Clinical trial results:
A Phase 1, Multicenter, Open-Label Study of Oral Entrectinib (RXDX-101) in Adult Patients with Locally Advanced or Metastatic Cancer Confirmed to be Positive for NTRK1, NTRK2, NTRK3, ROS1, or ALK Molecular Alterations

Summary

EudraCT number	2014-001326-15
Trial protocol	ES GB
Global end of trial date	02 June 2020

Results information

Result version number	v1 (current)
This version publication date	12 June 2021
First version publication date	12 June 2021

Trial information

Trial identification

Sponsor protocol code	RXDX-101-01

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02097810
WHO universal trial number (UTN)	-
Other trial identifiers	Sponsor Protocol Code: GO40784

Notes:

Sponsors

Sponsor organisation name	Hoffmann-La Roche
Sponsor organisation address	Grenzacherstrasse 124, Basel, Switzerland, CH-4070
Public contact	Medical Communications, F. Hoffmann-La Roche AG, +41 616878333, global.trial_information@roche.com
Scientific contact	Medical Communications, Hoffmann-La Roche, +41 616878333, global.trial_information@roche.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	01 April 2021
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	02 June 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Entrectinib (RXDX-101) is an orally available inhibitor of the tyrosine kinases TrkA (coded by the gene NTRK1), TrkB (coded by the gene NTRK2), TrkC (coded by the gene NTRK3), ROS1 (coded by the gene ROS1), and ALK (coded by the gene ALK). Molecular alterations to one or more of these targets are present in several different tumor types, including non-small cell lung cancer (NSCLC), colorectal cancer (CRC), prostate cancer, papillary thyroid cancer, pancreatic cancer, and neuroblastoma. Patients with locally advanced or metastatic cancer with a detectable molecular alteration in targets of interest may be eligible for enrollment. Phase 1 assessed safety and tolerability of entrectinib via standard dose escalation scheme and determine the recommended Phase 2 dose. Safety and efficacy were assessed in the dose expansion portion of the study.

Protection of trial subjects:

Protection of trial subjectsThis study was conducted in accordance with the protocol and with the following: - Consensus ethical principles derived from international guidelines including the Declaration of Helsinki and Council for International Organizations of Medical Sciences (CIOMS) International Ethical Guidelines - Applicable ICH Good Clinical Practice (GCP) Guidelines -Applicable laws and regulations

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	28 July 2014
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	Korea, Republic of: 9
Country: Number of subjects enrolled	United States: 74
Worldwide total number of subjects	83
EEA total number of subjects	0

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)	59
From 65 to 84 years	23
85 years and over	1

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Adult participants who had histologically or cytologically confirmed diagnosis of relapsed or refractory locally advanced or metastatic solid tumors for whom no alternative effective standard therapy was available or for whom standard therapy was considered unsuitable or intolerable, were enrolled on the STARTRK-1 study.

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	Entrectinib (RXDX-101) 100 mg/m2

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Entrectinib
Investigational medicinal product code	
Other name	RXDX-101
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

RXDX-101 at a dose of 100mg/m2 is administered as home-based treatment and should be taken at approximately the same time each morning. All subjects received repeated cycles (1 cycle = 4 weeks) of RXDX-101 orally once daily for 28 consecutive days. Drug administration occured in a fed state (i.e., patients should eat 1 hour prior to study drug administration).

Arm title	Entrectinib (RXDX-101) 200 mg/m2

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Entrectinib
Investigational medicinal product code	
Other name	RXDX-101
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

RXDX-101 at a dose of 200mg/m2 is administered as home-based treatment and should be taken at approximately the same time each morning. All subjects received repeated cycles (1 cycle = 4 weeks) of RXDX-101 orally once daily for 28 consecutive days. Drug administration occured in a fed state (i.e., patients should eat 1 hour prior to study drug administration).

Arm title	Entrectinib (RXDX-101) 400 mg/m2

Arm description: -

Arm type	Experimental

Investigational medicinal product name	Entrectinib
Investigational medicinal product code	
Other name	RXDX-101
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

RXDX-101 at a dose of 400mg/m2 is administered as home-based treatment and should be taken at approximately the same time each morning. All subjects received repeated cycles (1 cycle = 4 weeks) of RXDX-101 orally once daily for 28 consecutive days. Drug administration occured in a fed state (i.e., patients should eat 1 hour prior to study drug administration).

Arm title	Entrectinib (RXDX-101) 800 mg

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Entrectinib
Investigational medicinal product code	
Other name	RXDX-101
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

RXDX-101 at a dose of 800mg/m2 is administered as home-based treatment and should be taken at approximately the same time each morning. All subjects received repeated cycles (1 cycle = 4 weeks) of RXDX-101 orally once daily for 28 consecutive days. Drug administration occured in a fed state (i.e., patients should eat 1 hour prior to study drug administration).

Arm title	Entrectinib (RXDX-101) 600-800 mg by BSA

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Entrectinib
Investigational medicinal product code	
Other name	RXDX-101
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

RXDX-101 at a dose of 600-800mg/m2 by Body Surface Area is administered as home-based treatment and should be taken at approximately the same time each morning. All subjects received repeated cycles (1 cycle = 4 weeks) of RXDX-101 orally once daily for 28 consecutive days. Drug administration occured in a fed state (i.e., patients should eat 1 hour prior to study drug administration).

Arm title	Entrectinib (RXDX-101) 600 mg F1

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Entrectinib
Investigational medicinal product code	
Other name	RXDX-101
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

RXDX-101 at a dose of 600mg is administered as home-based treatment and should be taken at approximately the same time each morning. All subjects received repeated cycles (1 cycle = 4 weeks) of RXDX-101 orally once daily for 28 consecutive days. Drug administration occured in a fed state (i.e., patients should eat 1 hour prior to study drug administration).

Arm title	Entrectinib (RXDX-101) 600 mg QD F2A

Arm description: -

Arm type	Experimental

Investigational medicinal product name	Entrectinib
Investigational medicinal product code	
Other name	RXDX-101
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

RXDX-101 at a dose of 600mg is administered as home-based treatment and should be taken at approximately the same time each morning. All subjects received repeated cycles (1 cycle = 4 weeks) of RXDX-101 orally once daily for 28 consecutive days. Drug administration occured in a fed state (i.e., patients should eat 1 hour prior to study drug administration).

Arm title	Entrectinib (RXDX-101) 600 mg EXP

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Entrectinib
Investigational medicinal product code	
Other name	RXDX-101
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

RXDX-101 at a dose of 600mg is administered as home-based treatment and should be taken at approximately the same time each morning. All subjects received repeated cycles (1 cycle = 4 weeks) of RXDX-101 orally once daily for 28 consecutive days. Drug administration occured in a fed state (i.e., patients should eat 1 hour prior to study drug administration).

Number of subjects in period 1	Entrectinib (RXDX-101) 100 mg/m2	Entrectinib (RXDX-101) 200 mg/m2	Entrectinib (RXDX-101) 400 mg/m2
Started	5	5	10
Completed	0	0	0
Not completed	5	5	10
Consent withdrawn by subject	2	1	2
Death	2	-	4
Progressive Disease	-	-	-
Subject started different therapy	1	3	4
Lost to follow-up	-	1	-

Number of subjects in period 1	Entrectinib (RXDX-101) 800 mg	Entrectinib (RXDX-101) 600-800 mg by BSA	Entrectinib (RXDX-101) 600 mg F1
Started	9	5	22
Completed	0	0	0
Not completed	9	5	22
Consent withdrawn by subject	4	1	5
Death	1	1	4
Progressive Disease	-	-	2
Subject started different therapy	3	2	11
Lost to follow-up	1	1	-

Number of subjects in period 1	Entrectinib (RXDX-101) 600 mg QD F2A	Entrectinib (RXDX-101) 600 mg EXP
Started	20	7
Completed	0	0
Not completed	20	7
Consent withdrawn by subject	7	2
Death	5	3
Progressive Disease	-	1
Subject started different therapy	7	1
Lost to follow-up	1	-

Baseline characteristics

Reporting groups	
Reporting group title	Entrectinib (RXDX-101) 100 mg/m2
Reporting group description: -	
Reporting group title	Entrectinib (RXDX-101) 200 mg/m2
Reporting group description: -	
Reporting group title	Entrectinib (RXDX-101) 400 mg/m2
Reporting group description: -	
Reporting group title	Entrectinib (RXDX-101) 800 mg
Reporting group description: -	
Reporting group title	Entrectinib (RXDX-101) 600-800 mg by BSA
Reporting group description: -	
Reporting group title	Entrectinib (RXDX-101) 600 mg F1
Reporting group description: -	
Reporting group title	Entrectinib (RXDX-101) 600 mg QD F2A
Reporting group description: -	
Reporting group title	Entrectinib (RXDX-101) 600 mg EXP
Reporting group description: -	

Reporting group values	Entrectinib (RXDX-101) 100 mg/m2	Entrectinib (RXDX-101) 200 mg/m2	Entrectinib (RXDX-101) 400 mg/m2
Number of subjects	5	5	10
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)	2	3	9
From 65-84 years	3	2	1
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	59.6	60.2	51.5
standard deviation	± 18.3	± 9.7	± 8.4
Gender categorical Units: Subjects			
Female	0	4	7
Male	5	1	3
Race Units: Subjects			
Asian	0	1	2
Black or African American	0	0	2
White	5	4	5
Other	0	0	1

Ethnicity Units: Subjects			
Hispanic or Latino	0	1	0
Not Hispanic or Latino	5	4	9
Not Stated	0	0	0
Unknown	0	0	1

Reporting group values	Entrectinib (RXDX-101) 800 mg	Entrectinib (RXDX-101) 600-800 mg by BSA	Entrectinib (RXDX-101) 600 mg F1
Number of subjects	9	5	22
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)	6	3	20
From 65-84 years	3	2	2
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	55.9	55.0	51.7
standard deviation	± 14.1	± 23.4	± 14.7
Gender categorical Units: Subjects			
Female	8	2	10
Male	1	3	12
Race Units: Subjects			
Asian	0	1	11
Black or African American	0	0	2
White	7	4	9
Other	2	0	0
Ethnicity Units: Subjects			
Hispanic or Latino	1	0	0
Not Hispanic or Latino	8	5	19
Not Stated	0	0	1
Unknown	0	0	2

Reporting group values	Entrectinib (RXDX-101) 600 mg QD F2A	Entrectinib (RXDX-101) 600 mg EXP	Total
Number of subjects	20	7	83
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)	13	3	59
From 65-84 years	7	3	23
85 years and over	0	1	1
Age continuous			
Units: years			
arithmetic mean	55.0	69.0	
standard deviation	± 17.1	± 10.6	-
Gender categorical			
Units: Subjects			
Female	9	5	45
Male	11	2	38
Race			
Units: Subjects			
Asian	0	0	15
Black or African American	0	1	5
White	18	6	58
Other	2	0	5
Ethnicity			
Units: Subjects			
Hispanic or Latino	0	0	2
Not Hispanic or Latino	18	7	75
Not Stated	0	0	1
Unknown	2	0	5

End points

End points reporting groups

Reporting group title	Entrectinib (RXDX-101) 100 mg/m2
Reporting group description: -	
Reporting group title	Entrectinib (RXDX-101) 200 mg/m2
Reporting group description: -	
Reporting group title	Entrectinib (RXDX-101) 400 mg/m2
Reporting group description: -	
Reporting group title	Entrectinib (RXDX-101) 800 mg
Reporting group description: -	
Reporting group title	Entrectinib (RXDX-101) 600-800 mg by BSA
Reporting group description: -	
Reporting group title	Entrectinib (RXDX-101) 600 mg F1
Reporting group description: -	
Reporting group title	Entrectinib (RXDX-101) 600 mg QD F2A
Reporting group description: -	
Reporting group title	Entrectinib (RXDX-101) 600 mg EXP
Reporting group description: -	

Primary: Dose-Limiting Toxicity (DLT)

End point title	Dose-Limiting Toxicity (DLT)[1][2]
End point description:	
Determine dose-limiting toxicities of entrectinib.	
End point type	Primary
End point timeframe:	
28 days following first dose of entrectinib	

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 analysis provided

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No analysis provided

End point values	Entrectinib (RXDX-101) 100 mg/m2	Entrectinib (RXDX-101) 200 mg/m2	Entrectinib (RXDX-101) 400 mg/m2	Entrectinib (RXDX-101) 800 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	3	3	5
Units: SUbjects				
Any Dose-Limiting Toxicity	0	0	0	3
Central Nervous System	0	0	0	1
Non-Hematological Toxicity -	0	0	0	2

Statistical analyses

No statistical analyses for this end point

Primary: Overall Response Rate (ORR) - Efficacy Analysis Set, Dose Escalation

End point title	Overall Response Rate (ORR) - Efficacy Analysis Set, Dose Escalation[3][4]

End point description:

ORR defined as the proportion of subjects with a confirmed CR or PR according to RECIST v.1.1 as assessed by the Investigator relative to the total population of response-evaluable subjects. Here, results are presented as Objective Response Rate in %.

0000= NA
9999= NA

End point type	Primary

End point timeframe:

Screening, at end of cycle 1 and approx. every 8 weeks thereafter and at End of Treatment, if more than 4 weeks have passed from last tumor imaging.

Notes:

[3] - 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 analysis provided

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No analysis provided

End point values	Entrectinib (RXDX-101) 100 mg/m2	Entrectinib (RXDX-101) 200 mg/m2	Entrectinib (RXDX-101) 400 mg/m2	Entrectinib (RXDX-101) 800 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	5	10	9
Units: Percentage				
number (confidence interval 95%)	0 (0000 to 0000)	0 (0000 to 0000)	20.0 (0000 to 9999)	0 (0000 to 0000)

End point values	Entrectinib (RXDX-101) 600-800 mg by BSA	Entrectinib (RXDX-101) 600 mg F1	Entrectinib (RXDX-101) 600 mg QD F2A	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	4	20	15	
Units: Percentage				
number (confidence interval 95%)	0 (0 to 0)	30.0 (11.9 to 54.3)	33.3 (11.8 to 61.6)	

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Response Rate (ORR) - Efficacy Analysis Set, Dose Expansion

End point title	Overall Response Rate (ORR) - Efficacy Analysis Set, Dose Expansion[5]

End point description:

ORR defined as the proportion of subjects with a confirmed CR or PR according to RECIST v.1.1 as assessed by the Investigator relative to the total population of response-evaluable subjects. Here, results are presented as Objective Response Rate in %.

End point type	Secondary

End point timeframe:

Screening, at end of cycle 1 and approx. every 8 weeks thereafter and at End of Treatment, if more than 4 weeks have passed from last tumor imaging.

Notes:

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No analysis provided

End point values	Entrectinib (RXDX-101) 600 mg EXP			
Subject group type	Reporting group			
Number of subjects analysed	6			
Units: Percentage				
number (confidence interval 95%)	0 (0 to 0)			

Statistical analyses

No statistical analyses for this end point

Secondary: Disease Control - Efficacy Analysis Set

End point title	Disease Control - Efficacy Analysis Set

End point description:

Disease Control Rate (also known as Clinical Benefit Rate) defined as the proportion of subjects with a confirmed CR, PR, or SD > 6 months according to RECIST v.1.1 Here, results are presented as Clinical Benefit Rate in %.

0000= NA
9999= NA

End point type	Secondary

End point timeframe:

Screening, at end of cycle 1 and approx. every 8 weeks thereafter and at End of Treatment, if more than 4 weeks have passed from last tumor imaging.

End point values	Entrectinib (RXDX-101) 100 mg/m2	Entrectinib (RXDX-101) 200 mg/m2	Entrectinib (RXDX-101) 400 mg/m2	Entrectinib (RXDX-101) 800 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	5	10	9
Units: Subjects				
number (confidence interval 95%)	0 (0000 to 0000)	0 (00000 to 00000)	30.0 (0000 to 9999)	11.1 (0000 to 9999)

End point values	Entrectinib (RXDX-101) 600-800 mg by BSA	Entrectinib (RXDX-101) 600 mg F1	Entrectinib (RXDX-101) 600 mg QD F2A	Entrectinib (RXDX-101) 600 mg EXP
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	20	15	6
Units: Subjects				
number (confidence interval 95%)	0 (0 to 0)	35.0 (15.4 to 59.2)	33.3 (11.8 to 61.6)	16.7 (0.4 to 64.1)

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Response - Efficacy Analysis Set

End point title	Duration of Response - Efficacy Analysis Set[6]

End point description:

Duration of tumor response as defined from the first date a response is identified (either CR or PR) until the date of disease progression. Here results are presented for subjects with with an Objective Response. 9999=NA

End point type	Secondary

End point timeframe:

Screening, at end of cycle 1 and approx. every 8 weeks thereafter and at End of Treatment, if more than 4 weeks have passed from last tumor imaging.

Notes:

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No analysis provided

End point values	Entrectinib (RXDX-101) 600 mg F1	Entrectinib (RXDX-101) 600 mg QD F2A	Entrectinib (RXDX-101) 600 mg EXP	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	6	5	0[7]	
Units: Months				
median (confidence interval 95%)	19.844 (4.665 to 37.881)	11.072 (7.359 to 9999)	(to)	

Notes:

[7] - No subjects with an objective response, the duration of response was not applicable.

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival (OS) - Efficacy Analysis Set

End point title	Overall Survival (OS) - Efficacy Analysis Set[8]

End point description:

OS defined as time from first dose of entrectinib to death due to any cause. The median overall survival (OS) was not reached for the 600 mg F1 and 600 mg F2A dose groups (9999 = NA)

End point type	Secondary

End point timeframe:

First dose to death from any cause

Notes:

[8] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No analysis provided

End point values	Entrectinib (RXDX-101) 600 mg F1	Entrectinib (RXDX-101) 600 mg QD F2A	Entrectinib (RXDX-101) 600 mg EXP	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	20	15	6	
Units: Months				
median (confidence interval 95%)	9999 (8.476 to 9999)	9999 (2.267 to 9999)	9.281 (5.191 to 12.747)	

Statistical analyses

No statistical analyses for this end point

Secondary: Progression-Free Survival (PFS) - Efficacy Analysis Set

End point title	Progression-Free Survival (PFS) - Efficacy Analysis Set[9]

End point description:

PFS defined as time from first dose of entrectinib to tumor progression or death due to any cause. 9999 = NA

End point type	Secondary

End point timeframe:

First dose of entrectinib to tumor progression or death due to any cause

Notes:

[9] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No analysis provided

End point values	Entrectinib (RXDX-101) 600 mg F1	Entrectinib (RXDX-101) 600 mg QD F2A	Entrectinib (RXDX-101) 600 mg EXP	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	20	15	6	
Units: Months				
median (confidence interval 95%)	4.895 (2.694 to 19.088)	1.708 (0.756 to 9.922)	2.431 (0.723 to 9999)	

Statistical analyses

No statistical analyses for this end point

Secondary: Tmax, time of maximum plasma concentration of Entrectinib

End point title	Tmax, time of maximum plasma concentration of Entrectinib[10]

End point description:

End point type	Secondary

End point timeframe:

Cycle 1 Days 1, 14

Notes:

[10] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No analysis provided

End point values	Entrectinib (RXDX-101) 100 mg/m2	Entrectinib (RXDX-101) 200 mg/m2	Entrectinib (RXDX-101) 400 mg/m2	Entrectinib (RXDX-101) 800 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	5	7	6
Units: hours				
median (full range (min-max))				
Cycle 1 Day 1	6 (4 to 8)	6 (4 to 8)	4 (2 to 8)	4 (4 to 8)
Cycle 1 Day 14	2 (2 to 6)	6 (6 to 8)	4 (2 to 6)	6 (2 to 8)

End point values	Entrectinib (RXDX-101) 600-800 mg by BSA	Entrectinib (RXDX-101) 600 mg F1	Entrectinib (RXDX-101) 600 mg QD F2A	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	3	17	12	
Units: hours				
median (full range (min-max))				
Cycle 1 Day 1	4 (2 to 4)	4 (1 to 8)	4 (2 to 8)	
Cycle 1 Day 14	4 (4 to 4)	4 (2 to 8)	4 (2 to 6)	

Statistical analyses

No statistical analyses for this end point

Secondary: Cmax, maximum plasma concentration of Entrectinib

End point title	Cmax, maximum plasma concentration of Entrectinib[11]

End point description:

End point type	Secondary

End point timeframe:

Cycle 1: Day 1, Day 14

Notes:

[11] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No analysis provided

End point values	Entrectinib (RXDX-101) 100 mg/m2	Entrectinib (RXDX-101) 200 mg/m2	Entrectinib (RXDX-101) 400 mg/m2	Entrectinib (RXDX-101) 800 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	5	10	9
Units: nM				
geometric mean (geometric coefficient of variation)				
Cycle 1 Day 1	549 (± 37.6)	1460 (± 50.7)	2730 (± 43.3)	3780 (± 47.6)
Cycle 1 Day 2	1120 (± 41.2)	1820 (± 58.7)	4570 (± 52.3)	5320 (± 61.1)

End point values	Entrectinib (RXDX-101) 600-800 mg by BSA	Entrectinib (RXDX-101) 600 mg F1	Entrectinib (RXDX-101) 600 mg QD F2A	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	5	22	20	
Units: nM				
geometric mean (geometric coefficient of variation)				
Cycle 1 Day 1	3100 (± 4.70)	2020 (± 37.8)	2560 (± 52.3)	
Cycle 1 Day 2	3110 (± 27.0)	3140 (± 53.3)	3720 (± 52.0)	

Statistical analyses

No statistical analyses for this end point

Secondary: Tlast, time of occurrence of the last observed quantifiable concentration of Entrectinib

End point title	Tlast, time of occurrence of the last observed quantifiable concentration of Entrectinib[12]

End point description:

End point type	Secondary

End point timeframe:

Cycle 1: Day 1, Day 14

Notes:

[12] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No analysis provided

End point values	Entrectinib (RXDX-101) 100 mg/m2	Entrectinib (RXDX-101) 200 mg/m2	Entrectinib (RXDX-101) 400 mg/m2	Entrectinib (RXDX-101) 800 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	5	10	9
Units: hours				
median (full range (min-max))				
Cycle 1 Day 1	24.0 (22.4 to 25.9)	24.0 (24.0 to 24.0)	24.0 (6.00 to 25.8)	24.0 (24.0 to 26.4)

Cycle 1 Day 14	24.0 (24.0 to 24.0)	24.0 (8.0 to 24.0)	24.0 (24.0 to 24.0)	24.0 (8.0 to 24.0)

End point values	Entrectinib (RXDX-101) 600-800 mg by BSA	Entrectinib (RXDX-101) 600 mg F1	Entrectinib (RXDX-101) 600 mg QD F2A	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	5	22	20	
Units: hours				
median (full range (min-max))				
Cycle 1 Day 1	24.0 (8.0 to 24.0)	24.0 (8.0 to 24.0)	24.0 (6.0 to 24.0)	
Cycle 1 Day 14	24.0 (24.0 to 24.0)	24.0 (8.0 to 24.0)	24.0 (8.0 to 24.0)	

Statistical analyses

No statistical analyses for this end point

Secondary: Clast, last measurable concentration of Entrectinib

End point title	Clast, last measurable concentration of Entrectinib[13]

End point description:

End point type	Secondary

End point timeframe:

Cycle 1: Day 1, Day 14

Notes:

[13] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No analysis provided

End point values	Entrectinib (RXDX-101) 100 mg/m2	Entrectinib (RXDX-101) 200 mg/m2	Entrectinib (RXDX-101) 400 mg/m2	Entrectinib (RXDX-101) 800 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	5	10	9
Units: nM				
geometric mean (geometric coefficient of variation)				
Cycle 1 Day 1	204 (± 41.3)	510 (± 39.4)	1190 (± 61.8)	1420 (± 56.0)
Cycle 1 Day 14	567 (± 55.4)	936 (± 78.9)	2340 (± 54.3)	3350 (± 73.1)

End point values	Entrectinib (RXDX-101) 600-800 mg by BSA	Entrectinib (RXDX-101) 600 mg F1	Entrectinib (RXDX-101) 600 mg QD F2A	

Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	5	22	20	
Units: nM				
geometric mean (geometric coefficient of variation)				
Cycle 1 Day 1	1370 (± 43.1)	712 (± 58.1)	885 (± 42.1)	
Cycle 1 Day 14	1410 (± 26.1)	1750 (± 75.7)	2120 (± 62.5)	

Statistical analyses

No statistical analyses for this end point

Secondary: AUC0-6, area under the plasma concentration-time curve from time 0 to 6 hours postdose of Entrectinib

End point title	AUC0-6, area under the plasma concentration-time curve from time 0 to 6 hours postdose of Entrectinib[14]

End point description:

End point type	Secondary

End point timeframe:

Cycle 1: Day 1, Day 14

Notes:

[14] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No analysis provided

End point values	Entrectinib (RXDX-101) 100 mg/m2	Entrectinib (RXDX-101) 200 mg/m2	Entrectinib (RXDX-101) 400 mg/m2	Entrectinib (RXDX-101) 800 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	5	10	9
Units: nM·h				
geometric mean (geometric coefficient of variation)				
Cycle 1 Day 1	1520 (± 50.1)	5320 (± 79.4)	10300 (± 32.9)	14200 (± 51.4)
Cycle 1 Day 14	5490 (± 46.0)	8400 (± 69.6)	22700 (± 54.6)	24500 (± 77.3)

End point values	Entrectinib (RXDX-101) 600-800 mg by BSA	Entrectinib (RXDX-101) 600 mg F1	Entrectinib (RXDX-101) 600 mg QD F2A	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	5	22	20	
Units: nM·h				
geometric mean (geometric coefficient of variation)				
Cycle 1 Day 1	12600 (± 8.02)	7860 (± 44.7)	10600 (± 64.0)	
Cycle 1 Day 14	13200 (± 17.9)	14800 (± 57.0)	18300 (± 52.3)	

Statistical analyses

No statistical analyses for this end point

Secondary: AUC0-24, area under the plasma concentration-time curve from time 0 to 24 hours postdose of Entrectinib

End point title	AUC0-24, area under the plasma concentration-time curve from time 0 to 24 hours postdose of Entrectinib[15]

End point description:

End point type	Secondary

End point timeframe:

Cycle 1: Day 1, Day 14

Notes:

[15] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No analysis provided

End point values	Entrectinib (RXDX-101) 100 mg/m2	Entrectinib (RXDX-101) 200 mg/m2	Entrectinib (RXDX-101) 400 mg/m2	Entrectinib (RXDX-101) 800 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	5	8	9
Units: nM·h				
geometric mean (geometric coefficient of variation)				
Cycle 1 Day 1	7480 (± 30.4)	21000 (± 40.6)	43000 (± 52.3)	54900 (± 52.3)
Cycle 1 Day 14	18900 (± 48.6)	28300 (± 72.0)	78900 (± 54.3)	93200 (± 75.3)

End point values	Entrectinib (RXDX-101) 600-800 mg by BSA	Entrectinib (RXDX-101) 600 mg F1	Entrectinib (RXDX-101) 600 mg QD F2A	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	5	19	16	
Units: nM·h				
geometric mean (geometric coefficient of variation)				
Cycle 1 Day 1	41600 (± 17.8)	24800 (± 43.8)	34900 (± 44.0)	
Cycle 1 Day 14	51200 (± 24.9)	51500 (± 60.7)	55500 (± 43.3)	

Statistical analyses

No statistical analyses for this end point

Secondary: AUClast, area under the plasma concentration-time curve from time 0 to the last measurable concentration postdos of Entrectinib

End point title	AUClast, area under the plasma concentration-time curve from time 0 to the last measurable concentration postdos of Entrectinib[16]

End point description:

End point type	Secondary

End point timeframe:

Cycle 1: Day 1, Day 14

Notes:

[16] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No analysis provided

End point values	Entrectinib (RXDX-101) 100 mg/m2	Entrectinib (RXDX-101) 200 mg/m2	Entrectinib (RXDX-101) 400 mg/m2	Entrectinib (RXDX-101) 800 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	5	10	9
Units: nM·h				
geometric mean (geometric coefficient of variation)				
Cycle 1 Day 1	7530 (± 30.2)	21000 (± 40.6)	37000 (± 63.7)	55800 (± 52.3)
Cycle 1 Day 14	18900 (± 48.5)	25400 (± 74.1)	78900 (± 54.3)	82300 (± 83.8)

End point values	Entrectinib (RXDX-101) 600-800 mg by BSA	Entrectinib (RXDX-101) 600 mg F1	Entrectinib (RXDX-101) 600 mg QD F2A	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	5	22	20	
Units: nM·h				
geometric mean (geometric coefficient of variation)				
Cycle 1 Day 1	37300 (± 33.8)	22600 (± 50.4)	34900 (± 44.0)	
Cycle 1 Day 14	51200 (± 24.9)	47300 (± 67.2)	49500 (± 49.5)	

Statistical analyses

No statistical analyses for this end point

Secondary: C24h, Entrectinib concentration in the plasma measured at 24h postdose

End point title	C24h, Entrectinib concentration in the plasma measured at 24h postdose[17]

End point description:

End point type	Secondary

End point timeframe:

Cycle 1: Day 1, Day 14

Notes:

[17] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: No analysis provided

End point values	Entrectinib (RXDX-101) 100 mg/m2	Entrectinib (RXDX-101) 200 mg/m2	Entrectinib (RXDX-101) 400 mg/m2	Entrectinib (RXDX-101) 800 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	5	7	8
Units: nM				
geometric mean (geometric coefficient of variation)				
Cycle 1 Day 1	229 (± 43.1)	510 (± 39.4)	1140 (± 64.3)	1240 (± 50.5)
Cycle 1 Day 14	567 (± 55.4)	695 (± 83.8)	2340 (± 54.3)	3020 (± 85.6)

End point values	Entrectinib (RXDX-101) 600-800 mg by BSA	Entrectinib (RXDX-101) 600 mg F1	Entrectinib (RXDX-101) 600 mg QD F2A	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	4	17	16	
Units: nM				
geometric mean (geometric coefficient of variation)				
Cycle 1 Day 1	1160 (± 35.7)	578 (± 43.8)	805 (± 38.2)	
Cycle 1 Day 14	1410 (± 26.1)	1650 (± 68.6)	1650 (± 50.4)	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
From Cycle Day 1 to 30 days after last dose (approximately 6 years)	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	23.0

Reporting groups	
Reporting group title	RXDX-101 200 mg/m2
Reporting group description:	
Subjects receive entrectinib administered orally for 28 consecutive days in repeated 4-week cycles at the at a dose of 200 mg/m2.	
Reporting group title	RXDX-101 100 mg/m2
Reporting group description:	
Subjects receive entrectinib administered orally for 28 consecutive days in repeated 4-week cycles at the at a dose of 100 mg/m2.	
Reporting group title	RXDX-101 400 mg/m2
Reporting group description:	
Subjects receive entrectinib administered orally for 28 consecutive days in repeated 4-week cycles at the at a dose of 400 mg/m2	
Reporting group title	RXDX-101 600 mg/day
Reporting group description:	
Subjects receive entrectinib administered orally for 28 consecutive days in repeated 4-week cycles at the at a dose of 600 mg/m2.	
Reporting group title	RXDX-101 600 mg/day (EXP)
Reporting group description:	
Subjects receive entrectinib administered orally for 28 consecutive days in repeated 4-week cycles at the at a dose of 600 mg/m2.	
Reporting group title	RXDX-101 600 mg/day (F2)
Reporting group description:	
Subjects receive entrectinib administered orally for 28 consecutive days in repeated 4-week cycles at the at a dose of 600 mg/m2.	
Reporting group title	RXDX-101 800 mg/day
Reporting group description:	
Subjects receive entrectinib administered orally for 28 consecutive days in repeated 4-week cycles at the at a dose of 800 mg/m2.	
Reporting group title	RXDX-101 by BSA 600 mg/day or 800 mg/day
Reporting group description:	
Subjects receive entrectinib administered orally for 28 consecutive days in repeated 4-week cycles at the at a dose of 600-800 mg/m2.	

Serious adverse events	RXDX-101 200 mg/m2	RXDX-101 100 mg/m2	RXDX-101 400 mg/m2
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	4 / 10 (40.00%)
number of deaths (all causes)	0	2	4
number of deaths resulting from adverse events	0	0	0

Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Metastases to meninges			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 10 (10.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Vascular disorders			
Hypotension			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (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
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (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 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (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
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 10 (10.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Pleural effusion			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (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
Pulmonary embolism			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 10 (10.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory failure			

subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 10 (10.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Psychiatric disorders			
Confusional state			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (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
Mental disorder			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (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
Mental status changes			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 10 (10.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (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
Humerus fracture			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (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
Meniscus injury			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (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
Post procedural inflammation			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (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

Stress fracture			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (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
Wound dehiscence			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (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			
Atrial flutter			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (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
Myocarditis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (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
Nervous system disorders			
Ataxia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (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
Cauda equina syndrome			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (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
Cognitive disorder			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (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
Cranial nerve palsies multiple			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (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

Hydrocephalus			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 10 (10.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (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
Blood and lymphatic system disorders			
Febrile neutropenia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (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
Eye disorders			
Vision blurred			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (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
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (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
Abdominal pain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (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
Ascites			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (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
Dysphagia			

subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (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
Large intestine perforation			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (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
Small intestinal obstruction			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (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
Vomiting			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (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
Endocrine disorders			
Steroid withdrawal syndrome			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 10 (10.00%)
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	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (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
Osteonecrosis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (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
Pathological fracture			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (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			
Abdominal abscess			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (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
Localised infection			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 10 (10.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Parasitic gastroenteritis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 10 (10.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 10 (10.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (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
Shunt infection			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (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
Metabolism and nutrition disorders			
Hyponatraemia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (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
Tumour lysis syndrome			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (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

Serious adverse events	RXDX-101 600 mg/day	RXDX-101 600 mg/day (EXP)	RXDX-101 600 mg/day (F2)
Total subjects affected by serious adverse events			
subjects affected / exposed	7 / 22 (31.82%)	3 / 7 (42.86%)	13 / 20 (65.00%)
number of deaths (all causes)	4	3	5
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Metastases to meninges			
subjects affected / exposed	1 / 22 (4.55%)	0 / 7 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Vascular disorders			
Hypotension			
subjects affected / exposed	0 / 22 (0.00%)	0 / 7 (0.00%)	0 / 20 (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
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	0 / 22 (0.00%)	0 / 7 (0.00%)	1 / 20 (5.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			
subjects affected / exposed	0 / 22 (0.00%)	0 / 7 (0.00%)	0 / 20 (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
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	0 / 22 (0.00%)	0 / 7 (0.00%)	0 / 20 (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
Pleural effusion			
subjects affected / exposed	1 / 22 (4.55%)	0 / 7 (0.00%)	0 / 20 (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
Pulmonary embolism			

subjects affected / exposed	0 / 22 (0.00%)	0 / 7 (0.00%)	0 / 20 (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
Respiratory failure			
subjects affected / exposed	0 / 22 (0.00%)	0 / 7 (0.00%)	0 / 20 (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 / 22 (0.00%)	0 / 7 (0.00%)	1 / 20 (5.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mental disorder			
subjects affected / exposed	0 / 22 (0.00%)	0 / 7 (0.00%)	1 / 20 (5.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mental status changes			
subjects affected / exposed	1 / 22 (4.55%)	0 / 7 (0.00%)	1 / 20 (5.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 22 (0.00%)	0 / 7 (0.00%)	0 / 20 (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
Humerus fracture			
subjects affected / exposed	0 / 22 (0.00%)	1 / 7 (14.29%)	0 / 20 (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
Meniscus injury			
subjects affected / exposed	0 / 22 (0.00%)	0 / 7 (0.00%)	1 / 20 (5.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Post procedural inflammation			
subjects affected / exposed	1 / 22 (4.55%)	0 / 7 (0.00%)	0 / 20 (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
Stress fracture			
subjects affected / exposed	0 / 22 (0.00%)	0 / 7 (0.00%)	0 / 20 (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
Wound dehiscence			
subjects affected / exposed	0 / 22 (0.00%)	0 / 7 (0.00%)	1 / 20 (5.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Atrial flutter			
subjects affected / exposed	0 / 22 (0.00%)	0 / 7 (0.00%)	1 / 20 (5.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocarditis			
subjects affected / exposed	0 / 22 (0.00%)	0 / 7 (0.00%)	0 / 20 (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
Nervous system disorders			
Ataxia			
subjects affected / exposed	0 / 22 (0.00%)	0 / 7 (0.00%)	1 / 20 (5.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cauda equina syndrome			
subjects affected / exposed	0 / 22 (0.00%)	0 / 7 (0.00%)	1 / 20 (5.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cognitive disorder			
subjects affected / exposed	1 / 22 (4.55%)	0 / 7 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Cranial nerve palsies multiple			
subjects affected / exposed	0 / 22 (0.00%)	1 / 7 (14.29%)	0 / 20 (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
Hydrocephalus			
subjects affected / exposed	1 / 22 (4.55%)	0 / 7 (0.00%)	0 / 20 (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
Syncope			
subjects affected / exposed	0 / 22 (0.00%)	0 / 7 (0.00%)	1 / 20 (5.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Febrile neutropenia			
subjects affected / exposed	0 / 22 (0.00%)	0 / 7 (0.00%)	1 / 20 (5.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Vision blurred			
subjects affected / exposed	1 / 22 (4.55%)	0 / 7 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	0 / 22 (0.00%)	0 / 7 (0.00%)	0 / 20 (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
Abdominal pain			
subjects affected / exposed	0 / 22 (0.00%)	0 / 7 (0.00%)	0 / 20 (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
Ascites			

subjects affected / exposed	0 / 22 (0.00%)	1 / 7 (14.29%)	0 / 20 (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
Dysphagia			
subjects affected / exposed	1 / 22 (4.55%)	0 / 7 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Large intestine perforation			
subjects affected / exposed	0 / 22 (0.00%)	0 / 7 (0.00%)	1 / 20 (5.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Small intestinal obstruction			
subjects affected / exposed	0 / 22 (0.00%)	1 / 7 (14.29%)	0 / 20 (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
Vomiting			
subjects affected / exposed	0 / 22 (0.00%)	0 / 7 (0.00%)	0 / 20 (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
Endocrine disorders			
Steroid withdrawal syndrome			
subjects affected / exposed	0 / 22 (0.00%)	0 / 7 (0.00%)	0 / 20 (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
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 22 (4.55%)	0 / 7 (0.00%)	1 / 20 (5.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteonecrosis			
subjects affected / exposed	1 / 22 (4.55%)	0 / 7 (0.00%)	1 / 20 (5.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Pathological fracture			
subjects affected / exposed	0 / 22 (0.00%)	0 / 7 (0.00%)	1 / 20 (5.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Abdominal abscess			
subjects affected / exposed	0 / 22 (0.00%)	0 / 7 (0.00%)	1 / 20 (5.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Localised infection			
subjects affected / exposed	0 / 22 (0.00%)	0 / 7 (0.00%)	0 / 20 (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
Parasitic gastroenteritis			
subjects affected / exposed	0 / 22 (0.00%)	0 / 7 (0.00%)	0 / 20 (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 / 22 (0.00%)	1 / 7 (14.29%)	1 / 20 (5.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	0 / 22 (0.00%)	0 / 7 (0.00%)	1 / 20 (5.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Shunt infection			
subjects affected / exposed	1 / 22 (4.55%)	0 / 7 (0.00%)	0 / 20 (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
Metabolism and nutrition disorders			
Hyponatraemia			
subjects affected / exposed	1 / 22 (4.55%)	0 / 7 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Tumour lysis syndrome			
subjects affected / exposed	0 / 22 (0.00%)	0 / 7 (0.00%)	1 / 20 (5.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1

Serious adverse events	RXDX-101 800 mg/day	RXDX-101 by BSA 600 mg/day or 800 mg/day	
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 9 (44.44%)	3 / 5 (60.00%)	
number of deaths (all causes)	1	1	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Metastases to meninges			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Hypotension			
subjects affected / exposed	1 / 9 (11.11%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	0 / 9 (0.00%)	1 / 5 (20.00%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			
subjects affected / exposed	1 / 9 (11.11%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Pleural effusion			
subjects affected / exposed	1 / 9 (11.11%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory failure			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Confusional state			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mental disorder			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mental status changes			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 9 (0.00%)	1 / 5 (20.00%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Humerus fracture			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Meniscus injury			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural inflammation			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Stress fracture			
subjects affected / exposed	1 / 9 (11.11%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound dehiscence			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Atrial flutter			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocarditis			
subjects affected / exposed	0 / 9 (0.00%)	1 / 5 (20.00%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Ataxia			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cauda equina syndrome			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Cognitive disorder			
subjects affected / exposed	0 / 9 (0.00%)	1 / 5 (20.00%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cranial nerve palsies multiple			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hydrocephalus			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Febrile neutropenia			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Vision blurred			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	1 / 9 (11.11%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain			

subjects affected / exposed	1 / 9 (11.11%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ascites			
subjects affected / exposed	1 / 9 (11.11%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dysphagia			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Large intestine perforation			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small intestinal obstruction			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	1 / 9 (11.11%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocrine disorders			
Steroid withdrawal syndrome			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Osteonecrosis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pathological fracture			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Abdominal abscess			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Localised infection			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Parasitic gastroenteritis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Shunt infection			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			

Hyponatraemia			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tumour lysis syndrome			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	RXDX-101 200 mg/m2	RXDX-101 100 mg/m2	RXDX-101 400 mg/m2
Total subjects affected by non-serious adverse events			
subjects affected / exposed	5 / 5 (100.00%)	4 / 5 (80.00%)	10 / 10 (100.00%)
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Hypertension			
subjects affected / exposed	0 / 5 (0.00%)	1 / 5 (20.00%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Hypotension			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Orthostatic hypotension			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Phlebitis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Thrombophlebitis superficial			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
General disorders and administration site conditions			

Balance disturbances			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Asthenia			
subjects affected / exposed	1 / 5 (20.00%)	0 / 5 (0.00%)	2 / 10 (20.00%)
occurrences (all)	1	0	2
Chest discomfort			
subjects affected / exposed	1 / 5 (20.00%)	0 / 5 (0.00%)	1 / 10 (10.00%)
occurrences (all)	1	0	1
Chest pain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Chills			
subjects affected / exposed	1 / 5 (20.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	2	0	0
Face oedema			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Facial pain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Fatigue			
subjects affected / exposed	3 / 5 (60.00%)	2 / 5 (40.00%)	8 / 10 (80.00%)
occurrences (all)	3	3	18
Gait disturbance			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	2
Generalised oedema			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Malaise			
subjects affected / exposed	1 / 5 (20.00%)	0 / 5 (0.00%)	1 / 10 (10.00%)
occurrences (all)	1	0	1
Mucosal inflammation			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0

Oedema			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Oedema peripheral			
subjects affected / exposed	1 / 5 (20.00%)	1 / 5 (20.00%)	3 / 10 (30.00%)
occurrences (all)	1	1	3
Pain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Peripheral swelling			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Pyrexia			
subjects affected / exposed	1 / 5 (20.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Suprapubic pain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Temperature intolerance			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Unevaluable event			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Reproductive system and breast disorders			
Breast pain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Pelvic pain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	2 / 5 (40.00%)	0 / 5 (0.00%)	3 / 10 (30.00%)
occurrences (all)	2	0	3
Dysphonia			

subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Dyspnoea			
subjects affected / exposed	2 / 5 (40.00%)	0 / 5 (0.00%)	2 / 10 (20.00%)
occurrences (all)	3	0	3
Dyspnoea exertional			
subjects affected / exposed	0 / 5 (0.00%)	1 / 5 (20.00%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Epistaxis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Hypoxia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Nasal congestion			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Oropharyngeal pain			
subjects affected / exposed	1 / 5 (20.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Pleural effusion			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Productive cough			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Pulmonary embolism			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	2 / 10 (20.00%)
occurrences (all)	0	0	2
Rhinitis allergic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Rhinorrhoea			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Sinus congestion			

subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Sleep apnoea syndrome			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Throat irritation			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Wheezing			
subjects affected / exposed	1 / 5 (20.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Confusional state			
subjects affected / exposed	0 / 5 (0.00%)	1 / 5 (20.00%)	1 / 10 (10.00%)
occurrences (all)	0	1	1
Disorientation			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Insomnia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Libido decreased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Mood swings			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Sleep disorder			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Investigations			
Alanine aminotransferase increased			

subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Amylase increased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	2 / 10 (20.00%)
occurrences (all)	0	0	4
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Blood bilirubin increased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	2 / 10 (20.00%)
occurrences (all)	0	0	4
Blood creatinine increased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	2 / 10 (20.00%)
occurrences (all)	0	0	2
Blood uric acid increased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Electrocardiogram QT prolonged			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Electrocardiogram T wave abnormal			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Electrocardiogram abnormal			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
International normalised ratio increased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Lipase increased			

subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Neutrophil count decreased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Protein total decreased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Weight increased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	2 / 10 (20.00%)
occurrences (all)	0	0	2
White blood cell count decreased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
White blood cell count increased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Ankle fracture			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Contusion			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Fall			
subjects affected / exposed	1 / 5 (20.00%)	0 / 5 (0.00%)	1 / 10 (10.00%)
occurrences (all)	1	0	1
Humerus fracture			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Ligament sprain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Limb injury			

subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Meniscus injury			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Muscle rupture			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Radiation necrosis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Skin abrasion			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Stress fracture			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Tendon rupture			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Wound dehiscence			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Bradycardia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Tachycardia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Amnesia			

subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Aphasia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Asterixis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Ataxia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Autonomic nervous system imbalance			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Balance disorder			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Cognitive disorder			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Disturbance in attention			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	2 / 10 (20.00%)
occurrences (all)	0	0	2
Dizziness			
subjects affected / exposed	2 / 5 (40.00%)	0 / 5 (0.00%)	6 / 10 (60.00%)
occurrences (all)	3	0	8
Dizziness exertional			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Dysarthria			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Dysgeusia			
subjects affected / exposed	2 / 5 (40.00%)	0 / 5 (0.00%)	6 / 10 (60.00%)
occurrences (all)	3	0	6

Headache			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	3 / 10 (30.00%)
occurrences (all)	0	0	4
Hyperaesthesia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Hypoaesthesia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Memory impairment			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Neuropathy peripheral			
subjects affected / exposed	2 / 5 (40.00%)	0 / 5 (0.00%)	1 / 10 (10.00%)
occurrences (all)	2	0	1
Paraesthesia			
subjects affected / exposed	0 / 5 (0.00%)	1 / 5 (20.00%)	5 / 10 (50.00%)
occurrences (all)	0	1	6
Peripheral motor neuropathy			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Peripheral sensory neuropathy			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Psychomotor skills impaired			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Seizure			
subjects affected / exposed	0 / 5 (0.00%)	1 / 5 (20.00%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Somnolence			
subjects affected / exposed	0 / 5 (0.00%)	1 / 5 (20.00%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Taste disorder			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1

Tremor			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Vibratory sense increased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	2 / 5 (40.00%)	0 / 5 (0.00%)	3 / 10 (30.00%)
occurrences (all)	2	0	3
Lymphadenopathy			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Neutropenia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Thrombocytopenia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
External ear inflammation			
subjects affected / exposed	0 / 5 (0.00%)	1 / 5 (20.00%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Hypoacusis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Vertigo			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Asthenopia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Conjunctivitis allergic			

subjects affected / exposed	0 / 5 (0.00%)	1 / 5 (20.00%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Diplopia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Dry eye			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Eye pain			
subjects affected / exposed	0 / 5 (0.00%)	1 / 5 (20.00%)	1 / 10 (10.00%)
occurrences (all)	0	1	1
Eye swelling			
subjects affected / exposed	0 / 5 (0.00%)	1 / 5 (20.00%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Ocular discomfort			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Swelling of eyelid			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Vision blurred			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	3 / 10 (30.00%)
occurrences (all)	0	0	7
Visual impairment			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Vitreous floaters			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	1 / 5 (20.00%)	1 / 5 (20.00%)	0 / 10 (0.00%)
occurrences (all)	1	1	0
Abdominal pain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	2 / 10 (20.00%)
occurrences (all)	0	0	2

Abdominal pain upper			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	2
Abdominal tenderness			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Ascites			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Constipation			
subjects affected / exposed	2 / 5 (40.00%)	2 / 5 (40.00%)	2 / 10 (20.00%)
occurrences (all)	2	2	2
Diarrhoea			
subjects affected / exposed	1 / 5 (20.00%)	0 / 5 (0.00%)	2 / 10 (20.00%)
occurrences (all)	1	0	7
Dry mouth			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Dyspepsia			
subjects affected / exposed	1 / 5 (20.00%)	1 / 5 (20.00%)	0 / 10 (0.00%)
occurrences (all)	1	1	0
Dysphagia			
subjects affected / exposed	1 / 5 (20.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Flatulence			
subjects affected / exposed	1 / 5 (20.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Gingival pain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Haematochezia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0

Hypoaesthesia oral			
subjects affected / exposed	1 / 5 (20.00%)	0 / 5 (0.00%)	1 / 10 (10.00%)
occurrences (all)	1	0	1
Ileus			
subjects affected / exposed	1 / 5 (20.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Lip dry			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	3 / 5 (60.00%)	1 / 5 (20.00%)	5 / 10 (50.00%)
occurrences (all)	4	1	6
Odynophagia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Oesophageal pain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Oral pain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Paraesthesia oral			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Stomatitis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Tooth development disorder			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Vomiting			
subjects affected / exposed	2 / 5 (40.00%)	0 / 5 (0.00%)	1 / 10 (10.00%)
occurrences (all)	2	0	1
Hepatobiliary disorders			
Hepatic function abnormal			

subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Hyperbilirubinaemia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Dermatitis acneiform			
subjects affected / exposed	1 / 5 (20.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Dermatitis allergic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Dry skin			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Erythema			
subjects affected / exposed	1 / 5 (20.00%)	0 / 5 (0.00%)	1 / 10 (10.00%)
occurrences (all)	1	0	1
Hypertrichosis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Night sweats			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Pain of skin			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Panniculitis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Photosensitivity reaction			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0

Pruritus			
subjects affected / exposed	1 / 5 (20.00%)	0 / 5 (0.00%)	1 / 10 (10.00%)
occurrences (all)	1	0	1
Rash maculo-papular			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Rash pruritic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Sensitive skin			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Skin lesion			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Calcified, non-functioning right kidney			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Acute kidney injury			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Bladder spasm			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Haematuria			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Micturition urgency			
subjects affected / exposed	1 / 5 (20.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Nocturia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Pollakiuria			

subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Polyuria			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Proteinuria			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Renal failure			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Urinary hesitation			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Urinary tract pain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 5 (20.00%)	0 / 5 (0.00%)	2 / 10 (20.00%)
occurrences (all)	1	0	3
Back pain			
subjects affected / exposed	2 / 5 (40.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	2	0	0
Bursitis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Flank pain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Intervertebral disc protrusion			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Joint stiffness			

subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Joint swelling			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	2 / 10 (20.00%)
occurrences (all)	0	0	2
Muscle fatigue			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Muscle spasms			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Muscular weakness			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	4 / 10 (40.00%)
occurrences (all)	0	0	4
Musculoskeletal chest pain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Musculoskeletal pain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Myalgia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	4 / 10 (40.00%)
occurrences (all)	0	0	4
Neck pain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Osteonecrosis of jaw			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Pain in extremity			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	2 / 10 (20.00%)
occurrences (all)	0	0	3
Pain in jaw			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Rotator cuff syndrome			

subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Abdominal abscess			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Bronchitis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Cellulitis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Ear infection			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Escherichia infection			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Laryngitis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Localised infection			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Medical device site infection			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Oesophageal candidiasis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Oral candidiasis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1

Pneumonia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Rash pustular			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Respiratory tract infection			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Respiratory tract infection viral			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Sinusitis bacterial			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Skin infection			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Upper respiratory tract infection			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Urinary tract infection			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	1 / 5 (20.00%)	1 / 5 (20.00%)	3 / 10 (30.00%)
occurrences (all)	1	1	3
Dehydration			
subjects affected / exposed	1 / 5 (20.00%)	1 / 5 (20.00%)	1 / 10 (10.00%)
occurrences (all)	1	1	1
Hypercalcaemia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Hyperglycaemia			

subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Hyperkalaemia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	2 / 10 (20.00%)
occurrences (all)	0	0	2
Hypernatraemia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Hyperuricaemia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Hypoalbuminaemia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Hypocalcaemia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Hypokalaemia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Hypomagnesaemia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Hyponatraemia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	2 / 10 (20.00%)
occurrences (all)	0	0	2
Hypophosphataemia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	3 / 10 (30.00%)
occurrences (all)	0	0	5
Hypovolaemia			
subjects affected / exposed	0 / 5 (0.00%)	1 / 5 (20.00%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Increased appetite			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1

Non-serious adverse events	RXDX-101 600 mg/day	RXDX-101 600 mg/day (EXP)	RXDX-101 600 mg/day (F2)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	22 / 22 (100.00%)	7 / 7 (100.00%)	20 / 20 (100.00%)
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	0 / 22 (0.00%)	0 / 7 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Hypertension			
subjects affected / exposed	0 / 22 (0.00%)	0 / 7 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Hypotension			
subjects affected / exposed	2 / 22 (9.09%)	0 / 7 (0.00%)	5 / 20 (25.00%)
occurrences (all)	3	0	7
Orthostatic hypotension			
subjects affected / exposed	1 / 22 (4.55%)	0 / 7 (0.00%)	1 / 20 (5.00%)
occurrences (all)	1	0	1
Phlebitis			
subjects affected / exposed	0 / 22 (0.00%)	0 / 7 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Thrombophlebitis superficial			
subjects affected / exposed	0 / 22 (0.00%)	0 / 7 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Balance disturbances			
subjects affected / exposed	0 / 22 (0.00%)	0 / 7 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Asthenia			
subjects affected / exposed	2 / 22 (9.09%)	1 / 7 (14.29%)	1 / 20 (5.00%)
occurrences (all)	3	1	1
Chest discomfort			
subjects affected / exposed	0 / 22 (0.00%)	0 / 7 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Chest pain			
subjects affected / exposed	0 / 22 (0.00%)	0 / 7 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Chills			

subjects affected / exposed	0 / 22 (0.00%)	2 / 7 (28.57%)	3 / 20 (15.00%)
occurrences (all)	0	2	4
Face oedema			
subjects affected / exposed	2 / 22 (9.09%)	0 / 7 (0.00%)	0 / 20 (0.00%)
occurrences (all)	3	0	0
Facial pain			
subjects affected / exposed	0 / 22 (0.00%)	0 / 7 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Fatigue			
subjects affected / exposed	14 / 22 (63.64%)	4 / 7 (57.14%)	10 / 20 (50.00%)
occurrences (all)	18	7	20
Gait disturbance			
subjects affected / exposed	1 / 22 (4.55%)	1 / 7 (14.29%)	3 / 20 (15.00%)
occurrences (all)	1	3	6
Generalised oedema			
subjects affected / exposed	2 / 22 (9.09%)	0 / 7 (0.00%)	2 / 20 (10.00%)
occurrences (all)	6	0	3
Malaise			
subjects affected / exposed	0 / 22 (0.00%)	0 / 7 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Mucosal inflammation			
subjects affected / exposed	0 / 22 (0.00%)	0 / 7 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Oedema			
subjects affected / exposed	1 / 22 (4.55%)	0 / 7 (0.00%)	1 / 20 (5.00%)
occurrences (all)	2	0	1
Oedema peripheral			
subjects affected / exposed	6 / 22 (27.27%)	1 / 7 (14.29%)	6 / 20 (30.00%)
occurrences (all)	6	2	8
Pain			
subjects affected / exposed	1 / 22 (4.55%)	0 / 7 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Peripheral swelling			
subjects affected / exposed	0 / 22 (0.00%)	0 / 7 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Pyrexia			

subjects affected / exposed	2 / 22 (9.09%)	0 / 7 (0.00%)	5 / 20 (25.00%)
occurrences (all)	2	0	6
Suprapubic pain			
subjects affected / exposed	0 / 22 (0.00%)	0 / 7 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Temperature intolerance			
subjects affected / exposed	0 / 22 (0.00%)	1 / 7 (14.29%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Unevaluable event			
subjects affected / exposed	0 / 22 (0.00%)	0 / 7 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Reproductive system and breast disorders			
Breast pain			
subjects affected / exposed	0 / 22 (0.00%)	0 / 7 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Pelvic pain			
subjects affected / exposed	1 / 22 (4.55%)	0 / 7 (0.00%)	1 / 20 (5.00%)
occurrences (all)	1	0	1
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	4 / 22 (18.18%)	0 / 7 (0.00%)	5 / 20 (25.00%)
occurrences (all)	5	0	6
Dysphonia			
subjects affected / exposed	1 / 22 (4.55%)	0 / 7 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Dyspnoea			
subjects affected / exposed	7 / 22 (31.82%)	0 / 7 (0.00%)	5 / 20 (25.00%)
occurrences (all)	8	0	9
Dyspnoea exertional			
subjects affected / exposed	1 / 22 (4.55%)	1 / 7 (14.29%)	1 / 20 (5.00%)
occurrences (all)	1	1	2
Epistaxis			
subjects affected / exposed	0 / 22 (0.00%)	0 / 7 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Hypoxia			

subjects affected / exposed	1 / 22 (4.55%)	0 / 7 (0.00%)	2 / 20 (10.00%)
occurrences (all)	1	0	3
Nasal congestion			
subjects affected / exposed	1 / 22 (4.55%)	0 / 7 (0.00%)	4 / 20 (20.00%)
occurrences (all)	1	0	5
Oropharyngeal pain			
subjects affected / exposed	1 / 22 (4.55%)	0 / 7 (0.00%)	1 / 20 (5.00%)
occurrences (all)	1	0	1
Pleural effusion			
subjects affected / exposed	0 / 22 (0.00%)	0 / 7 (0.00%)	2 / 20 (10.00%)
occurrences (all)	0	0	2
Productive cough			
subjects affected / exposed	2 / 22 (9.09%)	0 / 7 (0.00%)	1 / 20 (5.00%)
occurrences (all)	2	0	2
Pulmonary embolism			
subjects affected / exposed	1 / 22 (4.55%)	0 / 7 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Rhinitis allergic			
subjects affected / exposed	0 / 22 (0.00%)	0 / 7 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Rhinorrhoea			
subjects affected / exposed	0 / 22 (0.00%)	0 / 7 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Sinus congestion			
subjects affected / exposed	0 / 22 (0.00%)	0 / 7 (0.00%)	2 / 20 (10.00%)
occurrences (all)	0	0	2
Sleep apnoea syndrome			
subjects affected / exposed	0 / 22 (0.00%)	0 / 7 (0.00%)	2 / 20 (10.00%)
occurrences (all)	0	0	2
Throat irritation			
subjects affected / exposed	0 / 22 (0.00%)	1 / 7 (14.29%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Wheezing			
subjects affected / exposed	0 / 22 (0.00%)	0 / 7 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Psychiatric disorders			

Anxiety			
subjects affected / exposed	1 / 22 (4.55%)	0 / 7 (0.00%)	1 / 20 (5.00%)
occurrences (all)	1	0	1
Confusional state			
subjects affected / exposed	1 / 22 (4.55%)	2 / 7 (28.57%)	3 / 20 (15.00%)
occurrences (all)	1	2	7
Disorientation			
subjects affected / exposed	0 / 22 (0.00%)	1 / 7 (14.29%)	0 / 20 (0.00%)
occurrences (all)	0	2	0
Insomnia			
subjects affected / exposed	1 / 22 (4.55%)	1 / 7 (14.29%)	0 / 20 (0.00%)
occurrences (all)	1	1	0
Libido decreased			
subjects affected / exposed	0 / 22 (0.00%)	0 / 7 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Mood swings			
subjects affected / exposed	0 / 22 (0.00%)	0 / 7 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Sleep disorder			
subjects affected / exposed	0 / 22 (0.00%)	0 / 7 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	3 / 22 (13.64%)	0 / 7 (0.00%)	1 / 20 (5.00%)
occurrences (all)	3	0	1
Amylase increased			
subjects affected / exposed	1 / 22 (4.55%)	0 / 7 (0.00%)	1 / 20 (5.00%)
occurrences (all)	1	0	1
Aspartate aminotransferase increased			
subjects affected / exposed	3 / 22 (13.64%)	0 / 7 (0.00%)	2 / 20 (10.00%)
occurrences (all)	3	0	2
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 22 (0.00%)	0 / 7 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Blood bilirubin increased			

subjects affected / exposed	0 / 22 (0.00%)	0 / 7 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Blood creatinine increased			
subjects affected / exposed	4 / 22 (18.18%)	2 / 7 (28.57%)	4 / 20 (20.00%)
occurrences (all)	11	2	5
Blood uric acid increased			
subjects affected / exposed	0 / 22 (0.00%)	0 / 7 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Electrocardiogram QT prolonged			
subjects affected / exposed	0 / 22 (0.00%)	0 / 7 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Electrocardiogram T wave abnormal			
subjects affected / exposed	0 / 22 (0.00%)	1 / 7 (14.29%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Electrocardiogram abnormal			
subjects affected / exposed	0 / 22 (0.00%)	1 / 7 (14.29%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
International normalised ratio increased			
subjects affected / exposed	0 / 22 (0.00%)	0 / 7 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Lipase increased			
subjects affected / exposed	2 / 22 (9.09%)	0 / 7 (0.00%)	0 / 20 (0.00%)
occurrences (all)	2	0	0
Neutrophil count decreased			
subjects affected / exposed	2 / 22 (9.09%)	0 / 7 (0.00%)	1 / 20 (5.00%)
occurrences (all)	4	0	1
Protein total decreased			
subjects affected / exposed	0 / 22 (0.00%)	1 / 7 (14.29%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Weight increased			
subjects affected / exposed	7 / 22 (31.82%)	0 / 7 (0.00%)	9 / 20 (45.00%)
occurrences (all)	12	0	12
White blood cell count decreased			
subjects affected / exposed	1 / 22 (4.55%)	0 / 7 (0.00%)	1 / 20 (5.00%)
occurrences (all)	7	0	3

White blood cell count increased			
subjects affected / exposed	0 / 22 (0.00%)	1 / 7 (14.29%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Injury, poisoning and procedural complications			
Ankle fracture			
subjects affected / exposed	0 / 22 (0.00%)	0 / 7 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Contusion			
subjects affected / exposed	0 / 22 (0.00%)	0 / 7 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Fall			
subjects affected / exposed	0 / 22 (0.00%)	0 / 7 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Humerus fracture			
subjects affected / exposed	0 / 22 (0.00%)	1 / 7 (14.29%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Ligament sprain			
subjects affected / exposed	0 / 22 (0.00%)	0 / 7 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Limb injury			
subjects affected / exposed	0 / 22 (0.00%)	0 / 7 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Meniscus injury			
subjects affected / exposed	0 / 22 (0.00%)	0 / 7 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Muscle rupture			
subjects affected / exposed	0 / 22 (0.00%)	0 / 7 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Radiation necrosis			
subjects affected / exposed	0 / 22 (0.00%)	0 / 7 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Skin abrasion			
subjects affected / exposed	0 / 22 (0.00%)	0 / 7 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Stress fracture			

subjects affected / exposed	0 / 22 (0.00%)	0 / 7 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Tendon rupture			
subjects affected / exposed	0 / 22 (0.00%)	0 / 7 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Wound dehiscence			
subjects affected / exposed	0 / 22 (0.00%)	0 / 7 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	1 / 22 (4.55%)	0 / 7 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Bradycardia			
subjects affected / exposed	0 / 22 (0.00%)	0 / 7 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Tachycardia			
subjects affected / exposed	0 / 22 (0.00%)	1 / 7 (14.29%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Nervous system disorders			
Amnesia			
subjects affected / exposed	1 / 22 (4.55%)	0 / 7 (0.00%)	2 / 20 (10.00%)
occurrences (all)	1	0	2
Aphasia			
subjects affected / exposed	0 / 22 (0.00%)	0 / 7 (0.00%)	2 / 20 (10.00%)
occurrences (all)	0	0	2
Asterixis			
subjects affected / exposed	0 / 22 (0.00%)	0 / 7 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Ataxia			
subjects affected / exposed	2 / 22 (9.09%)	0 / 7 (0.00%)	0 / 20 (0.00%)
occurrences (all)	2	0	0
Autonomic nervous system imbalance			
subjects affected / exposed	0 / 22 (0.00%)	0 / 7 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Balance disorder			

subjects affected / exposed	0 / 22 (0.00%)	1 / 7 (14.29%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Cognitive disorder			
subjects affected / exposed	3 / 22 (13.64%)	0 / 7 (0.00%)	3 / 20 (15.00%)
occurrences (all)	4	0	3
Disturbance in attention			
subjects affected / exposed	2 / 22 (9.09%)	0 / 7 (0.00%)	1 / 20 (5.00%)
occurrences (all)	2	0	1
Dizziness			
subjects affected / exposed	8 / 22 (36.36%)	1 / 7 (14.29%)	7 / 20 (35.00%)
occurrences (all)	12	4	11
Dizziness exertional			
subjects affected / exposed	0 / 22 (0.00%)	0 / 7 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Dysarthria			
subjects affected / exposed	1 / 22 (4.55%)	0 / 7 (0.00%)	1 / 20 (5.00%)
occurrences (all)	2	0	1
Dysgeusia			
subjects affected / exposed	11 / 22 (50.00%)	0 / 7 (0.00%)	3 / 20 (15.00%)
occurrences (all)	12	0	3
Headache			
subjects affected / exposed	3 / 22 (13.64%)	0 / 7 (0.00%)	3 / 20 (15.00%)
occurrences (all)	7	0	3
Hyperaesthesia			
subjects affected / exposed	2 / 22 (9.09%)	0 / 7 (0.00%)	0 / 20 (0.00%)
occurrences (all)	2	0	0
Hypoaesthesia			
subjects affected / exposed	1 / 22 (4.55%)	2 / 7 (28.57%)	0 / 20 (0.00%)
occurrences (all)	1	2	0
Memory impairment			
subjects affected / exposed	1 / 22 (4.55%)	0 / 7 (0.00%)	1 / 20 (5.00%)
occurrences (all)	1	0	1
Neuropathy peripheral			
subjects affected / exposed	1 / 22 (4.55%)	0 / 7 (0.00%)	2 / 20 (10.00%)
occurrences (all)	1	0	4
Paraesthesia			

subjects affected / exposed	4 / 22 (18.18%)	0 / 7 (0.00%)	2 / 20 (10.00%)
occurrences (all)	5	0	2
Peripheral motor neuropathy			
subjects affected / exposed	1 / 22 (4.55%)	0 / 7 (0.00%)	1 / 20 (5.00%)
occurrences (all)	1	0	1
Peripheral sensory neuropathy			
subjects affected / exposed	3 / 22 (13.64%)	0 / 7 (0.00%)	7 / 20 (35.00%)
occurrences (all)	5	0	12
Psychomotor skills impaired			
subjects affected / exposed	0 / 22 (0.00%)	0 / 7 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Seizure			
subjects affected / exposed	0 / 22 (0.00%)	0 / 7 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Somnolence			
subjects affected / exposed	1 / 22 (4.55%)	0 / 7 (0.00%)	1 / 20 (5.00%)
occurrences (all)	1	0	3
Taste disorder			
subjects affected / exposed	1 / 22 (4.55%)	0 / 7 (0.00%)	2 / 20 (10.00%)
occurrences (all)	1	0	2
Tremor			
subjects affected / exposed	0 / 22 (0.00%)	1 / 7 (14.29%)	3 / 20 (15.00%)
occurrences (all)	0	1	3
Vibratory sense increased			
subjects affected / exposed	0 / 22 (0.00%)	0 / 7 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	4 / 22 (18.18%)	3 / 7 (42.86%)	6 / 20 (30.00%)
occurrences (all)	9	9	10
Lymphadenopathy			
subjects affected / exposed	0 / 22 (0.00%)	0 / 7 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Neutropenia			
subjects affected / exposed	1 / 22 (4.55%)	0 / 7 (0.00%)	2 / 20 (10.00%)
occurrences (all)	5	0	23

Thrombocytopenia			
subjects affected / exposed	0 / 22 (0.00%)	0 / 7 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	0 / 22 (0.00%)	0 / 7 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
External ear inflammation			
subjects affected / exposed	0 / 22 (0.00%)	0 / 7 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Hypoacusis			
subjects affected / exposed	0 / 22 (0.00%)	1 / 7 (14.29%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Vertigo			
subjects affected / exposed	0 / 22 (0.00%)	1 / 7 (14.29%)	1 / 20 (5.00%)
occurrences (all)	0	1	1
Eye disorders			
Asthenopia			
subjects affected / exposed	0 / 22 (0.00%)	0 / 7 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Conjunctivitis allergic			
subjects affected / exposed	0 / 22 (0.00%)	0 / 7 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Diplopia			
subjects affected / exposed	4 / 22 (18.18%)	0 / 7 (0.00%)	0 / 20 (0.00%)
occurrences (all)	6	0	0
Dry eye			
subjects affected / exposed	0 / 22 (0.00%)	0 / 7 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Eye pain			
subjects affected / exposed	0 / 22 (0.00%)	0 / 7 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Eye swelling			
subjects affected / exposed	0 / 22 (0.00%)	0 / 7 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Ocular discomfort			

subjects affected / exposed	0 / 22 (0.00%)	0 / 7 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Swelling of eyelid			
subjects affected / exposed	0 / 22 (0.00%)	0 / 7 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Vision blurred			
subjects affected / exposed	3 / 22 (13.64%)	2 / 7 (28.57%)	3 / 20 (15.00%)
occurrences (all)	4	2	4
Visual impairment			
subjects affected / exposed	0 / 22 (0.00%)	1 / 7 (14.29%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Vitreous floaters			
subjects affected / exposed	1 / 22 (4.55%)	0 / 7 (0.00%)	1 / 20 (5.00%)
occurrences (all)	1	0	1
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	2 / 22 (9.09%)	0 / 7 (0.00%)	1 / 20 (5.00%)
occurrences (all)	2	0	1
Abdominal pain			
subjects affected / exposed	2 / 22 (9.09%)	0 / 7 (0.00%)	2 / 20 (10.00%)
occurrences (all)	2	0	2
Abdominal pain upper			
subjects affected / exposed	1 / 22 (4.55%)	0 / 7 (0.00%)	1 / 20 (5.00%)
occurrences (all)	1	0	1
Abdominal tenderness			
subjects affected / exposed	0 / 22 (0.00%)	0 / 7 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Ascites			
subjects affected / exposed	1 / 22 (4.55%)	1 / 7 (14.29%)	0 / 20 (0.00%)
occurrences (all)	1	1	0
Constipation			
subjects affected / exposed	12 / 22 (54.55%)	1 / 7 (14.29%)	7 / 20 (35.00%)
occurrences (all)	14	1	9
Diarrhoea			
subjects affected / exposed	4 / 22 (18.18%)	1 / 7 (14.29%)	7 / 20 (35.00%)
occurrences (all)	5	1	8

Dry mouth			
subjects affected / exposed	2 / 22 (9.09%)	0 / 7 (0.00%)	0 / 20 (0.00%)
occurrences (all)	2	0	0
Dyspepsia			
subjects affected / exposed	2 / 22 (9.09%)	0 / 7 (0.00%)	3 / 20 (15.00%)
occurrences (all)	2	0	3
Dysphagia			
subjects affected / exposed	2 / 22 (9.09%)	0 / 7 (0.00%)	4 / 20 (20.00%)
occurrences (all)	2	0	4
Flatulence			
subjects affected / exposed	0 / 22 (0.00%)	1 / 7 (14.29%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 22 (0.00%)	0 / 7 (0.00%)	3 / 20 (15.00%)
occurrences (all)	0	0	3
Gingival pain			
subjects affected / exposed	0 / 22 (0.00%)	0 / 7 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Haematochezia			
subjects affected / exposed	0 / 22 (0.00%)	1 / 7 (14.29%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Hypoaesthesia oral			
subjects affected / exposed	0 / 22 (0.00%)	1 / 7 (14.29%)	1 / 20 (5.00%)
occurrences (all)	0	1	2
Ileus			
subjects affected / exposed	0 / 22 (0.00%)	0 / 7 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Lip dry			
subjects affected / exposed	0 / 22 (0.00%)	1 / 7 (14.29%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Nausea			
subjects affected / exposed	8 / 22 (36.36%)	1 / 7 (14.29%)	10 / 20 (50.00%)
occurrences (all)	10	1	14
Odynophagia			
subjects affected / exposed	0 / 22 (0.00%)	0 / 7 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1

Oesophageal pain			
subjects affected / exposed	0 / 22 (0.00%)	0 / 7 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Oral pain			
subjects affected / exposed	0 / 22 (0.00%)	0 / 7 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Paraesthesia oral			
subjects affected / exposed	2 / 22 (9.09%)	0 / 7 (0.00%)	0 / 20 (0.00%)
occurrences (all)	2	0	0
Stomatitis			
subjects affected / exposed	0 / 22 (0.00%)	0 / 7 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Tooth development disorder			
subjects affected / exposed	0 / 22 (0.00%)	0 / 7 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Vomiting			
subjects affected / exposed	6 / 22 (27.27%)	1 / 7 (14.29%)	5 / 20 (25.00%)
occurrences (all)	11	1	5
Hepatobiliary disorders			
Hepatic function abnormal			
subjects affected / exposed	0 / 22 (0.00%)	0 / 7 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Hyperbilirubinaemia			
subjects affected / exposed	0 / 22 (0.00%)	0 / 7 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	0 / 22 (0.00%)	0 / 7 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Dermatitis acneiform			
subjects affected / exposed	1 / 22 (4.55%)	0 / 7 (0.00%)	1 / 20 (5.00%)
occurrences (all)	2	0	1
Dermatitis allergic			
subjects affected / exposed	0 / 22 (0.00%)	0 / 7 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Dry skin			

subjects affected / exposed	2 / 22 (9.09%)	0 / 7 (0.00%)	2 / 20 (10.00%)
occurrences (all)	2	0	3
Erythema			
subjects affected / exposed	0 / 22 (0.00%)	0 / 7 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Hypertrichosis			
subjects affected / exposed	0 / 22 (0.00%)	0 / 7 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Night sweats			
subjects affected / exposed	0 / 22 (0.00%)	0 / 7 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Pain of skin			
subjects affected / exposed	0 / 22 (0.00%)	0 / 7 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Panniculitis			
subjects affected / exposed	0 / 22 (0.00%)	0 / 7 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Photosensitivity reaction			
subjects affected / exposed	2 / 22 (9.09%)	0 / 7 (0.00%)	2 / 20 (10.00%)
occurrences (all)	2	0	2
Pruritus			
subjects affected / exposed	0 / 22 (0.00%)	0 / 7 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Rash maculo-papular			
subjects affected / exposed	0 / 22 (0.00%)	0 / 7 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	2
Rash pruritic			
subjects affected / exposed	0 / 22 (0.00%)	0 / 7 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Sensitive skin			
subjects affected / exposed	0 / 22 (0.00%)	0 / 7 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Skin lesion			
subjects affected / exposed	0 / 22 (0.00%)	0 / 7 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Renal and urinary disorders			

Calcified, non-functioning right kidney			
subjects affected / exposed	0 / 22 (0.00%)	0 / 7 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Acute kidney injury			
subjects affected / exposed	0 / 22 (0.00%)	0 / 7 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Bladder spasm			
subjects affected / exposed	0 / 22 (0.00%)	0 / 7 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Haematuria			
subjects affected / exposed	0 / 22 (0.00%)	0 / 7 (0.00%)	2 / 20 (10.00%)
occurrences (all)	0	0	2
Micturition urgency			
subjects affected / exposed	0 / 22 (0.00%)	0 / 7 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Nocturia			
subjects affected / exposed	1 / 22 (4.55%)	0 / 7 (0.00%)	1 / 20 (5.00%)
occurrences (all)	1	0	1
Pollakiuria			
subjects affected / exposed	1 / 22 (4.55%)	0 / 7 (0.00%)	1 / 20 (5.00%)
occurrences (all)	1	0	1
Polyuria			
subjects affected / exposed	0 / 22 (0.00%)	0 / 7 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Proteinuria			
subjects affected / exposed	1 / 22 (4.55%)	0 / 7 (0.00%)	1 / 20 (5.00%)
occurrences (all)	1	0	1
Renal failure			
subjects affected / exposed	0 / 22 (0.00%)	0 / 7 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Urinary hesitation			
subjects affected / exposed	0 / 22 (0.00%)	0 / 7 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	2
Urinary tract pain			

subjects affected / exposed	0 / 22 (0.00%)	0 / 7 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	2 / 22 (9.09%)	1 / 7 (14.29%)	6 / 20 (30.00%)
occurrences (all)	3	1	7
Back pain			
subjects affected / exposed	4 / 22 (18.18%)	0 / 7 (0.00%)	3 / 20 (15.00%)
occurrences (all)	9	0	4
Bursitis			
subjects affected / exposed	0 / 22 (0.00%)	0 / 7 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Flank pain			
subjects affected / exposed	0 / 22 (0.00%)	0 / 7 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Intervertebral disc protrusion			
subjects affected / exposed	0 / 22 (0.00%)	0 / 7 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Joint stiffness			
subjects affected / exposed	0 / 22 (0.00%)	1 / 7 (14.29%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Joint swelling			
subjects affected / exposed	0 / 22 (0.00%)	0 / 7 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Muscle fatigue			
subjects affected / exposed	0 / 22 (0.00%)	0 / 7 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Muscle spasms			
subjects affected / exposed	1 / 22 (4.55%)	1 / 7 (14.29%)	0 / 20 (0.00%)
occurrences (all)	1	1	0
Muscular weakness			
subjects affected / exposed	1 / 22 (4.55%)	0 / 7 (0.00%)	2 / 20 (10.00%)
occurrences (all)	1	0	3
Musculoskeletal chest pain			

subjects affected / exposed	1 / 22 (4.55%)	0 / 7 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal pain			
subjects affected / exposed	0 / 22 (0.00%)	0 / 7 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Myalgia			
subjects affected / exposed	10 / 22 (45.45%)	1 / 7 (14.29%)	3 / 20 (15.00%)
occurrences (all)	11	1	4
Neck pain			
subjects affected / exposed	0 / 22 (0.00%)	0 / 7 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Osteonecrosis of jaw			
subjects affected / exposed	0 / 22 (0.00%)	0 / 7 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Pain in extremity			
subjects affected / exposed	1 / 22 (4.55%)	0 / 7 (0.00%)	0 / 20 (0.00%)
occurrences (all)	2	0	0
Pain in jaw			
subjects affected / exposed	0 / 22 (0.00%)	0 / 7 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Rotator cuff syndrome			
subjects affected / exposed	1 / 22 (4.55%)	0 / 7 (0.00%)	1 / 20 (5.00%)
occurrences (all)	1	0	1
Infections and infestations			
Abdominal abscess			
subjects affected / exposed	0 / 22 (0.00%)	0 / 7 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Bronchitis			
subjects affected / exposed	2 / 22 (9.09%)	0 / 7 (0.00%)	0 / 20 (0.00%)
occurrences (all)	2	0	0
Cellulitis			
subjects affected / exposed	0 / 22 (0.00%)	0 / 7 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Ear infection			
subjects affected / exposed	0 / 22 (0.00%)	0 / 7 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1

Escherichia infection			
subjects affected / exposed	0 / 22 (0.00%)	0 / 7 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Laryngitis			
subjects affected / exposed	0 / 22 (0.00%)	0 / 7 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Localised infection			
subjects affected / exposed	0 / 22 (0.00%)	0 / 7 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	2
Medical device site infection			
subjects affected / exposed	0 / 22 (0.00%)	0 / 7 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			
subjects affected / exposed	0 / 22 (0.00%)	0 / 7 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Oesophageal candidiasis			
subjects affected / exposed	0 / 22 (0.00%)	0 / 7 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Oral candidiasis			
subjects affected / exposed	0 / 22 (0.00%)	0 / 7 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Pneumonia			
subjects affected / exposed	1 / 22 (4.55%)	0 / 7 (0.00%)	1 / 20 (5.00%)
occurrences (all)	1	0	1
Rash pustular			
subjects affected / exposed	0 / 22 (0.00%)	0 / 7 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Respiratory tract infection			
subjects affected / exposed	0 / 22 (0.00%)	1 / 7 (14.29%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Respiratory tract infection viral			
subjects affected / exposed	0 / 22 (0.00%)	0 / 7 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Sinusitis bacterial			
subjects affected / exposed	0 / 22 (0.00%)	0 / 7 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0

Skin infection			
subjects affected / exposed	1 / 22 (4.55%)	0 / 7 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Upper respiratory tract infection			
subjects affected / exposed	0 / 22 (0.00%)	0 / 7 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Urinary tract infection			
subjects affected / exposed	1 / 22 (4.55%)	2 / 7 (28.57%)	5 / 20 (25.00%)
occurrences (all)	1	2	9
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	4 / 22 (18.18%)	0 / 7 (0.00%)	3 / 20 (15.00%)
occurrences (all)	5	0	3
Dehydration			
subjects affected / exposed	3 / 22 (13.64%)	0 / 7 (0.00%)	2 / 20 (10.00%)
occurrences (all)	3	0	4
Hypercalcaemia			
subjects affected / exposed	0 / 22 (0.00%)	1 / 7 (14.29%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Hyperglycaemia			
subjects affected / exposed	0 / 22 (0.00%)	0 / 7 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Hyperkalaemia			
subjects affected / exposed	1 / 22 (4.55%)	0 / 7 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Hypernatraemia			
subjects affected / exposed	0 / 22 (0.00%)	0 / 7 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Hyperuricaemia			
subjects affected / exposed	0 / 22 (0.00%)	1 / 7 (14.29%)	2 / 20 (10.00%)
occurrences (all)	0	1	3
Hypoalbuminaemia			
subjects affected / exposed	0 / 22 (0.00%)	1 / 7 (14.29%)	1 / 20 (5.00%)
occurrences (all)	0	1	2
Hypocalcaemia			

subjects affected / exposed	1 / 22 (4.55%)	2 / 7 (28.57%)	0 / 20 (0.00%)
occurrences (all)	1	2	0
Hypokalaemia			
subjects affected / exposed	2 / 22 (9.09%)	0 / 7 (0.00%)	0 / 20 (0.00%)
occurrences (all)	2	0	0
Hypomagnesaemia			
subjects affected / exposed	1 / 22 (4.55%)	0 / 7 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Hyponatraemia			
subjects affected / exposed	0 / 22 (0.00%)	0 / 7 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Hypophosphataemia			
subjects affected / exposed	3 / 22 (13.64%)	0 / 7 (0.00%)	3 / 20 (15.00%)
occurrences (all)	4	0	3
Hypovolaemia			
subjects affected / exposed	0 / 22 (0.00%)	0 / 7 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Increased appetite			
subjects affected / exposed	0 / 22 (0.00%)	0 / 7 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	RXDX-101 800 mg/day	RXDX-101 by BSA 600 mg/day or 800 mg/day	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	9 / 9 (100.00%)	5 / 5 (100.00%)	
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Hypertension			
subjects affected / exposed	0 / 9 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	1	
Hypotension			
subjects affected / exposed	3 / 9 (33.33%)	0 / 5 (0.00%)	
occurrences (all)	3	0	
Orthostatic hypotension			

subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Phlebitis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Thrombophlebitis superficial			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
General disorders and administration site conditions			
Balance disturbances			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Asthenia			
subjects affected / exposed	1 / 9 (11.11%)	1 / 5 (20.00%)	
occurrences (all)	1	1	
Chest discomfort			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Chest pain			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Chills			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Face oedema			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Facial pain			
subjects affected / exposed	0 / 9 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	1	
Fatigue			
subjects affected / exposed	6 / 9 (66.67%)	4 / 5 (80.00%)	
occurrences (all)	9	6	
Gait disturbance			

subjects affected / exposed	2 / 9 (22.22%)	0 / 5 (0.00%)	
occurrences (all)	6	0	
Generalised oedema			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Malaise			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Mucosal inflammation			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Oedema			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Oedema peripheral			
subjects affected / exposed	2 / 9 (22.22%)	2 / 5 (40.00%)	
occurrences (all)	2	3	
Pain			
subjects affected / exposed	0 / 9 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	1	
Peripheral swelling			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Pyrexia			
subjects affected / exposed	2 / 9 (22.22%)	1 / 5 (20.00%)	
occurrences (all)	2	1	
Suprapubic pain			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Temperature intolerance			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Unevaluable event			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Reproductive system and breast			

disorders			
Breast pain			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Pelvic pain			
subjects affected / exposed	1 / 9 (11.11%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	3 / 9 (33.33%)	0 / 5 (0.00%)	
occurrences (all)	3	0	
Dysphonia			
subjects affected / exposed	0 / 9 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	1	
Dyspnoea			
subjects affected / exposed	2 / 9 (22.22%)	0 / 5 (0.00%)	
occurrences (all)	2	0	
Dyspnoea exertional			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Epistaxis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Hypoxia			
subjects affected / exposed	1 / 9 (11.11%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Nasal congestion			
subjects affected / exposed	1 / 9 (11.11%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Oropharyngeal pain			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Pleural effusion			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Productive cough			

subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Pulmonary embolism			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Rhinitis allergic			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Rhinorrhoea			
subjects affected / exposed	1 / 9 (11.11%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Sinus congestion			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Sleep apnoea syndrome			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Throat irritation			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Wheezing			
subjects affected / exposed	1 / 9 (11.11%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 9 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	1	
Confusional state			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Disorientation			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Insomnia			
subjects affected / exposed	1 / 9 (11.11%)	0 / 5 (0.00%)	
occurrences (all)	1	0	

Libido decreased			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Mood swings			
subjects affected / exposed	0 / 9 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	1	
Sleep disorder			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Amylase increased			
subjects affected / exposed	1 / 9 (11.11%)	0 / 5 (0.00%)	
occurrences (all)	2	0	
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Blood bilirubin increased			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Blood creatinine increased			
subjects affected / exposed	2 / 9 (22.22%)	2 / 5 (40.00%)	
occurrences (all)	3	2	
Blood uric acid increased			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Electrocardiogram QT prolonged			
subjects affected / exposed	1 / 9 (11.11%)	1 / 5 (20.00%)	
occurrences (all)	1	1	
Electrocardiogram T wave abnormal			

subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Electrocardiogram abnormal			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
International normalised ratio increased			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Lipase increased			
subjects affected / exposed	1 / 9 (11.11%)	1 / 5 (20.00%)	
occurrences (all)	2	1	
Neutrophil count decreased			
subjects affected / exposed	0 / 9 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	1	
Protein total decreased			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Weight increased			
subjects affected / exposed	1 / 9 (11.11%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
White blood cell count decreased			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
White blood cell count increased			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Injury, poisoning and procedural complications			
Ankle fracture			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Contusion			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Fall			

subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Humerus fracture			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Ligament sprain			
subjects affected / exposed	0 / 9 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	1	
Limb injury			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Meniscus injury			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Muscle rupture			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Radiation necrosis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Skin abrasion			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Stress fracture			
subjects affected / exposed	0 / 9 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	5	
Tendon rupture			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Wound dehiscence			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	0 / 9 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	1	

Bradycardia			
subjects affected / exposed	0 / 9 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	1	
Tachycardia			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Nervous system disorders			
Amnesia			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Aphasia			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Asterixis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Ataxia			
subjects affected / exposed	1 / 9 (11.11%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Autonomic nervous system imbalance			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Balance disorder			
subjects affected / exposed	0 / 9 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	1	
Cognitive disorder			
subjects affected / exposed	2 / 9 (22.22%)	1 / 5 (20.00%)	
occurrences (all)	3	1	
Disturbance in attention			
subjects affected / exposed	1 / 9 (11.11%)	1 / 5 (20.00%)	
occurrences (all)	1	1	
Dizziness			
subjects affected / exposed	2 / 9 (22.22%)	2 / 5 (40.00%)	
occurrences (all)	2	3	
Dizziness exertional			

subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Dysarthria			
subjects affected / exposed	1 / 9 (11.11%)	0 / 5 (0.00%)	
occurrences (all)	2	0	
Dysgeusia			
subjects affected / exposed	5 / 9 (55.56%)	3 / 5 (60.00%)	
occurrences (all)	5	3	
Headache			
subjects affected / exposed	0 / 9 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	1	
Hyperaesthesia			
subjects affected / exposed	1 / 9 (11.11%)	1 / 5 (20.00%)	
occurrences (all)	1	1	
Hypoaesthesia			
subjects affected / exposed	1 / 9 (11.11%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Memory impairment			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Neuropathy peripheral			
subjects affected / exposed	1 / 9 (11.11%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Paraesthesia			
subjects affected / exposed	2 / 9 (22.22%)	1 / 5 (20.00%)	
occurrences (all)	2	2	
Peripheral motor neuropathy			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Peripheral sensory neuropathy			
subjects affected / exposed	1 / 9 (11.11%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Psychomotor skills impaired			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Seizure			

subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Somnolence			
subjects affected / exposed	0 / 9 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	1	
Taste disorder			
subjects affected / exposed	1 / 9 (11.11%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Tremor			
subjects affected / exposed	1 / 9 (11.11%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Vibratory sense increased			
subjects affected / exposed	0 / 9 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	1	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	3 / 9 (33.33%)	1 / 5 (20.00%)	
occurrences (all)	3	1	
Lymphadenopathy			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Neutropenia			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Thrombocytopenia			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
External ear inflammation			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Hypoacusis			

subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Vertigo			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Eye disorders			
Asthenopia			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Conjunctivitis allergic			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Diplopia			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Dry eye			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Eye pain			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Eye swelling			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Ocular discomfort			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Swelling of eyelid			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Vision blurred			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Visual impairment			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	

Vitreous floaters			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Abdominal pain			
subjects affected / exposed	1 / 9 (11.11%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Abdominal pain upper			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Abdominal tenderness			
subjects affected / exposed	1 / 9 (11.11%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Ascites			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Constipation			
subjects affected / exposed	1 / 9 (11.11%)	2 / 5 (40.00%)	
occurrences (all)	1	5	
Diarrhoea			
subjects affected / exposed	2 / 9 (22.22%)	3 / 5 (60.00%)	
occurrences (all)	3	8	
Dry mouth			
subjects affected / exposed	3 / 9 (33.33%)	1 / 5 (20.00%)	
occurrences (all)	3	1	
Dyspepsia			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Dysphagia			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Flatulence			

subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)		
occurrences (all)	0	0		
Gastrooesophageal reflux disease				
subjects affected / exposed	1 / 9 (11.11%)	1 / 5 (20.00%)		
occurrences (all)	1	1		
Gingival pain				
subjects affected / exposed	1 / 9 (11.11%)	0 / 5 (0.00%)		
occurrences (all)	1	0		
Haematochezia				
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)		
occurrences (all)	0	0		
Hypoaesthesia oral				
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)		
occurrences (all)	0	0		
Ileus				
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)		
occurrences (all)	0	0		
Lip dry				
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)		
occurrences (all)	0	0		
Nausea				
subjects affected / exposed	1 / 9 (11.11%)	0 / 5 (0.00%)		
occurrences (all)	1	0		
Odynophagia				
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)		
occurrences (all)	0	0		
Oesophageal pain				
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)		
occurrences (all)	0	0		
Oral pain				
subjects affected / exposed	0 / 9 (0.00%)	1 / 5 (20.00%)		
occurrences (all)	0	2		
Paraesthesia oral				
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)		
occurrences (all)	0	0		
Stomatitis				

subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Tooth development disorder			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Vomiting			
subjects affected / exposed	1 / 9 (11.11%)	2 / 5 (40.00%)	
occurrences (all)	1	4	
Hepatobiliary disorders			
Hepatic function abnormal			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Hyperbilirubinaemia			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	1 / 9 (11.11%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Dermatitis acneiform			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Dermatitis allergic			
subjects affected / exposed	0 / 9 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	1	
Dry skin			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Erythema			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Hypertrichosis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Night sweats			

subjects affected / exposed	2 / 9 (22.22%)	0 / 5 (0.00%)	
occurrences (all)	2	0	
Pain of skin			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Panniculitis			
subjects affected / exposed	0 / 9 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	1	
Photosensitivity reaction			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Pruritus			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Rash maculo-papular			
subjects affected / exposed	0 / 9 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	1	
Rash pruritic			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Sensitive skin			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Skin lesion			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Renal and urinary disorders			
Calcified, non-functioning right kidney			
subjects affected / exposed	1 / 9 (11.11%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Acute kidney injury			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Bladder spasm			

subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Haematuria			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Micturition urgency			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Nocturia			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Pollakiuria			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Polyuria			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Proteinuria			
subjects affected / exposed	1 / 9 (11.11%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Renal failure			
subjects affected / exposed	1 / 9 (11.11%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Urinary hesitation			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Urinary tract pain			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 9 (11.11%)	3 / 5 (60.00%)	
occurrences (all)	1	4	
Back pain			

subjects affected / exposed	2 / 9 (22.22%)	0 / 5 (0.00%)	
occurrences (all)	2	0	
Bursitis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Flank pain			
subjects affected / exposed	1 / 9 (11.11%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Intervertebral disc protrusion			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Joint stiffness			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Joint swelling			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Muscle fatigue			
subjects affected / exposed	0 / 9 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	1	
Muscle spasms			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Muscular weakness			
subjects affected / exposed	2 / 9 (22.22%)	1 / 5 (20.00%)	
occurrences (all)	3	1	
Musculoskeletal chest pain			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Musculoskeletal pain			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Myalgia			
subjects affected / exposed	0 / 9 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	2	
Neck pain			

subjects affected / exposed	1 / 9 (11.11%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Osteonecrosis of jaw			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Pain in extremity			
subjects affected / exposed	1 / 9 (11.11%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Pain in jaw			
subjects affected / exposed	0 / 9 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	1	
Rotator cuff syndrome			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Infections and infestations			
Abdominal abscess			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Bronchitis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Cellulitis			
subjects affected / exposed	0 / 9 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	1	
Ear infection			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Escherichia infection			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Laryngitis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Localised infection			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	

Medical device site infection			
subjects affected / exposed	0 / 9 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	1	
Nasopharyngitis			
subjects affected / exposed	0 / 9 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	1	
Oesophageal candidiasis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Oral candidiasis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Pneumonia			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Rash pustular			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Respiratory tract infection			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Respiratory tract infection viral			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Sinusitis bacterial			
subjects affected / exposed	1 / 9 (11.11%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Skin infection			
subjects affected / exposed	0 / 9 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	1	
Upper respiratory tract infection			
subjects affected / exposed	1 / 9 (11.11%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Urinary tract infection			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	

Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Dehydration			
subjects affected / exposed	0 / 9 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	1	
Hypercalcaemia			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Hyperglycaemia			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Hyperkalaemia			
subjects affected / exposed	1 / 9 (11.11%)	0 / 5 (0.00%)	
occurrences (all)	2	0	
Hypernatraemia			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Hyperuricaemia			
subjects affected / exposed	2 / 9 (22.22%)	0 / 5 (0.00%)	
occurrences (all)	2	0	
Hypoalbuminaemia			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Hypocalcaemia			
subjects affected / exposed	1 / 9 (11.11%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Hypokalaemia			
subjects affected / exposed	3 / 9 (33.33%)	0 / 5 (0.00%)	
occurrences (all)	4	0	
Hypomagnesaemia			
subjects affected / exposed	1 / 9 (11.11%)	0 / 5 (0.00%)	
occurrences (all)	2	0	
Hyponatraemia			

subjects affected / exposed	0 / 9 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	1	
Hypophosphataemia			
subjects affected / exposed	0 / 9 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	2	
Hypovolaemia			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Increased appetite			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
26 March 2014	This version incorporates FDA comments related to patient safety. The main procedural change concerns the Phase 1 Dose Escalation Segment. The duration of Cycle 1 was changed to 6 weeks instead of 4 weeks. All subsequent cycles are 4 weeks. To accommodate this procedural change, assessments have been modified or incorporated, including vital signs, weight, serum pregnancy test, and PK
16 April 2014	This version incorporates changes for clarification concerning study personnel, Phase 1-Cycle 1 timing, visit windows, dose modifications, concomitant medications, recording/reporting of adverse events, table footnotes, and study visit section headings.
08 October 2014	The requirement for patients to have tumors that harbor genes with molecular alterations of NTRK1, NTRK2, NTRK3, ROS1, or ALK was removed for patients enrolling in the dose escalation segment of the study. An option to evaluate entrectinib when administered as a twice daily dosing regimen, in addition to the once daily dosing regimen, was added to the dose escalation segment as well as the option to enroll additional patients to obtain additional data. The information used to select the RP2D was expanded to include all available safety, tolerability, PK, and PD data from different dose levels, regimens, and schedules tested. Eligibility criteria were changed.
23 April 2015	Increased the number of potential study centers from "up to 40" to "up to 60." Incorporated language that allowed evaluation of alternate entrectinib formulations. The length of cycle 1 in the dose escalation segment was reduced from 6 weeks (42 days) to 4 weeks (28 days). Additionally, all references to visits and procedures for cycle 1, days 35 and 42, were removed. Subsequently, any relevant procedures that were previously conducted on cycle 1, day 42 were added to cycle 1, day 28 as appropriate (eg, ECOG performance status, ECG, tumor imaging, entrectinib accountability and dispensation, serum pregnancy test). The number of PK and PD samples collected in the dose expansion segment was reduced from all patients to a subset of patients. Modifications were made to define 6 cohorts in the dose expansion segment of the study with NTRK1, NTRK2, NTRK3, ROS1, or ALK rearrangements. Thus, the number of planned patients was subsequently increased from approximately 120 patients to approximately 150 patients. Inclusion and exclusion criteria were modified and/or language was added for clarification.
16 August 2016	The main reason for this amendment is to remove the Phase 2a portion of the study due to the start of the Sponsor's separate Phase 2 Global Study RXDX-101-02 (STARTRK-2), which is also open at the Phase 1 clinical trial sites. The current STARTRK-1 study will revert back to a Phase 1 design comprised of a dose escalation portion (already completed) followed by dose expansion at the RP2D (600 mg QD) in patients with solid tumors that harbor other NTRK1/2/3, ROS1, and ALK molecular alterations of interest to continue to explore alternative (non-gene fusion) oncogenic drivers. In addition, the study will remain open to provide an opportunity to collect pharmacokinetics for future formulations of entrectinib, and finally, to enroll patients who may not be eligible for STARTRK-2, but who are otherwise of clinical and scientific interest.
20 September 2018	F. Hoffmann-La Roche Ltd took over the future development of study drug entrectinib (RXDX-101) from Ignyta, Inc. With the change in Sponsor, a new Medical Monitor was assigned.

04 February 2019	Pharmacokinetic (PK) analysis for the Primary CSR (October 2018) was sufficient. Further blood draws for remaining patients was considered as additional burden and would have had limited value. Therefore, collection of PK samples was discontinued. Pharmacodynamic urine sampling was discontinued due to logistical challenges (collection and storage). Removing sample collections from overall study procedures/assessments would not have impacted patient safety and would have been less burdensome for patients

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported