



Clinical trial results:

Phase 2, Open-label, Dose-escalation and Dose-expansion Study of Infigratinib, an FGFR 1-3-selective Tyrosine Kinase Inhibitor, in Children with Achondroplasia: PROPEL 2

Summary

EudraCT number	2019-002954-21
Trial protocol	FR GB
Global end of trial date	21 October 2024

Results information

Result version number	v1 (current)
This version publication date	29 May 2026
First version publication date	29 May 2026

Trial information

Trial identification

Sponsor protocol code	QBGJ398-201
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04265651
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	QED Therapeutics, Inc.
Sponsor organisation address	1800 Owens Street, 12th Floor, San Francisco, United States, 94158
Public contact	Daniela Rogoff, QED Therapeutics, 011 8772805655, daniela.rogoff@bridgebio.com
Scientific contact	Daniela Rogoff, QED Therapeutics, 011 8772805655, daniela.rogoff@bridgebio.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMA-002594-PIP02-20
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?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	21 October 2024
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	21 October 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective of the dose escalation part of the trial was to identify a dose of oral infigratinib, based on safety and efficacy evaluations, for children with achondroplasia (ACH) to be used for further study.

The main objective of the dose expansion part of the trial was to provide preliminary evidence of efficacy of oral infigratinib for the treatment of ACH, as assessed by change from baseline in height velocity in children with ACH.

Protection of trial subjects:

This clinical trial was conducted in accordance with the International Council for Harmonisation (ICH) Harmonised Tripartite Guidelines for Good Clinical Practice (GCP), with applicable local regulations (including European Directive 2001/20/EC and US Code of Federal Regulations Title 21), and with the ethical principles laid down in the Declaration of Helsinki.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	15 July 2020
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy
Long term follow-up duration	10 Years
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Australia: 10
Country: Number of subjects enrolled	Canada: 3
Country: Number of subjects enrolled	United States: 11
Country: Number of subjects enrolled	Spain: 20
Country: Number of subjects enrolled	United Kingdom: 27
Country: Number of subjects enrolled	France: 13
Worldwide total number of subjects	84
EEA total number of subjects	33

Notes:

Subjects enrolled per age group

In utero	0
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Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	84
Adolescents (12-17 years)	0
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants were enrolled across 19 trial centers in Europe (France, Great Britain, Spain), North America (Canada, US), and Australia between 15 July 2020 and 21 October 2024.

Long-term follow up is planned to go ahead under the open label extension trial protocol QBGJ398-203.

Pre-assignment

Screening details:

Children 3 to 11 years of age with ACH who previously participated in the PROPEL trial (Protocol QBGJ398-001) for at least 6 months and met eligibility criteria were eligible to enroll onto this open label trial.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Dose Escalation Cohort 1 (0.016 mg/kg)

Arm description:

Participants received once daily oral treatment with infigratinib at 0.016 mg/kg for at least 6 months. Dose increases were allowed at Month 6 and Month 12 if criteria were met.

Arm type	Experimental
Investigational medicinal product name	Infigratinib
Investigational medicinal product code	BGJ398
Other name	BBP-831
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Infigratinib was provided as a pediatric formulation of minitablets for daily oral administration.

Arm title	Dose Escalation Cohort 2 (0.032 mg/kg)
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Arm description:

Participants received once daily oral treatment with infigratinib at 0.032 mg/kg for at least 6 months. Dose increases were allowed at Month 6 and Month 12 if criteria were met.

Arm type	Experimental
Investigational medicinal product name	Infigratinib
Investigational medicinal product code	BGJ398
Other name	BBP-831
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Infigratinib was provided as a pediatric formulation of minitablets for daily oral administration.

Arm title	Dose Escalation Cohort 3 (0.064 mg/kg)
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Arm description:

Participants received once daily oral treatment with infigratinib at 0.064 mg/kg for at least 6 months.

Arm type	Experimental
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Investigational medicinal product name	Infigratinib
Investigational medicinal product code	BGJ398
Other name	BBP-831
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Infigratinib was provided as a pediatric formulation of minitablets for daily oral administration.

Arm title	Dose Escalation Cohort 4 (0.128 mg/kg)
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Arm description:

Participants received once daily oral treatment with infigratinib at 0.128 mg/kg for at least 6 months.

Arm type	Experimental
Investigational medicinal product name	Infigratinib
Investigational medicinal product code	BGJ398
Other name	BBP-831
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Infigratinib was provided as a pediatric formulation of minitablets for daily oral administration.

Arm title	Dose Escalation Cohort 5 (0.25 mg/kg)
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Arm description:

Participants received once daily oral treatment with infigratinib at 0.25mg/kg for at least 6 months.

Arm type	Experimental
Investigational medicinal product name	Infigratinib
Investigational medicinal product code	BGJ398
Other name	BBP-831
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Infigratinib was provided as a pediatric formulation of minitablets for daily oral administration.

Arm title	Dose Expansion Cohort (0.25 mg/kg)
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Arm description:

Participants received once daily oral treatment with infigratinib at 0.25 mg/kg for 12 months.

Arm type	Experimental
Investigational medicinal product name	Infigratinib
Investigational medicinal product code	BGJ398
Other name	BBP-831
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Infigratinib was provided as a pediatric formulation of sprinkle capsules for daily oral administration. In this presentation minitablets were provided inside nonlocking gelatin capsules.

Number of subjects in period 1	Dose Escalation Cohort 1 (0.016 mg/kg)	Dose Escalation Cohort 2 (0.032 mg/kg)	Dose Escalation Cohort 3 (0.064 mg/kg)
Started	8	19	16
Completed	7	17	16
Not completed	1	2	0
Consent withdrawn by subject	1	1	-
Planned to undergo prohibited surgery	-	1	-

Number of subjects in period 1	Dose Escalation Cohort 4 (0.128 mg/kg)	Dose Escalation Cohort 5 (0.25 mg/kg)	Dose Expansion Cohort (0.25 mg/kg)
Started	16	13	12
Completed	16	11	12
Not completed	0	2	0
Consent withdrawn by subject	-	2	-
Planned to undergo prohibited surgery	-	-	-

Baseline characteristics

Reporting groups

Reporting group title	Dose Escalation Cohort 1 (0.016 mg/kg)
Reporting group description:	
Participants received once daily oral treatment with infigratinib at 0.016 mg/kg for at least 6 months. Dose increases were allowed at Month 6 and Month 12 if criteria were met.	
Reporting group title	Dose Escalation Cohort 2 (0.032 mg/kg)
Reporting group description:	
Participants received once daily oral treatment with infigratinib at 0.032 mg/kg for at least 6 months. Dose increases were allowed at Month 6 and Month 12 if criteria were met.	
Reporting group title	Dose Escalation Cohort 3 (0.064 mg/kg)
Reporting group description:	
Participants received once daily oral treatment with infigratinib at 0.064 mg/kg for at least 6 months.	
Reporting group title	Dose Escalation Cohort 4 (0.128 mg/kg)
Reporting group description:	
Participants received once daily oral treatment with infigratinib at 0.128 mg/kg for at least 6 months.	
Reporting group title	Dose Escalation Cohort 5 (0.25 mg/kg)
Reporting group description:	
Participants received once daily oral treatment with infigratinib at 0.25mg/kg for at least 6 months.	
Reporting group title	Dose Expansion Cohort (0.25 mg/kg)
Reporting group description:	
Participants received once daily oral treatment with infigratinib at 0.25 mg/kg for 12 months.	

Reporting group values	Dose Escalation Cohort 1 (0.016 mg/kg)	Dose Escalation Cohort 2 (0.032 mg/kg)	Dose Escalation Cohort 3 (0.064 mg/kg)
Number of subjects	8	19	16
Age categorical			
Units: Subjects			

Age continuous			
Units: years			
arithmetic mean	7.69	8.29	7.70
standard deviation	± 2.834	± 1.836	± 2.401
Gender categorical			
Units: Subjects			
Female	6	14	7
Male	2	5	9
Race			
Units: Subjects			
White	5	10	13
Black or African American	2	1	0
Asian	0	2	0
Multiple	0	1	0
Other	1	1	0
Not Reported	0	4	3
Height-for-Age Percentile			
Height percentile based on children with achondroplasia is from data entered in EDC.			
Units: percent			

arithmetic mean	51.19	46.24	44.53
standard deviation	± 22.941	± 23.677	± 25.153

Reporting group values	Dose Escalation Cohort 4 (0.128 mg/kg)	Dose Escalation Cohort 5 (0.25 mg/kg)	Dose Expansion Cohort (0.25 mg/kg)
Number of subjects	16	13	12
Age categorical Units: Subjects			

Age continuous Units: years			
arithmetic mean	6.61	7.05	6.75
standard deviation	± 2.082	± 1.987	± 2.374
Gender categorical Units: Subjects			
Female	7	8	6
Male	9	5	6
Race Units: Subjects			
White	9	7	9
Black or African American	0	1	0
Asian	2	2	1
Multiple	0	1	2
Other	1	0	0
Not Reported	4	2	0
Height-for-Age Percentile			
Height percentile based on children with achondroplasia is from data entered in EDC.			
Units: percent			
arithmetic mean	44.00	61.04	46.04
standard deviation	± 28.286	± 19.802	± 27.935

Reporting group values	Total		
Number of subjects	84		
Age categorical Units: Subjects			

Age continuous Units: years			
arithmetic mean	-		
standard deviation			
Gender categorical Units: Subjects			
Female	48		
Male	36		
Race Units: Subjects			
White	53		
Black or African American	4		
Asian	7		
Multiple	4		

Other	3		
Not Reported	13		

Height-for-Age Percentile			
Height percentile based on children with achondroplasia is from data entered in EDC.			
Units: percent			
arithmetic mean			
standard deviation	-		

End points

End points reporting groups

Reporting group title	Dose Escalation Cohort 1 (0.016 mg/kg)
Reporting group description: Participants received once daily oral treatment with infigratinib at 0.016 mg/kg for at least 6 months. Dose increases were allowed at Month 6 and Month 12 if criteria were met.	
Reporting group title	Dose Escalation Cohort 2 (0.032 mg/kg)
Reporting group description: Participants received once daily oral treatment with infigratinib at 0.032 mg/kg for at least 6 months. Dose increases were allowed at Month 6 and Month 12 if criteria were met.	
Reporting group title	Dose Escalation Cohort 3 (0.064 mg/kg)
Reporting group description: Participants received once daily oral treatment with infigratinib at 0.064 mg/kg for at least 6 months.	
Reporting group title	Dose Escalation Cohort 4 (0.128 mg/kg)
Reporting group description: Participants received once daily oral treatment with infigratinib at 0.128 mg/kg for at least 6 months.	
Reporting group title	Dose Escalation Cohort 5 (0.25 mg/kg)
Reporting group description: Participants received once daily oral treatment with infigratinib at 0.25mg/kg for at least 6 months.	
Reporting group title	Dose Expansion Cohort (0.25 mg/kg)
Reporting group description: Participants received once daily oral treatment with infigratinib at 0.25 mg/kg for 12 months.	

Primary: Dose Escalation Part: Number of Participants with Treatment-emergent Adverse Events (TEAEs) that Led to Dose Decrease or Discontinuation

End point title	Dose Escalation Part: Number of Participants with Treatment-emergent Adverse Events (TEAEs) that Led to Dose Decrease or Discontinuation ^{[1][2]}
End point description: A TEAE was defined as an AE that started on or after the first dose date through the last dose date +30 days. TEAEs requiring dose reduction or discontinuation in an individual participant were managed by the Investigator according to protocol-defined criteria.	
Safety analysis set: participants who received at least 1 dose of study drug.	
End point type	Primary
End point timeframe: Day 1 to 18 months	

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: There was no pre-specified data analysis for this endpoint.

[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: Results are only reported for the dose escalation cohorts for this endpoint.

End point values	Dose Escalation Cohort 1 (0.016 mg/kg)	Dose Escalation Cohort 2 (0.032 mg/kg)	Dose Escalation Cohort 3 (0.064 mg/kg)	Dose Escalation Cohort 4 (0.128 mg/kg)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	8	19	16	16
Units: participants				
Dose Decrease	0	0	1	0
Dose Discontinuation	0	0	0	0

End point values	Dose Escalation Cohort 5 (0.25 mg/kg)			
Subject group type	Reporting group			
Number of subjects analysed	13			
Units: participants				
Dose Decrease	0			
Dose Discontinuation	0			

Statistical analyses

No statistical analyses for this end point

Primary: Dose Escalation Part: Change from Baseline in Annualized Height Velocity (AHV)

End point title	Dose Escalation Part: Change from Baseline in Annualized Height Velocity (AHV) ^{[3][4]}
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End point description:

AHV is defined as the annualized height change between the height at the analysis visit and the Baseline height. Baseline is defined as the AHV obtained from a minimum of 6 months of observation in the PROPEL study (QBGJ398-001). Analysis of AHV (cm/year) was anchored at Baseline by initial dose level for Dose Escalation. Height velocity was calculated from the anthropometric measurements.

N = 8, 18, 16, 16, 12 | 7, 17, 16, 16, 11 | 7, 17, 16, 16, 11

Efficacy analysis set: participants who have received at least 1 dose of study drug, and have a baseline and at least 1 postbaseline standing height measurement.

End point type	Primary
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End point timeframe:

Baseline up to 18 months

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: There was no pre-specified data analysis for this endpoint.

[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: Results are only reported for the dose escalation cohorts for this endpoint.

End point values	Dose Escalation Cohort 1 (0.016 mg/kg)	Dose Escalation Cohort 2 (0.032 mg/kg)	Dose Escalation Cohort 3 (0.064 mg/kg)	Dose Escalation Cohort 4 (0.128 mg/kg)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	8	19	16	16
Units: cm/year				
arithmetic mean (standard deviation)				
Month 6	-1.82 (± 3.752)	1.13 (± 1.327)	-0.06 (± 1.632)	0.94 (± 1.493)
Month 12	-0.68 (± 2.379)	0.98 (± 1.306)	-0.28 (± 1.117)	0.94 (± 1.447)
Month 18	-1.01 (± 2.086)	0.85 (± 1.302)	-0.26 (± 0.918)	0.95 (± 1.446)

End point values	Dose Escalation Cohort 5 (0.25 mg/kg)			
Subject group type	Reporting group			
Number of subjects analysed	12			
Units: cm/year				
arithmetic mean (standard deviation)				
Month 6	3.38 (± 2.704)			
Month 12	2.51 (± 2.211)			
Month 18	2.50 (± 1.914)			

Statistical analyses

No statistical analyses for this end point

Primary: Dose Expansion Part: Change from Baseline in AHV

End point title	Dose Expansion Part: Change from Baseline in AHV ^[5] ^[6]
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End point description:

AHV is defined as the annualized height change between the height at the analysis visit and the baseline height. Baseline is defined as the AHV obtained from a minimum of 6 months of observation in the PROPEL study. Analysis of AHV (cm/year) was anchored at Baseline by Initial Dose Level for Dose Escalation.

Efficacy analysis set: participants who have received at least 1 dose of study drug, and have a baseline and at least 1 postbaseline standing height measurement.

End point type	Primary
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End point timeframe:

Baseline up to 12 months

Notes:

[5] - 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: There was no pre-specified data analysis for this endpoint.

[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: Results are only reported for the dose expansion cohorts for this endpoint.

End point values	Dose Expansion Cohort (0.25 mg/kg)			
Subject group type	Reporting group			
Number of subjects analysed	12			
Units: cm/year				
arithmetic mean (standard deviation)				
Month 6	2.67 ($\pm$ 1.575)			
Month 12	1.93 ($\pm$ 1.332)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Standing Height Z-score

End point title	Change from Baseline in Standing Height Z-score
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End point description:

Height was converted to age-and sex-appropriate standard score (Z-score). By comparison with mean and SD height for children with achondroplasia, ACH height Z-score was derived by (standing height – ACH height) divided by SD.

Efficacy analysis set: participants who have received at least 1 dose of study drug, and have a baseline and at least 1 postbaseline standing height measurement.

999 = Values at 18 months were not measured for the dose expansion cohort.

End point type	Secondary
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End point timeframe:

Dose escalation cohorts: Baseline and 18 months

Dose expansion cohort: Baseline and 12 months

End point values	Dose Escalation Cohort 1 (0.016 mg/kg)	Dose Escalation Cohort 2 (0.032 mg/kg)	Dose Escalation Cohort 3 (0.064 mg/kg)	Dose Escalation Cohort 4 (0.128 mg/kg)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7	17	16	16
Units: Z-score				
arithmetic mean (standard deviation)				
Month 12	0.13 ($\pm$ 0.252)	0.18 ($\pm$ 0.166)	-0.02 ($\pm$ 0.226)	0.20 ($\pm$ 0.204)
Month 18	0.15 ($\pm$ 0.258)	0.28 ($\pm$ 0.245)	-0.01 ($\pm$ 0.276)	0.32 ($\pm$ 0.331)

End point values	Dose Escalation Cohort 5 (0.25 mg/kg)	Dose Expansion Cohort (0.25 mg/kg)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	12		
Units: Z-score				
arithmetic mean (standard deviation)				
Month 12	0.36 (± 0.283)	0.47 (± 0.266)		
Month 18	0.54 (± 0.280)	999 (± 999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Ratio of Upper to Lower Body Segment

End point title	Change from Baseline in Ratio of Upper to Lower Body Segment ^[7]
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End point description:

The ratio was calculated as sitting height/(standing height – sitting height).

Efficacy analysis set: participants who have received at least 1 dose of study drug, and have a baseline and at least 1 postbaseline standing height measurement.

999 = Values at 18 months were not measured for the dose expansion cohort.

End point type	Secondary
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End point timeframe:

Dose escalation cohorts: Baseline and 18 months Dose expansion cohort: Baseline and 12 months

Notes:

[7] - 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: Results are only reported for the dose escalation cohorts for this endpoint.

End point values	Dose Escalation Cohort 1 (0.016 mg/kg)	Dose Escalation Cohort 2 (0.032 mg/kg)	Dose Escalation Cohort 3 (0.064 mg/kg)	Dose Escalation Cohort 4 (0.128 mg/kg)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7	17	16	16
Units: ratio				
arithmetic mean (standard deviation)				
Month 12	-0.01 (± 0.071)	-0.03 (± 0.112)	-0.06 (± 0.095)	-0.07 (± 0.090)
Month 18	-0.01 (± 0.070)	-0.05 (± 0.096)	-0.07 (± 0.096)	-0.06 (± 0.127)

End point values	Dose Escalation Cohort 5 (0.25 mg/kg)			
Subject group type	Reporting group			
Number of subjects analysed	11			

Units: ratio				
arithmetic mean (standard deviation)				
Month 12	-0.04 (± 0.078)			
Month 18	-0.12 (± 0.089)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Dose escalation part: Up to 18 months. Dose expansion part: Up to 12 months.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	23.1
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Reporting groups

Reporting group title	Dose Escalation Cohort 1 (0.016 mg/kg)
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Reporting group description:

Participants received once daily oral treatment with infigratinib at 0.016 mg/kg for 18 months.

Reporting group title	Dose Escalation Cohort 2 (0.032 mg/kg)
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Reporting group description:

Participants received once daily oral treatment with infigratinib at 0.032 mg/kg for 18 months.

Reporting group title	Dose Escalation Cohort 3 (0.064mg/kg)
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Reporting group description:

Participants received once daily oral treatment with infigratinib at 0.064 mg/kg for 18 months.

Reporting group title	Dose Escalation Cohort 4 (0.128 mg/kg)
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Reporting group description:

Participants received once daily oral treatment with infigratinib at 0.128 mg/kg for 18 months.

Reporting group title	Dose Escalation Cohort 5 (0.25 mg/kg)
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Reporting group description:

Participants received once daily oral treatment with infigratinib at 0.25mg/kg for 18 months.

Reporting group title	Dose Expansion Cohort (0.25 mg/kg)
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Reporting group description:

Participants received once daily oral treatment with infigratinib at 0.25 mg/kg for 12 months.

Serious adverse events	Dose Escalation Cohort 1 (0.016 mg/kg)	Dose Escalation Cohort 2 (0.032 mg/kg)	Dose Escalation Cohort 3 (0.064mg/kg)
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 8 (0.00%)	0 / 19 (0.00%)	0 / 16 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Nervous system disorders			
Hydrocephalus			
subjects affected / exposed	0 / 8 (0.00%)	0 / 19 (0.00%)	0 / 16 (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			
Lower respiratory tract infection			

subjects affected / exposed	0 / 8 (0.00%)	0 / 19 (0.00%)	0 / 16 (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	Dose Escalation Cohort 4 (0.128 mg/kg)	Dose Escalation Cohort 5 (0.25 mg/kg)	Dose Expansion Cohort (0.25 mg/kg)
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 16 (0.00%)	0 / 13 (0.00%)	1 / 12 (8.33%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Nervous system disorders			
Hydrocephalus			
subjects affected / exposed	0 / 16 (0.00%)	0 / 13 (0.00%)	1 / 12 (8.33%)
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			
Lower respiratory tract infection			
subjects affected / exposed	0 / 16 (0.00%)	0 / 13 (0.00%)	1 / 12 (8.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Dose Escalation Cohort 1 (0.016 mg/kg)	Dose Escalation Cohort 2 (0.032 mg/kg)	Dose Escalation Cohort 3 (0.064mg/kg)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	8 / 8 (100.00%)	19 / 19 (100.00%)	16 / 16 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Cholesteatoma			
subjects affected / exposed	0 / 8 (0.00%)	0 / 19 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Enchondromatosis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 19 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Vascular disorders			

Vasculitis			
subjects affected / exposed	0 / 8 (0.00%)	1 / 19 (5.26%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Hypertension			
subjects affected / exposed	0 / 8 (0.00%)	0 / 19 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	1 / 8 (12.50%)	4 / 19 (21.05%)	6 / 16 (37.50%)
occurrences (all)	1	4	10
Fatigue			
subjects affected / exposed	0 / 8 (0.00%)	0 / 19 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Malaise			
subjects affected / exposed	1 / 8 (12.50%)	0 / 19 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Asthenia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 19 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Influenza like illness			
subjects affected / exposed	0 / 8 (0.00%)	0 / 19 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Catheter site pain			
subjects affected / exposed	0 / 8 (0.00%)	1 / 19 (5.26%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Discomfort			
subjects affected / exposed	0 / 8 (0.00%)	1 / 19 (5.26%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Facial pain			
subjects affected / exposed	0 / 8 (0.00%)	0 / 19 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Feeling of body temperature change			
subjects affected / exposed	0 / 8 (0.00%)	0 / 19 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Gait disturbance			

subjects affected / exposed	0 / 8 (0.00%)	1 / 19 (5.26%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Injection site discomfort			
subjects affected / exposed	0 / 8 (0.00%)	0 / 19 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Medical device pain			
subjects affected / exposed	1 / 8 (12.50%)	0 / 19 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Swelling			
subjects affected / exposed	0 / 8 (0.00%)	0 / 19 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Vaccination site pain			
subjects affected / exposed	0 / 8 (0.00%)	0 / 19 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Immune system disorders			
Seasonal allergy			
subjects affected / exposed	0 / 8 (0.00%)	0 / 19 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Hypersensitivity			
subjects affected / exposed	0 / 8 (0.00%)	0 / 19 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Rhinitis allergic			
subjects affected / exposed	0 / 8 (0.00%)	0 / 19 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Social circumstances			
Poor personal hygiene			
subjects affected / exposed	0 / 8 (0.00%)	0 / 19 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Reproductive system and breast disorders			
Breast mass			
subjects affected / exposed	0 / 8 (0.00%)	1 / 19 (5.26%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Genital labial adhesions			
subjects affected / exposed	0 / 8 (0.00%)	1 / 19 (5.26%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Gynaecomastia			

subjects affected / exposed	0 / 8 (0.00%)	1 / 19 (5.26%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 8 (0.00%)	1 / 19 (5.26%)	3 / 16 (18.75%)
occurrences (all)	0	1	12
Oropharyngeal pain			
subjects affected / exposed	0 / 8 (0.00%)	2 / 19 (10.53%)	4 / 16 (25.00%)
occurrences (all)	0	2	5
Epistaxis			
subjects affected / exposed	0 / 8 (0.00%)	2 / 19 (10.53%)	1 / 16 (6.25%)
occurrences (all)	0	4	1
Nasal congestion			
subjects affected / exposed	2 / 8 (25.00%)	0 / 19 (0.00%)	2 / 16 (12.50%)
occurrences (all)	2	0	9
Rhinorrhoea			
subjects affected / exposed	0 / 8 (0.00%)	1 / 19 (5.26%)	2 / 16 (12.50%)
occurrences (all)	0	1	2
Sleep apnoea syndrome			
subjects affected / exposed	2 / 8 (25.00%)	0 / 19 (0.00%)	1 / 16 (6.25%)
occurrences (all)	2	0	1
Adenoidal hypertrophy			
subjects affected / exposed	0 / 8 (0.00%)	1 / 19 (5.26%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Aphonia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 19 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Asthma			
subjects affected / exposed	0 / 8 (0.00%)	0 / 19 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Bronchospasm			
subjects affected / exposed	0 / 8 (0.00%)	0 / 19 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Influenza			

subjects affected / exposed	0 / 8 (0.00%)	0 / 19 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Pharyngeal erythema			
subjects affected / exposed	0 / 8 (0.00%)	0 / 19 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Sneezing			
subjects affected / exposed	0 / 8 (0.00%)	0 / 19 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Tonsillar hypertrophy			
subjects affected / exposed	0 / 8 (0.00%)	1 / 19 (5.26%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Nasal discomfort			
subjects affected / exposed	0 / 8 (0.00%)	0 / 19 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Attention deficit hyperactivity disorder			
subjects affected / exposed	0 / 8 (0.00%)	1 / 19 (5.26%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Anger			
subjects affected / exposed	1 / 8 (12.50%)	0 / 19 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Anxiety			
subjects affected / exposed	1 / 8 (12.50%)	0 / 19 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Depressed mood			
subjects affected / exposed	0 / 8 (0.00%)	0 / 19 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Enuresis			
subjects affected / exposed	0 / 8 (0.00%)	1 / 19 (5.26%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Intentional self-injury			
subjects affected / exposed	1 / 8 (12.50%)	0 / 19 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Sleep disorder			

subjects affected / exposed	0 / 8 (0.00%)	0 / 19 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Sleep terror			
subjects affected / exposed	0 / 8 (0.00%)	0 / 19 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Stress			
subjects affected / exposed	0 / 8 (0.00%)	1 / 19 (5.26%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Investigations			
Vitamin D decreased			
subjects affected / exposed	0 / 8 (0.00%)	0 / 19 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Blood 25-hydroxycholecalciferol decreased			
subjects affected / exposed	0 / 8 (0.00%)	0 / 19 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Blood cholesterol increased			
subjects affected / exposed	0 / 8 (0.00%)	2 / 19 (10.53%)	0 / 16 (0.00%)
occurrences (all)	0	2	0
Blood calcium decreased			
subjects affected / exposed	1 / 8 (12.50%)	0 / 19 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Blood phosphorus increased			
subjects affected / exposed	0 / 8 (0.00%)	0 / 19 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Blood creatinine decreased			
subjects affected / exposed	0 / 8 (0.00%)	0 / 19 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Blood glucose increased			
subjects affected / exposed	0 / 8 (0.00%)	1 / 19 (5.26%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Blood triglycerides increased			
subjects affected / exposed	0 / 8 (0.00%)	1 / 19 (5.26%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Blood urine present			

subjects affected / exposed	0 / 8 (0.00%)	0 / 19 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Electrocardiogram QT prolonged			
subjects affected / exposed	0 / 8 (0.00%)	0 / 19 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Hepatic enzyme increased			
subjects affected / exposed	0 / 8 (0.00%)	0 / 19 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Platelet count decreased			
subjects affected / exposed	0 / 8 (0.00%)	0 / 19 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Vitamin D increased			
subjects affected / exposed	0 / 8 (0.00%)	0 / 19 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Platelet count increased			
subjects affected / exposed	0 / 8 (0.00%)	0 / 19 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Arthropod bite			
subjects affected / exposed	0 / 8 (0.00%)	3 / 19 (15.79%)	2 / 16 (12.50%)
occurrences (all)	0	5	2
Fall			
subjects affected / exposed	1 / 8 (12.50%)	1 / 19 (5.26%)	1 / 16 (6.25%)
occurrences (all)	1	2	1
Head injury			
subjects affected / exposed	2 / 8 (25.00%)	1 / 19 (5.26%)	1 / 16 (6.25%)
occurrences (all)	2	1	1
Wound			
subjects affected / exposed	0 / 8 (0.00%)	3 / 19 (15.79%)	0 / 16 (0.00%)
occurrences (all)	0	3	0
Ligament sprain			
subjects affected / exposed	1 / 8 (12.50%)	1 / 19 (5.26%)	0 / 16 (0.00%)
occurrences (all)	1	1	0
Procedural pain			

subjects affected / exposed	0 / 8 (0.00%)	0 / 19 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Face injury			
subjects affected / exposed	0 / 8 (0.00%)	0 / 19 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Foreign body ingestion			
subjects affected / exposed	0 / 8 (0.00%)	1 / 19 (5.26%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Incision site rash			
subjects affected / exposed	0 / 8 (0.00%)	0 / 19 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Joint injury			
subjects affected / exposed	1 / 8 (12.50%)	0 / 19 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Lip injury			
subjects affected / exposed	0 / 8 (0.00%)	0 / 19 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Skin abrasion			
subjects affected / exposed	0 / 8 (0.00%)	0 / 19 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Foreign body in ear			
subjects affected / exposed	0 / 8 (0.00%)	0 / 19 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Skin laceration			
subjects affected / exposed	0 / 8 (0.00%)	0 / 19 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	2
Venomous sting			
subjects affected / exposed	0 / 8 (0.00%)	0 / 19 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Congenital, familial and genetic disorders			
Anodontia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 19 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Tooth hypoplasia			

subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	0 / 19 (0.00%) 0	1 / 16 (6.25%) 1
Hypodontia subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	0 / 19 (0.00%) 0	0 / 16 (0.00%) 0
Cardiac disorders Defect conduction intraventricular subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	0 / 19 (0.00%) 0	1 / 16 (6.25%) 1
Tachycardia subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	0 / 19 (0.00%) 0	1 / 16 (6.25%) 1
Nervous system disorders Headache subjects affected / exposed occurrences (all)	1 / 8 (12.50%) 2	6 / 19 (31.58%) 10	7 / 16 (43.75%) 14
Dizziness subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	2 / 19 (10.53%) 2	4 / 16 (25.00%) 4
Hypoaesthesia subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	1 / 19 (5.26%) 1	1 / 16 (6.25%) 1
Dysgeusia subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	0 / 19 (0.00%) 0	1 / 16 (6.25%) 1
Paraesthesia subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	0 / 19 (0.00%) 0	0 / 16 (0.00%) 0
Presyncope subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	1 / 19 (5.26%) 1	0 / 16 (0.00%) 0
Tremor subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	0 / 19 (0.00%) 0	1 / 16 (6.25%) 1
Blood and lymphatic system disorders			

Lymphadenopathy			
subjects affected / exposed	0 / 8 (0.00%)	0 / 19 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Leukopenia			
subjects affected / exposed	0 / 8 (0.00%)	1 / 19 (5.26%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Lymphadenitis			
subjects affected / exposed	0 / 8 (0.00%)	1 / 19 (5.26%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Normocytic anaemia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 19 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Anaemia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 19 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Iron deficiency anaemia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 19 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Neutropenia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 19 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	0 / 8 (0.00%)	3 / 19 (15.79%)	2 / 16 (12.50%)
occurrences (all)	0	5	2
Otitis media			
subjects affected / exposed	0 / 8 (0.00%)	2 / 19 (10.53%)	0 / 16 (0.00%)
occurrences (all)	0	2	0
Excessive cerumen production			
subjects affected / exposed	0 / 8 (0.00%)	1 / 19 (5.26%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Deafness			
subjects affected / exposed	0 / 8 (0.00%)	1 / 19 (5.26%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Deafness neurosensory			

subjects affected / exposed	1 / 8 (12.50%)	0 / 19 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Ear discomfort			
subjects affected / exposed	0 / 8 (0.00%)	0 / 19 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Motion sickness			
subjects affected / exposed	0 / 8 (0.00%)	1 / 19 (5.26%)	0 / 16 (0.00%)
occurrences (all)	0	3	0
Otitis media acute			
subjects affected / exposed	0 / 8 (0.00%)	0 / 19 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Otorrhoea			
subjects affected / exposed	0 / 8 (0.00%)	0 / 19 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Vertigo			
subjects affected / exposed	0 / 8 (0.00%)	1 / 19 (5.26%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Hypoacusis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 19 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Inner ear disorder			
subjects affected / exposed	0 / 8 (0.00%)	0 / 19 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Middle ear effusion			
subjects affected / exposed	0 / 8 (0.00%)	0 / 19 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Optic atrophy			
subjects affected / exposed	0 / 8 (0.00%)	0 / 19 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Amblyopia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 19 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Chalazion			
subjects affected / exposed	0 / 8 (0.00%)	0 / 19 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0

Eye discharge			
subjects affected / exposed	0 / 8 (0.00%)	0 / 19 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Eye pruritus			
subjects affected / exposed	0 / 8 (0.00%)	1 / 19 (5.26%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Hypermetropia			
subjects affected / exposed	0 / 8 (0.00%)	1 / 19 (5.26%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Lacrimation increased			
subjects affected / exposed	0 / 8 (0.00%)	0 / 19 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Strabismus			
subjects affected / exposed	0 / 8 (0.00%)	1 / 19 (5.26%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Vision blurred			
subjects affected / exposed	0 / 8 (0.00%)	0 / 19 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Visual impairment			
subjects affected / exposed	0 / 8 (0.00%)	1 / 19 (5.26%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Conjunctivitis allergic			
subjects affected / exposed	0 / 8 (0.00%)	0 / 19 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	3 / 8 (37.50%)	4 / 19 (21.05%)	5 / 16 (31.25%)
occurrences (all)	3	4	13
Abdominal pain			
subjects affected / exposed	0 / 8 (0.00%)	3 / 19 (15.79%)	2 / 16 (12.50%)
occurrences (all)	0	9	2
Diarrhoea			
subjects affected / exposed	0 / 8 (0.00%)	1 / 19 (5.26%)	4 / 16 (25.00%)
occurrences (all)	0	2	13
Nausea			

subjects affected / exposed	0 / 8 (0.00%)	0 / 19 (0.00%)	4 / 16 (25.00%)
occurrences (all)	0	0	19
Abdominal pain upper			
subjects affected / exposed	1 / 8 (12.50%)	0 / 19 (0.00%)	4 / 16 (25.00%)
occurrences (all)	2	0	10
Constipation			
subjects affected / exposed	1 / 8 (12.50%)	0 / 19 (0.00%)	2 / 16 (12.50%)
occurrences (all)	1	0	2
Dental caries			
subjects affected / exposed	0 / 8 (0.00%)	2 / 19 (10.53%)	0 / 16 (0.00%)
occurrences (all)	0	2	0
Dyspepsia			
subjects affected / exposed	0 / 8 (0.00%)	1 / 19 (5.26%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Odynophagia			
subjects affected / exposed	0 / 8 (0.00%)	2 / 19 (10.53%)	0 / 16 (0.00%)
occurrences (all)	0	4	0
Tooth development disorder			
subjects affected / exposed	0 / 8 (0.00%)	1 / 19 (5.26%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Abdominal discomfort			
subjects affected / exposed	1 / 8 (12.50%)	0 / 19 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Aphthous ulcer			
subjects affected / exposed	0 / 8 (0.00%)	0 / 19 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Faeces soft			
subjects affected / exposed	0 / 8 (0.00%)	1 / 19 (5.26%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Flatulence			
subjects affected / exposed	0 / 8 (0.00%)	1 / 19 (5.26%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Gastrointestinal disorder			
subjects affected / exposed	0 / 8 (0.00%)	0 / 19 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Gingival bleeding			

subjects affected / exposed	1 / 8 (12.50%)	0 / 19 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 8 (0.00%)	0 / 19 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Gingival pain			
subjects affected / exposed	0 / 8 (0.00%)	0 / 19 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Lip haemorrhage			
subjects affected / exposed	0 / 8 (0.00%)	0 / 19 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Malocclusion			
subjects affected / exposed	0 / 8 (0.00%)	0 / 19 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Malpositioned teeth			
subjects affected / exposed	0 / 8 (0.00%)	0 / 19 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Mouth ulceration			
subjects affected / exposed	0 / 8 (0.00%)	0 / 19 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Tooth demineralisation			
subjects affected / exposed	1 / 8 (12.50%)	0 / 19 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Tooth malformation			
subjects affected / exposed	0 / 8 (0.00%)	0 / 19 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Toothache			
subjects affected / exposed	0 / 8 (0.00%)	0 / 19 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Hepatobiliary disorders			
Hyperbilirubinaemia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 19 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	2
Hypertransaminasaemia			
subjects affected / exposed	0 / 8 (0.00%)	1 / 19 (5.26%)	0 / 16 (0.00%)
occurrences (all)	0	2	0

Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	1 / 8 (12.50%)	0 / 19 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Urticaria			
subjects affected / exposed	0 / 8 (0.00%)	0 / 19 (0.00%)	2 / 16 (12.50%)
occurrences (all)	0	0	2
Dermatitis			
subjects affected / exposed	0 / 8 (0.00%)	2 / 19 (10.53%)	0 / 16 (0.00%)
occurrences (all)	0	2	0
Miliaria			
subjects affected / exposed	0 / 8 (0.00%)	2 / 19 (10.53%)	0 / 16 (0.00%)
occurrences (all)	0	2	0
Acanthosis nigricans			
subjects affected / exposed	0 / 8 (0.00%)	0 / 19 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Dermatitis contact			
subjects affected / exposed	0 / 8 (0.00%)	0 / 19 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Ecchymosis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 19 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Erythema			
subjects affected / exposed	0 / 8 (0.00%)	0 / 19 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Pityriasis rosea			
subjects affected / exposed	0 / 8 (0.00%)	0 / 19 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Pruritus			
subjects affected / exposed	0 / 8 (0.00%)	0 / 19 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Skin reaction			
subjects affected / exposed	0 / 8 (0.00%)	1 / 19 (5.26%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Sweat discolouration			

subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	1 / 19 (5.26%) 1	0 / 16 (0.00%) 0
Rash erythematous subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	0 / 19 (0.00%) 0	0 / 16 (0.00%) 0
Renal and urinary disorders			
Haematuria subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	1 / 19 (5.26%) 1	0 / 16 (0.00%) 0
Pollakiuria subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	1 / 19 (5.26%) 1	0 / 16 (0.00%) 0
Urinary incontinence subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	0 / 19 (0.00%) 0	0 / 16 (0.00%) 0
Musculoskeletal and connective tissue disorders			
Pain in extremity subjects affected / exposed occurrences (all)	2 / 8 (25.00%) 2	3 / 19 (15.79%) 7	8 / 16 (50.00%) 16
Arthralgia subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	3 / 19 (15.79%) 4	2 / 16 (12.50%) 2
Back pain subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	1 / 19 (5.26%) 1	2 / 16 (12.50%) 5
Muscle spasms subjects affected / exposed occurrences (all)	1 / 8 (12.50%) 1	0 / 19 (0.00%) 0	1 / 16 (6.25%) 1
Neck pain subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	0 / 19 (0.00%) 0	1 / 16 (6.25%) 1
Torticollis subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	1 / 19 (5.26%) 1	0 / 16 (0.00%) 0
Knee deformity			

subjects affected / exposed	0 / 8 (0.00%)	0 / 19 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Muscle fatigue			
subjects affected / exposed	0 / 8 (0.00%)	0 / 19 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Muscle twitching			
subjects affected / exposed	0 / 8 (0.00%)	0 / 19 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Muscular weakness			
subjects affected / exposed	0 / 8 (0.00%)	0 / 19 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Musculoskeletal discomfort			
subjects affected / exposed	0 / 8 (0.00%)	1 / 19 (5.26%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Myalgia			
subjects affected / exposed	0 / 8 (0.00%)	1 / 19 (5.26%)	0 / 16 (0.00%)
occurrences (all)	0	5	0
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	4 / 8 (50.00%)	9 / 19 (47.37%)	7 / 16 (43.75%)
occurrences (all)	5	16	25
COVID-19			
subjects affected / exposed	1 / 8 (12.50%)	8 / 19 (42.11%)	8 / 16 (50.00%)
occurrences (all)	1	9	9
Ear infection			
subjects affected / exposed	3 / 8 (37.50%)	3 / 19 (15.79%)	2 / 16 (12.50%)
occurrences (all)	11	3	5
Rhinitis			
subjects affected / exposed	0 / 8 (0.00%)	2 / 19 (10.53%)	4 / 16 (25.00%)
occurrences (all)	0	3	5
Viral infection			
subjects affected / exposed	1 / 8 (12.50%)	2 / 19 (10.53%)	1 / 16 (6.25%)
occurrences (all)	1	4	1
Upper respiratory tract infection			
subjects affected / exposed	3 / 8 (37.50%)	1 / 19 (5.26%)	1 / 16 (6.25%)
occurrences (all)	4	1	1

Gastroenteritis			
subjects affected / exposed	0 / 8 (0.00%)	2 / 19 (10.53%)	2 / 16 (12.50%)
occurrences (all)	0	2	2
Tonsillitis			
subjects affected / exposed	0 / 8 (0.00%)	2 / 19 (10.53%)	1 / 16 (6.25%)
occurrences (all)	0	2	1
Gastroenteritis viral			
subjects affected / exposed	0 / 8 (0.00%)	0 / 19 (0.00%)	2 / 16 (12.50%)
occurrences (all)	0	0	2
Urinary tract infection			
subjects affected / exposed	1 / 8 (12.50%)	0 / 19 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Varicella			
subjects affected / exposed	0 / 8 (0.00%)	1 / 19 (5.26%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Asymptomatic COVID-19			
subjects affected / exposed	0 / 8 (0.00%)	1 / 19 (5.26%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Conjunctivitis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 19 (0.00%)	2 / 16 (12.50%)
occurrences (all)	0	0	2
Croup infectious			
subjects affected / exposed	0 / 8 (0.00%)	0 / 19 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Influenza			
subjects affected / exposed	0 / 8 (0.00%)	0 / 19 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Molluscum contagiosum			
subjects affected / exposed	0 / 8 (0.00%)	1 / 19 (5.26%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Otitis media			
subjects affected / exposed	0 / 8 (0.00%)	0 / 19 (0.00%)	2 / 16 (12.50%)
occurrences (all)	0	0	2
Pharyngitis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 19 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	4

Tooth abscess			
subjects affected / exposed	0 / 8 (0.00%)	0 / 19 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Viral upper respiratory tract infection			
subjects affected / exposed	1 / 8 (12.50%)	0 / 19 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Bacillus infection			
subjects affected / exposed	0 / 8 (0.00%)	0 / 19 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Beta haemolytic streptococcal infection			
subjects affected / exposed	0 / 8 (0.00%)	0 / 19 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Candida infection			
subjects affected / exposed	0 / 8 (0.00%)	1 / 19 (5.26%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Coronavirus infection			
subjects affected / exposed	0 / 8 (0.00%)	1 / 19 (5.26%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Enterobiasis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 19 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Enterovirus infection			
subjects affected / exposed	0 / 8 (0.00%)	0 / 19 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Herpes zoster			
subjects affected / exposed	0 / 8 (0.00%)	0 / 19 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Infectious mononucleosis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 19 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Laryngitis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 19 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Lice infestation			

subjects affected / exposed	0 / 8 (0.00%)	0 / 19 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	8
Localised infection			
subjects affected / exposed	0 / 8 (0.00%)	0 / 19 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Lower respiratory tract infection			
subjects affected / exposed	0 / 8 (0.00%)	0 / 19 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Oral candidiasis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 19 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Otitis externa			
subjects affected / exposed	0 / 8 (0.00%)	0 / 19 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Parasitic gastroenteritis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 19 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Pharyngitis bacterial			
subjects affected / exposed	0 / 8 (0.00%)	0 / 19 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Pharyngotonsillitis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 19 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Respiratory syncytial virus infection			
subjects affected / exposed	0 / 8 (0.00%)	0 / 19 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Respiratory tract infection			
subjects affected / exposed	0 / 8 (0.00%)	0 / 19 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Scarlet fever			
subjects affected / exposed	0 / 8 (0.00%)	0 / 19 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Suspected COVID-19			
subjects affected / exposed	0 / 8 (0.00%)	1 / 19 (5.26%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Tooth infection			

subjects affected / exposed	0 / 8 (0.00%)	0 / 19 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Viral rash			
subjects affected / exposed	0 / 8 (0.00%)	0 / 19 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Fungal infection			
subjects affected / exposed	0 / 8 (0.00%)	0 / 19 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal viral infection			
subjects affected / exposed	0 / 8 (0.00%)	0 / 19 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Hand-foot-and-mouth disease			
subjects affected / exposed	0 / 8 (0.00%)	0 / 19 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Impetigo			
subjects affected / exposed	0 / 8 (0.00%)	0 / 19 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 8 (0.00%)	1 / 19 (5.26%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Vitamin D deficiency			
subjects affected / exposed	0 / 8 (0.00%)	3 / 19 (15.79%)	2 / 16 (12.50%)
occurrences (all)	0	3	2
Hypercholesterolaemia			
subjects affected / exposed	0 / 8 (0.00%)	2 / 19 (10.53%)	0 / 16 (0.00%)
occurrences (all)	0	2	0
Hyperphosphataemia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 19 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Hypoglycaemia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 19 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Increased appetite			
subjects affected / exposed	0 / 8 (0.00%)	0 / 19 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1

Non-serious adverse events	Dose Escalation Cohort 4 (0.128 mg/kg)	Dose Escalation Cohort 5 (0.25 mg/kg)	Dose Expansion Cohort (0.25 mg/kg)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	16 / 16 (100.00%)	13 / 13 (100.00%)	12 / 12 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Cholesteatoma			
subjects affected / exposed	0 / 16 (0.00%)	0 / 13 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Enchondromatosis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 13 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Vascular disorders			
Vasculitis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 13 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Hypertension			
subjects affected / exposed	0 / 16 (0.00%)	0 / 13 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	4 / 16 (25.00%)	4 / 13 (30.77%)	2 / 12 (16.67%)
occurrences (all)	10	11	2
Fatigue			
subjects affected / exposed	1 / 16 (6.25%)	1 / 13 (7.69%)	0 / 12 (0.00%)
occurrences (all)	1	1	0
Malaise			
subjects affected / exposed	2 / 16 (12.50%)	0 / 13 (0.00%)	0 / 12 (0.00%)
occurrences (all)	3	0	0
Asthenia			
subjects affected / exposed	1 / 16 (6.25%)	0 / 13 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Influenza like illness			
subjects affected / exposed	0 / 16 (0.00%)	0 / 13 (0.00%)	2 / 12 (16.67%)
occurrences (all)	0	0	4
Catheter site pain			

subjects affected / exposed	0 / 16 (0.00%)	0 / 13 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Discomfort			
subjects affected / exposed	0 / 16 (0.00%)	0 / 13 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Facial pain			
subjects affected / exposed	0 / 16 (0.00%)	0 / 13 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Feeling of body temperature change			
subjects affected / exposed	0 / 16 (0.00%)	0 / 13 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Gait disturbance			
subjects affected / exposed	0 / 16 (0.00%)	0 / 13 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Injection site discomfort			
subjects affected / exposed	0 / 16 (0.00%)	1 / 13 (7.69%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Medical device pain			
subjects affected / exposed	0 / 16 (0.00%)	0 / 13 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Swelling			
subjects affected / exposed	1 / 16 (6.25%)	0 / 13 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Vaccination site pain			
subjects affected / exposed	1 / 16 (6.25%)	0 / 13 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Immune system disorders			
Seasonal allergy			
subjects affected / exposed	1 / 16 (6.25%)	0 / 13 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Hypersensitivity			
subjects affected / exposed	0 / 16 (0.00%)	1 / 13 (7.69%)	2 / 12 (16.67%)
occurrences (all)	0	1	2
Rhinitis allergic			
subjects affected / exposed	0 / 16 (0.00%)	0 / 13 (0.00%)	2 / 12 (16.67%)
occurrences (all)	0	0	2

Social circumstances Poor personal hygiene subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	1 / 13 (7.69%) 1	0 / 12 (0.00%) 0
Reproductive system and breast disorders Breast mass subjects affected / exposed occurrences (all) Genital labial adhesions subjects affected / exposed occurrences (all) Gynaecomastia subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0 0 / 16 (0.00%) 0 0 / 16 (0.00%) 0	0 / 13 (0.00%) 0 0 / 13 (0.00%) 0 0 / 13 (0.00%) 0	0 / 12 (0.00%) 0 0 / 12 (0.00%) 0 0 / 12 (0.00%) 0
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all) Oropharyngeal pain subjects affected / exposed occurrences (all) Epistaxis subjects affected / exposed occurrences (all) Nasal congestion subjects affected / exposed occurrences (all) Rhinorrhoea subjects affected / exposed occurrences (all) Sleep apnoea syndrome subjects affected / exposed occurrences (all) Adenoidal hypertrophy subjects affected / exposed occurrences (all)	4 / 16 (25.00%) 8 2 / 16 (12.50%) 2 1 / 16 (6.25%) 3 0 / 16 (0.00%) 0 0 / 16 (0.00%) 0 0 / 16 (0.00%) 0 0 / 16 (0.00%) 0	3 / 13 (23.08%) 3 1 / 13 (7.69%) 1 2 / 13 (15.38%) 6 0 / 13 (0.00%) 0 1 / 13 (7.69%) 3 0 / 13 (0.00%) 0 0 / 13 (0.00%) 0	2 / 12 (16.67%) 6 1 / 12 (8.33%) 1 1 / 12 (8.33%) 2 3 / 12 (25.00%) 13 1 / 12 (8.33%) 2 2 / 12 (16.67%) 2 0 / 12 (0.00%) 0

Aphonia			
subjects affected / exposed	1 / 16 (6.25%)	0 / 13 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Asthma			
subjects affected / exposed	1 / 16 (6.25%)	0 / 13 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Bronchospasm			
subjects affected / exposed	1 / 16 (6.25%)	0 / 13 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Influenza			
subjects affected / exposed	1 / 16 (6.25%)	0 / 13 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Pharyngeal erythema			
subjects affected / exposed	1 / 16 (6.25%)	0 / 13 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Sneezing			
subjects affected / exposed	0 / 16 (0.00%)	1 / 13 (7.69%)	1 / 12 (8.33%)
occurrences (all)	0	1	1
Tonsillar hypertrophy			
subjects affected / exposed	0 / 16 (0.00%)	0 / 13 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Nasal discomfort			
subjects affected / exposed	0 / 16 (0.00%)	0 / 13 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Psychiatric disorders			
Attention deficit hyperactivity disorder			
subjects affected / exposed	0 / 16 (0.00%)	2 / 13 (15.38%)	0 / 12 (0.00%)
occurrences (all)	0	2	0
Anger			
subjects affected / exposed	0 / 16 (0.00%)	0 / 13 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Anxiety			
subjects affected / exposed	0 / 16 (0.00%)	0 / 13 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Depressed mood			

subjects affected / exposed	1 / 16 (6.25%)	0 / 13 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Enuresis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 13 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Intentional self-injury			
subjects affected / exposed	0 / 16 (0.00%)	0 / 13 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Sleep disorder			
subjects affected / exposed	0 / 16 (0.00%)	1 / 13 (7.69%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Sleep terror			
subjects affected / exposed	1 / 16 (6.25%)	0 / 13 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Stress			
subjects affected / exposed	0 / 16 (0.00%)	0 / 13 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Investigations			
Vitamin D decreased			
subjects affected / exposed	1 / 16 (6.25%)	1 / 13 (7.69%)	0 / 12 (0.00%)
occurrences (all)	1	1	0
Blood 25-hydroxycholecalciferol decreased			
subjects affected / exposed	1 / 16 (6.25%)	0 / 13 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Blood cholesterol increased			
subjects affected / exposed	0 / 16 (0.00%)	0 / 13 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Blood calcium decreased			
subjects affected / exposed	0 / 16 (0.00%)	0 / 13 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Blood phosphorus increased			
subjects affected / exposed	0 / 16 (0.00%)	1 / 13 (7.69%)	1 / 12 (8.33%)
occurrences (all)	0	1	1
Blood creatinine decreased			

subjects affected / exposed	1 / 16 (6.25%)	0 / 13 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Blood glucose increased			
subjects affected / exposed	0 / 16 (0.00%)	0 / 13 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Blood triglycerides increased			
subjects affected / exposed	0 / 16 (0.00%)	0 / 13 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Blood urine present			
subjects affected / exposed	1 / 16 (6.25%)	0 / 13 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Electrocardiogram QT prolonged			
subjects affected / exposed	0 / 16 (0.00%)	1 / 13 (7.69%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Hepatic enzyme increased			
subjects affected / exposed	0 / 16 (0.00%)	1 / 13 (7.69%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Platelet count decreased			
subjects affected / exposed	0 / 16 (0.00%)	0 / 13 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Vitamin D increased			
subjects affected / exposed	0 / 16 (0.00%)	1 / 13 (7.69%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Platelet count increased			
subjects affected / exposed	0 / 16 (0.00%)	0 / 13 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Injury, poisoning and procedural complications			
Arthropod bite			
subjects affected / exposed	0 / 16 (0.00%)	0 / 13 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Fall			
subjects affected / exposed	0 / 16 (0.00%)	1 / 13 (7.69%)	3 / 12 (25.00%)
occurrences (all)	0	1	4
Head injury			

subjects affected / exposed	0 / 16 (0.00%)	0 / 13 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Wound			
subjects affected / exposed	0 / 16 (0.00%)	1 / 13 (7.69%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Ligament sprain			
subjects affected / exposed	1 / 16 (6.25%)	0 / 13 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Procedural pain			
subjects affected / exposed	0 / 16 (0.00%)	1 / 13 (7.69%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Face injury			
subjects affected / exposed	0 / 16 (0.00%)	1 / 13 (7.69%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Foreign body ingestion			
subjects affected / exposed	0 / 16 (0.00%)	0 / 13 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Incision site rash			
subjects affected / exposed	0 / 16 (0.00%)	0 / 13 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Joint injury			
subjects affected / exposed	0 / 16 (0.00%)	0 / 13 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Lip injury			
subjects affected / exposed	0 / 16 (0.00%)	1 / 13 (7.69%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Skin abrasion			
subjects affected / exposed	0 / 16 (0.00%)	1 / 13 (7.69%)	1 / 12 (8.33%)
occurrences (all)	0	1	1
Foreign body in ear			
subjects affected / exposed	0 / 16 (0.00%)	0 / 13 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Skin laceration			
subjects affected / exposed	0 / 16 (0.00%)	0 / 13 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Venomous sting			

subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	0 / 13 (0.00%) 0	0 / 12 (0.00%) 0
Congenital, familial and genetic disorders			
Anodontia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 13 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Tooth hypoplasia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 13 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Hypodontia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 13 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Cardiac disorders			
Defect conduction intraventricular			
subjects affected / exposed	0 / 16 (0.00%)	0 / 13 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Tachycardia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 13 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Headache			
subjects affected / exposed	4 / 16 (25.00%)	6 / 13 (46.15%)	6 / 12 (50.00%)
occurrences (all)	16	23	10
Dizziness			
subjects affected / exposed	0 / 16 (0.00%)	0 / 13 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Hypoaesthesia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 13 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Dysgeusia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 13 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Praesthesia			
subjects affected / exposed	1 / 16 (6.25%)	0 / 13 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Presyncope			

subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	0 / 13 (0.00%) 0	0 / 12 (0.00%) 0
Tremor subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	0 / 13 (0.00%) 0	0 / 12 (0.00%) 0
Blood and lymphatic system disorders			
Lymphadenopathy subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 3	0 / 13 (0.00%) 0	0 / 12 (0.00%) 0
Leukopenia subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	0 / 13 (0.00%) 0	0 / 12 (0.00%) 0
Lymphadenitis subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	0 / 13 (0.00%) 0	0 / 12 (0.00%) 0
Normocytic anaemia subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	0 / 13 (0.00%) 0	0 / 12 (0.00%) 0
Anaemia subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	0 / 13 (0.00%) 0	1 / 12 (8.33%) 1
Iron deficiency anaemia subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	0 / 13 (0.00%) 0	1 / 12 (8.33%) 2
Neutropenia subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	0 / 13 (0.00%) 0	1 / 12 (8.33%) 1
Ear and labyrinth disorders			
Ear pain subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1	2 / 13 (15.38%) 2	2 / 12 (16.67%) 3
Otitis media subjects affected / exposed occurrences (all)	2 / 16 (12.50%) 4	2 / 13 (15.38%) 1	2 / 12 (16.67%) 2
Excessive cerumen production			

subjects affected / exposed	1 / 16 (6.25%)	0 / 13 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Deafness			
subjects affected / exposed	0 / 16 (0.00%)	0 / 13 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Deafness neurosensory			
subjects affected / exposed	0 / 16 (0.00%)	0 / 13 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Ear discomfort			
subjects affected / exposed	0 / 16 (0.00%)	1 / 13 (7.69%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Motion sickness			
subjects affected / exposed	0 / 16 (0.00%)	0 / 13 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Otitis media acute			
subjects affected / exposed	1 / 16 (6.25%)	0 / 13 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Otorrhoea			
subjects affected / exposed	0 / 16 (0.00%)	1 / 13 (7.69%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Vertigo			
subjects affected / exposed	0 / 16 (0.00%)	0 / 13 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Hypoacusis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 13 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Inner ear disorder			
subjects affected / exposed	0 / 16 (0.00%)	0 / 13 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Middle ear effusion			
subjects affected / exposed	0 / 16 (0.00%)	0 / 13 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Eye disorders			
Optic atrophy			
subjects affected / exposed	1 / 16 (6.25%)	0 / 13 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0

Amblyopia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 13 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Chalazion			
subjects affected / exposed	1 / 16 (6.25%)	0 / 13 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Eye discharge			
subjects affected / exposed	1 / 16 (6.25%)	0 / 13 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Eye pruritus			
subjects affected / exposed	0 / 16 (0.00%)	0 / 13 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Hypermetropia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 13 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Lacrimation increased			
subjects affected / exposed	0 / 16 (0.00%)	0 / 13 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Strabismus			
subjects affected / exposed	0 / 16 (0.00%)	0 / 13 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Vision blurred			
subjects affected / exposed	0 / 16 (0.00%)	0 / 13 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Visual impairment			
subjects affected / exposed	0 / 16 (0.00%)	0 / 13 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Conjunctivitis allergic			
subjects affected / exposed	0 / 16 (0.00%)	0 / 13 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	8 / 16 (50.00%)	4 / 13 (30.77%)	2 / 12 (16.67%)
occurrences (all)	17	9	5
Abdominal pain			

subjects affected / exposed	4 / 16 (25.00%)	2 / 13 (15.38%)	1 / 12 (8.33%)
occurrences (all)	4	5	1
Diarrhoea			
subjects affected / exposed	3 / 16 (18.75%)	3 / 13 (23.08%)	1 / 12 (8.33%)
occurrences (all)	4	5	1
Nausea			
subjects affected / exposed	3 / 16 (18.75%)	2 / 13 (15.38%)	0 / 12 (0.00%)
occurrences (all)	3	3	0
Abdominal pain upper			
subjects affected / exposed	2 / 16 (12.50%)	1 / 13 (7.69%)	1 / 12 (8.33%)
occurrences (all)	2	1	1
Constipation			
subjects affected / exposed	1 / 16 (6.25%)	0 / 13 (0.00%)	1 / 12 (8.33%)
occurrences (all)	1	0	1
Dental caries			
subjects affected / exposed	0 / 16 (0.00%)	0 / 13 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Dyspepsia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 13 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Odynophagia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 13 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Tooth development disorder			
subjects affected / exposed	0 / 16 (0.00%)	0 / 13 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Abdominal discomfort			
subjects affected / exposed	0 / 16 (0.00%)	0 / 13 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Aphthous ulcer			
subjects affected / exposed	1 / 16 (6.25%)	0 / 13 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Faeces soft			
subjects affected / exposed	0 / 16 (0.00%)	0 / 13 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Flatulence			

subjects affected / exposed	0 / 16 (0.00%)	0 / 13 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorder			
subjects affected / exposed	0 / 16 (0.00%)	1 / 13 (7.69%)	0 / 12 (0.00%)
occurrences (all)	0	2	0
Gingival bleeding			
subjects affected / exposed	0 / 16 (0.00%)	0 / 13 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Gastroesophageal reflux disease			
subjects affected / exposed	0 / 16 (0.00%)	0 / 13 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Gingival pain			
subjects affected / exposed	0 / 16 (0.00%)	1 / 13 (7.69%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Lip haemorrhage			
subjects affected / exposed	1 / 16 (6.25%)	0 / 13 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Malocclusion			
subjects affected / exposed	0 / 16 (0.00%)	0 / 13 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Malpositioned teeth			
subjects affected / exposed	0 / 16 (0.00%)	0 / 13 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Mouth ulceration			
subjects affected / exposed	0 / 16 (0.00%)	1 / 13 (7.69%)	0 / 12 (0.00%)
occurrences (all)	0	2	0
Tooth demineralisation			
subjects affected / exposed	0 / 16 (0.00%)	0 / 13 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Tooth malformation			
subjects affected / exposed	0 / 16 (0.00%)	1 / 13 (7.69%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Toothache			
subjects affected / exposed	0 / 16 (0.00%)	1 / 13 (7.69%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Hepatobiliary disorders			

Hyperbilirubinaemia subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	0 / 13 (0.00%) 0	0 / 12 (0.00%) 0
Hypertransaminasaemia subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	0 / 13 (0.00%) 0	0 / 12 (0.00%) 0
Skin and subcutaneous tissue disorders			
Rash subjects affected / exposed occurrences (all)	2 / 16 (12.50%) 2	1 / 13 (7.69%) 1	0 / 12 (0.00%) 0
Urticaria subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 3	0 / 13 (0.00%) 0	0 / 12 (0.00%) 0
Dermatitis subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	0 / 13 (0.00%) 0	1 / 12 (8.33%) 1
Miliaria subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	0 / 13 (0.00%) 0	0 / 12 (0.00%) 0
Acanthosis nigricans subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	1 / 13 (7.69%) 1	0 / 12 (0.00%) 0
Dermatitis contact subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	0 / 13 (0.00%) 0	0 / 12 (0.00%) 0
Ecchymosis subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	1 / 13 (7.69%) 1	0 / 12 (0.00%) 0
Erythema subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1	0 / 13 (0.00%) 0	0 / 12 (0.00%) 0
Pityriasis rosea subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	1 / 13 (7.69%) 1	0 / 12 (0.00%) 0
Pruritus			

subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	0 / 13 (0.00%) 0	0 / 12 (0.00%) 0
Skin reaction subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	0 / 13 (0.00%) 0	0 / 12 (0.00%) 0
Sweat discolouration subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	0 / 13 (0.00%) 0	0 / 12 (0.00%) 0
Rash erythematous subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	0 / 13 (0.00%) 0	1 / 12 (8.33%) 1
Renal and urinary disorders Haematuria subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	0 / 13 (0.00%) 0	0 / 12 (0.00%) 0
Pollakiuria subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	0 / 13 (0.00%) 0	0 / 12 (0.00%) 0
Urinary incontinence subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1	0 / 13 (0.00%) 0	0 / 12 (0.00%) 0
Musculoskeletal and connective tissue disorders Pain in extremity subjects affected / exposed occurrences (all)	2 / 16 (12.50%) 3	4 / 13 (30.77%) 5	2 / 12 (16.67%) 3
Arthralgia subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	1 / 13 (7.69%) 1	1 / 12 (8.33%) 1
Back pain subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1	1 / 13 (7.69%) 1	1 / 12 (8.33%) 1
Muscle spasms subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	0 / 13 (0.00%) 0	0 / 12 (0.00%) 0
Neck pain			

subjects affected / exposed	0 / 16 (0.00%)	1 / 13 (7.69%)	1 / 12 (8.33%)
occurrences (all)	0	1	1
Torticollis			
subjects affected / exposed	1 / 16 (6.25%)	0 / 13 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Knee deformity			
subjects affected / exposed	0 / 16 (0.00%)	0 / 13 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Muscle fatigue			
subjects affected / exposed	0 / 16 (0.00%)	0 / 13 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Muscle twitching			
subjects affected / exposed	0 / 16 (0.00%)	0 / 13 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Muscular weakness			
subjects affected / exposed	0 / 16 (0.00%)	0 / 13 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal discomfort			
subjects affected / exposed	0 / 16 (0.00%)	0 / 13 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Myalgia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 13 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	4 / 16 (25.00%)	5 / 13 (38.46%)	6 / 12 (50.00%)
occurrences (all)	8	9	7
COVID-19			
subjects affected / exposed	5 / 16 (31.25%)	1 / 13 (7.69%)	0 / 12 (0.00%)
occurrences (all)	5	1	0
Ear infection			
subjects affected / exposed	7 / 16 (43.75%)	4 / 13 (30.77%)	0 / 12 (0.00%)
occurrences (all)	10	7	0
Rhinitis			
subjects affected / exposed	3 / 16 (18.75%)	2 / 13 (15.38%)	0 / 12 (0.00%)
occurrences (all)	6	4	0

Viral infection			
subjects affected / exposed	3 / 16 (18.75%)	4 / 13 (30.77%)	3 / 12 (25.00%)
occurrences (all)	4	5	3
Upper respiratory tract infection			
subjects affected / exposed	3 / 16 (18.75%)	2 / 13 (15.38%)	2 / 12 (16.67%)
occurrences (all)	3	2	3
Gastroenteritis			
subjects affected / exposed	1 / 16 (6.25%)	1 / 13 (7.69%)	0 / 12 (0.00%)
occurrences (all)	1	1	0
Tonsillitis			
subjects affected / exposed	1 / 16 (6.25%)	0 / 13 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Gastroenteritis viral			
subjects affected / exposed	0 / 16 (0.00%)	1 / 13 (7.69%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Urinary tract infection			
subjects affected / exposed	0 / 16 (0.00%)	2 / 13 (15.38%)	0 / 12 (0.00%)
occurrences (all)	0	2	0
Varicella			
subjects affected / exposed	2 / 16 (12.50%)	0 / 13 (0.00%)	0 / 12 (0.00%)
occurrences (all)	2	0	0
Asymptomatic COVID-19			
subjects affected / exposed	1 / 16 (6.25%)	0 / 13 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Conjunctivitis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 13 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Croup infectious			
subjects affected / exposed	1 / 16 (6.25%)	1 / 13 (7.69%)	0 / 12 (0.00%)
occurrences (all)	3	1	0
Influenza			
subjects affected / exposed	0 / 16 (0.00%)	1 / 13 (7.69%)	0 / 12 (0.00%)
occurrences (all)	0	2	0
Molluscum contagiosum			
subjects affected / exposed	0 / 16 (0.00%)	0 / 13 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1

Otitis media			
subjects affected / exposed	0 / 16 (0.00%)	0 / 13 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Pharyngitis			
subjects affected / exposed	1 / 16 (6.25%)	0 / 13 (0.00%)	1 / 12 (8.33%)
occurrences (all)	1	0	1
Tooth abscess			
subjects affected / exposed	2 / 16 (12.50%)	0 / 13 (0.00%)	0 / 12 (0.00%)
occurrences (all)	2	0	0
Viral upper respiratory tract infection			
subjects affected / exposed	1 / 16 (6.25%)	0 / 13 (0.00%)	1 / 12 (8.33%)
occurrences (all)	1	0	1
Bacillus infection			
subjects affected / exposed	1 / 16 (6.25%)	0 / 13 (0.00%)	0 / 12 (0.00%)
occurrences (all)	2	0	0
Beta haemolytic streptococcal infection			
subjects affected / exposed	0 / 16 (0.00%)	1 / 13 (7.69%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Candida infection			
subjects affected / exposed	0 / 16 (0.00%)	0 / 13 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Coronavirus infection			
subjects affected / exposed	0 / 16 (0.00%)	0 / 13 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Enterobiasis			
subjects affected / exposed	1 / 16 (6.25%)	0 / 13 (0.00%)	1 / 12 (8.33%)
occurrences (all)	1	0	1
Enterovirus infection			
subjects affected / exposed	0 / 16 (0.00%)	0 / 13 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Herpes zoster			
subjects affected / exposed	1 / 16 (6.25%)	0 / 13 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Infectious mononucleosis			

subjects affected / exposed	0 / 16 (0.00%)	0 / 13 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Laryngitis			
subjects affected / exposed	0 / 16 (0.00%)	1 / 13 (7.69%)	0 / 12 (0.00%)
occurrences (all)	0	2	0
Lice infestation			
subjects affected / exposed	0 / 16 (0.00%)	0 / 13 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Localised infection			
subjects affected / exposed	0 / 16 (0.00%)	1 / 13 (7.69%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Lower respiratory tract infection			
subjects affected / exposed	0 / 16 (0.00%)	1 / 13 (7.69%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Oral candidiasis			
subjects affected / exposed	1 / 16 (6.25%)	0 / 13 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Otitis externa			
subjects affected / exposed	0 / 16 (0.00%)	0 / 13 (0.00%)	2 / 12 (16.67%)
occurrences (all)	0	0	2
Parasitic gastroenteritis			
subjects affected / exposed	1 / 16 (6.25%)	0 / 13 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Pharyngitis bacterial			
subjects affected / exposed	0 / 16 (0.00%)	0 / 13 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Pharyngotonsillitis			
subjects affected / exposed	0 / 16 (0.00%)	1 / 13 (7.69%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Respiratory syncytial virus infection			
subjects affected / exposed	1 / 16 (6.25%)	0 / 13 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Respiratory tract infection			
subjects affected / exposed	1 / 16 (6.25%)	0 / 13 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Scarlet fever			

subjects affected / exposed	1 / 16 (6.25%)	0 / 13 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Suspected COVID-19			
subjects affected / exposed	0 / 16 (0.00%)	0 / 13 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Tooth infection			
subjects affected / exposed	0 / 16 (0.00%)	0 / 13 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Viral rash			
subjects affected / exposed	0 / 16 (0.00%)	1 / 13 (7.69%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Fungal infection			
subjects affected / exposed	0 / 16 (0.00%)	0 / 13 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Gastrointestinal viral infection			
subjects affected / exposed	0 / 16 (0.00%)	0 / 13 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	2
Hand-foot-and-mouth disease			
subjects affected / exposed	0 / 16 (0.00%)	0 / 13 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Impetigo			
subjects affected / exposed	0 / 16 (0.00%)	0 / 13 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	2 / 16 (12.50%)	1 / 13 (7.69%)	0 / 12 (0.00%)
occurrences (all)	2	1	0
Vitamin D deficiency			
subjects affected / exposed	0 / 16 (0.00%)	0 / 13 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Hypercholesterolaemia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 13 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Hyperphosphataemia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 13 (0.00%)	2 / 12 (16.67%)
occurrences (all)	0	0	2

Hypoglycaemia			
subjects affected / exposed	1 / 16 (6.25%)	0 / 13 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Increased appetite			
subjects affected / exposed	0 / 16 (0.00%)	0 / 13 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
15 October 2020	• PK Substudy was added. • Assessment of biomarkers to evaluate infigratinib activity was added. • Subsection to define adverse events of special interest (AESIs) and a requirement for expedited reporting of these events was added. • Collection of PK and biomarker sample at Month 3 was added. • Collection of laboratory sample at EOT/ET visit was added. • Exclusion of participants with functioning ventriculo-peritoneal shunt was added. • Assessment of estimated glomerular filtration rate (eGFR) was added. • List of prohibited medications and medications to be used with caution per the most recently available nonclinical and clinical data was updated. • Number of participants to be enrolled was updated from 5 in cohort 1, to 3 in cohort 1, 19 in cohort 2, 16 in cohort 3 and 16 in cohort 4.
23 May 2022	• Assessment of health-related quality of life (Quality of Life in Short Stature Youth (QoLISSY)), overall body pain (Pain-Numeric Rating Scale (NRS)), and functional abilities (Functional Independence Measure for Children (WeeFIM)), were added, and it was clarified that Pediatric Quality of Life questionnaire (PedsQL) would be assessed in all participants but QoLISSY, Pain-NRS, and WeeFIM would only be assessed in Dose Expansion participants. • It was clarified that samples for biomarkers of infigratinib activity would be collected for Dose Escalation and PK Substudy Cohorts 2-4 only. • Protocol was revised to allow enrollment of additional participants (up to 30) if needed by sponsor and when maximum dose not reached. • Protocol was revised to allow additional PK cohort(s). • Duration of study was revised from 3 years to 5 years. • Exclusion criterion #3 was modified to add use of country-specific height for age tables when determining if participant's height was <-2 or $>+2$ SDs for age and sex. • Exclusion criterion #10 was modified to allow participation of children with vitamin D supplementation initiated ≥ 1 month before screening. • Exclusion criterion #18 was modified to increase the time participants must not have experienced bone fractures from 6 months to 12 months prior to screening. • Statement was added that study drug formulation may be updated following identification of dose to explore further. • Vitamin D analogues, calcidiol, and medications that alter the pH of gastrointestinal tract were added as prohibited medications. • Deletion of phosphorus value specified in criteria for dose decrease/discontinuation in individual participants to include the above the age-adjusted upper limit of normal (ULN) for laboratory reporting. • Cohort 5 was added with 12 participants to be enrolled.

10 March 2023	• Added details for newly introduced drug presentation (sprinkle capsules) for use in Dose Expansion. • Added language defining the screening period as a 28-day window and that the baseline period was a 14-day window starting after enrollment. • Clarified that the last dose of study drug should be administered the day before the EOT/ET visit. • Added that Pain-NRS child report should be completed by children 6 years of age or older and parent report should be completed by all parents regardless of age of participating child. • Added that QoLISSY child report should be completed by children 8 years of age or older and parent report completed by parents of children 4 years or older. • Specified that retraining of subject and parent/legally authorized representative (LAR) should be implemented by site staff if there were issues with drug accountability. • Defined a phosphorus level (>6.0 mg/dL) which could result in dose reduction/discontinuation. • Number of participants to be enrolled was updated to 13 in the dose escalation cohort.
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Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported