsules of CFG920 were supplied to the Investigators at dose strengths of 25 mg and 100 mg. Patients continuously received daily dosing of oral CFG920 capsule.

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

Dosage and administration details:

Commercially available prednisone tablets were supplied to the Investigators at dose strengths of 5 mg. Patients continuously received daily dosing of oral CFG920 capsule co-administered with prednisone twice daily for 28 day (4 week) cycles, with no breaks between cycles.

Number of subjects in period 1	CFG920 50mg bid + 5mg prednisone bid	CFG920 100mg bid + 5mg prednisone bid	CFG920 150mg bid + 5mg prednisone bid
	Started	6	9
Completed	0	0	0
Not completed	6	9	6
Adverse event, non-fatal	-	2	2
disease progression	6	7	4

Number of subjects in period 1	CFG920 200mg bid + 5mg prednisone bid
Started	10
Completed	0
Not completed	10
Adverse event, non-fatal	3
disease progression	7

Baseline characteristics

Reporting groups

Reporting group title	CFG920 50mg bid + 5mg prednisone bid
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Reporting group description:

The initial dose of CFG920 was 50 mg bid co-administered with 5 mg bid of prednisone for 28 day cycles. Dose escalation continued until the MTD/RP2D was estimated.

Reporting group title	CFG920 100mg bid + 5mg prednisone bid
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Reporting group description:

The dose of CFG920 was 100 mg bid co-administered with 5 mg bid of prednisone for 28 day cycles. Dose escalation continued until the MTD/RP2D was estimated.

Reporting group title	CFG920 150mg bid + 5mg prednisone bid
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Reporting group description:

The initial dose of CFG920 was 150 mg bid co-administered with 5 mg bid of prednisone for 28 day cycles. Dose escalation continued until the MTD/RP2D was estimated.

Reporting group title	CFG920 200mg bid + 5mg prednisone bid
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Reporting group description:

The initial dose of CFG920 was 150 mg bid co-administered with 5 mg bid of prednisone for 28 day cycles. Dose escalation continued until the MTD/RP2D was estimated.

Reporting group values	CFG920 50mg bid + 5mg prednisone bid	CFG920 100mg bid + 5mg prednisone bid	CFG920 150mg bid + 5mg prednisone bid
Number of subjects	6	9	6
Age categorical Units: Subjects			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age continuous Units: years			
arithmetic mean	66.3	67.1	68.8
standard deviation	± 4.84	± 8.81	± 6.85
Gender categorical Units: Subjects			
Female	0	0	0
Male	6	9	6

Reporting group values	CFG920 200mg bid + 5mg prednisone bid	Total	
Number of subjects	10	31	

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			
arithmetic mean	67.6		
standard deviation	± 7.26	-	
Gender categorical Units: Subjects			
Female	0	0	
Male	10	31	

End points

End points reporting groups

Reporting group title	CFG920 50mg bid + 5mg prednisone bid
Reporting group description: The initial dose of CFG920 was 50 mg bid co-administered with 5 mg bid of prednisone for 28 day cycles. Dose escalation continued until the MTD/RP2D was estimated.	
Reporting group title	CFG920 100mg bid + 5mg prednisone bid
Reporting group description: The dose of CFG920 was 100 mg bid co-administered with 5 mg bid of prednisone for 28 day cycles. Dose escalation continued until the MTD/RP2D was estimated.	
Reporting group title	CFG920 150mg bid + 5mg prednisone bid
Reporting group description: The initial dose of CFG920 was 150 mg bid co-administered with 5 mg bid of prednisone for 28 day cycles. Dose escalation continued until the MTD/RP2D was estimated.	
Reporting group title	CFG920 200mg bid + 5mg prednisone bid
Reporting group description: The initial dose of CFG920 was 150 mg bid co-administered with 5 mg bid of prednisone for 28 day cycles. Dose escalation continued until the MTD/RP2D was estimated.	

Primary: Determination of MTD/RP2D of CFG920 by DLTs occurring in first cycle

End point title	Determination of MTD/RP2D of CFG920 by DLTs occurring in first cycle ^[1]
End point description: 4 dose levels of CFG920 (50 mg bid, 100 mg bid, 150 mg bid, 200 mg bid) were investigated in the dose escalation part of the study. 150 mg bid was excluded from the candidate doses of maximum tolerated dose (MTD)/ recommended phase II dose (R2PD) as only 4 subjects were eligible for dose determining set (DDS) at this dose level. The RP2D selected was to be either the MTD or a dose below the MTD based on safety & pharmacokinetic/pharmacodynamic considerations. DLTs - dose limiting toxicities: by primary system organ class, preferred term & treatment group per DDS (consisted of all subjects from the safety set who either met the minimum exposure criterion & had sufficient safety evaluations, or had experienced a DLT during cycle 1 .	
End point type	Primary
End point timeframe: Cycle 1 = first 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 primary outcome measure.

End point values	CFG920 50mg bid + 5mg prednisone bid	CFG920 100mg bid + 5mg prednisone bid	CFG920 150mg bid + 5mg prednisone bid	CFG920 200mg bid + 5mg prednisone bid
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	9	4	7
Units: Subjects				
Any primary system class	0	1	1	1
Metabolism & nutrition disorders	0	1	1	1
Hyperglycaemia	0	0	0	1
Hyperkalaemia	0	0	1	0
Hyponatraemia	0	1	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Summary of Efficacy measured with Prostrate Specific Antigen (PSA)

End point title	Summary of Efficacy measured with Prostrate Specific Antigen (PSA)
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End point description:

PSA observed after first dose of CFG920. For patients who discontinued before 12 weeks, the last obtained PSA value was used.

End point type	Secondary
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End point timeframe:

Baseline, 12 Weeks

End point values	CFG920 50mg bid + 5mg prednisone bid	CFG920 100mg bid + 5mg prednisone bid	CFG920 150mg bid + 5mg prednisone bid	CFG920 200mg bid + 5mg prednisone bid
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	9	5	10
Units: Percentage change				
arithmetic mean (standard deviation)				
PSA change at 12 weeks from baseline	110.5 (± 251.94)	41.4 (± 109.85)	152.1 (± 146.98)	21.9 (± 92.94)
Best PSA change from baseline	-13.6 (± 57.51)	35.4 (± 111.97)	69.5 (± 90.86)	-20.2 (± 56.6)

Statistical analyses

No statistical analyses for this end point

Secondary: PSA \geq 50% reduction at or after 12 weeks

End point title	PSA \geq 50% reduction at or after 12 weeks
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End point description:

Number of subjects with PSA reduction \geq 50% at or after 12 weeks, after first dose of CFG920. For subjects who discontinued before 12 weeks, the last obtained PSA value was used.

End point type	Secondary
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End point timeframe:

Baseline, 12 weeks

End point values	CFG920 50mg bid + 5mg prednisone bid	CFG920 100mg bid + 5mg prednisone bid	CFG920 150mg bid + 5mg prednisone bid	CFG920 200mg bid + 5mg prednisone bid
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	9	6	10
Units: Subjects				
Yes	1	2	1	4
No	5	7	4	6
Missing	0	0	1	0

Statistical analyses

No statistical analyses for this end point

Secondary: PK parameter: Tmax for CFG920

End point title	PK parameter: Tmax for CFG920
End point description:	The time to reach Cmax for CFG920.
End point type	Secondary
End point timeframe:	Cycle 1 Day 1 (C1D1), Cycle 1 Day 15 (C1D15), Cycle 2 Day 1 (C2D1)

End point values	CFG920 50mg bid + 5mg prednisone bid	CFG920 100mg bid + 5mg prednisone bid	CFG920 150mg bid + 5mg prednisone bid	CFG920 200mg bid + 5mg prednisone bid
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	9	5	10
Units: hr				
median (full range (min-max))				
Tmax: C1D1	0.583 (0.5 to 2)	1 (0.467 to 3)	1 (0.5 to 2.07)	1.06 (0.5 to 2.02)
Tmax: C1D15	1.03 (0.5 to 3)	1 (0.5 to 3.88)	1 (0.5 to 2.1)	2 (0.483 to 4)
Tmax: C2D1	0.959 (0.5 to 2)	2 (1.07 to 3)	1.92 (0.533 to 2)	1.17 (1 to 2)

Statistical analyses

No statistical analyses for this end point

Secondary: PK parameter Cmax of CFG920

End point title	PK parameter Cmax of CFG920
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End point description:

The maximum concentration of CFG920.

End point type Secondary

End point timeframe:

C1D1, C1D15, C2D1

End point values	CFG920 50mg bid + 5mg prednisone bid	CFG920 100mg bid + 5mg prednisone bid	CFG920 150mg bid + 5mg prednisone bid	CFG920 200mg bid + 5mg prednisone bid
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	9	5	10
Units: ng/mL				
arithmetic mean (standard deviation)				
Cmax: C1D1	677 (± 149)	1250 (± 473)	1620 (± 435)	2480 (± 798)
Cmax: C1D15	468 (± 208)	1040 (± 388)	1450 (± 692)	2850 (± 1230)
Cmax: C2D1	523 (± 126)	1110 (± 269)	1220 (± 787)	1880 (± 874)

Statistical analyses

No statistical analyses for this end point

Secondary: PK parameter AUCinf of CFG920

End point title PK parameter AUCinf of CFG920

End point description:

Area under the concentration - time curve from time zero to infinity.

End point type Secondary

End point timeframe:

C1D1, C1D15, C2D1

End point values	CFG920 50mg bid + 5mg prednisone bid	CFG920 100mg bid + 5mg prednisone bid	CFG920 150mg bid + 5mg prednisone bid	CFG920 200mg bid + 5mg prednisone bid
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	5	4	7
Units: h*ng/mL				
arithmetic mean (standard deviation)				
AUCinf: C1D1	4030 (± 1390)	11300 (± 6170)	20400 (± 12000)	21900 (± 9190)
AUCinf: C1D15	995 (± 381)	3320 (± 2360)	3540 (± 0)	6990 (± 474)
AUCinf: C2D1	1430 (± 673)	3030 (± 1020)	3410 (± 1170)	7370 (± 3000)

Statistical analyses

No statistical analyses for this end point

Secondary: PK parameter AUC0-12h of CFG920

End point title	PK parameter AUC0-12h of CFG920
End point description:	Area under the concentration - time curve from time zero to 12 hours.
End point type	Secondary
End point timeframe:	C1D1, C1D15, C2D1

End point values	CFG920 50mg bid + 5mg prednisone bid	CFG920 100mg bid + 5mg prednisone bid	CFG920 150mg bid + 5mg prednisone bid	CFG920 200mg bid + 5mg prednisone bid
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	9	5	10
Units: h*ng/mL				
arithmetic mean (standard deviation)				
AUC0-12h: C1D1	3310 (± 727)	8560 (± 2960)	11500 (± 5370)	17000 (± 5440)
AUC0-12h: C1D15	1760 (± 1560)	4170 (± 2410)	9080 (± 5970)	15300 (± 6440)
AUC0-12h: C2D1	1710 (± 955)	5200 (± 2280)	6870 (± 6270)	10100 (± 7030)

Statistical analyses

No statistical analyses for this end point

Secondary: PK parameter T1/2 for CFG920

End point title	PK parameter T1/2 for CFG920
End point description:	The half-life for CFG920.
End point type	Secondary
End point timeframe:	C1D1, C1D15, C2D1

End point values	CFG920 50mg bid + 5mg prednisone bid	CFG920 100mg bid + 5mg prednisone bid	CFG920 150mg bid + 5mg prednisone bid	CFG920 200mg bid + 5mg prednisone bid
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	5	4	7
Units: hr				
arithmetic mean (standard deviation)				
T1/2: C1D1	3.47 (± 1.92)	3.52 (± 1.52)	6.98 (± 3.01)	4.88 (± 2.14)
T1/2: C1D15	1.27 (± 0.362)	1.7 (± 0.525)	1.77 (± 0)	1.99 (± 0.619)

T1/2: C2D1	1.75 (± 0.679)	1.56 (± 0.247)	2.2 (± 1.04)	2.03 (± 0.765)
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Statistical analyses

No statistical analyses for this end point

Secondary: PK parameter CL/F for CFG920

End point title	PK parameter CL/F for CFG920
End point description:	Apparent total clearance of the drug from plasma after oral administration.
End point type	Secondary
End point timeframe:	C1D1, C1D15, C2D1

End point values	CFG920 50mg bid + 5mg prednisone bid	CFG920 100mg bid + 5mg prednisone bid	CFG920 150mg bid + 5mg prednisone bid	CFG920 200mg bid + 5mg prednisone bid
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	5	4	7
Units: L/h				
arithmetic mean (standard deviation)				
CL/F: C1D1	13.6 (± 4.83)	10.9 (± 5.21)	9.87 (± 6.33)	11 (± 5.63)
CL/F: C1D15	56.9 (± 25.4)	40.3 (± 19)	42.9 (± 0)	29.4 (± 2.78)
CL/F: C2D1	40.9 (± 14.8)	35.4 (± 11.8)	48.1 (± 14.6)	30.5 (± 9.28)

Statistical analyses

No statistical analyses for this end point

Secondary: PK parameter Vz/F for CFG920

End point title	PK parameter Vz/F for CFG920
End point description:	Apparent volume of distribution during terminal phase after non-intravenous administration.
End point type	Secondary
End point timeframe:	C1D1, C1D15, C2D1

End point values	CFG920 50mg bid + 5mg prednisone bid	CFG920 100mg bid + 5mg prednisone bid	CFG920 150mg bid + 5mg prednisone bid	CFG920 200mg bid + 5mg prednisone bid
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	5	4	7
Units: Litre				
arithmetic mean (standard deviation)				
Vz/F: C1D1	61.2 (± 18.3)	48.4 (± 15.7)	79 (± 19.8)	70.1 (± 29.6)
Vz/F: C1D15	96.3 (± 16.5)	88.4 (± 26.1)	109 (± 0)	85.6 (± 34.3)
Vz/F: C2D1	92.2 (± 11.8)	85.5 (± 22.7)	141 (± 25.7)	83.3 (± 18.2)

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 reported in this record are from date of 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
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	18.1
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Reporting groups

Reporting group title	CFG920 50 mg BID
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Reporting group description:

CFG920 50 mg BID

Reporting group title	CFG920 100 mg BID
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Reporting group description:

CFG920 100 mg BID

Reporting group title	CFG920 150 mg BID
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Reporting group description:

CFG920 150 mg BID

Reporting group title	CFG920 200 mg BID
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Reporting group description:

CFG920 200 mg BID

Serious adverse events	CFG920 50 mg BID	CFG920 100 mg BID	CFG920 150 mg BID
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 6 (33.33%)	4 / 9 (44.44%)	2 / 6 (33.33%)
number of deaths (all causes)	1	1	0
number of deaths resulting from adverse events	0	0	0
Investigations			
Blood creatinine increased			
subjects affected / exposed	0 / 6 (0.00%)	1 / 9 (11.11%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Platelet count decreased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Weight decreased subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Cardiac arrest subjects affected / exposed	0 / 6 (0.00%)	1 / 9 (11.11%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Nervous system disorders			
Spinal cord compression subjects affected / exposed	1 / 6 (16.67%)	0 / 9 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia subjects affected / exposed	1 / 6 (16.67%)	0 / 9 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombocytopenia subjects affected / exposed	0 / 6 (0.00%)	1 / 9 (11.11%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Asthenia subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	1 / 6 (16.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fatigue subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			

subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	1 / 6 (16.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	0 / 6 (0.00%)	1 / 9 (11.11%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Inguinal hernia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 9 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 6 (0.00%)	1 / 9 (11.11%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cough			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Confusional state			
subjects affected / exposed	0 / 6 (0.00%)	1 / 9 (11.11%)	1 / 6 (16.67%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Acute kidney injury			

subjects affected / exposed	0 / 6 (0.00%)	1 / 9 (11.11%)	1 / 6 (16.67%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal failure			
subjects affected / exposed	0 / 6 (0.00%)	1 / 9 (11.11%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary incontinence			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	1 / 6 (16.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 6 (16.67%)	0 / 9 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bone pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Muscular weakness			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Endocarditis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 9 (11.11%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Urinary tract infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urosepsis			
subjects affected / exposed	0 / 6 (0.00%)	1 / 9 (11.11%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dehydration			
subjects affected / exposed	0 / 6 (0.00%)	1 / 9 (11.11%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperkalaemia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 9 (11.11%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolic acidosis			
subjects affected / exposed	0 / 6 (0.00%)	1 / 9 (11.11%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	CFG920 200 mg BID		
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 10 (50.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Investigations			
Blood creatinine increased			

subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Platelet count decreased			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Weight decreased			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Cardiac arrest			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Spinal cord compression			
subjects affected / exposed	1 / 10 (10.00%)		
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	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Thrombocytopenia			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Asthenia			

subjects affected / exposed	1 / 10 (10.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Fatigue			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pyrexia			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Inguinal hernia			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cough			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Dyspnoea			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Psychiatric disorders Confusional state subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	 0 / 10 (0.00%) 0 / 0 0 / 0		
Renal and urinary disorders Acute kidney injury subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	 0 / 10 (0.00%) 0 / 0 0 / 0		
Renal failure subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	 0 / 10 (0.00%) 0 / 0 0 / 0		
Urinary incontinence subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	 0 / 10 (0.00%) 0 / 0 0 / 0		
Musculoskeletal and connective tissue disorders Back pain subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	 0 / 10 (0.00%) 0 / 0 0 / 0		
Bone pain subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	 1 / 10 (10.00%) 0 / 1 0 / 0		
Muscular weakness subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	 1 / 10 (10.00%) 0 / 1 0 / 0		
Infections and infestations Endocarditis			

subjects affected / exposed	1 / 10 (10.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumonia			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Urinary tract infection			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Urosepsis			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Dehydration			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hyperkalaemia			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Metabolic acidosis			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	CFG920 50 mg BID	CFG920 100 mg BID	CFG920 150 mg BID
Total subjects affected by non-serious adverse events			
subjects affected / exposed	6 / 6 (100.00%)	9 / 9 (100.00%)	6 / 6 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Tumour pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Vascular disorders			
Angiopathy			
subjects affected / exposed	0 / 6 (0.00%)	1 / 9 (11.11%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Flushing			
subjects affected / exposed	1 / 6 (16.67%)	0 / 9 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Hot flush			
subjects affected / exposed	0 / 6 (0.00%)	1 / 9 (11.11%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Hypertension			
subjects affected / exposed	1 / 6 (16.67%)	0 / 9 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Hypotension			
subjects affected / exposed	0 / 6 (0.00%)	1 / 9 (11.11%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 6 (0.00%)	2 / 9 (22.22%)	0 / 6 (0.00%)
occurrences (all)	0	2	0
Fatigue			
subjects affected / exposed	5 / 6 (83.33%)	3 / 9 (33.33%)	3 / 6 (50.00%)
occurrences (all)	6	3	3
Malaise			

subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	1 / 9 (11.11%) 1	0 / 6 (0.00%) 0
Oedema peripheral subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 9 (0.00%) 0	1 / 6 (16.67%) 1
Pain subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	1 / 9 (11.11%) 1	1 / 6 (16.67%) 1
Pyrexia subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1	0 / 9 (0.00%) 0	1 / 6 (16.67%) 1
Systemic inflammatory response syndrome subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	1 / 9 (11.11%) 1	0 / 6 (0.00%) 0
Respiratory, thoracic and mediastinal disorders			
Cough subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1	2 / 9 (22.22%) 2	0 / 6 (0.00%) 0
Dyspnoea subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 9 (0.00%) 0	0 / 6 (0.00%) 0
Epistaxis subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	1 / 9 (11.11%) 1	0 / 6 (0.00%) 0
Hypoxia subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	1 / 9 (11.11%) 1	0 / 6 (0.00%) 0
Psychiatric disorders			
Agitation subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	1 / 9 (11.11%) 1	0 / 6 (0.00%) 0
Alcohol abuse subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	1 / 9 (11.11%) 1	0 / 6 (0.00%) 0
Anxiety			

subjects affected / exposed	1 / 6 (16.67%)	0 / 9 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Confusional state			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Depression			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Insomnia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Irritability			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Panic attack			
subjects affected / exposed	0 / 6 (0.00%)	1 / 9 (11.11%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Sleep disorder			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Tobacco abuse			
subjects affected / exposed	0 / 6 (0.00%)	1 / 9 (11.11%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 6 (0.00%)	2 / 9 (22.22%)	2 / 6 (33.33%)
occurrences (all)	0	2	2
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 6 (0.00%)	3 / 9 (33.33%)	3 / 6 (50.00%)
occurrences (all)	0	3	3
Blood albumin decreased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Blood alkaline phosphatase increased			

subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1	1 / 9 (11.11%) 3	4 / 6 (66.67%) 5
Blood bilirubin increased subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	1 / 9 (11.11%) 1	0 / 6 (0.00%) 0
Blood calcium decreased subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 9 (0.00%) 0	1 / 6 (16.67%) 1
Blood creatinine increased subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 3	1 / 9 (11.11%) 1	0 / 6 (0.00%) 0
Blood phosphorus decreased subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 9 (0.00%) 0	0 / 6 (0.00%) 0
Blood sodium decreased subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 9 (0.00%) 0	1 / 6 (16.67%) 1
Blood urea increased subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	1 / 9 (11.11%) 1	0 / 6 (0.00%) 0
Gamma-glutamyltransferase increased subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	1 / 9 (11.11%) 1	3 / 6 (50.00%) 3
Platelet count decreased subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	1 / 9 (11.11%) 3	1 / 6 (16.67%) 1
Protein total decreased subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 9 (0.00%) 0	0 / 6 (0.00%) 0
Weight decreased subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1	1 / 9 (11.11%) 1	0 / 6 (0.00%) 0
Injury, poisoning and procedural complications			

Animal bite subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Contusion subjects affected / exposed	1 / 6 (16.67%)	0 / 9 (0.00%)	0 / 6 (0.00%)
occurrences (all)	3	0	0
Ligament sprain subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Atrial fibrillation subjects affected / exposed	0 / 6 (0.00%)	1 / 9 (11.11%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Sinus tachycardia subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Nervous system disorders			
Dizziness subjects affected / exposed	0 / 6 (0.00%)	1 / 9 (11.11%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Dysgeusia subjects affected / exposed	0 / 6 (0.00%)	1 / 9 (11.11%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Headache subjects affected / exposed	1 / 6 (16.67%)	0 / 9 (0.00%)	1 / 6 (16.67%)
occurrences (all)	1	0	2
Monoparesis subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Muscle contractions involuntary subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Paraesthesia subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Presyncope			

subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	1 / 9 (11.11%) 1	0 / 6 (0.00%) 0
Radiculopathy subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	1 / 9 (11.11%) 1	0 / 6 (0.00%) 0
Syncope subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	1 / 9 (11.11%) 1	0 / 6 (0.00%) 0
Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all)	2 / 6 (33.33%) 2	4 / 9 (44.44%) 5	2 / 6 (33.33%) 2
Lymphopenia subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 9 (0.00%) 0	0 / 6 (0.00%) 0
Thrombocytopenia subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	2 / 9 (22.22%) 2	1 / 6 (16.67%) 1
Eye disorders Cataract subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 9 (0.00%) 0	1 / 6 (16.67%) 1
Dry eye subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 9 (0.00%) 0	1 / 6 (16.67%) 1
Visual acuity reduced subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 9 (0.00%) 0	0 / 6 (0.00%) 0
Gastrointestinal disorders Abdominal pain upper subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1	0 / 9 (0.00%) 0	0 / 6 (0.00%) 0
Abnormal faeces subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 9 (0.00%) 0	0 / 6 (0.00%) 0
Aphthous ulcer			

subjects affected / exposed	0 / 6 (0.00%)	1 / 9 (11.11%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Constipation			
subjects affected / exposed	1 / 6 (16.67%)	3 / 9 (33.33%)	2 / 6 (33.33%)
occurrences (all)	1	4	2
Diarrhoea			
subjects affected / exposed	2 / 6 (33.33%)	2 / 9 (22.22%)	0 / 6 (0.00%)
occurrences (all)	4	2	0
Dry mouth			
subjects affected / exposed	2 / 6 (33.33%)	0 / 9 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
Dyspepsia			
subjects affected / exposed	0 / 6 (0.00%)	2 / 9 (22.22%)	1 / 6 (16.67%)
occurrences (all)	0	2	1
Faecal incontinence			
subjects affected / exposed	0 / 6 (0.00%)	1 / 9 (11.11%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Faeces discoloured			
subjects affected / exposed	1 / 6 (16.67%)	0 / 9 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Flatulence			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 6 (0.00%)	1 / 9 (11.11%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Nausea			
subjects affected / exposed	4 / 6 (66.67%)	4 / 9 (44.44%)	1 / 6 (16.67%)
occurrences (all)	4	4	1
Odynophagia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Steatorrhoea			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Vomiting			

subjects affected / exposed occurrences (all)	3 / 6 (50.00%) 4	2 / 9 (22.22%) 2	0 / 6 (0.00%) 0
Hepatobiliary disorders			
Hepatitis			
subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1	0 / 9 (0.00%) 0	0 / 6 (0.00%) 0
Hyperbilirubinaemia			
subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	1 / 9 (11.11%) 1	0 / 6 (0.00%) 0
Skin and subcutaneous tissue disorders			
Hyperhidrosis			
subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 9 (0.00%) 0	0 / 6 (0.00%) 0
Ingrown hair			
subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1	0 / 9 (0.00%) 0	0 / 6 (0.00%) 0
Pruritus			
subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 9 (0.00%) 0	1 / 6 (16.67%) 1
Rash			
subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	1 / 9 (11.11%) 1	0 / 6 (0.00%) 0
Rash maculo-papular			
subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 9 (0.00%) 0	1 / 6 (16.67%) 1
Urticaria			
subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 9 (0.00%) 0	0 / 6 (0.00%) 0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 9 (0.00%) 0	0 / 6 (0.00%) 0
Dysuria			
subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 9 (0.00%) 0	1 / 6 (16.67%) 1
Haematuria			

subjects affected / exposed	1 / 6 (16.67%)	0 / 9 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Pollakiuria			
subjects affected / exposed	1 / 6 (16.67%)	0 / 9 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Urinary incontinence			
subjects affected / exposed	2 / 6 (33.33%)	0 / 9 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
Urinary retention			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	2 / 6 (33.33%)	1 / 9 (11.11%)	1 / 6 (16.67%)
occurrences (all)	2	1	1
Back pain			
subjects affected / exposed	0 / 6 (0.00%)	3 / 9 (33.33%)	2 / 6 (33.33%)
occurrences (all)	0	3	2
Bone pain			
subjects affected / exposed	3 / 6 (50.00%)	1 / 9 (11.11%)	0 / 6 (0.00%)
occurrences (all)	6	1	0
Groin pain			
subjects affected / exposed	1 / 6 (16.67%)	0 / 9 (0.00%)	1 / 6 (16.67%)
occurrences (all)	1	0	1
Muscle spasms			
subjects affected / exposed	2 / 6 (33.33%)	0 / 9 (0.00%)	2 / 6 (33.33%)
occurrences (all)	3	0	4
Muscular weakness			
subjects affected / exposed	2 / 6 (33.33%)	0 / 9 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
Musculoskeletal chest pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Musculoskeletal pain			

subjects affected / exposed	1 / 6 (16.67%)	2 / 9 (22.22%)	0 / 6 (0.00%)
occurrences (all)	1	2	0
Musculoskeletal stiffness			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Myalgia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 9 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Myopathy			
subjects affected / exposed	1 / 6 (16.67%)	0 / 9 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Infections and infestations			
Folliculitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal viral infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			
subjects affected / exposed	0 / 6 (0.00%)	1 / 9 (11.11%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Sepsis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Tooth infection			
subjects affected / exposed	0 / 6 (0.00%)	1 / 9 (11.11%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Upper respiratory tract infection			
subjects affected / exposed	0 / 6 (0.00%)	1 / 9 (11.11%)	1 / 6 (16.67%)
occurrences (all)	0	1	2
Urinary tract infection			
subjects affected / exposed	1 / 6 (16.67%)	1 / 9 (11.11%)	1 / 6 (16.67%)
occurrences (all)	1	1	1
Viral infection			
subjects affected / exposed	0 / 6 (0.00%)	1 / 9 (11.11%)	0 / 6 (0.00%)
occurrences (all)	0	1	0

Viral upper respiratory tract infection subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1	0 / 9 (0.00%) 0	0 / 6 (0.00%) 0
Metabolism and nutrition disorders			
Decreased appetite subjects affected / exposed occurrences (all)	2 / 6 (33.33%) 2	2 / 9 (22.22%) 3	1 / 6 (16.67%) 1
Dehydration subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	1 / 9 (11.11%) 1	0 / 6 (0.00%) 0
Hypercalcaemia subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	1 / 9 (11.11%) 1	0 / 6 (0.00%) 0
Hyperglycaemia subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 9 (0.00%) 0	0 / 6 (0.00%) 0
Hyperkalaemia subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 9 (0.00%) 0	1 / 6 (16.67%) 2
Hypernatraemia subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 9 (0.00%) 0	1 / 6 (16.67%) 1
Hypoalbuminaemia subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	1 / 9 (11.11%) 1	0 / 6 (0.00%) 0
Hypocalcaemia subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	2 / 9 (22.22%) 2	0 / 6 (0.00%) 0
Hypoglycaemia subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	1 / 9 (11.11%) 1	0 / 6 (0.00%) 0
Hypokalaemia subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	1 / 9 (11.11%) 1	0 / 6 (0.00%) 0
Hyponatraemia			

subjects affected / exposed	0 / 6 (0.00%)	2 / 9 (22.22%)	0 / 6 (0.00%)
occurrences (all)	0	2	0
Hypophosphataemia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 9 (11.11%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Hypoproteinaemia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Metabolic acidosis			
subjects affected / exposed	0 / 6 (0.00%)	1 / 9 (11.11%)	0 / 6 (0.00%)
occurrences (all)	0	1	0

Non-serious adverse events	CFG920 200 mg BID		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	10 / 10 (100.00%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Tumour pain			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Vascular disorders			
Angiopathy			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Flushing			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Hot flush			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Hypertension			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Hypotension			

subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0		
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Fatigue			
subjects affected / exposed	5 / 10 (50.00%)		
occurrences (all)	5		
Malaise			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Oedema peripheral			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Pain			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Pyrexia			
subjects affected / exposed	3 / 10 (30.00%)		
occurrences (all)	3		
Systemic inflammatory response syndrome			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Dyspnoea			
subjects affected / exposed	2 / 10 (20.00%)		
occurrences (all)	2		
Epistaxis			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Hypoxia			

subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0		
Psychiatric disorders			
Agitation			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Alcohol abuse			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Anxiety			
subjects affected / exposed	2 / 10 (20.00%)		
occurrences (all)	2		
Confusional state			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Depression			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Insomnia			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Irritability			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Panic attack			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Sleep disorder			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Tobacco abuse			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Investigations			
Alanine aminotransferase increased			

subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Blood albumin decreased			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Blood alkaline phosphatase increased			
subjects affected / exposed	3 / 10 (30.00%)		
occurrences (all)	3		
Blood bilirubin increased			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Blood calcium decreased			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Blood creatinine increased			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Blood phosphorus decreased			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	2		
Blood sodium decreased			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Blood urea increased			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Gamma-glutamyltransferase increased			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	2		
Platelet count decreased			

<p>subjects affected / exposed occurrences (all)</p> <p>Protein total decreased subjects affected / exposed occurrences (all)</p> <p>Weight decreased subjects affected / exposed occurrences (all)</p>	<p>4 / 10 (40.00%) 4</p> <p>1 / 10 (10.00%) 1</p> <p>1 / 10 (10.00%) 1</p>		
<p>Injury, poisoning and procedural complications</p> <p>Animal bite subjects affected / exposed occurrences (all)</p> <p>Contusion subjects affected / exposed occurrences (all)</p> <p>Ligament sprain subjects affected / exposed occurrences (all)</p>	<p>1 / 10 (10.00%) 1</p> <p>3 / 10 (30.00%) 3</p> <p>1 / 10 (10.00%) 1</p>		
<p>Cardiac disorders</p> <p>Atrial fibrillation subjects affected / exposed occurrences (all)</p> <p>Sinus tachycardia subjects affected / exposed occurrences (all)</p>	<p>0 / 10 (0.00%) 0</p> <p>0 / 10 (0.00%) 0</p>		
<p>Nervous system disorders</p> <p>Dizziness subjects affected / exposed occurrences (all)</p> <p>Dysgeusia subjects affected / exposed occurrences (all)</p> <p>Headache subjects affected / exposed occurrences (all)</p> <p>Monoparesis</p>	<p>3 / 10 (30.00%) 3</p> <p>1 / 10 (10.00%) 1</p> <p>0 / 10 (0.00%) 0</p>		

subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Muscle contractions involuntary			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	3		
Paraesthesia			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	2		
Presyncope			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Radiculopathy			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Syncope			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	3 / 10 (30.00%)		
occurrences (all)	5		
Lymphopenia			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Thrombocytopenia			
subjects affected / exposed	4 / 10 (40.00%)		
occurrences (all)	13		
Eye disorders			
Cataract			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Dry eye			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Visual acuity reduced			

subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1		
Gastrointestinal disorders			
Abdominal pain upper subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0		
Abnormal faeces subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1		
Aphthous ulcer subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0		
Constipation subjects affected / exposed occurrences (all)	3 / 10 (30.00%) 3		
Diarrhoea subjects affected / exposed occurrences (all)	2 / 10 (20.00%) 5		
Dry mouth subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0		
Dyspepsia subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1		
Faecal incontinence subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0		
Faeces discoloured subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0		
Flatulence subjects affected / exposed occurrences (all)	2 / 10 (20.00%) 2		
Gastrooesophageal reflux disease subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0		

Nausea			
subjects affected / exposed	3 / 10 (30.00%)		
occurrences (all)	4		
Odynophagia			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Steatorrhoea			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Vomiting			
subjects affected / exposed	4 / 10 (40.00%)		
occurrences (all)	4		
Hepatobiliary disorders			
Hepatitis			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Hyperbilirubinaemia			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Skin and subcutaneous tissue disorders			
Hyperhidrosis			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Ingrown hair			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Pruritus			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Rash			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Rash maculo-papular			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Urticaria			

subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1		
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Dysuria			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Haematuria			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Pollakiuria			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Urinary incontinence			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Urinary retention			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	2 / 10 (20.00%)		
occurrences (all)	3		
Back pain			
subjects affected / exposed	2 / 10 (20.00%)		
occurrences (all)	2		
Bone pain			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Groin pain			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Muscle spasms			

subjects affected / exposed occurrences (all)	2 / 10 (20.00%) 2		
Muscular weakness subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1		
Musculoskeletal chest pain subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 2		
Musculoskeletal pain subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0		
Musculoskeletal stiffness subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1		
Myalgia subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1		
Myopathy subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0		
Infections and infestations			
Folliculitis subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1		
Gastrointestinal viral infection subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1		
Nasopharyngitis subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0		
Sepsis subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1		
Tooth infection subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0		

Upper respiratory tract infection subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1		
Urinary tract infection subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1		
Viral infection subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0		
Viral upper respiratory tract infection subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0		
Metabolism and nutrition disorders			
Decreased appetite subjects affected / exposed occurrences (all)	2 / 10 (20.00%) 2		
Dehydration subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0		
Hypercalcaemia subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1		
Hyperglycaemia subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 3		
Hyperkalaemia subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0		
Hypernatraemia subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0		
Hypoalbuminaemia subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0		
Hypocalcaemia			

subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Hypoglycaemia			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Hypokalaemia			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Hyponatraemia			
subjects affected / exposed	3 / 10 (30.00%)		
occurrences (all)	3		
Hypophosphataemia			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Hypoproteinaemia			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Metabolic acidosis			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
21 August 2012	<p>Amendment 1 was issued prior to enrollment of patients into the study. The main purpose of this amendment was to incorporate changes that Novartis has agreed to as per the agreement with the U.S. Food and Drug Administration.</p> <p>Eligibility Criteria To better define the eligible patient population, more specific inclusion requirements for prior treatment with docetaxel and ABI were added. Due to plausible mechanistic toxicities, laboratory criteria for potassium were added. To further define the DLT criteria for thrombocytopenia, additional details were included with regard to bleeding. Due to potential for mechanistic toxicities, additional dose modification, toxicity monitoring, and toxicity management guidance were added. To modify dose escalation criteria, the language in the guidelines was revised. Following reviewer recommendation, the starting dose was reduced to 50 mg bid.</p>
01 March 2013	<p>Amendment 2:</p> <p>To improve site and patient compliance and protocol execution, PD assessment was included as an exploratory endpoint. To address emerging data and to inform future decisions, a change from baseline of 30% decline in PSA was added as a secondary endpoint. To assess genetic abnormalities that were thought to be important in cancer, the collection of tumor biopsy specimens was added as an exploratory endpoint. With the addition of the mandatory tumor collection at Screening, receiving any additional tissue was not likely. To address the ensuing limited availability of paired fresh tissue biopsies, the optional fresh pre and post dose biopsies that were to be used to assess the suppression of AR signaling in tumor tissue and potential correlations with clinical outcomes and investigate the change in tumor androgens were eliminated. To allow for a better defining of progression per radiological assessment, the secondary Phase II endpoint to assess efficacy at MTD/RP2D via radiological progression free survival is renamed to radiological time to progression. To assess genetic abnormalities that are thought to be important in cancer, the requirement to collect tumor tissue was added to the inclusion criteria. To prevent premature discontinuation of patients from treatment and thus allowing the continued exploration of higher safe doses of CFG920, the management of blood bilirubin toxicity was revised to be in line with the management of toxicity of other molecules of the same class. To allow for better characterizing toxicity, the use of the adrenocortical insufficiency was changed to mineralocorticoid imbalance. To allow for more frequent assessment of plasma renin activity (PRA), the guidance for the management of adrenocortical insufficiency/ mineralocorticoid imbalance was revised. Because of its potential androgen receptor agonist activity, spironolactone was added as a prohibited medication.</p>

17 July 2013	<p>Amendment 3:</p> <p>Given the lack of evidence from preclinical studies of a difference in the clinical benefit between these primary and secondary ABI resistant CRPC arms, these two arms were combined into a single ABI resistant CRPC arm (Arm 2) in the Phase II part of the study. A supportive sub-group analysis to further investigate the effect of primary and secondary ABI resistance on CFG920 activity was to be performed retrospectively. Patient numbers were adjusted to match these changes.</p> <p>Because of the potential hyperglycemic effects of prednisone, glucose and HbA1c control (inclusion criteria) and monitoring of glucose levels (DLT and dose modification criteria) were added for patient safety. The DLT criteria were modified to allow for observation of possible hyperglycemia with the control of blood sugar prior to declaration of a DLT. In addition, the dose modification criteria were revised to provide guidance on the management of hyperglycemia as well as the clinical management of the discontinuation of prednisone.</p> <p>Monitoring frequency of PRA was revised to monitor potential changes in plasma renin activity (PRA) within the first five cycles of CFG920 initiation or dose modification.</p> <p>As part of protocol amendment 2, androstenedione was removed from the hormonal assessments. To ensure alignment within the protocol, androstenedione was also removed from the efficacy evaluation section.</p>
14 January 2014	<p>Amendment 4:</p> <p>In response to the request from Health Authorities, the inclusion criterion for ABI naïve patients in the Phase II part of the study was revised to include patients' refusal of ABI as follows: no prior treatment with CYP17 inhibitors (ABI, ketoconazole, etc.) or enzalutamide, and refused ABI.</p> <p>Erstwhile data from the ongoing trial indicated that treatment with CFG920 could lead to increased risk of thrombocytopenia. To assess the potential effects of CFG920 on myeloid development, including that of megakaryocytes, the collection of a bone marrow biopsy and aspirate in patients who present with grade 3 or 4 thrombocytopenia was added.</p> <p>The interim analysis evaluated the PSA response, defined as a $\geq 50\%$ reduction in PSA from baseline to ≥ 12 weeks of treatment that was confirmed 4 weeks later. As such, the timing of the interim analysis was revised to be performed after patients had completed at least 16 weeks of treatment.</p>
28 October 2014	<p>Amendment 6:</p> <p>Introduced a reduced visit schedule to address patients continuing beyond the study data cut off for the primary analysis (15-Aug-2014).</p> <p>Added the date of the data cutoff for the primary clinical study report (CSR).</p> <p>For all efficacy, safety and tolerability, and laboratory evaluation assessments, added the modified collection time points for patients following the reduced visit evaluation schedule.</p> <p>Clarified that the end of treatment collection would not be performed for patients following the reduced visit evaluation schedule.</p> <p>For all efficacy, safety and tolerability, and laboratory evaluation assessments, added the modified collection time points for patients following the reduced visit evaluation schedule.</p>

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Since patient enrollment was stopped after the completion of the dose-escalation part (Phase I), all analyses related to the phase II part were not conducted. Recruitment halt was implemented after completion of Phase I.

Notes: