



Clinical trial results:

An Open-Label, Multi-Center, Single Arm Study to Evaluate the Safety and Tolerability of Intravenous Zanamivir in the Treatment of Hospitalized Adult, Adolescent and Pediatric Subjects with Confirmed Influenza Infection

Summary

EudraCT number	2009-016035-35
Trial protocol	FR ES DE GB Outside EU/EEA
Global end of trial date	13 February 2015

Results information

Result version number	v1 (current)
This version publication date	10 July 2016
First version publication date	10 July 2016

Trial information

Trial identification

Sponsor protocol code	NAI113678
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Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	GlaxoSmithKline
Sponsor organisation address	980 Great West Road, Brentford, Middlesex, United Kingdom,
Public contact	GSK Response Center, GlaxoSmithKline, 1 866-435-7343,
Scientific contact	GSK Response Center, GlaxoSmithKline, 1 866-435-7343,

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMA-001318-PIP01-12
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	24 June 2015
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	13 February 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the safety and tolerability of IV zanamivir in the treatment of hospitalized adult, adolescent and pediatric subjects with influenza infection.

Protection of trial subjects:

N/A

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	20 November 2009
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Spain: 32
Country: Number of subjects enrolled	United Kingdom: 6
Country: Number of subjects enrolled	France: 36
Country: Number of subjects enrolled	Thailand: 12
Country: Number of subjects enrolled	Australia: 9
Country: Number of subjects enrolled	South Africa: 1
Country: Number of subjects enrolled	Canada: 6
Country: Number of subjects enrolled	Russian Federation: 1
Country: Number of subjects enrolled	United States: 95
Country: Number of subjects enrolled	Japan: 3
Worldwide total number of subjects	201
EEA total number of subjects	74

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	18

months)	
Children (2-11 years)	36
Adolescents (12-17 years)	17
Adults (18-64 years)	106
From 65 to 84 years	23
85 years and over	1

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Male or female participants who were ≥ 6 months of age, hospitalized with laboratory-confirmed influenza, and able to receive study drug within 7 days of influenza symptom onset were enrolled in the study.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Cohort 6: Adults (18 years and older)

Arm description:

Participants ≥ 18 years of age received 600 milligrams (mg) zanamivir by intravenous (IV) infusion over 30 minutes twice daily, adjusted for renal function, for 5 days. Treatment could have been extended for up to 5 additional days if viral shedding or clinical symptoms warranted further treatment.

Arm type	Experimental
Investigational medicinal product name	zanamivir
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

600 mg twice daily, adjusted for renal function

Arm title	Cohort 1: Infants (6 months to <1 year of age)
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Arm description:

Participants 6 months to <1 year of age received 14 mg per kilogram (mg/kg) zanamivir by IV infusion over 30 minutes twice daily, adjusted for renal function, for 5 days. Treatment could have been extended for up to 5 additional days if viral shedding or clinical symptoms warranted further treatment.

Arm type	Experimental
Investigational medicinal product name	zanamivir
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

14 mg/kg twice daily, adjusted for renal function

Arm title	Cohort 2: Children (1 to <2 years of age)
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Arm description:

Participants 1 year to <2 years of age received 14 mg/kg zanamivir by IV infusion over 30 minutes twice daily, adjusted for renal function, for 5 days. Treatment could have been extended for up to 5 additional days if viral shedding or clinical symptoms warranted further treatment.

Arm type	Experimental
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Investigational medicinal product name	zanamivir
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use
Dosage and administration details:	
14 mg/kg twice daily, adjusted for renal function	
Arm title	Cohort 3: Children (2 to <6 years of age)

Arm description:

Participants 2 years to <6 years of age received 14 mg/kg zanamivir with a maximum dose of 600 mg by IV infusion over 30 minutes twice daily, adjusted for renal function, for 5 days. Treatment could have been extended for up to 5 additional days if viral shedding or clinical symptoms warranted further treatment.

Arm type	Experimental
Investigational medicinal product name	zanamivir
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use
Dosage and administration details:	
14 mg/kg twice daily, adjusted for renal function	
Arm title	Cohort 4: Children (6 to <13 years of age)

Arm description:

Participants 6 years to <13 years of age received 12 mg/kg zanamivir with a maximum dose of 600 mg by IV infusion over 30 minutes twice daily, adjusted for renal function, for 5 days. Treatment could have been extended for up to 5 additional days if viral shedding or clinical symptoms warranted further treatment.

Arm type	Experimental
Investigational medicinal product name	zanamivir
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use
Dosage and administration details:	
12 mg/kg (maximum dose of 600 mg) twice daily, adjusted for renal function	
Arm title	Cohort 5: Adolescents (13 to <18 years of age)

Arm description:

Participants 13 to <18 years of age received 12 mg/kg zanamivir with a maximum dose of 600 mg by IV infusion over 30 minutes twice daily, adjusted for renal function, for 5 days. Treatment could have been extended for up to 5 additional days if viral shedding or clinical symptoms warranted further treatment.

Arm type	Experimental
Investigational medicinal product name	zanamivir
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use
Dosage and administration details:	
12 mg/kg (maximum dose of 600 mg) twice daily, adjusted for renal function	

Number of subjects in period 1	Cohort 6: Adults (18 years and older)	Cohort 1: Infants (6 months to <1 year of age)	Cohort 2: Children (1 to <2 years of age)
Started	130	7	11
Completed	107	7	9
Not completed	23	0	2
Adverse event, serious fatal	20	-	1
Consent withdrawn by subject	1	-	-
Physician decision	1	-	-
Lost to follow-up	1	-	1

Number of subjects in period 1	Cohort 3: Children (2 to <6 years of age)	Cohort 4: Children (6 to <13 years of age)	Cohort 5: Adolescents (13 to <18 years of age)
Started	12	27	14
Completed	12	26	11
Not completed	0	1	3
Adverse event, serious fatal	-	1	3
Consent withdrawn by subject	-	-	-
Physician decision	-	-	-
Lost to follow-up	-	-	-

Baseline characteristics

Reporting groups

Reporting group title	Cohort 6: Adults (18 years and older)
Reporting group description: Participants ≥ 18 years of age received 600 milligrams (mg) zanamivir by intravenous (IV) infusion over 30 minutes twice daily, adjusted for renal function, for 5 days. Treatment could have been extended for up to 5 additional days if viral shedding or clinical symptoms warranted further treatment.	
Reporting group title	Cohort 1: Infants (6 months to <1 year of age)
Reporting group description: Participants 6 months to <1 year of age received 14 mg per kilogram (mg/kg) zanamivir by IV infusion over 30 minutes twice daily, adjusted for renal function, for 5 days. Treatment could have been extended for up to 5 additional days if viral shedding or clinical symptoms warranted further treatment.	
Reporting group title	Cohort 2: Children (1 to <2 years of age)
Reporting group description: Participants 1 year to <2 years of age received 14 mg/kg zanamivir by IV infusion over 30 minutes twice daily, adjusted for renal function, for 5 days. Treatment could have been extended for up to 5 additional days if viral shedding or clinical symptoms warranted further treatment.	
Reporting group title	Cohort 3: Children (2 to <6 years of age)
Reporting group description: Participants 2 years to <6 years of age received 14 mg/kg zanamivir with a maximum dose of 600 mg by IV infusion over 30 minutes twice daily, adjusted for renal function, for 5 days. Treatment could have been extended for up to 5 additional days if viral shedding or clinical symptoms warranted further treatment.	
Reporting group title	Cohort 4: Children (6 to <13 years of age)
Reporting group description: Participants 6 years to <13 years of age received 12 mg/kg zanamivir with a maximum dose of 600 mg by IV infusion over 30 minutes twice daily, adjusted for renal function, for 5 days. Treatment could have been extended for up to 5 additional days if viral shedding or clinical symptoms warranted further treatment.	
Reporting group title	Cohort 5: Adolescents (13 to <18 years of age)
Reporting group description: Participants 13 to <18 years of age received 12 mg/kg zanamivir with a maximum dose of 600 mg by IV infusion over 30 minutes twice daily, adjusted for renal function, for 5 days. Treatment could have been extended for up to 5 additional days if viral shedding or clinical symptoms warranted further treatment.	

Reporting group values	Cohort 6: Adults (18 years and older)	Cohort 1: Infants (6 months to <1 year of age)	Cohort 2: Children (1 to <2 years of age)
Number of subjects	130	7	11
Age categorical Units: Subjects			

Age continuous Units: years arithmetic mean standard deviation	48.3 ± 16.19	0.76 ± 0.127	1.33 ± 0.22
Gender categorical Units: Subjects Female Male	56 74	1 6	4 7
Race, Customized Units: Subjects African American/African Heritage	10	1	4

American Indian or Alaska Native	1	0	0
Asian - East Asian Heritage	4	0	0
Asian - South East Asian Heritage	10	0	0
Asian - Japanese Heritage	0	1	0
Native Hawaiian or Other Pacific Islander	0	0	0
White - Arabic/North African Heritage	6	0	0
White - White/Caucasian/European Heritage	97	5	7
Unknown	2	0	0
Mixed Race	0	0	0

Reporting group values	Cohort 3: Children (2 to <6 years of age)	Cohort 4: Children (6 to <13 years of age)	Cohort 5: Adolescents (13 to <18 years of age)
Number of subjects	12	27	14
Age categorical Units: Subjects			

Age continuous Units: years arithmetic mean standard deviation	3.74 ± 1.201	8.67 ± 1.861	15.36 ± 1.151
Gender categorical Units: Subjects			
Female	4	9	6
Male	8	18	8
Race, Customized Units: Subjects			
African American/African Heritage	1	4	3
American Indian or Alaska Native	0	0	0
Asian - East Asian Heritage	0	0	0
Asian - South East Asian Heritage	0	0	0
Asian - Japanese Heritage	2	0	0
Native Hawaiian or Other Pacific Islander	0	1	0
White - Arabic/North African Heritage	1	1	0
White - White/Caucasian/European Heritage	7	18	11
Unknown	0	1	0
Mixed Race	1	2	0

Reporting group values	Total		
Number of subjects	201		
Age categorical Units: Subjects			

Age continuous Units: years arithmetic mean standard deviation	-		
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Gender categorical			
Units: Subjects			
Female	80		
Male	121		
Race, Customized			
Units: Subjects			
African American/African Heritage	23		
American Indian or Alaska Native	1		
Asian - East Asian Heritage	4		
Asian - South East Asian Heritage	10		
Asian - Japanese Heritage	3		
Native Hawaiian or Other Pacific Islander	1		
White - Arabic/North African Heritage	8		
White - White/Caucasian/European Heritage	145		
Unknown	3		
Mixed Race	3		

End points

End points reporting groups

Reporting group title	Cohort 6: Adults (18 years and older)
Reporting group description: Participants ≥ 18 years of age received 600 milligrams (mg) zanamivir by intravenous (IV) infusion over 30 minutes twice daily, adjusted for renal function, for 5 days. Treatment could have been extended for up to 5 additional days if viral shedding or clinical symptoms warranted further treatment.	
Reporting group title	Cohort 1: Infants (6 months to <1 year of age)
Reporting group description: Participants 6 months to <1 year of age received 14 mg per kilogram (mg/kg) zanamivir by IV infusion over 30 minutes twice daily, adjusted for renal function, for 5 days. Treatment could have been extended for up to 5 additional days if viral shedding or clinical symptoms warranted further treatment.	
Reporting group title	Cohort 2: Children (1 to <2 years of age)
Reporting group description: Participants 1 year to <2 years of age received 14 mg/kg zanamivir by IV infusion over 30 minutes twice daily, adjusted for renal function, for 5 days. Treatment could have been extended for up to 5 additional days if viral shedding or clinical symptoms warranted further treatment.	
Reporting group title	Cohort 3: Children (2 to <6 years of age)
Reporting group description: Participants 2 years to <6 years of age received 14 mg/kg zanamivir with a maximum dose of 600 mg by IV infusion over 30 minutes twice daily, adjusted for renal function, for 5 days. Treatment could have been extended for up to 5 additional days if viral shedding or clinical symptoms warranted further treatment.	
Reporting group title	Cohort 4: Children (6 to <13 years of age)
Reporting group description: Participants 6 years to <13 years of age received 12 mg/kg zanamivir with a maximum dose of 600 mg by IV infusion over 30 minutes twice daily, adjusted for renal function, for 5 days. Treatment could have been extended for up to 5 additional days if viral shedding or clinical symptoms warranted further treatment.	
Reporting group title	Cohort 5: Adolescents (13 to <18 years of age)
Reporting group description: Participants 13 to <18 years of age received 12 mg/kg zanamivir with a maximum dose of 600 mg by IV infusion over 30 minutes twice daily, adjusted for renal function, for 5 days. Treatment could have been extended for up to 5 additional days if viral shedding or clinical symptoms warranted further treatment.	
Subject analysis set title	Cohort 6: Adults (18 years and older)
Subject analysis set type	Intention-to-treat
Subject analysis set description: Participants ≥ 18 years of age received 600 mg zanamivir by IV infusion over 30 minutes twice daily, adjusted for renal function, for 5 days. Treatment could have been extended for up to 5 additional days if viral shedding or clinical symptoms warranted further treatment.	
Subject analysis set title	Cohorts 1-5: Pediatrics/adolescents (6 months to <18 years)
Subject analysis set type	Intention-to-treat
Subject analysis set description: Participants 6 months to <18 years of age received 14 mg/kg zanamivir (participants from 6 months to <6 years of age) or 12 mg/kg zanamivir (participants from 6 years to <18 years of age) with a maximum dose of 600 mg by IV infusion over 30 minutes twice daily, adjusted for renal function for 5 days. Treatment could be extended for up to 5 additional days if viral shedding or clinical symptoms warranted further treatment.	
Subject analysis set title	Cohort 6: Adults (18 years and older); zanamivir ≤ 5 days
Subject analysis set type	Intention-to-treat
Subject analysis set description: Participants ≥ 18 years of age received 600 mg zanamivir by IV infusion over 30 minutes twice daily, adjusted for renal function, for 5 days.	
Subject analysis set title	Cohort 6: Adults (18 years and older); zanamivir >5 days
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Participants ≥ 18 years of age received 600 mg zanamivir by IV infusion over 30 minutes twice daily, adjusted for renal function, for >5 days and up to 10 days if viral shedding or clinical symptoms warranted further treatment.

Subject analysis set title	Cohort 1: Infants (6 months to <1 year of age)
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Participants 6 months to <1 year of age received 14 mg/kg zanamivir by IV infusion over 30 minutes twice daily, adjusted for renal function, for 5 days. Treatment could have been extended for up to 5 additional days if viral shedding or clinical symptoms warranted further treatment.

Subject analysis set title	Cohort 2: Children (1 to <2 years of age)
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Participants 1 year to <2 years of age received 14 mg/kg zanamivir by IV infusion over 30 minutes twice daily, adjusted for renal function, for 5 days. Treatment could have been extended for up to 5 additional days if viral shedding or clinical symptoms warranted further treatment.

Subject analysis set title	Cohort 3: Children (2 to <6 years of age)
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Participants 2 years to <6 years of age received 14 mg/kg zanamivir with a maximum dose of 600 mg by IV infusion over 30 minutes twice daily, adjusted for renal function, for 5 days. Treatment could have been extended for up to 5 additional days if viral shedding or clinical symptoms warranted further treatment.

Subject analysis set title	Cohort 4: Children (6 to <13 years of age)
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Participants 6 years to <13 years of age received 12 mg/kg zanamivir with a maximum dose of 600 mg by IV infusion over 30 minutes twice daily, adjusted for renal function, for 5 days. Treatment could have been extended for up to 5 additional days if viral shedding or clinical symptoms warranted further treatment.

Subject analysis set title	Cohort 5: Adolescents (13 to <18 years of age)
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Participants 13 to <18 years of age received 12 mg/kg zanamivir with a maximum dose of 600 mg by IV infusion over 30 minutes twice daily, adjusted for renal function, for 5 days. Treatment could have been extended for up to 5 additional days if viral shedding or clinical symptoms warranted further treatment.

Primary: Number of participants with any adverse event (AE) considered to be related to study treatment

End point title	Number of participants with any adverse event (AE) considered to be related to study treatment ^[1]
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End point description:

An AE is defined as any untoward medical occurrence in a participant temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product. An AE can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease (new or exacerbated) temporally associated with the use of a medicinal product. All AEs were assessed by the Investigator as related or not related to the study treatment.

End point type	Primary
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End point timeframe:

Up to post-treatment (PT) + 23 days

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Statistical analysis was not conducted for this endpoint; there are no data to report.

End point values	Cohort 6: Adults (18 years and older)	Cohorts 1-5: Pediatrics/adol escents (6 months to <18 years)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	130 ^[2]	71 ^[3]		
Units: Participants	28	5		

Notes:

[2] - Safety Population: participants who received ≥ 1 dose of study medication.

[3] - Safety Population: participants who received ≥ 1 dose of study medication.

Statistical analyses

No statistical analyses for this end point

Primary: Number of participants with any severe or Grade 3/4 AEs

End point title	Number of participants with any severe or Grade 3/4 AEs ^[4]
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End point description:

An AE is defined as any untoward medical occurrence in a participant temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product. An AE can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease (new or exacerbated) temporally associated with the use of a medicinal product. AEs that occurred during the study were evaluated by the Investigator and graded according to the Division of Acquired Immunodeficiency Syndrome (DAIDS) table for grading the severity of adult and pediatric AEs. Grade 3=severe; Grade 4=potentially life threatening.

End point type	Primary
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End point timeframe:

Up to post-treatment (PT) + 23 days

Notes:

[4] - 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: Statistical analysis was not conducted for this endpoint; there are no data to report.

End point values	Cohort 6: Adults (18 years and older)	Cohorts 1-5: Pediatrics/adol escents (6 months to <18 years)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	130 ^[5]	71 ^[6]		
Units: Participants	57	23		

Notes:

[5] - Safety Population

[6] - Safety Population

Statistical analyses

No statistical analyses for this end point

Primary: Number of participants with any severe or Grade 3/4 treatment-related AE

End point title	Number of participants with any severe or Grade 3/4 treatment-related AE ^[7]
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End point description:

An AE is defined as any untoward medical occurrence in a participant temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product. An AE can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or

disease (new or exacerbated) temporally associated with the use of a medicinal product. AEs that occurred during the study were evaluated by the Investigator and graded according to the DAIDS table for grading the severity of adult and pediatric AEs. Grade 3=severe; Grade 4=potentially life threatening. All AEs were assessed by the Investigator as related or not related to the study treatment.

End point type	Primary
End point timeframe:	
Up to post-treatment (PT) + 23 days	

Notes:

[7] - 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: Statistical analysis was not conducted for this endpoint; there are no data to report.

End point values	Cohort 6: Adults (18 years and older)	Cohorts 1-5: Pediatrics/adolescents (6 months to <18 years)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	130 ^[8]	71 ^[9]		
Units: Participants	16	2		

Notes:

[8] - Safety Population

[9] - Safety Population

Statistical analyses

No statistical analyses for this end point

Primary: Number of participants who permanently discontinued the study treatment due to an AE

End point title	Number of participants who permanently discontinued the study treatment due to an AE ^[10]
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End point description:

An AE is defined as any untoward medical occurrence in a participant temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product. An AE can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease (new or exacerbated) temporally associated with the use of a medicinal product.

End point type	Primary
End point timeframe:	
Up to 10 days	

Notes:

[10] - 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: Statistical analysis was not conducted for this endpoint; there are no data to report.

End point values	Cohort 6: Adults (18 years and older)	Cohorts 1-5: Pediatrics/adolescents (6 months to <18 years)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	130 ^[11]	71 ^[12]		
Units: Participants	17	2		

Notes:

[11] - Safety Population

[12] - Safety Population

Statistical analyses

No statistical analyses for this end point

Primary: Number of participants who were permanently discontinued from the study due to an AE

End point title	Number of participants who were permanently discontinued from the study due to an AE ^[13]
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End point description:

An AE is defined as any untoward medical occurrence in a participant temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product. An AE can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease (new or exacerbated) temporally associated with the use of a medicinal product.

End point type	Primary
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End point timeframe:

Up to post-treatment (PT) + 23 days

Notes:

[13] - 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: Statistical analysis was not conducted for this endpoint; there are no data to report.

End point values	Cohort 6: Adults (18 years and older)	Cohorts 1-5: Pediatrics/adol escents (6 months to <18 years)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	130 ^[14]	71 ^[15]		
Units: Participants	20	5		

Notes:

[14] - Safety Population

[15] - Safety Population

Statistical analyses

No statistical analyses for this end point

Primary: Number of participants with the indicated clinical chemistry values relative to the normal range at Baseline (Day 1) and Day 5

End point title	Number of participants with the indicated clinical chemistry values relative to the normal range at Baseline (Day 1) and Day 5 ^[16]
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End point description:

Blood samples for laboratory assessments were collected at Baseline (Day [D] 1), Days 3 and 5, and on post-treatment +2 days (if hospitalized) and post-treatment +23 days. Clinical chemistry parameters summarized here include alanine aminotransferase (ALT), direct bilirubin (DB), total bilirubin (TB), and creatinine. The number of participants with values that were high (H)/normal (N)/low (L) relative to the normal range at Baseline (D 1) and D 5 for the indicated clinical chemistry parameters are summarized. Baseline is defined as the last pre-treatment value collected. Only those participants available at the specified time points were analyzed (represented by n=X, X in the category titles).

End point type	Primary
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End point timeframe:

Baseline (Day 1) and Day 5

Notes:

[16] - 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: Statistical analysis was not conducted for this endpoint; there are no data to report.

End point values	Cohort 6: Adults (18 years and older)	Cohorts 1-5: Pediatrics/adol escents (6 months to <18 years)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	130 ^[17]	71 ^[18]		
Units: Participants				
D 1, H ALT, n=129, 71	48	21		
D 1, N ALT, n=129, 71	79	49		
D 1, L ALT, n=129, 71	1	1		
D 5, H ALT, n=102, 45	41	16		
D 5, N ALT, n=102, 45	60	27		
D 5, L ALT, n=102, 45	1	1		
D 1, H DB, n=83, 60	17	9		
D 1, N DB, n=83, 60	61	45		
D 1, L DB, n=83, 60	2	3		
D 5, H DB, n=70, 36	20	4		
D 5, N DB, n=70, 36	46	28		
D 5, L DB, n=70, 36	1	1		
D 1, H TB, n=128, 71	11	13		
D 1, N TB, n=128, 71	110	50		
D 1, L TB, n=128, 71	7	7		
D 5, H TB, n=102, 42	13	6		
D 5, N TB, n=102, 42	85	32		
D 5, L TB, n=102, 42	4	2		
D 1, H Creatinine, n=128, 71	27	6		
D 1, N Creatinine, n=128, 71	50	56		
D 1, L Creatinine, n=128, 71	51	9		
D 5, H Creatinine, n=111, 46	31	7		
D 5, N Creatinine, n=111, 46	46	34		
D 5, L Creatinine, n=111, 46	34	5		

Notes:

[17] - Safety Population

[18] - Safety Population

Statistical analyses

No statistical analyses for this end point

Primary: Number of participants with the indicated hematology values relative to the normal range at Baseline (Day 1) and Day 5

End point title	Number of participants with the indicated hematology values relative to the normal range at Baseline (Day 1) and Day 5 ^[19]
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End point description:

Blood samples for laboratory assessments were collected at Baseline (Day [D] 1), Days 3 and 5, and on post-treatment +2 days (if hospitalized) and post-treatment +23 days. Hematology parameters summarized here include hemoglobin, total neutrophils (TN), and white blood cell (WBC) count. The number of participants with values that were high (H)/normal (N)/low (L) relative to the normal range at Baseline (D 1) and D 5 for the indicated hematology parameters are summarized. Baseline is defined as the last pre-treatment value collected. Only those participants available at the specified time points were analyzed (represented by n=X, X in the category titles).

End point type	Primary
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End point timeframe:

Baseline (Day 1) and Day 5

Notes:

[19] - 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: Statistical analysis was not conducted for this endpoint; there are no data to report.

End point values	Cohort 6: Adults (18 years and older)	Cohorts 1-5: Pediatrics/adol escents (6 months to <18 years)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	130 ^[20]	71 ^[21]		
Units: Participants				
D 1, H Hemoglobin, n=130, 71	0	1		
D 1, N Hemoglobin, n=130, 71	48	30		
D 1, L Hemoglobin, n=130, 71	82	40		
D 5, H Hemoglobin, n=114, 47	1	0		
D 5, N Hemoglobin, n=114, 47	25	16		
D 5, L Hemoglobin, n=114, 47	88	31		
D 1, H TN, n=123, 70	51	34		
D 1, N TN, n=123, 70	59	29		
D 1, L TN, n=123, 70	13	7		
D 5, H TN, n=106, 45	49	20		
D 5, N TN, n=106, 45	49	18		
D 5, L TN, n=106, 45	8	7		
D 1, H WBC Count, n=130, 71	29	9		
D 1, N WBC Count, n=130, 71	71	42		
D 1, L WBC Count, n=130, 71	30	20		
D 5, H WBC Count, n=114, 47	50	12		
D 5, N WBC Count, n=114, 47	49	30		
D 5, L WBC Count, n=114, 47	15	5		

Notes:

[20] - Safety Population

[21] - Safety Population

Statistical analyses

No statistical analyses for this end point

Primary: Number of participants with the indicated treatment-emergent (TE) Grade 3/4 clinical chemistry toxicities

End point title	Number of participants with the indicated treatment-emergent (TE) Grade 3/4 clinical chemistry toxicities ^[22]
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End point description:

A toxicity was considered to be TE if it was greater than the Baseline grade, and if it had developed or increased post-Baseline in intensity (and prior to the last dose of investigational product). Clinical chemistry parameters summarized here include ALT, TB, and creatinine. Per the DAIDS table for grading the severity of adult and pediatric AEs, Grade 3=severe and Grade 4=potentially life threatening. Baseline is defined as the last pre-treatment value collected. Only those participants available at the specified time points were analyzed (represented by n=X, X in the category titles).

End point type	Primary
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End point timeframe:

Up to post-treatment (PT) + 23 days

Notes:

[22] - 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: Statistical analysis was not conducted for this endpoint; there are no data to report.

End point values	Cohort 6: Adults (18 years and older)	Cohorts 1-5: Pediatrics/adol escents (6 months to <18 years)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	130 ^[23]	71 ^[24]		
Units: Participants				
ALT, Grade 3, n=128, 68	10	1		
ALT, Grade 4, n=128, 68	5	0		
TB, Grade 3, n=127, 68	3	1		
TB, Grade 4, n=127, 68	3	4		
Creatinine, Grade 3, n=129, 68	6	3		
Creatinine, Grade 4, n=129, 68	5	2		

Notes:

[23] - Safety Population

[24] - Safety Population

Statistical analyses

No statistical analyses for this end point

Primary: Number of participants with the indicated treatment-emergent (TE) Grade 3/4 hematology toxicities

End point title	Number of participants with the indicated treatment-emergent (TE) Grade 3/4 hematology toxicities ^[25]
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End point description:

A toxicity was considered to be TE if it was greater than the Baseline grade, and if it had developed or increased post-Baseline in intensity (and prior to the last dose of investigational product). The hematology parameters summarized here include hemoglobin, TN, and WBC count. Per the DAIDS table for grading the severity of adult and pediatric AEs, Grade 3=severe and Grade 4=potentially life threatening. Baseline is defined as the last pre-treatment value collected. Only those participants available at the specified time points were analyzed (represented by n=X, X in the category titles).

End point type	Primary
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End point timeframe:

Up to post-treatment (PT) + 23 days

Notes:

[25] - 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: Statistical analysis was not conducted for this endpoint; there are no data to report.

End point values	Cohort 6: Adults (18 years and older)	Cohorts 1-5: Pediatrics/adol escents (6 months to <18 years)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	130 ^[26]	71 ^[27]		
Units: Participants				
Hemoglobin, Grade 3, n=129, 68	40	12		
Hemoglobin, Grade 4, n=129, 68	9	2		
TN, Grade 3, n=122, 66	0	3		

TN, Grade 4, n=122, 66	1	2		
WBC count, Grade 3, n=129, 68	2	1		
WBC count, Grade 4, n=129, 68	2	0		

Notes:

[26] - Safety Population

[27] - Safety Population

Statistical analyses

No statistical analyses for this end point

Primary: Median heart rate at Baseline (Day 1) and Day 5

End point title	Median heart rate at Baseline (Day 1) and Day 5 ^[28]
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End point description:

Heart rate was measured at Baseline (Day 1); Days 2, 3, 4, 5, 6, 7, 8, 9, and 10; post-treatment +2 days, +5 days, +9 days, +16 days (assessments to be done if participant remained hospitalized), and +23 days. Heart rate was assessed once daily during inpatient or outpatient follow-up visits. Heart rate values at Baseline (Day 1) and Day 5 are summarized. Baseline is defined as the last pre-treatment value collected. Only those participants available at the specified time points were analyzed (represented by n=X, X, X, X, X, X, X in the category titles).

End point type	Primary
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End point timeframe:

Baseline (Day 1) and Day 5

Notes:

[28] - 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: Statistical analysis was not conducted for this endpoint; there are no data to report.

End point values	Cohort 6: Adults (18 years and older); zanamivir ≤5 days	Cohort 6: Adults (18 years and older); zanamivir >5 days	Cohort 1: Infants (6 months to <1 year of age)	Cohort 2: Children (1 to <2 years of age)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	87 ^[29]	43 ^[30]	7 ^[31]	11 ^[32]
Units: Beats per minute (bpm)				
median (full range (min-max))				
Day 1, n=87, 43, 7, 11, 12, 27, 14	93 (58 to 143)	95 (50 to 140)	119 (95 to 156)	144 (121 to 195)
Day 5, n=73, 42, 7, 6, 9, 15, 10	87 (50 to 140)	93.5 (60 to 134)	127 (93 to 152)	122.5 (98 to 146)

Notes:

[29] - Safety Population

[30] - Safety Population

[31] - Safety Population

[32] - Safety Population

End point values	Cohort 3: Children (2 to <6 years of age)	Cohort 4: Children (6 to <13 years of age)	Cohort 5: Adolescents (13 to <18 years of age)	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	12 ^[33]	27 ^[34]	14 ^[35]	
Units: Beats per minute (bpm)				
median (full range (min-max))				

Day 1, n=87, 43, 7, 11, 12, 27, 14	115.5 (92 to 160)	112 (59 to 185)	99 (74 to 134)	
Day 5, n=73, 42, 7, 6, 9, 15, 10	112 (85 to 123)	102 (67 to 128)	79.5 (58 to 113)	

Notes:

[33] - Safety Population

[34] - Safety Population

[35] - Safety Population

Statistical analyses

No statistical analyses for this end point

Primary: Median systolic blood pressure (SBP) and diastolic blood pressure (DBP) at Baseline (Day 1) and Day 5

End point title	Median systolic blood pressure (SBP) and diastolic blood pressure (DBP) at Baseline (Day 1) and Day 5 ^[36]
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End point description:

SBP and DBP were measured at Baseline (Day 1), Days 2, 3, 4, 5, 6, 7, 8, 9, and 10; post-treatment +2 days, +5 days, +9 days, +16 days (assessments to be done if participant remained hospitalized), and +23 days. SBP and DBP were assessed once daily during inpatient or outpatient follow-up visits. SBP and DBP values at Baseline (Day 1) and Day 5 are summarized. Baseline is defined as the last pre-treatment value collected. Only those participants available at the specified time points were analyzed (represented by n=X, X, X, X, X, X, X in the category titles).

End point type	Primary
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End point timeframe:

Baseline (Day 1) and Day 5

Notes:

[36] - 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: Statistical analysis was not conducted for this endpoint; there are no data to report.

End point values	Cohort 6: Adults (18 years and older); zanamivir ≤5 days	Cohort 6: Adults (18 years and older); zanamivir >5 days	Cohort 1: Infants (6 months to <1 year of age)	Cohort 2: Children (1 to <2 years of age)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	87 ^[37]	43 ^[38]	7 ^[39]	11 ^[40]
Units: Millimeters of mercury (mmHg)				
median (full range (min-max))				
SBP, Day 1, n=87, 43, 7, 11, 12, 27, 14	126 (70 to 175)	118 (80 to 180)	102 (83 to 116)	100 (77 to 144)
SBP, Day 5, n=73, 43, 7, 5, 9, 15, 10	128 (51 to 182)	132 (88 to 220)	103 (86 to 130)	98 (87 to 120)
DBP, Day 1, n=87, 43, 7, 11, 12, 27, 14	68 (32 to 96)	63 (40 to 97)	53 (42 to 64)	60 (39 to 78)
DBP, Day 5, n=73, 43, 7, 5, 9, 15, 10	70 (29 to 106)	66 (50 to 100)	60 (42 to 83)	60 (45 to 73)

Notes:

[37] - Safety Population

[38] - Safety Population

[39] - Safety Population

[40] - Safety Population

End point values	Cohort 3: Children (2 to <6 years of age)	Cohort 4: Children (6 to <13 years of age)	Cohort 5: Adolescents (13 to <18 years of age)	
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Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	12 ^[41]	27 ^[42]	14 ^[43]	
Units: Millimeters of mercury (mmHg)				
median (full range (min-max))				
SBP, Day 1, n=87, 43, 7, 11, 12, 27, 14	105.5 (82 to 124)	108 (70 to 136)	107 (95 to 137)	
SBP, Day 5, n=73, 43, 7, 5, 9, 15, 10	117 (83 to 140)	110 (96 to 135)	108.5 (95 to 121)	
DBP, Day 1, n=87, 43, 7, 11, 12, 27, 14	58 (37 to 86)	57 (41 to 82)	62 (36 to 74)	
DBP, Day 5, n=73, 43, 7, 5, 9, 15, 10	67 (43 to 89)	68 (47 to 80)	54.5 (35 to 72)	

Notes:

[41] - Safety Population

[42] - Safety Population

[43] - Safety Population

Statistical analyses

No statistical analyses for this end point

Primary: Median oxygen saturation measured via transcutaneous oximetry (TCPO2) at Baseline (Day 1) and Day 5

End point title	Median oxygen saturation measured via transcutaneous oximetry (TCPO2) at Baseline (Day 1) and Day 5 ^[44]
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End point description:

TCPO2 is a noninvasive test that directly measures the oxygen level of tissue beneath the skin. Because oxygen is carried to tissues by blood flow in the arteries, TCPO2 is an indirect measure of blood flow. The percent (%) oxygen saturation was measured at Baseline (Day 1), Days 2, 3, 4, 5, 6, 7, 8, 9, and 10; and post-treatment +2 days, +5 days, +9 days, +16 days (assessments to be done if participant remained hospitalized), and +23 days. Oxygen saturation was assessed once daily during inpatient follow-up visits. The median oxygen saturation values at Baseline (Day 1) and Day 5 are summarized. Baseline is defined as the last pre-treatment value collected. Only those participants available at the specified time points were analyzed (represented by n=X, X, X, X, X, X, X in the category titles).

End point type	Primary
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End point timeframe:

Baseline (Day 1) and Day 5

Notes:

[44] - 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: Statistical analysis was not conducted for this endpoint; there are no data to report.

End point values	Cohort 6: Adults (18 years and older); zanamivir ≤5 days	Cohort 6: Adults (18 years and older); zanamivir >5 days	Cohort 1: Infants (6 months to <1 year of age)	Cohort 2: Children (1 to <2 years of age)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	87 ^[45]	43 ^[46]	7 ^[47]	11 ^[48]
Units: Percentage of oxygen level in blood				
median (full range (min-max))				
Day 1, n=87, 43, 7, 11, 12, 27, 14	97 (82 to 100)	96 (70 to 100)	98 (76 to 100)	100 (93 to 100)
Day 5, n=70, 43, 7, 6, 9, 15, 9	97 (73 to 100)	96 (45 to 100)	100 (96 to 100)	95.5 (85 to 100)

Notes:

[45] - Safety Population

[46] - Safety Population

[47] - Safety Population

[48] - Safety Population

End point values	Cohort 3: Children (2 to <6 years of age)	Cohort 4: Children (6 to <13 years of age)	Cohort 5: Adolescents (13 to <18 years of age)	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	12 ^[49]	27 ^[50]	14 ^[51]	
Units: Percentage of oxygen level in blood				
median (full range (min-max))				
Day 1, n=87, 43, 7, 11, 12, 27, 14	98 (93 to 100)	98 (91 to 100)	97.5 (94 to 100)	
Day 5, n=70, 43, 7, 6, 9, 15, 9	97 (95 to 100)	97 (50 to 100)	96 (70 to 100)	

Notes:

[49] - Safety Population

[50] - Safety Population

[51] - Safety Population

Statistical analyses

No statistical analyses for this end point

Primary: Median respiration rate at Baseline (Day 1) and Day 5

End point title	Median respiration rate at Baseline (Day 1) and Day 5 ^[52]
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End point description:

Respiration rate was measured at Baseline (Day 1), Days 2, 3, 4, 5, 6, 7, 8, 9, and 10; and post-treatment +2 days, +5 days, +9 days, +16 days (assessments to be done if participant remained hospitalized), and +23 days. Respiration rate was assessed once daily during inpatient or outpatient follow-up visits. The median respiration rate at Baseline (Day 1) and Day 5 is summarized. Baseline is defined as the last pre-treatment value collected. Only those participants available at the specified time points were analyzed (represented by n=X, X, X, X, X, X, X in the category titles).

End point type	Primary
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End point timeframe:

Baseline (Day 1) and Day 5

Notes:

[52] - 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: Statistical analysis was not conducted for this endpoint; there are no data to report.

End point values	Cohort 6: Adults (18 years and older); zanamivir <=5 days	Cohort 6: Adults (18 years and older); zanamivir >5 days	Cohort 1: Infants (6 months to <1 year of age)	Cohort 2: Children (1 to <2 years of age)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	87 ^[53]	43 ^[54]	7 ^[55]	11 ^[56]
Units: Breaths per minute				
median (full range (min-max))				
Day 1, n=87, 43, 7, 11, 12, 27, 14	23 (6 to 47)	22 (10 to 40)	32 (28 to 46)	34 (20 to 40)
Day 5, n=67, 42, 7, 6, 9, 15, 10	20 (10 to 42)	23.5 (8 to 41)	40 (28 to 48)	31 (10 to 50)

Notes:

[53] - Safety Population

[54] - Safety Population

[55] - Safety Population

[56] - Safety Population

End point values	Cohort 3: Children (2 to <6 years of age)	Cohort 4: Children (6 to <13 years of age)	Cohort 5: Adolescents (13 to <18 years of age)	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	12 ^[57]	27 ^[58]	14 ^[59]	
Units: Breaths per minute				
median (full range (min-max))				
Day 1, n=87, 43, 7, 11, 12, 27, 14	29.5 (22 to 66)	20 (4 to 49)	21 (0 to 98)	
Day 5, n=67, 42, 7, 6, 9, 15, 10	30 (22 to 44)	23 (8 to 48)	19 (0 to 28)	

Notes:

[57] - Safety Population

[58] - Safety Population

[59] - Safety Population

Statistical analyses

No statistical analyses for this end point

Primary: Median body temperature at Baseline (Day 1) and Day 5

End point title	Median body temperature at Baseline (Day 1) and Day 5 ^[60]
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End point description:

Body temperature was recorded at Baseline (Day 1), Days 2, 3, 4, 5, 6, 7, 8, 9, and 10; and post-treatment +2 days, +5 days, +9 days, +16 days (assessments to be done if participant remained hospitalized), and +23 days. Body temperature was recorded once daily during inpatient or outpatient follow-up visits. Median body temperature at Baseline (Day 1) and Day 5 is summarized. Baseline is defined as the last pre-treatment value collected. Only those participants available at the specified time points were analyzed (represented by n=X, X, X, X, X, X, X in the category titles).

End point type	Primary
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End point timeframe:

Baseline (Day 1) and Day 5

Notes:

[60] - 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: Statistical analysis was not conducted for this endpoint; there are no data to report.

End point values	Cohort 6: Adults (18 years and older); zanamivir ≤5 days	Cohort 6: Adults (18 years and older); zanamivir >5 days	Cohort 1: Infants (6 months to <1 year of age)	Cohort 2: Children (1 to <2 years of age)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	87 ^[61]	43 ^[62]	7 ^[63]	11 ^[64]
Units: Degrees centigrade				
median (full range (min-max))				
Day 1, n=87, 43, 7, 11, 12, 27, 14	37.3 (33.4 to 40.1)	37.3 (35.3 to 40.4)	36.8 (36 to 40)	37.3 (34 to 40)
Day 5, n=73, 42, 7, 6, 9, 15, 10	37 (35.3 to 38.8)	37.15 (34.5 to 39.8)	37 (36 to 38)	36.8 (36 to 38)

Notes:

- [61] - Safety Population
- [62] - Safety Population
- [63] - Safety Population
- [64] - Safety Population

End point values	Cohort 3: Children (2 to <6 years of age)	Cohort 4: Children (6 to <13 years of age)	Cohort 5: Adolescents (13 to <18 years of age)	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	12 ^[65]	27 ^[66]	14 ^[67]	
Units: Degrees centigrade				
median (full range (min-max))				
Day 1, n=87, 43, 7, 11, 12, 27, 14	37.5 (36 to 39)	37.3 (33 to 39)	37.5 (36 to 40)	
Day 5, n=73, 42, 7, 6, 9, 15, 10	37.3 (37 to 38)	37.1 (37 to 39)	37.1 (37 to 39)	

Notes:

- [65] - Safety Population
- [66] - Safety Population
- [67] - Safety Population

Statistical analyses

No statistical analyses for this end point

Primary: Number of participants assessed as normal/abnormal (clinically significant [CS] and not clinically significant [NCS]) for 12-lead electrocardiogram (ECG) at Baseline (Day 1)

End point title	Number of participants assessed as normal/abnormal (clinically significant [CS] and not clinically significant [NCS]) for 12-lead electrocardiogram (ECG) at Baseline (Day 1) ^[68]
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End point description:

The number of participants with an ECG status of normal and abnormal CS or NCS, as determined by the Investigator, is reported. Normal=all ECG parameters within the accepted normal ranges. Abnormal=ECG findings outside of normal ranges. CS=ECG with a CS abnormality that meets exclusion criteria. NCS=ECG with an abnormality that is not CS nor meets exclusion criteria, per Investigator, based on reasonable standards of clinical judgment. Only those participants available at the specified time points were analyzed (represented by n=X, X, X, X, X, X in the category titles).

End point type	Primary
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End point timeframe:

Baseline (Day 1)

Notes:

[68] - 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: Statistical analysis was not conducted for this endpoint; there are no data to report.

End point values	Cohort 6: Adults (18 years and older)	Cohort 1: Infants (6 months to <1 year of age)	Cohort 2: Children (1 to <2 years of age)	Cohort 3: Children (2 to <6 years of age)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	130 ^[69]	7 ^[70]	11 ^[71]	12 ^[72]
Units: Participants				
Normal, n=128, 7, 10, 12, 25, 13	68	5	7	8
Abnormal NCS, n=128, 7, 10, 12, 25, 13	57	2	2	4
Abnormal CS, n=128, 7, 10, 12, 25, 13	7	0	1	0

Notes:

[69] - Safety Population

[70] - Safety Population

[71] - Safety Population

[72] - Safety Population

End point values	Cohort 4: Children (6 to <13 years of age)	Cohort 5: Adolescents (13 to <18 years of age)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	27 ^[73]	14 ^[74]		
Units: Participants				
Normal, n=128, 7, 10, 12, 25, 13	20	8		
Abnormal NCS, n=128, 7, 10, 12, 25, 13	5	5		
Abnormal CS, n=128, 7, 10, 12, 25, 13	0	0		

Notes:

[73] - Safety Population

[74] - Safety Population

Statistical analyses

No statistical analyses for this end point

Primary: Median corrected QT interval (QTc) for heart rate by Fridericia's formula (QTcF) and Bazett's formula (QTcB) at Baseline (Day 1) and Day 5

End point title	Median corrected QT interval (QTc) for heart rate by Fridericia's formula (QTcF) and Bazett's formula (QTcB) at Baseline (Day 1) and Day 5 ^[75]
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End point description:

Twelve-lead ECGs were recorded for the parameters of QTcF and QTcB. The first set of pre-dose ECG values at Baseline (Day 1) and the pre-dose ECG values at Day 5 are presented. Baseline is defined as the last pre-treatment value collected. Only those participants available at the specified time points were analyzed (represented by n=X, X, X, X, X, X, X in the category titles). "99999" indicates that data are not available/analysis was not performed.

End point type	Primary
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End point timeframe:

Baseline (Day 1) and Day 5

Notes:

[75] - 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: Statistical analysis was not conducted for this endpoint; there are no data to report.

End point values	Cohort 6: Adults (18 years and older); zanamivir ≤5 days	Cohort 6: Adults (18 years and older); zanamivir >5 days	Cohort 1: Infants (6 months to <1 year of age)	Cohort 2: Children (1 to <2 years of age)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	87 ^[76]	43 ^[77]	7 ^[78]	11 ^[79]
Units: Milliseconds				
median (full range (min-max))				
QTcF, Baseline, n=87, 42, 6, 9, 11, 24, 13	400.6 (204 to 584)	413.5 (285 to 502)	356 (0 to 465)	362 (331 to 426)

QTcF, Day 5, n=68, 40, 0, 1, 3, 3, 5	406.6 (298 to 610)	405.5 (339 to 555)	99999 (99999 to 99999)	373 (373 to 373)
QTcB, Baseline, n=87, 42, 6, 9, 11, 24, 13	424 (231 to 642)	432 (310 to 514)	412 (0 to 443)	422 (389 to 502)
QTcB, Day 5, n=68, 40, 0, 1, 3, 3, 5	422 (325 to 649)	434 (334 to 535)	99999 (99999 to 99999)	416 (416 to 416)

Notes:

[76] - Safety Population

[77] - Safety Population

[78] - Safety Population

[79] - Safety Population

End point values	Cohort 3: Children (2 to <6 years of age)	Cohort 4: Children (6 to <13 years of age)	Cohort 5: Adolescents (13 to <18 years of age)	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	12 ^[80]	27 ^[81]	14 ^[82]	
Units: Milliseconds				
median (full range (min-max))				
QTcF, Baseline, n=87, 42, 6, 9, 11, 24, 13	365 (297 to 483)	387.5 (267 to 544)	387 (271 to 424)	
QTcF, Day 5, n=68, 40, 0, 1, 3, 3, 5	394 (291 to 411)	353 (310 to 392)	389 (179 to 409)	
QTcB, Baseline, n=87, 42, 6, 9, 11, 24, 13	410 (330 to 493)	422.5 (264 to 497)	415 (316 to 467)	
QTcB, Day 5, n=68, 40, 0, 1, 3, 3, 5	444 (321 to 475)	380 (350 to 410)	399 (189 to 422)	

Notes:

[80] - Safety Population

[81] - Safety Population

[82] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Median time to virologic improvement

End point title	Median time to virologic improvement
End point description: Time to virologic improvement is defined as a 2-log drop in viral load or undetectable viral ribonucleic acid (RNA) as measured by quantitative reverse transcriptase-polymerase chain reaction (RT-PCR) from nasopharyngeal samples (PCR positive at Baseline). Only those participants available at the specified time points were analyzed.	
End point type	Secondary
End point timeframe: Up to post-treatment (PT) + 23 days	

End point values	Cohort 6: Adults (18 years and older)	Cohort 1: Infants (6 months to <1 year of age)	Cohort 2: Children (1 to <2 years of age)	Cohort 3: Children (2 to <6 years of age)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	76 ^[83]	5 ^[84]	7 ^[85]	9 ^[86]
Units: Days				
median (full range (min-max))	3 (1 to 26)	4 (2 to 9)	4 (3 to 25)	3 (3 to 7)

Notes:

[83] - ITT-E Population

[84] - ITT-E Population

[85] - ITT-E Population

[86] - ITT-E Population

End point values	Cohort 4: Children (6 to <13 years of age)	Cohort 5: Adolescents (13 to <18 years of age)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	13 ^[87]	7 ^[88]		
Units: Days				
median (full range (min-max))	5 (3 to 6)	4 (2 to 13)		

Notes:

[87] - ITT-E Population

[88] - ITT-E Population

Statistical analyses

No statistical analyses for this end point

Secondary: Median change from Baseline (Influenza A or B quantitative PCR, as appropriate) in viral load at the indicated time points

End point title	Median change from Baseline (Influenza A or B quantitative PCR, as appropriate) in viral load at the indicated time points
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End point description:

Change from Baseline in viral load was measured from nasopharyngeal swab samples, as determined by RT-PCR (PCR positive at Baseline). Nasopharyngeal swab samples were collected at Baseline (Day 1); Day 2, Day 3, Day 4, Day 5, Day 7, and Day 10; and, only if the participants had continued symptoms and were hospitalized, post-treatment (PT) samples were collected at +2 days, +5 days, +9 days, +16 days, and +23 days. 'PT +23 days' also comprises viral load values at early study withdrawal. Only those participants available at the specified time points were analyzed (represented by n=X, X, X, X, X, X in the category titles). "99999" indicates that data are not available/analysis was not performed.

End point type	Secondary
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End point timeframe:

Baseline (Day 1); Days 2, 3, 4, 5, 7, and 10; and post-treatment +2, +5, +9, +16, +23 days

End point values	Cohort 6: Adults (18 years and older)	Cohort 1: Infants (6 months to <1 year of age)	Cohort 2: Children (1 to <2 years of age)	Cohort 3: Children (2 to <6 years of age)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	130 ^[89]	7 ^[90]	11 ^[91]	12 ^[92]
Units: Log10 copies per milliliter				
median (full range (min-max))				

Day 2, n=89, 0, 0, 2, 3, 2	-0.92 (-4 to 2)	99999 (99999 to 99999)	99999 (99999 to 99999)	-3.75 (-3.87 to 3.63)
Day 3, n=82, 4, 7, 10, 15, 7	-1.42 (-3.38 to 1.08)	-1.655 (-3.15 to -0.94)	-1.93 (-4.36 to 0.55)	-2.215 (-6.16 to -0.49)
Day 4, n=84, 0, 0, 2, 2, 1	-1.59 (-5.4 to 1.38)	99999 (99999 to 99999)	99999 (99999 to 99999)	-4.895 (-5.01 to -4.78)
Day 5, n=75, 5, 4, 8, 12, 5	-1.57 (-5.06 to 2.05)	-2.72 (-4.92 to -0.12)	-3.705 (-6.2 to 0.24)	-3.285 (-6.16 to -1.81)
Day 7, n=23, 1, 1, 1, 3, 1	-1.58 (-3.52 to 3.02)	-1.82 (-1.82 to -1.82)	-6.2 (-6.2 to -6.2)	-3.03 (-3.03 to -3.03)
Day 10, n=19, 0, 2, 1, 4, 1	-1.75 (-4 to 2.04)	99999 (99999 to 99999)	-5.385 (-6.2 to -4.57)	-6.43 (-6.43 to -6.43)
PT +2 days, n=32, 0, 1, 2, 6, 3	-1.38 (-4.86 to 0.46)	99999 (99999 to 99999)	-6.2 (-6.2 to -6.2)	-2.495 (-2.91 to -2.08)
PT +5 days, n=26, 0, 2, 0, 5, 2	-1.84 (-5.21 to -0.4)	99999 (99999 to 99999)	-5.385 (-6.2 to -4.57)	99999 (99999 to 99999)
PT +9 days, n=27, 0, 1, 0, 3, 2	-2.58 (-5.21 to -0.41)	99999 (99999 to 99999)	-6.2 (-6.2 to -6.2)	99999 (99999 to 99999)
PT +16 days, n=21, 0, 1, 0, 4, 1	-2.48 (-5.21 to -0.41)	99999 (99999 to 99999)	-2.95 (-2.95 to -2.95)	99999 (99999 to 99999)
PT +23 days, n=21, 2, 4, 0, 4, 0	-2.89 (-5.21 to -0.46)	-4.455 (-4.92 to -3.99)	-4.67 (-6.2 to -2.95)	99999 (99999 to 99999)

Notes:

[89] - ITT-E Population

[90] - ITT-E Population

[91] - ITT-E Population

[92] - ITT-E Population

End point values	Cohort 4: Children (6 to <13 years of age)	Cohort 5: Adolescents (13 to <18 years of age)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	27 ^[93]	14 ^[94]		
Units: Log10 copies per milliliter				
median (full range (min-max))				
Day 2, n=89, 0, 0, 2, 3, 2	-1.16 (-1.87 to 0.5)	-2.28 (-2.55 to -2.01)		
Day 3, n=82, 4, 7, 10, 15, 7	-1.33 (-5.19 to 0.62)	-2.55 (-4.01 to -0.29)		
Day 4, n=84, 0, 0, 2, 2, 1	-2.06 (-2.06 to -1.52)	-2.55 (-2.55 to -2.55)		
Day 5, n=75, 5, 4, 8, 12, 5	-2.93 (-6.71 to -1.53)	-2.55 (-4.01 to -1.4)		
Day 7, n=23, 1, 1, 1, 3, 1	-3.04 (-3.46 to -1.26)	-1.61 (-1.61 to -1.61)		
Day 10, n=19, 0, 2, 1, 4, 1	-4.76 (-5.42 to -2.48)	-1.67 (-1.67 to -1.67)		
PT +2 days, n=32, 0, 1, 2, 6, 3	-3.825 (-5.42 to -1.6)	-3.06 (-4.61 to -1.63)		
PT +5 days, n=26, 0, 2, 0, 5, 2	-4.19 (-5.42 to -1.6)	-3.275 (-3.43 to -3.12)		
PT +9 days, n=27, 0, 1, 0, 3, 2	-4.19 (-5.42 to -1.6)	-3.865 (-4.61 to -3.12)		
PT +16 days, n=21, 0, 1, 0, 4, 1	-3.825 (-4.56 to -1.6)	-4.61 (-4.61 to -4.61)		
PT +23 days, n=21, 2, 4, 0, 4, 0	-3.825 (-4.56 to -1.6)	99999 (99999 to 99999)		

Notes:

[93] - ITT-E Population

[94] - ITT-E Population

Statistical analyses

No statistical analyses for this end point

Secondary: Mean viral susceptibility to zanamivir at Baseline (Day 1) and all Post-Baseline visits collectively

End point title	Mean viral susceptibility to zanamivir at Baseline (Day 1) and all Post-Baseline visits collectively ^[95]
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End point description:

Viral susceptibility to zanamivir at Baseline and at all post-Baseline visits collectively was assessed by neuraminidase (NA) enzyme inhibition assay. The mean IC50 data are summarized by subtype (A/H1N1, A/H3N2, B) and by visit. IC50 is defined as the concentration of zanamvir required to inhibit NA activity by 50%. Only those participants available at the specified time points were analyzed (represented by n=X, X in the category titles). "99999" indicates that data are not available/analysis was not performed.

End point type	Secondary
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End point timeframe:

Baseline and up to post-treatment (PT) + 23 days

Notes:

[95] - 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: Statistical analysis was not conducted for all arms; there are no data to report.

End point values	Cohort 6: Adults (18 years and older)			
Subject group type	Reporting group			
Number of subjects analysed	130 ^[96]			
Units: Nanomolar (nM)				
arithmetic mean (standard deviation)				
A/H1N1, Day 1, n=22	0.2091 (± 0.06886)			
A/H1N1, All Post-Baseline, n=8	0.18 (± 0.04)			
A/H3N2, Day 1, n=5	0.266 (± 0.08385)			
A/H3N2, All Post-Baseline, n=2	0.23 (± 0.01414)			
B, Day 1, n=2	1.61 (± 0.35355)			
B, All Post-Baseline, n=0	99999 (± 99999)			

Notes:

[96] - ITT-E Population

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with treatment-emergent (TE) mutations

End point title	Number of participants with treatment-emergent (TE) mutations ^[97]
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End point description:

Viral RNA isolated from participants at Baseline (Day 1) and post-Baseline visits were sequenced to determine the presence of TE neuraminidase (NA) and hemagglutinin (HA) mutations resulting from selective pressure. A mutation was considered to be TE if it was not present at Baseline and was present in the post-Baseline sample analyzed. These mutations were classified as either known to confer zanamvir resistance or novel mutations with unknown clinical significance.

End point type	Secondary
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End point timeframe:

Baseline and up to post-treatment (PT) + 23 days

Notes:

[97] - 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: Statistical analysis was not conducted for all arms; there are no data to report.

End point values	Cohort 6: Adults (18 years and older)			
Subject group type	Reporting group			
Number of subjects analysed	130 ^[98]			
Units: Participants				
Known Zanamivir-Resistant NA Mutations	0			
Novel NA Mutations	5			
Resistant HA Mutations	2			
Novel HA Mutations	4			

Notes:

[98] - ITT-E Population

Statistical analyses

No statistical analyses for this end point

Secondary: Median time to resolution of individual vital signs

End point title	Median time to resolution of individual vital signs
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End point description:

Times to return to afebrile status (normal body temperature), normal respiratory status, normal heart rate, and normal systolic blood pressure were assessed. Afebrile status is defined as a temperature ≤ 36.6 axilla, ≤ 37.2 oral, or ≤ 37.7 rectal, core or tympanic, degrees Centigrade. A return to normal respiratory status is defined as either: (a) return to pre-morbid oxygen requirement; or (b) return to no need for supplemental oxygen; or (c) respiratory rate ≤ 60 , ≤ 40 , ≤ 34 , ≤ 30 , ≤ 24 or ≤ 24 breaths/minute (without supplemental oxygen) for Cohorts 1-6 respectively. A normal HR is defined as ≤ 160 , ≤ 150 , ≤ 140 , ≤ 120 , ≤ 100 or ≤ 100 bpm for Cohorts 1-6 respectively, and a normal SBP is defined as ≥ 70 , ≥ 74 , ≥ 76 , ≥ 80 , ≥ 90 or ≥ 90 mmHg for Cohorts 1-6 respectively. Only those participants available at the specified time points were analyzed (represented by n=X, X, X, X, X, X in the category titles).

End point type	Secondary
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End point timeframe:

Up to post-treatment (PT) + 23 days

End point values	Cohort 6: Adults (18 years and older)	Cohort 1: Infants (6 months to <1 year of age)	Cohort 2: Children (1 to <2 years of age)	Cohort 3: Children (2 to <6 years of age)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	130 ^[99]	7 ^[100]	11 ^[101]	12 ^[102]
Units: Days				
median (full range (min-max))				
Afebrile Status, n=120, 7, 11, 7, 24, 13	3 (2 to 34)	4 (2 to 26)	2 (1 to 30)	25 (2 to 32)
Respiratory Status, n=89, 7, 10, 12, 23, 9	8 (2 to 36)	5 (2 to 16)	2 (1 to 21)	3.5 (2 to 21)
HR, n=121, 7, 11, 12, 27, 13	2 (2 to 22)	2 (2 to 2)	2 (1 to 25)	2 (2 to 3)
SBP, n=128, 7, 11, 12, 27, 14	2 (2 to 3)	2 (2 to 2)	2 (1 to 3)	2 (2 to 3)

Notes:

[99] - ITT-E Population

[100] - ITT-E Population

[101] - ITT-E Population

[102] - ITT-E Population

End point values	Cohort 4: Children (6 to <13 years of age)	Cohort 5: Adolescents (13 to <18 years of age)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	27 ^[103]	14 ^[104]		
Units: Days				
median (full range (min-max))				
Afebrile Status, n=120, 7, 11, 7, 24, 13	3 (2 to 26)	3 (2 to 15)		
Respiratory Status, n=89, 7, 10, 12, 23, 9	3 (2 to 33)	2 (2 to 20)		
HR, n=121, 7, 11, 12, 27, 13	2 (2 to 31)	2 (2 to 5)		
SBP, n=128, 7, 11, 12, 27, 14	2 (2 to 24)	2 (2 to 3)		

Notes:

[103] - ITT-E Population

[104] - ITT-E Population

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with the indicated ventilation status: modality of supplemental oxygen delivery and mechanical ventilation

End point title	Number of participants with the indicated ventilation status: modality of supplemental oxygen delivery and mechanical ventilation
End point description:	
Ventilation status was measured at Baseline (Day 1); Days 2, 3, 4, 5, 6, 7, 8, 9, and 10; and post-treatment +2 days, +5 days, +9 days, +16 days (assessments to be done if participant remained hospitalized), and +23 days. Ventilation status was assessed once daily during inpatient follow-up visits. The number of participants reported for machine-assisted: extracorporeal membrane oxygenation (ECMO), endotracheal mechanical ventilation, and supplemental oxygen delivery (SOD) at "any time (AT) on study" and at Baseline (Day 1) are summarized.	
End point type	Secondary
End point timeframe:	
Up to post-treatment (PT) + 23 days	

End point values	Cohort 6: Adults (18 years and older)	Cohort 1: Infants (6 months to <1 year of age)	Cohort 2: Children (1 to <2 years of age)	Cohort 3: Children (2 to <6 years of age)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	130 ^[105]	7 ^[106]	11 ^[107]	12 ^[108]
Units: Participants				
AT on Study, Machine-Assisted: ECMO	4	0	1	0
AT on Study, Machine-Assisted: Endotracheal	74	3	5	4
AT on Study, SOD	91	3	5	7
Day 1, Machine-Assisted: ECMO	3	0	1	0
Day 1, Machine-Assisted: Endotracheal	60	2	3	4
Day 1, SOD	46	1	3	1

Notes:

[105] - ITT-E Population

[106] - ITT-E Population

[107] - ITT-E Population

[108] - ITT-E Population

End point values	Cohort 4: Children (6 to <13 years of age)	Cohort 5: Adolescents (13 to <18 years of age)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	27 ^[109]	14 ^[110]		
Units: Participants				
AT on Study, Machine-Assisted: ECMO	2	1		
AT on Study, Machine-Assisted: Endotracheal	14	4		
AT on Study, SOD	13	5		
Day 1, Machine-Assisted: ECMO	2	1		
Day 1, Machine-Assisted: Endotracheal	11	4		
Day 1, SOD	6	1		

Notes:

[109] - ITT-E Population

[110] - ITT-E Population

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of mechanical ventilation and supplemental oxygen use

End point title	Duration of mechanical ventilation and supplemental oxygen use
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End point description:

Due to the conditional nature of data collection post treatment, the duration of mechanical ventilation and supplemental oxygen use were not determined.

End point type	Secondary
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End point timeframe:

Up to discharge from the hospital

End point values	Cohort 6: Adults (18 years and older)	Cohort 1: Infants (6 months to <1 year of age)	Cohort 2: Children (1 to <2 years of age)	Cohort 3: Children (2 to <6 years of age)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	0 ^[111]	0 ^[112]	0 ^[113]	0 ^[114]
Units: Days				
median (full range (min-max))	(to)	(to)	(to)	(to)

Notes:

[111] - ITT-E Population

[112] - ITT-E Population

[113] - ITT-E Population

[114] - ITT-E Population

End point values	Cohort 4: Children (6 to <13 years of age)	Cohort 5: Adolescents (13 to <18 years of age)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	0 ^[115]	0 ^[116]		
Units: Days				
median (full range (min-max))	(to)	(to)		

Notes:

[115] - ITT-E Population

[116] - ITT-E Population

Statistical analyses

No statistical analyses for this end point

Secondary: Median time to return to pre-morbid functional status

End point title	Median time to return to pre-morbid functional status
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End point description:

Time to return to pre-morbid functional status was assessed on a 3-point scale (bed rest, limited ambulation, or unrestricted). Only those participants available at the specified time points were analyzed.

End point type	Secondary
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End point timeframe:

Up to post-treatment (PT) + 23 days

End point values	Cohort 6: Adults (18 years and older)	Cohort 1: Infants (6 months to <1 year of age)	Cohort 2: Children (1 to <2 years of age)	Cohort 3: Children (2 to <6 years of age)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	76 ^[117]	7 ^[118]	9 ^[119]	11 ^[120]
Units: Days				
median (full range (min-max))	10 (2 to 48)	8 (2 to 27)	3 (2 to 27)	5 (2 to 28)

Notes:

[117] - ITT-E Population

[118] - ITT-E Population

[119] - ITT-E Population

[120] - ITT-E Population

End point values	Cohort 4: Children (6 to <13 years of age)	Cohort 5: Adolescents (13 to <18 years of age)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	22 ^[121]	9 ^[122]		
Units: Days				
median (full range (min-max))	5.5 (2 to 34)	4 (2 to 8)		

Notes:

[121] - ITT-E Population

[122] - ITT-E Population

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with the indicated mortality status at Day 14 and Day 28

End point title	Number of participants with the indicated mortality status at Day 14 and Day 28
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End point description:

The number of participants who died on or before Study Day 14 and Study Day 28 was summarized. Only those participants available at the specified time points were analyzed.

End point type	Secondary
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End point timeframe:

Day 14 and Day 28

End point values	Cohort 6: Adults (18 years and older)	Cohort 1: Infants (6 months to <1 year of age)	Cohort 2: Children (1 to <2 years of age)	Cohort 3: Children (2 to <6 years of age)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	130 ^[123]	7 ^[124]	11 ^[125]	12 ^[126]
Units: Participants				
Died on or before Study Day 14, No	113	7	11	12
Died on or before Study Day 14, Yes	17	0	0	0
Died on or before Study Day 28, No	108	7	10	12
Died on or before Study Day 28, Yes	22	0	1	0

Notes:

[123] - ITT-E Population

[124] - ITT-E Population

[125] - ITT-E Population

[126] - ITT-E Population

End point values	Cohort 4: Children (6 to	Cohort 5: Adolescents		
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	<13 years of age)	(13 to <18 years of age)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	27 ^[127]	14 ^[128]		
Units: Participants				
Died on or before Study Day 14, No	26	12		
Died on or before Study Day 14, Yes	1	2		
Died on or before Study Day 28, No	26	11		
Died on or before Study Day 28, Yes	1	3		

Notes:

[127] - ITT-E Population

[128] - ITT-E Population

Statistical analyses

No statistical analyses for this end point

Secondary: Median time to clinical response (sustained resolution) of all vital signs (composite)

End point title	Median time to clinical response (sustained resolution) of all vital signs (composite)
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End point description:

Sustained resolution of the following vital signs (composite) was assessed: afebrile status, normal oxygen saturation, normal respiratory status, normal HR, and normal BP. Clinical response is defined as the resolution of at least four of five vital signs within the following resolution criteria, maintained for 24 hours or hospital discharge, whichever occurred first: Temperature in degrees Centigrade (≤ 36.6 axilla, ≤ 37.2 oral, ≤ 37.7 rectal, core or tympanic); oxygen saturation ($\geq 95\%$, without supplemental oxygen); respiratory status (return to pre-morbid oxygen requirement, or no need for supplemental oxygen, or respiratory rate ≤ 60 , ≤ 40 , ≤ 34 , ≤ 30 , ≤ 24 or ≤ 24 breaths/minute without supplemental oxygen for Cohorts 1-6 respectively); HR (≤ 160 , ≤ 150 , ≤ 140 , ≤ 120 , ≤ 100 or ≤ 100 bpm for Cohorts 1-6 respectively); SBP (≥ 70 , ≥ 74 , ≥ 76 , ≥ 80 , ≥ 90 or ≥ 90 mmHg for Cohorts 1-6 respectively). Only those participants available at the specified time points were analyzed.

End point type	Secondary
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End point timeframe:

Up to post-treatment (PT) + 23 days

End point values	Cohort 6: Adults (18 years and older)	Cohort 1: Infants (6 months to <1 year of age)	Cohort 2: Children (1 to <2 years of age)	Cohort 3: Children (2 to <6 years of age)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	81 ^[129]	7 ^[130]	10 ^[131]	12 ^[132]
Units: Days				
median (full range (min-max))	9 (2 to 32)	7 (2 to 23)	3.5 (1 to 21)	6.5 (2 to 37)

Notes:

[129] - ITT-E Population

[130] - ITT-E Population

[131] - ITT-E Population

[132] - ITT-E Population

End point values	Cohort 4: Children (6 to <13 years of	Cohort 5: Adolescents (13 to <18		
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	age)	years of age)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	25 ^[133]	11 ^[134]		
Units: Days				
median (full range (min-max))	4 (1 to 42)	5 (2 to 32)		

Notes:

[133] - ITT-E Population

[134] - ITT-E Population

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with any AE categorized as an influenza complication

End point title	Number of participants with any AE categorized as an influenza complication
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End point description:

An AE is defined as any untoward medical occurrence in a participant temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product. An AE can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease (new or exacerbated) temporally associated with the use of a medicinal product.

End point type	Secondary
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End point timeframe:

Up to post-treatment (PT) + 23 days

End point values	Cohort 6: Adults (18 years and older)	Cohort 1: Infants (6 months to <1 year of age)	Cohort 2: Children (1 to <2 years of age)	Cohort 3: Children (2 to <6 years of age)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	130 ^[135]	7 ^[136]	11 ^[137]	12 ^[138]
Units: Participants	45	4	4	3

Notes:

[135] - ITT-E Population

[136] - ITT-E Population

[137] - ITT-E Population

[138] - ITT-E Population

End point values	Cohort 4: Children (6 to <13 years of age)	Cohort 5: Adolescents (13 to <18 years of age)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	27 ^[139]	14 ^[140]		
Units: Participants	8	3		

Notes:

[139] - ITT-E Population

[140] - ITT-E Population

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants who used any concomitant antibiotic medications for complications of influenza

End point title	Number of participants who used any concomitant antibiotic medications for complications of influenza
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End point description:

Concomitant medications (prescription and non-prescription) were permitted during the course of the study at the Investigator's discretion (except for prohibited medications: during the treatment period with IV zanamivir, other influenza antiviral drugs were not permitted). The number of participants who were treated with antibiotics for influenza complications was summarized.

End point type	Secondary
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End point timeframe:

Up to post-treatment (PT) + 23 days

End point values	Cohort 6: Adults (18 years and older)	Cohort 1: Infants (6 months to <1 year of age)	Cohort 2: Children (1 to <2 years of age)	Cohort 3: Children (2 to <6 years of age)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	130 ^[141]	7 ^[142]	11 ^[143]	12 ^[144]
Units: Participants	63	5	7	7

Notes:

[141] - ITT-E Population

[142] - ITT-E Population

[143] - ITT-E Population

[144] - ITT-E Population

End point values	Cohort 4: Children (6 to <13 years of age)	Cohort 5: Adolescents (13 to <18 years of age)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	27 ^[145]	14 ^[146]		
Units: Participants	12	6		

Notes:

[145] - ITT-E Population

[146] - ITT-E Population

Statistical analyses

No statistical analyses for this end point

Secondary: Median duration of hospitalization and intensive care unit (ICU) stays

End point title	Median duration of hospitalization and intensive care unit (ICU) stays
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End point description:

The duration of hospitalization (H) reflects the number of hospitalization days between the date of the first dose of investigational product and the date of discharge. ICU stay includes total duration in ICU and may include days in ICU before entry into the study. For participants with a missing discharge date who were not discharged at the end of the study, the date of discharge was imputed to the last follow-up visit (post-treatment +23 days). Only those participants available at the specified time points were analyzed (represented by n=X in the category titles).

End point type	Secondary
End point timeframe:	
Up to discharge from hospital	

End point values	Cohort 6: Adults (18 years and older)	Cohort 1: Infants (6 months to <1 year of age)	Cohort 2: Children (1 to <2 years of age)	Cohort 3: Children (2 to <6 years of age)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	130 ^[147]	7 ^[148]	11 ^[149]	12 ^[150]
Units: Days				
median (full range (min-max))				
Duration of H, n=130, 7, 11, 12, 27, 14	15 (1 to 133)	7 (2 to 23)	4 (2 to 44)	6.5 (3 to 37)
Duration of H-ICU, n=108, 4, 6, 8, 19, 9	11.5 (1 to 104)	7.5 (5 to 24)	5 (3 to 19)	5.5 (2 to 26)

Notes:

[147] - ITT-E Population

[148] - ITT-E Population

[149] - ITT-E Population

[150] - ITT-E Population

End point values	Cohort 4: Children (6 to <13 years of age)	Cohort 5: Adolescents (13 to <18 years of age)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	27 ^[151]	14 ^[152]		
Units: Days				
median (full range (min-max))				
Duration of H, n=130, 7, 11, 12, 27, 14	6 (1 to 45)	6.5 (2 to 42)		
Duration of H-ICU, n=108, 4, 6, 8, 19, 9	8 (2 to 50)	8 (4 to 39)		

Notes:

[151] - ITT-E Population

[152] - ITT-E Population

Statistical analyses

No statistical analyses for this end point

Secondary: Geometric mean maximum serum concentration (Cmax) of zanamivir at the end of infusion

End point title	Geometric mean maximum serum concentration (Cmax) of zanamivir at the end of infusion
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End point description:

The Cmax of zanamivir was evaluated at the end of infusion. Serial blood samples for pharmacokinetic (PK) analysis were collected if possible in conjunction with the initial dose on Day 1 (5-7 serial samples) and over a dosing interval during repeat dosing on Days 3, 4, or 5 (5 serial samples). PK data for all participants with available blood samples were analyzed. PK data for those participants who were neither on extracorporeal membrane oxygenation (ECMO) nor on continuous renal replacement therapy (CRRT), who had CLcr ≥ 80 mL/minutes (≥ 80 mL/minute/1.73m² for cohorts 1-4) and who received an initial dose (ID) and a maintenance dose (MD) of 14 mg/kg (6 months to <6 years of age), 12 mg/kg, not to exceed 600 mg (6 to <18 years of age) or 600 mg zanamivir (≥ 18 years of age) (represented by n=X in the category titles) were summarized. "99999" indicates that data are not available/analysis was not performed.

End point type	Secondary
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End point timeframe:

Day 1 and Days 3, 4, or 5

End point values	Cohort 6: Adults (18 years and older)	Cohort 1: Infants (6 months to <1 year of age)	Cohort 2: Children (1 to <2 years of age)	Cohort 3: Children (2 to <6 years of age)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	130 ^[153]	7 ^[154]	6 ^[155]	12 ^[156]
Units: Micrograms per mL				
geometric mean (geometric coefficient of variation)				
ID, 600 mg, CLCr>=80, n=67, 0, 0, 0, 0, 6	32.77 (± 34)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)
ID, 12 mg/kg, CLCr>=80, n=0, 0, 0, 0, 9, 3	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)
ID, 14 mg/kg, CLCr>=80, n=0, 4, 5, 9, 0, 0	99999 (± 99999)	36.21 (± 21)	37.78 (± 24)	41.54 (± 23)
MD, 600 mg, CLCr>=80, n=72, 0, 0, 0, 0, 2	35.3 (± 32)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)
MD, 12 mg/kg, CLCr>=80, n=0, 0, 0, 0, 4, 0	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)
MD, 14 mg/kg, CLCr>=80, n=0, 0, 1, 4, 0, 0	99999 (± 99999)	99999 (± 99999)	38.01 (± 99999)	43.19 (± 9)

Notes:

[153] - PK Parameter Population: participants with one or more estimated zanamivir PK parameters

[154] - PK Parameter Population: participants with one or more estimated zanamivir PK parameters

[155] - PK Parameter Population: participants with one or more estimated zanamivir PK parameters

[156] - PK Parameter Population: participants with one or more estimated zanamivir PK parameters

End point values	Cohort 4: Children (6 to <13 years of age)	Cohort 5: Adolescents (13 to <18 years of age)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	15 ^[157]	13 ^[158]		
Units: Micrograms per mL				
geometric mean (geometric coefficient of variation)				
ID, 600 mg, CLCr>=80, n=67, 0, 0, 0, 0, 6	99999 (± 99999)	34.47 (± 27)		
ID, 12 mg/kg, CLCr>=80, n=0, 0, 0, 0, 9, 3	44.16 (± 47)	4.99 (± 3997)		
ID, 14 mg/kg, CLCr>=80, n=0, 4, 5, 9, 0, 0	99999 (± 99999)	99999 (± 99999)		
MD, 600 mg, CLCr>=80, n=72, 0, 0, 0, 0, 2	99999 (± 99999)	25.73 (± 52)		
MD, 12 mg/kg, CLCr>=80, n=0, 0, 0, 0, 4, 0	45.18 (± 48)	99999 (± 99999)		
MD, 14 mg/kg, CLCr>=80, n=0, 0, 1, 4, 0, 0	99999 (± 99999)	99999 (± 99999)		

Notes:

[157] - PK Parameter Population: participants with one or more estimated zanamivir PK parameters

[158] - PK Parameter Population: participants with one or more estimated zanamivir PK parameters

Statistical analyses

No statistical analyses for this end point

Secondary: Geometric mean area under the serum drug concentration-time curve (AUC) over a 12-hour dosing interval (AUC[0-tau]) and AUC extrapolated to infinity (AUC[0-inf]) of zanamivir

End point title	Geometric mean area under the serum drug concentration-time curve (AUC) over a 12-hour dosing interval (AUC[0-tau]) and AUC extrapolated to infinity (AUC[0-inf]) of zanamivir
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End point description:

The AUC(0-tau) during the repeat dose interval and AUC(0-inf) for the initial dose were evaluated. Serial blood samples for PK analysis were collected if possible in conjunction with the initial dose on Day 1 (5-7 serial samples) and over a dosing interval during repeat dosing on Days 3, 4, or 5 (5 serial samples). PK data for all participants with available blood samples were analyzed. PK data for those participants not on ECMO or CRRT with a CLcr ≥ 80 mL/minutes (≥ 80 mL/minute/1.73m² for cohorts 1-4) and who received an ID and a MD of 14 mg/kg (6 months to <6 years of age), 12 mg/kg, not to exceed 600 mg (6 to <18 years of age) or 600 mg zanamivir (≥ 18 years of age) (represented by n=X in the category titles) were summarized. "99999" indicates that data are not available/analysis was not performed.

End point type	Secondary
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End point timeframe:

Day 1 and Days 3, 4, or 5

End point values	Cohort 6: Adults (18 years and older)	Cohort 1: Infants (6 months to <1 year of age)	Cohort 2: Children (1 to <2 years of age)	Cohort 3: Children (2 to <6 years of age)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	130 ^[159]	7 ^[160]	6 ^[161]	12 ^[162]
Units: Micrograms per hour per milliliter				
geometric mean (geometric coefficient of variation)				
AUC(0-inf), ID, 600 mg, CLcr ≥ 80 , n=63,0,0,0,0,5	82.86 (± 36)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)
AUC(0-inf), ID, 12 mg/kg, CLcr ≥ 80 , n=0,0,0,0,8,1	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)
AUC(0-inf), ID, 14 mg/kg, CLcr ≥ 80 , n=0,3,4,9,0,0	99999 (± 99999)	75.31 (± 23)	72.42 (± 14)	80.28 (± 38)
AUC(0-tau), MD, 600 mg, CLcr ≥ 80 , n=65,0,0, 0,0,2	90.33 (± 36)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)
AUC(0-tau), MD, 12 mg/kg, CLcr ≥ 80 , n=0,0,0,0,4,0	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)
AUC(0-tau), MD, 14 mg/kg, CLcr ≥ 80 , n=0,0,1,4,0,0	99999 (± 99999)	99999 (± 99999)	68.2 (± 99999)	81.02 (± 28)

Notes:

[159] - PK Parameter Population

[160] - PK Parameter Population

[161] - PK Parameter Population

[162] - PK Parameter Population

End point values	Cohort 4: Children (6 to <13 years of age)	Cohort 5: Adolescents (13 to <18 years of age)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	15 ^[163]	13 ^[164]		

Units: Micrograms per hour per milliliter				
geometric mean (geometric coefficient of variation)				
AUC(0-inf), ID, 600 mg, CLcr>=80, n=63,0,0,0,5	99999 (± 99999)	91.07 (± 27)		
AUC(0-inf), ID, 12 mg/kg, CLcr>=80, n=0,0,0,0,8,1	107.21 (± 41)	135.22 (± 99999)		
AUC(0-inf), ID, 14 mg/kg, CLcr>=80, n=0,3,4,9,0,0	99999 (± 99999)	99999 (± 99999)		
AUC(0-tau), MD, 600 mg, CLcr>=80, n=65,0,0, 0,0,2	99999 (± 99999)	64.52 (± 30)		
AUC(0-tau), MD, 12 mg/kg, CLcr>=80, n=0,0,0,0,4,0	90.33 (± 45)	99999 (± 99999)		
AUC(0-tau), MD, 14 mg/kg, CLcr>=80, n=0,0,1,4,0,0	99999 (± 99999)	99999 (± 99999)		

Notes:

[163] - PK Parameter Population

[164] - PK Parameter Population

Statistical analyses

No statistical analyses for this end point

Secondary: Geometric mean terminal half life (t1/2) of zanamivir

End point title	Geometric mean terminal half life (t1/2) of zanamivir
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End point description:

The t1/2 of zanamivir was evaluated. Terminal half life is defined as the time it takes for a substance to lose half of its pharmacologic, physiologic, or radiologic activity. Serial blood samples for PK analysis were collected if possible in conjunction with the initial dose on Day 1 (5-7 serial samples) and over a dosing interval during repeat dosing on Day 3, 4, or 5 (5 serial samples). PK data for all participants with available blood samples were analyzed. PK data for those participants not on ECMO or CRRT with a CLcr>=80 mL/minutes (>=80 mL/minute/1.73m² for cohorts 1-4) and who received an ID and a MD of 14 mg/kg (6 months to <6 years of age), 12 mg/kg, not to exceed 600 mg (6 to <18 years of age) or 600 mg zanamivir (>=18 years of age) (represented by n=X in the category titles) were summarized. "99999" indicates that data are not available/analysis was not performed.

End point type	Secondary
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End point timeframe:

Day 1 and Days 3, 4, or 5

End point values	Cohort 6: Adults (18 years and older)	Cohort 1: Infants (6 months to <1 year of age)	Cohort 2: Children (1 to <2 years of age)	Cohort 3: Children (2 to <6 years of age)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	130 ^[165]	7 ^[166]	6 ^[167]	12 ^[168]
Units: Hours				
geometric mean (geometric coefficient of variation)				
ID, 600 mg, CLcr>=80, n=67, 0, 0, 0, 0, 5	2.39 (± 31)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)
ID, 12 mg/kg, CLcr>=80, n=0, 0, 0, 0, 8, 1	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)
ID, 14 mg/kg, CLcr>=80, n=0, 3, 5, 9, 0, 0	99999 (± 99999)	1.84 (± 19)	2.49 (± 118)	1.6 (± 34)
MD, 600 mg, CLcr>=80, n=68, 0, 0, 0, 0, 2	2.56 (± 34)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)

MD, 12 mg/kg, CLcr \geq 80, n=0, 0, 0, 0, 4, 0	99999 (\pm 99999)	99999 (\pm 99999)	99999 (\pm 99999)	99999 (\pm 99999)
MD, 14 mg/kg, CLcr \geq 80, n=0, 0, 1, 4, 0, 0	99999 (\pm 99999)	99999 (\pm 99999)	1.68 (\pm 99999)	1.76 (\pm 20)

Notes:

[165] - PK Parameter Population

[166] - PK Parameter Population

[167] - PK Parameter Population

[168] - PK Parameter Population

End point values	Cohort 4: Children (6 to <13 years of age)	Cohort 5: Adolescents (13 to <18 years of age)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	15 ^[169]	13 ^[170]		
Units: Hours				
geometric mean (geometric coefficient of variation)				
ID, 600 mg, CLcr \geq 80, n=67, 0, 0, 0, 0, 5	99999 (\pm 99999)	2.06 (\pm 47)		
ID, 12 mg/kg, CLcr \geq 80, n=0, 0, 0, 0, 8, 1	2.57 (\pm 55)	2.16 (\pm 99999)		
ID, 14 mg/kg, CLcr \geq 80, n=0, 3, 5, 9, 0, 0	99999 (\pm 99999)	99999 (\pm 99999)		
MD, 600 mg, CLcr \geq 80, n=68, 0, 0, 0, 0, 2	99999 (\pm 99999)	1.73 (\pm 21)		
MD, 12 mg/kg, CLcr \geq 80, n=0, 0, 0, 0, 4, 0	1.81 (\pm 41)	99999 (\pm 99999)		
MD, 14 mg/kg, CLcr \geq 80, n=0, 0, 1, 4, 0, 0	99999 (\pm 99999)	99999 (\pm 99999)		

Notes:

[169] - PK Parameter Population

[170] - PK Parameter Population

Statistical analyses

No statistical analyses for this end point

Secondary: Geometric mean serum clearance of zanamivir

End point title	Geometric mean serum clearance of zanamivir
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End point description:

The serum clearance of zanamivir was evaluated. Clearance is defined as the volume of zanamivir per unit time eliminated from serum. Serial blood samples for PK analysis were collected if possible in conjunction with the initial dose on Day 1 (5-7 serial samples) and over a dosing interval during repeat dosing on Days 3, 4, or 5 (5 serial samples). PK data for all participants with available blood samples were analyzed. PK data for those participants not on ECMO or CRRT with a CLcr \geq 80 mL/minutes (\geq 80 mL/minute/1.73m² for cohorts 1-4) and who received an ID and a MD 14 mg/kg (6 months to <6 years of age), 12 mg/kg, not to exceed 600 mg (6 to <18 years of age) or 600 mg zanamivir (\geq 18 years of age) (represented by n=X in the category titles) were summarized. "99999" indicates that data are not available/analysis was not performed.

End point type	Secondary
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End point timeframe:

Day 1 and Days 3, 4, or 5

End point values	Cohort 6: Adults (18 years and older)	Cohort 1: Infants (6 months to <1 year of age)	Cohort 2: Children (1 to <2 years of age)	Cohort 3: Children (2 to <6 years of age)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	130 ^[171]	7 ^[172]	6 ^[173]	12 ^[174]
Units: mL per minutes				
geometric mean (geometric coefficient of variation)				
ID, 600 mg, CLcr>=80, n=63, 0, 0, 0, 0, 5	120.68 (± 36)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)
ID, 12 mg/kg, CLcr>=80, n=0, 0, 0, 0, 8, 1	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)
ID, 14 mg/kg, CLcr>=80, n=0, 3, 4, 9, 0, 0	99999 (± 99999)	27.31 (± 32)	31 (± 12)	41.95 (± 37)
MD, 600 mg, CLcr>=80, n=65, 0, 0, 0, 0, 2	110.71 (± 36)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)
MD, 12 mg/kg, CLcr>=80, n=0, 0, 0, 0, 4, 0	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)
MD, 14 mg/kg, CLcr>=80, n=0, 0, 1, 4, 0, 0	99999 (± 99999)	99999 (± 99999)	31.78 (± 99999)	40.35 (± 35)

Notes:

[171] - PK Parameter Population

[172] - PK Parameter Population

[173] - PK Parameter Population

[174] - PK Parameter Population

End point values	Cohort 4: Children (6 to <13 years of age)	Cohort 5: Adolescents (13 to <18 years of age)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	15 ^[175]	13 ^[176]		
Units: mL per minutes				
geometric mean (geometric coefficient of variation)				
ID, 600 mg, CLcr>=80, n=63, 0, 0, 0, 0, 5	99999 (± 99999)	109.83 (± 27)		
ID, 12 mg/kg, CLcr>=80, n=0, 0, 0, 0, 8, 1	46.7 (± 47)	53.7 (± 99999)		
ID, 14 mg/kg, CLcr>=80, n=0, 3, 4, 9, 0, 0	99999 (± 99999)	99999 (± 99999)		
MD, 600 mg, CLcr>=80, n=65, 0, 0, 0, 0, 2	99999 (± 99999)	155.03 (± 30)		
MD, 12 mg/kg, CLcr>=80, n=0, 0, 0, 0, 4, 0	68.61 (± 34)	99999 (± 99999)		
MD, 14 mg/kg, CLcr>=80, n=0, 0, 1, 4, 0, 0	99999 (± 99999)	99999 (± 99999)		

Notes:

[175] - PK Parameter Population

[176] - PK Parameter Population

Statistical analyses

No statistical analyses for this end point

Secondary: Geometric mean volume of distribution (Vd) of zanamivir

End point title	Geometric mean volume of distribution (Vd) of zanamivir
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End point description:

The Vd of zanamivir was evaluated. Volume of distribution is defined as the apparent volume in which zanamivir is distributed. Serial blood samples for PK analysis were collected if possible in conjunction with the initial dose on Day 1 (5-7 serial samples) and over a dosing interval during repeat dosing on Days 3, 4, or 5 (5 serial samples). PK data for all participants with available blood samples were analyzed. PK data for those participants not on ECMO or CRRT with a CLcr \geq 80 mL/minutes (\geq 80 mL/minute/1.73m² for cohorts 1-4) and who received an ID and a MD of 14 mg/kg (6 months to <6 years of age), 12 mg/kg, not to exceed 600 mg (6 to <18 years of age) or 600 mg zanamivir (\geq 18 years of age) (represented by n=X in the category titles) were summarized. "99999" indicates that data are not available/analysis was not performed.

End point type Secondary

End point timeframe:

Day 1 and Days 3, 4, or 5

End point values	Cohort 6: Adults (18 years and older)	Cohort 1: Infants (6 months to <1 year of age)	Cohort 2: Children (1 to <2 years of age)	Cohort 3: Children (2 to <6 years of age)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	130 ^[177]	7 ^[178]	6 ^[179]	12 ^[180]
Units: Liters (L)				
geometric mean (geometric coefficient of variation)				
ID, 600 mg, CLcr \geq 80, n=63, 0, 0, 0, 0, 5	22.02 (\pm 30)	99999 (\pm 99999)	99999 (\pm 99999)	99999 (\pm 99999)
ID, 12 mg/kg, CLcr \geq 80, n=0, 0, 0, 0, 8, 1	99999 (\pm 99999)	99999 (\pm 99999)	99999 (\pm 99999)	99999 (\pm 99999)
ID, 14 mg/kg, CLcr \geq 80, n=0, 3, 4, 9, 0, 0	99999 (\pm 99999)	3.77 (\pm 12)	3.94 (\pm 29)	5.15 (\pm 20)
MD, 600 mg, CLcr \geq 80, n=65, 0, 0, 0, 0, 2	21.61 (\pm 33)	99999 (\pm 99999)	99999 (\pm 99999)	99999 (\pm 99999)
MD, 12 mg/kg, CLcr \geq 80, n=0, 0, 0, 0, 8, 0	99999 (\pm 99999)	99999 (\pm 99999)	99999 (\pm 99999)	99999 (\pm 99999)
MD, 14 mg/kg, CLcr \geq 80, n=0, 0, 1, 4, 0, 0	99999 (\pm 99999)	99999 (\pm 99999)	3.77 (\pm 99999)	5.23 (\pm 32)

Notes:

[177] - PK Parameter Population

[178] - PK Parameter Population

[179] - PK Parameter Population

[180] - PK Parameter Population

End point values	Cohort 4: Children (6 to <13 years of age)	Cohort 5: Adolescents (13 to <18 years of age)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	15 ^[181]	13 ^[182]		
Units: Liters (L)				
geometric mean (geometric coefficient of variation)				
ID, 600 mg, CLcr \geq 80, n=63, 0, 0, 0, 0, 5	99999 (\pm 99999)	18.57 (\pm 26)		
ID, 12 mg/kg, CLcr \geq 80, n=0, 0, 0, 0, 8, 1	9.21 (\pm 48)	10.09 (\pm 99999)		
ID, 14 mg/kg, CLcr \geq 80, n=0, 3, 4, 9, 0, 0	99999 (\pm 99999)	99999 (\pm 99999)		

MD, 600 mg, CLcr>=80, n=65, 0, 0, 0, 0, 2	99999 (± 99999)	23.2 (± 25)		
MD, 12 mg/kg, CLcr>=80, n=0, 0, 0, 0, 8, 0	9.82 (± 8)	99999 (± 99999)		
MD, 14 mg/kg, CLcr>=80, n=0, 0, 1, 4, 0, 0	99999 (± 99999)	99999 (± 99999)		

Notes:

[181] - PK Parameter Population

[182] - PK Parameter Population

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Non-serious adverse events (AEs) were collected from the start of study medication until follow-up (up to 33 days). Serious adverse events (SAEs) assessed as related to study participation were recorded from time of consent until any follow-up contact.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	17.1
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Reporting groups

Reporting group title	Cohort 6: Adults (18 years and older)
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Reporting group description:

Participants ≥ 18 years of age received 600 milligrams (mg) zanamivir by intravenous (IV) infusion over 30 minutes twice daily, adjusted for renal function, for 5 days. Treatment could have been extended for up to 5 additional days if viral shedding or clinical symptoms warranted further treatment.

Reporting group title	Cohort 1: Infants (6 months to <1 year of age)
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Reporting group description:

Participants 6 months to <1 year of age received 14 mg per kilogram (mg/kg) zanamivir by IV infusion over 30 minutes twice daily, adjusted for renal function, for 5 days. Treatment could have been extended for up to 5 additional days if viral shedding or clinical symptoms warranted further treatment.

Reporting group title	Cohort 2: Children (1 to <2 years of age)
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Reporting group description:

Participants 1 year to <2 years of age received 14 mg/kg zanamivir by IV infusion over 30 minutes twice daily, adjusted for renal function, for 5 days. Treatment could have been extended for up to 5 additional days if viral shedding or clinical symptoms warranted further treatment.

Reporting group title	Cohort 3: Children (2 to <6 years of age)
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Reporting group description:

Participants 2 years to <6 years of age received 14 mg/kg zanamivir with a maximum dose of 600 mg by IV infusion over 30 minutes twice daily, adjusted for renal function, for 5 days. Treatment could have been extended for up to 5 additional days if viral shedding or clinical symptoms warranted further treatment.

Reporting group title	Cohort 4: Children (6 to <13 years of age)
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Reporting group description:

Participants 6 years to <13 years of age received 12 mg/kg zanamivir with a maximum dose of 600 mg by IV infusion over 30 minutes twice daily, adjusted for renal function, for 5 days. Treatment could have been extended for up to 5 additional days if viral shedding or clinical symptoms warranted further treatment.

Reporting group title	Cohort 5: Adolescents (13 to <18 years of age)
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Reporting group description:

Participants 13 to <18 years of age received 12 mg/kg zanamivir with a maximum dose of 600 mg by IV infusion over 30 minutes twice daily, adjusted for renal function, for 5 days. Treatment could have been extended for up to 5 additional days if viral shedding or clinical symptoms warranted further treatment.

Serious adverse events	Cohort 6: Adults (18 years and older)	Cohort 1: Infants (6 months to <1 year of age)	Cohort 2: Children (1 to <2 years of age)
Total subjects affected by serious adverse events			
subjects affected / exposed	44 / 130 (33.85%)	1 / 7 (14.29%)	2 / 11 (18.18%)
number of deaths (all causes)	33	0	1
number of deaths resulting from adverse events			

Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Acute leukaemia			
subjects affected / exposed	1 / 130 (0.77%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	1 / 130 (0.77%)	0 / 7 (0.00%)	0 / 11 (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
Haemorrhage			
subjects affected / exposed	1 / 130 (0.77%)	0 / 7 (0.00%)	0 / 11 (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
Hypertension			
subjects affected / exposed	0 / 130 (0.00%)	0 / 7 (0.00%)	0 / 11 (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
Peripheral ischaemia			
subjects affected / exposed	1 / 130 (0.77%)	0 / 7 (0.00%)	0 / 11 (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
Shock haemorrhagic			
subjects affected / exposed	1 / 130 (0.77%)	0 / 7 (0.00%)	0 / 11 (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
General disorders and administration site conditions			
Multi-organ failure			
subjects affected / exposed	3 / 130 (2.31%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 3	0 / 0	0 / 0
Pyrexia			

subjects affected / exposed	0 / 130 (0.00%)	0 / 7 (0.00%)	0 / 11 (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			
Respiratory failure			
subjects affected / exposed	7 / 130 (5.38%)	1 / 7 (14.29%)	1 / 11 (9.09%)
occurrences causally related to treatment / all	0 / 7	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 5	0 / 0	0 / 1
Acute respiratory distress syndrome			
subjects affected / exposed	3 / 130 (2.31%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	3 / 130 (2.31%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Hypoxia			
subjects affected / exposed	2 / 130 (1.54%)	0 / 7 (0.00%)	0 / 11 (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
Chronic obstructive pulmonary disease			
subjects affected / exposed	1 / 130 (0.77%)	0 / 7 (0.00%)	0 / 11 (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
Haemothorax			
subjects affected / exposed	1 / 130 (0.77%)	0 / 7 (0.00%)	0 / 11 (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
Pneumothorax			
subjects affected / exposed	1 / 130 (0.77%)	0 / 7 (0.00%)	0 / 11 (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 haemorrhage			

subjects affected / exposed	1 / 130 (0.77%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory arrest			
subjects affected / exposed	1 / 130 (0.77%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Respiratory distress			
subjects affected / exposed	1 / 130 (0.77%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Psychiatric disorders			
Depression			
subjects affected / exposed	1 / 130 (0.77%)	0 / 7 (0.00%)	0 / 11 (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
Investigations			
Blood bilirubin increased			
subjects affected / exposed	0 / 130 (0.00%)	0 / 7 (0.00%)	0 / 11 (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
Injury, poisoning and procedural complications			
Brain herniation			
subjects affected / exposed	0 / 130 (0.00%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Cardiac arrest			
subjects affected / exposed	4 / 130 (3.08%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 4	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Cardio-respiratory arrest			

subjects affected / exposed	2 / 130 (1.54%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 2	0 / 0	0 / 0
Tachycardia			
subjects affected / exposed	0 / 130 (0.00%)	0 / 7 (0.00%)	1 / 11 (9.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrioventricular block complete			
subjects affected / exposed	1 / 130 (0.77%)	0 / 7 (0.00%)	0 / 11 (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
Cardiogenic shock			
subjects affected / exposed	1 / 130 (0.77%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Torsade de pointes			
subjects affected / exposed	1 / 130 (0.77%)	0 / 7 (0.00%)	0 / 11 (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
Ventricular arrhythmia			
subjects affected / exposed	1 / 130 (0.77%)	0 / 7 (0.00%)	0 / 11 (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
Ventricular tachycardia			
subjects affected / exposed	1 / 130 (0.77%)	0 / 7 (0.00%)	0 / 11 (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
Nervous system disorders			
Encephalopathy			
subjects affected / exposed	2 / 130 (1.54%)	0 / 7 (0.00%)	0 / 11 (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
Ischaemic stroke			

subjects affected / exposed	1 / 130 (0.77%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Status epilepticus			
subjects affected / exposed	0 / 130 (0.00%)	0 / 7 (0.00%)	0 / 11 (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			
Neutropenia			
subjects affected / exposed	0 / 130 (0.00%)	0 / 7 (0.00%)	0 / 11 (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			
Cyclic vomiting syndrome			
subjects affected / exposed	0 / 130 (0.00%)	0 / 7 (0.00%)	0 / 11 (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
Hepatobiliary disorders			
Hepatocellular injury			
subjects affected / exposed	3 / 130 (2.31%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	2 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Toxic skin eruption			
subjects affected / exposed	1 / 130 (0.77%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Renal failure			
subjects affected / exposed	2 / 130 (1.54%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Renal failure acute			

subjects affected / exposed	2 / 130 (1.54%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Pneumonia			
subjects affected / exposed	7 / 130 (5.38%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 9	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 3	0 / 0	0 / 0
Septic shock			
subjects affected / exposed	4 / 130 (3.08%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 5	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 2	0 / 0	0 / 0
Bronchopulmonary aspergillosis			
subjects affected / exposed	3 / 130 (2.31%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 3	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	3 / 130 (2.31%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 3	0 / 0	0 / 0
Bacteraemia			
subjects affected / exposed	1 / 130 (0.77%)	0 / 7 (0.00%)	0 / 11 (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
Acinetobacter bacteraemia			
subjects affected / exposed	1 / 130 (0.77%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	0 / 130 (0.00%)	0 / 7 (0.00%)	0 / 11 (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
Encephalitis			

subjects affected / exposed	0 / 130 (0.00%)	0 / 7 (0.00%)	0 / 11 (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
Endocarditis			
subjects affected / exposed	1 / 130 (0.77%)	0 / 7 (0.00%)	0 / 11 (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
Lung abscess			
subjects affected / exposed	1 / 130 (0.77%)	0 / 7 (0.00%)	0 / 11 (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
Pseudomonas infection			
subjects affected / exposed	1 / 130 (0.77%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Respiratory syncytial virus infection			
subjects affected / exposed	0 / 130 (0.00%)	0 / 7 (0.00%)	0 / 11 (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
Superinfection bacterial			
subjects affected / exposed	1 / 130 (0.77%)	0 / 7 (0.00%)	0 / 11 (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
Viral pericarditis			
subjects affected / exposed	1 / 130 (0.77%)	0 / 7 (0.00%)	0 / 11 (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 / 130 (0.77%)	0 / 7 (0.00%)	0 / 11 (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
Lactic acidosis			

subjects affected / exposed	0 / 130 (0.00%)	0 / 7 (0.00%)	0 / 11 (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	Cohort 3: Children (2 to <6 years of age)	Cohort 4: Children (6 to <13 years of age)	Cohort 5: Adolescents (13 to <18 years of age)
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 12 (0.00%)	8 / 27 (29.63%)	4 / 14 (28.57%)
number of deaths (all causes)	0	1	3
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Acute leukaemia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (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
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (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
Haemorrhage			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (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
Hypertension			
subjects affected / exposed	0 / 12 (0.00%)	1 / 27 (3.70%)	0 / 14 (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
Peripheral ischaemia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (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
Shock haemorrhagic			

subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (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			
Multi-organ failure			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	1 / 14 (7.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Pyrexia			
subjects affected / exposed	0 / 12 (0.00%)	1 / 27 (3.70%)	0 / 14 (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
Respiratory, thoracic and mediastinal disorders			
Respiratory failure			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (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
Acute respiratory distress syndrome			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (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 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (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
Hypoxia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (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
Chronic obstructive pulmonary disease			

subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (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
Haemothorax			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (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
Pneumothorax			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (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 haemorrhage			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (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 arrest			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (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 distress			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (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			
Depression			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (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
Investigations			
Blood bilirubin increased			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	1 / 14 (7.14%)
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			
Brain herniation			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	1 / 14 (7.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Cardiac disorders			
Cardiac arrest			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (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
Cardio-respiratory arrest			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (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
Tachycardia			
subjects affected / exposed	0 / 12 (0.00%)	1 / 27 (3.70%)	0 / 14 (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
Atrioventricular block complete			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (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
Cardiogenic shock			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (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
Torsade de pointes			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (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
Ventricular arrhythmia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (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

Ventricular tachycardia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (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			
Encephalopathy			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (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
Ischaemic stroke			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (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
Status epilepticus			
subjects affected / exposed	0 / 12 (0.00%)	1 / 27 (3.70%)	0 / 14 (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
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	0 / 12 (0.00%)	1 / 27 (3.70%)	0 / 14 (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
Gastrointestinal disorders			
Cyclic vomiting syndrome			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	1 / 14 (7.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Hepatocellular injury			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (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
Skin and subcutaneous tissue disorders			
Toxic skin eruption			

subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (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
Renal and urinary disorders			
Renal failure			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (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
Renal failure acute			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (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			
Pneumonia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (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
Septic shock			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (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
Bronchopulmonary aspergillosis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (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
Sepsis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (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
Bacteraemia			
subjects affected / exposed	0 / 12 (0.00%)	1 / 27 (3.70%)	0 / 14 (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
Acinetobacter bacteraemia			

subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (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
Cellulitis			
subjects affected / exposed	0 / 12 (0.00%)	1 / 27 (3.70%)	0 / 14 (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
Encephalitis			
subjects affected / exposed	0 / 12 (0.00%)	1 / 27 (3.70%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Endocarditis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (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
Lung abscess			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (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
Pseudomonas infection			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (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 syncytial virus infection			
subjects affected / exposed	0 / 12 (0.00%)	1 / 27 (3.70%)	0 / 14 (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
Superinfection bacterial			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (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
Viral pericarditis			

subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (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 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (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
Lactic acidosis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	1 / 14 (7.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Cohort 6: Adults (18 years and older)	Cohort 1: Infants (6 months to <1 year of age)	Cohort 2: Children (1 to <2 years of age)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	100 / 130 (76.92%)	4 / 7 (57.14%)	7 / 11 (63.64%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Chronic myeloid leukaemia			
subjects affected / exposed	1 / 130 (0.77%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Vascular disorders			
Hypotension			
subjects affected / exposed	15 / 130 (11.54%)	0 / 7 (0.00%)	1 / 11 (9.09%)
occurrences (all)	26	0	1
Hypertension			
subjects affected / exposed	11 / 130 (8.46%)	0 / 7 (0.00%)	1 / 11 (9.09%)
occurrences (all)	19	0	1
Deep vein thrombosis			
subjects affected / exposed	2 / 130 (1.54%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	2	0	0
Thrombophlebitis			

subjects affected / exposed	3 / 130 (2.31%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	4	0	0
Phlebitis			
subjects affected / exposed	2 / 130 (1.54%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	3	0	0
Venous thrombosis			
subjects affected / exposed	2 / 130 (1.54%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	2	0	0
Arterial thrombosis			
subjects affected / exposed	1 / 130 (0.77%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Circulatory collapse			
subjects affected / exposed	1 / 130 (0.77%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Extremity necrosis			
subjects affected / exposed	0 / 130 (0.00%)	0 / 7 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Haematoma			
subjects affected / exposed	1 / 130 (0.77%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Hypoperfusion			
subjects affected / exposed	0 / 130 (0.00%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Jugular vein thrombosis			
subjects affected / exposed	0 / 130 (0.00%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Poor peripheral circulation			
subjects affected / exposed	0 / 130 (0.00%)	0 / 7 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Venous thrombosis limb			
subjects affected / exposed	1 / 130 (0.77%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
General disorders and administration site conditions			
Pyrexia			

subjects affected / exposed	14 / 130 (10.77%)	1 / 7 (14.29%)	0 / 11 (0.00%)
occurrences (all)	14	1	0
Oedema			
subjects affected / exposed	7 / 130 (5.38%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	7	0	0
Asthenia			
subjects affected / exposed	2 / 130 (1.54%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	2	0	0
Pain			
subjects affected / exposed	3 / 130 (2.31%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	4	0	0
Drug withdrawal syndrome			
subjects affected / exposed	0 / 130 (0.00%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Chest pain			
subjects affected / exposed	2 / 130 (1.54%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	2	0	0
Generalised oedema			
subjects affected / exposed	0 / 130 (0.00%)	0 / 7 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Infusion site extravasation			
subjects affected / exposed	1 / 130 (0.77%)	1 / 7 (14.29%)	0 / 11 (0.00%)
occurrences (all)	1	1	0
Catheter site haemorrhage			
subjects affected / exposed	1 / 130 (0.77%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Device occlusion			
subjects affected / exposed	0 / 130 (0.00%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Facial pain			
subjects affected / exposed	1 / 130 (0.77%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Hypothermia			
subjects affected / exposed	0 / 130 (0.00%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Injection site reaction			

subjects affected / exposed	1 / 130 (0.77%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Multi-organ failure			
subjects affected / exposed	0 / 130 (0.00%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Oedema peripheral			
subjects affected / exposed	1 / 130 (0.77%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Thrombosis in device			
subjects affected / exposed	1 / 130 (0.77%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Unintentional medical device removal			
subjects affected / exposed	0 / 130 (0.00%)	1 / 7 (14.29%)	0 / 11 (0.00%)
occurrences (all)	0	2	0
Reproductive system and breast disorders			
Perineal rash			
subjects affected / exposed	1 / 130 (0.77%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Respiratory, thoracic and mediastinal disorders			
Pleural effusion			
subjects affected / exposed	6 / 130 (4.62%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	6	0	0
Dyspnoea			
subjects affected / exposed	4 / 130 (3.08%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	5	0	0
Bronchospasm			
subjects affected / exposed	3 / 130 (2.31%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	3	0	0
Pneumothorax			
subjects affected / exposed	3 / 130 (2.31%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	3	0	0
Pulmonary oedema			
subjects affected / exposed	2 / 130 (1.54%)	1 / 7 (14.29%)	0 / 11 (0.00%)
occurrences (all)	2	1	0
Respiratory distress			

subjects affected / exposed	1 / 130 (0.77%)	0 / 7 (0.00%)	1 / 11 (9.09%)
occurrences (all)	1	0	1
Respiratory failure			
subjects affected / exposed	1 / 130 (0.77%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Stridor			
subjects affected / exposed	0 / 130 (0.00%)	2 / 7 (28.57%)	0 / 11 (0.00%)
occurrences (all)	0	2	0
Cough			
subjects affected / exposed	1 / 130 (0.77%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Epistaxis			
subjects affected / exposed	0 / 130 (0.00%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Acute pulmonary oedema			
subjects affected / exposed	1 / 130 (0.77%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Acute respiratory distress syndrome			
subjects affected / exposed	1 / 130 (0.77%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Acute respiratory failure			
subjects affected / exposed	1 / 130 (0.77%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Adenoidal hypertrophy			
subjects affected / exposed	0 / 130 (0.00%)	1 / 7 (14.29%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Dysphonia			
subjects affected / exposed	1 / 130 (0.77%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Dyspnoea exertional			
subjects affected / exposed	1 / 130 (0.77%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Haemoptysis			
subjects affected / exposed	1 / 130 (0.77%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	2	0	0
Interstitial lung disease			

subjects affected / exposed	0 / 130 (0.00%)	1 / 7 (14.29%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Lung disorder			
subjects affected / exposed	1 / 130 (0.77%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Nasal congestion			
subjects affected / exposed	0 / 130 (0.00%)	0 / 7 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Nasal dryness			
subjects affected / exposed	1 / 130 (0.77%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Pneumonia aspiration			
subjects affected / exposed	0 / 130 (0.00%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Pulmonary congestion			
subjects affected / exposed	1 / 130 (0.77%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Pulmonary hypertension			
subjects affected / exposed	0 / 130 (0.00%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Rhinorrhoea			
subjects affected / exposed	0 / 130 (0.00%)	1 / 7 (14.29%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Tachypnoea			
subjects affected / exposed	1 / 130 (0.77%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Thoracic haemorrhage			
subjects affected / exposed	0 / 130 (0.00%)	0 / 7 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Wheezing			
subjects affected / exposed	0 / 130 (0.00%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Anxiety			
subjects affected / exposed	12 / 130 (9.23%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	12	0	0

Insomnia			
subjects affected / exposed	4 / 130 (3.08%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	4	0	0
Mental status changes			
subjects affected / exposed	2 / 130 (1.54%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	2	0	0
Agitation			
subjects affected / exposed	3 / 130 (2.31%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	3	0	0
Delirium			
subjects affected / exposed	1 / 130 (0.77%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Conduct disorder			
subjects affected / exposed	1 / 130 (0.77%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Confusional state			
subjects affected / exposed	1 / 130 (0.77%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Drug dependence			
subjects affected / exposed	0 / 130 (0.00%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Withdrawal syndrome			
subjects affected / exposed	1 / 130 (0.77%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	11 / 130 (8.46%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	11	0	0
Aspartate aminotransferase increased			
subjects affected / exposed	5 / 130 (3.85%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	5	0	0
Blood creatinine phosphokinase increased			
subjects affected / exposed	2 / 130 (1.54%)	0 / 7 (0.00%)	1 / 11 (9.09%)
occurrences (all)	2	0	1
Hepatic enzyme increased			

subjects affected / exposed	3 / 130 (2.31%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	3	0	0
Activated partial thromboplastin time prolonged			
subjects affected / exposed	1 / 130 (0.77%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Blood alkaline phosphatase increased			
subjects affected / exposed	2 / 130 (1.54%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	2	0	0
Blood creatinine increased			
subjects affected / exposed	1 / 130 (0.77%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Electrocardiogram QT prolonged			
subjects affected / exposed	2 / 130 (1.54%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	2	0	0
Oxygen saturation decreased			
subjects affected / exposed	2 / 130 (1.54%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	2	0	0
Transaminases increased			
subjects affected / exposed	2 / 130 (1.54%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	2	0	0
Blood glucose increased			
subjects affected / exposed	0 / 130 (0.00%)	0 / 7 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Blood pressure increased			
subjects affected / exposed	1 / 130 (0.77%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Blood sodium increased			
subjects affected / exposed	0 / 130 (0.00%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Blood triglycerides increased			
subjects affected / exposed	1 / 130 (0.77%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Chest X-ray abnormal			
subjects affected / exposed	0 / 130 (0.00%)	0 / 7 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1

Gamma-glutamyltransferase increased			
subjects affected / exposed	1 / 130 (0.77%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Gastric occult blood positive			
subjects affected / exposed	0 / 130 (0.00%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Haematocrit decreased			
subjects affected / exposed	1 / 130 (0.77%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Haemoglobin decreased			
subjects affected / exposed	0 / 130 (0.00%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
International normalised ratio increased			
subjects affected / exposed	1 / 130 (0.77%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Liver function test abnormal			
subjects affected / exposed	0 / 130 (0.00%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Occult blood positive			
subjects affected / exposed	0 / 130 (0.00%)	0 / 7 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Prothrombin time prolonged			
subjects affected / exposed	1 / 130 (0.77%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Pseudomonas test positive			
subjects affected / exposed	0 / 130 (0.00%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Troponin I increased			
subjects affected / exposed	0 / 130 (0.00%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Excoriation			
subjects affected / exposed	1 / 130 (0.77%)	1 / 7 (14.29%)	0 / 11 (0.00%)
occurrences (all)	1	1	0
Contusion			

subjects affected / exposed	1 / 130 (0.77%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Endotracheal intubation complication			
subjects affected / exposed	1 / 130 (0.77%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Foot fracture			
subjects affected / exposed	0 / 130 (0.00%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Overdose			
subjects affected / exposed	1 / 130 (0.77%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Procedural pain			
subjects affected / exposed	1 / 130 (0.77%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	6 / 130 (4.62%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	6	0	0
Tachycardia			
subjects affected / exposed	3 / 130 (2.31%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	3	0	0
Arrhythmia			
subjects affected / exposed	2 / 130 (1.54%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	2	0	0
Bundle branch block right			
subjects affected / exposed	2 / 130 (1.54%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	2	0	0
Aortic valve incompetence			
subjects affected / exposed	0 / 130 (0.00%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Bradycardia			
subjects affected / exposed	1 / 130 (0.77%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Bundle branch block left			
subjects affected / exposed	1 / 130 (0.77%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0

Cardiac failure congestive subjects affected / exposed occurrences (all)	1 / 130 (0.77%) 1	0 / 7 (0.00%) 0	0 / 11 (0.00%) 0
Dilatation ventricular subjects affected / exposed occurrences (all)	0 / 130 (0.00%) 0	0 / 7 (0.00%) 0	0 / 11 (0.00%) 0
Left ventricular dysfunction subjects affected / exposed occurrences (all)	1 / 130 (0.77%) 1	0 / 7 (0.00%) 0	0 / 11 (0.00%) 0
Left ventricular hypertrophy subjects affected / exposed occurrences (all)	0 / 130 (0.00%) 0	0 / 7 (0.00%) 0	0 / 11 (0.00%) 0
Mitral valve incompetence subjects affected / exposed occurrences (all)	0 / 130 (0.00%) 0	0 / 7 (0.00%) 0	0 / 11 (0.00%) 0
Right atrial dilatation subjects affected / exposed occurrences (all)	0 / 130 (0.00%) 0	0 / 7 (0.00%) 0	0 / 11 (0.00%) 0
Tricuspid valve incompetence subjects affected / exposed occurrences (all)	0 / 130 (0.00%) 0	0 / 7 (0.00%) 0	0 / 11 (0.00%) 0
Ventricular arrhythmia subjects affected / exposed occurrences (all)	0 / 130 (0.00%) 0	0 / 7 (0.00%) 0	1 / 11 (9.09%) 1
Nervous system disorders			
Headache subjects affected / exposed occurrences (all)	3 / 130 (2.31%) 3	0 / 7 (0.00%) 0	0 / 11 (0.00%) 0
Critical illness polyneuropathy subjects affected / exposed occurrences (all)	3 / 130 (2.31%) 3	0 / 7 (0.00%) 0	0 / 11 (0.00%) 0
Dizziness subjects affected / exposed occurrences (all)	1 / 130 (0.77%) 1	0 / 7 (0.00%) 0	0 / 11 (0.00%) 0
Neuromyopathy			

subjects affected / exposed	2 / 130 (1.54%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	2	0	0
Neuropathy peripheral			
subjects affected / exposed	2 / 130 (1.54%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	2	0	0
Aphasia			
subjects affected / exposed	0 / 130 (0.00%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Apraxia			
subjects affected / exposed	0 / 130 (0.00%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Brain injury			
subjects affected / exposed	0 / 130 (0.00%)	0 / 7 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Brain oedema			
subjects affected / exposed	0 / 130 (0.00%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Dizziness exertional			
subjects affected / exposed	1 / 130 (0.77%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Epilepsy			
subjects affected / exposed	1 / 130 (0.77%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Migraine			
subjects affected / exposed	1 / 130 (0.77%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Polyneuropathy			
subjects affected / exposed	1 / 130 (0.77%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Psychomotor hyperactivity			
subjects affected / exposed	1 / 130 (0.77%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Tremor			
subjects affected / exposed	0 / 130 (0.00%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			

Anaemia			
subjects affected / exposed	11 / 130 (8.46%)	0 / 7 (0.00%)	1 / 11 (9.09%)
occurrences (all)	12	0	1
Neutropenia			
subjects affected / exposed	1 / 130 (0.77%)	1 / 7 (14.29%)	2 / 11 (18.18%)
occurrences (all)	1	1	2
Thrombocytopenia			
subjects affected / exposed	4 / 130 (3.08%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	4	0	0
Leukocytosis			
subjects affected / exposed	2 / 130 (1.54%)	0 / 7 (0.00%)	1 / 11 (9.09%)
occurrences (all)	2	0	1
Leukopenia			
subjects affected / exposed	2 / 130 (1.54%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	2	0	0
Thrombocytosis			
subjects affected / exposed	2 / 130 (1.54%)	1 / 7 (14.29%)	0 / 11 (0.00%)
occurrences (all)	2	1	0
Coagulopathy			
subjects affected / exposed	1 / 130 (0.77%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Agranulocytosis			
subjects affected / exposed	1 / 130 (0.77%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Bandaemia			
subjects affected / exposed	0 / 130 (0.00%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Eosinophilia			
subjects affected / exposed	0 / 130 (0.00%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Haemolytic anaemia			
subjects affected / exposed	1 / 130 (0.77%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Lymphopenia			
subjects affected / exposed	1 / 130 (0.77%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0

Normochromic normocytic anaemia subjects affected / exposed occurrences (all)	0 / 130 (0.00%) 0	0 / 7 (0.00%) 0	0 / 11 (0.00%) 0
Eye disorders			
Conjunctival haemorrhage subjects affected / exposed occurrences (all)	1 / 130 (0.77%) 1	0 / 7 (0.00%) 0	0 / 11 (0.00%) 0
Conjunctival oedema subjects affected / exposed occurrences (all)	0 / 130 (0.00%) 0	0 / 7 (0.00%) 0	0 / 11 (0.00%) 0
Diplopia subjects affected / exposed occurrences (all)	0 / 130 (0.00%) 0	0 / 7 (0.00%) 0	0 / 11 (0.00%) 0
Dry eye subjects affected / exposed occurrences (all)	1 / 130 (0.77%) 1	0 / 7 (0.00%) 0	0 / 11 (0.00%) 0
Keratopathy subjects affected / exposed occurrences (all)	0 / 130 (0.00%) 0	0 / 7 (0.00%) 0	0 / 11 (0.00%) 0
Pupillary disorder subjects affected / exposed occurrences (all)	0 / 130 (0.00%) 0	0 / 7 (0.00%) 0	0 / 11 (0.00%) 0
Gastrointestinal disorders			
Constipation subjects affected / exposed occurrences (all)	10 / 130 (7.69%) 10	0 / 7 (0.00%) 0	1 / 11 (9.09%) 1
Diarrhoea subjects affected / exposed occurrences (all)	10 / 130 (7.69%) 16	0 / 7 (0.00%) 0	0 / 11 (0.00%) 0
Vomiting subjects affected / exposed occurrences (all)	4 / 130 (3.08%) 4	0 / 7 (0.00%) 0	0 / 11 (0.00%) 0
Nausea subjects affected / exposed occurrences (all)	6 / 130 (4.62%) 6	0 / 7 (0.00%) 0	0 / 11 (0.00%) 0
Abdominal pain			

subjects affected / exposed	3 / 130 (2.31%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	3	0	0
Dyspepsia			
subjects affected / exposed	2 / 130 (1.54%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	2	0	0
Abdominal compartment syndrome			
subjects affected / exposed	0 / 130 (0.00%)	0 / 7 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Abdominal discomfort			
subjects affected / exposed	0 / 130 (0.00%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Abdominal distension			
subjects affected / exposed	1 / 130 (0.77%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Gastritis erosive			
subjects affected / exposed	1 / 130 (0.77%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Gastrointestinal haemorrhage			
subjects affected / exposed	1 / 130 (0.77%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 130 (0.77%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Ileus			
subjects affected / exposed	1 / 130 (0.77%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Impaired gastric emptying			
subjects affected / exposed	1 / 130 (0.77%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Mouth haemorrhage			
subjects affected / exposed	0 / 130 (0.00%)	0 / 7 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Oral disorder			
subjects affected / exposed	1 / 130 (0.77%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Rectal haemorrhage			

subjects affected / exposed	1 / 130 (0.77%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Volvulus			
subjects affected / exposed	1 / 130 (0.77%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Hepatobiliary disorders			
Hyperbilirubinaemia			
subjects affected / exposed	2 / 130 (1.54%)	0 / 7 (0.00%)	1 / 11 (9.09%)
occurrences (all)	2	0	1
Hepatocellular injury			
subjects affected / exposed	4 / 130 (3.08%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	4	0	0
Cholestasis			
subjects affected / exposed	3 / 130 (2.31%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	3	0	0
Cholelithiasis			
subjects affected / exposed	0 / 130 (0.00%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Hepatomegaly			
subjects affected / exposed	1 / 130 (0.77%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	5 / 130 (3.85%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	5	0	0
Decubitus ulcer			
subjects affected / exposed	2 / 130 (1.54%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	2	0	0
Skin disorder			
subjects affected / exposed	1 / 130 (0.77%)	0 / 7 (0.00%)	1 / 11 (9.09%)
occurrences (all)	1	0	1
Dermatitis diaper			
subjects affected / exposed	0 / 130 (0.00%)	2 / 7 (28.57%)	0 / 11 (0.00%)
occurrences (all)	0	2	0
Drug eruption			

subjects affected / exposed	1 / 130 (0.77%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Blister			
subjects affected / exposed	0 / 130 (0.00%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Prurigo			
subjects affected / exposed	1 / 130 (0.77%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Pruritus			
subjects affected / exposed	0 / 130 (0.00%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Rash erythematous			
subjects affected / exposed	1 / 130 (0.77%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Rash macular			
subjects affected / exposed	0 / 130 (0.00%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Rash vesicular			
subjects affected / exposed	1 / 130 (0.77%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Skin discolouration			
subjects affected / exposed	1 / 130 (0.77%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Skin exfoliation			
subjects affected / exposed	0 / 130 (0.00%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Subcutaneous emphysema			
subjects affected / exposed	1 / 130 (0.77%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Urticaria			
subjects affected / exposed	1 / 130 (0.77%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Renal and urinary disorders			
Renal failure			
subjects affected / exposed	3 / 130 (2.31%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	3	0	0

Renal failure acute subjects affected / exposed occurrences (all)	2 / 130 (1.54%) 2	0 / 7 (0.00%) 0	0 / 11 (0.00%) 0
Dysuria subjects affected / exposed occurrences (all)	1 / 130 (0.77%) 1	0 / 7 (0.00%) 0	0 / 11 (0.00%) 0
Glycosuria subjects affected / exposed occurrences (all)	0 / 130 (0.00%) 0	0 / 7 (0.00%) 0	1 / 11 (9.09%) 1
Polyuria subjects affected / exposed occurrences (all)	1 / 130 (0.77%) 1	0 / 7 (0.00%) 0	0 / 11 (0.00%) 0
Renal impairment subjects affected / exposed occurrences (all)	1 / 130 (0.77%) 1	0 / 7 (0.00%) 0	0 / 11 (0.00%) 0
Renal tubular necrosis subjects affected / exposed occurrences (all)	0 / 130 (0.00%) 0	0 / 7 (0.00%) 0	1 / 11 (9.09%) 1
Endocrine disorders Adrenal insufficiency subjects affected / exposed occurrences (all)	1 / 130 (0.77%) 1	0 / 7 (0.00%) 0	0 / 11 (0.00%) 0
Hyperparathyroidism secondary subjects affected / exposed occurrences (all)	1 / 130 (0.77%) 1	0 / 7 (0.00%) 0	0 / 11 (0.00%) 0
Musculoskeletal and connective tissue disorders Back pain subjects affected / exposed occurrences (all)	3 / 130 (2.31%) 3	0 / 7 (0.00%) 0	0 / 11 (0.00%) 0
Muscle atrophy subjects affected / exposed occurrences (all)	1 / 130 (0.77%) 1	0 / 7 (0.00%) 0	0 / 11 (0.00%) 0
Muscle spasms subjects affected / exposed occurrences (all)	1 / 130 (0.77%) 1	0 / 7 (0.00%) 0	0 / 11 (0.00%) 0
Muscular weakness			

subjects affected / exposed	1 / 130 (0.77%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal stiffness			
subjects affected / exposed	1 / 130 (0.77%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Myalgia			
subjects affected / exposed	1 / 130 (0.77%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Myositis ossificans			
subjects affected / exposed	0 / 130 (0.00%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Neck pain			
subjects affected / exposed	1 / 130 (0.77%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Rhabdomyolysis			
subjects affected / exposed	1 / 130 (0.77%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Infections and infestations			
Pneumonia			
subjects affected / exposed	2 / 130 (1.54%)	2 / 7 (28.57%)	0 / 11 (0.00%)
occurrences (all)	2	2	0
Urinary tract infection			
subjects affected / exposed	4 / 130 (3.08%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	4	0	0
Oral herpes			
subjects affected / exposed	4 / 130 (3.08%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	4	0	0
Bronchitis			
subjects affected / exposed	3 / 130 (2.31%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	3	0	0
Candida infection			
subjects affected / exposed	3 / 130 (2.31%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	3	0	0
Oral candidiasis			
subjects affected / exposed	3 / 130 (2.31%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	3	0	0

Bronchopneumonia			
subjects affected / exposed	2 / 130 (1.54%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	2	0	0
Fungal skin infection			
subjects affected / exposed	0 / 130 (0.00%)	0 / 7 (0.00%)	2 / 11 (18.18%)
occurrences (all)	0	0	2
Lung infection			
subjects affected / exposed	2 / 130 (1.54%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	2	0	0
Pneumonia bacterial			
subjects affected / exposed	1 / 130 (0.77%)	1 / 7 (14.29%)	0 / 11 (0.00%)
occurrences (all)	1	1	0
Sepsis			
subjects affected / exposed	0 / 130 (0.00%)	0 / 7 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Sinusitis			
subjects affected / exposed	1 / 130 (0.77%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Bacterial disease carrier			
subjects affected / exposed	1 / 130 (0.77%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Bronchiolitis			
subjects affected / exposed	0 / 130 (0.00%)	1 / 7 (14.29%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Clostridium difficile colitis			
subjects affected / exposed	1 / 130 (0.77%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Clostridium difficile infection			
subjects affected / exposed	1 / 130 (0.77%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Croup infectious			
subjects affected / exposed	0 / 130 (0.00%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Device related infection			
subjects affected / exposed	1 / 130 (0.77%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0

Empyema			
subjects affected / exposed	0 / 130 (0.00%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Enterococcal infection			
subjects affected / exposed	1 / 130 (0.77%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Genital herpes			
subjects affected / exposed	1 / 130 (0.77%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Hordeolum			
subjects affected / exposed	1 / 130 (0.77%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Oesophageal candidiasis			
subjects affected / exposed	1 / 130 (0.77%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Ophthalmic herpes simplex			
subjects affected / exposed	1 / 130 (0.77%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Otitis media			
subjects affected / exposed	0 / 130 (0.00%)	1 / 7 (14.29%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Otitis media acute			
subjects affected / exposed	0 / 130 (0.00%)	0 / 7 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Penile infection			
subjects affected / exposed	1 / 130 (0.77%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Pneumonia haemophilus			
subjects affected / exposed	0 / 130 (0.00%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Pneumonia necrotising			
subjects affected / exposed	0 / 130 (0.00%)	0 / 7 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Pneumonia staphylococcal			
subjects affected / exposed	1 / 130 (0.77%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0

Pneumonia viral			
subjects affected / exposed	1 / 130 (0.77%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Pseudomonas bronchitis			
subjects affected / exposed	1 / 130 (0.77%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Respiratory moniliasis			
subjects affected / exposed	0 / 130 (0.00%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Rhinitis			
subjects affected / exposed	0 / 130 (0.00%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Staphylococcal sepsis			
subjects affected / exposed	1 / 130 (0.77%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Tracheitis			
subjects affected / exposed	1 / 130 (0.77%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Upper respiratory tract infection			
subjects affected / exposed	1 / 130 (0.77%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Vulvovaginal mycotic infection			
subjects affected / exposed	1 / 130 (0.77%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Metabolism and nutrition disorders			
Hypokalaemia			
subjects affected / exposed	16 / 130 (12.31%)	1 / 7 (14.29%)	0 / 11 (0.00%)
occurrences (all)	17	1	0
Hypoalbuminaemia			
subjects affected / exposed	7 / 130 (5.38%)	1 / 7 (14.29%)	0 / 11 (0.00%)
occurrences (all)	7	1	0
Hypophosphataemia			
subjects affected / exposed	6 / 130 (4.62%)	0 / 7 (0.00%)	1 / 11 (9.09%)
occurrences (all)	7	0	1
Hyperglycaemia			

subjects affected / exposed	4 / 130 (3.08%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	4	0	0
Hypocalcaemia			
subjects affected / exposed	6 / 130 (4.62%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	6	0	0
Hyperkalaemia			
subjects affected / exposed	5 / 130 (3.85%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	5	0	0
Hypernatraemia			
subjects affected / exposed	2 / 130 (1.54%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	3	0	0
Acidosis			
subjects affected / exposed	3 / 130 (2.31%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	4	0	0
Hypoglycaemia			
subjects affected / exposed	3 / 130 (2.31%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	3	0	0
Hypomagnesaemia			
subjects affected / exposed	1 / 130 (0.77%)	1 / 7 (14.29%)	0 / 11 (0.00%)
occurrences (all)	1	1	0
Hyponatraemia			
subjects affected / exposed	3 / 130 (2.31%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	3	0	0
Metabolic acidosis			
subjects affected / exposed	2 / 130 (1.54%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	2	0	0
Metabolic alkalosis			
subjects affected / exposed	3 / 130 (2.31%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	3	0	0
Food intolerance			
subjects affected / exposed	0 / 130 (0.00%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Hyperphosphataemia			
subjects affected / exposed	1 / 130 (0.77%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Hypochloraemia			

subjects affected / exposed	0 / 130 (0.00%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Lactic acidosis			
subjects affected / exposed	1 / 130 (0.77%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Fluid overload			
subjects affected / exposed	1 / 130 (0.77%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Fluid retention			
subjects affected / exposed	0 / 130 (0.00%)	1 / 7 (14.29%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Hyperchloraemia			
subjects affected / exposed	0 / 130 (0.00%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Hypophagia			
subjects affected / exposed	0 / 130 (0.00%)	1 / 7 (14.29%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Malnutrition			
subjects affected / exposed	1 / 130 (0.77%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Vitamin B12 deficiency			
subjects affected / exposed	1 / 130 (0.77%)	0 / 7 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0

Non-serious adverse events	Cohort 3: Children (2 to <6 years of age)	Cohort 4: Children (6 to <13 years of age)	Cohort 5: Adolescents (13 to <18 years of age)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	8 / 12 (66.67%)	20 / 27 (74.07%)	9 / 14 (64.29%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Chronic myeloid leukaemia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Vascular disorders			
Hypotension			
subjects affected / exposed	0 / 12 (0.00%)	2 / 27 (7.41%)	0 / 14 (0.00%)
occurrences (all)	0	2	0
Hypertension			

subjects affected / exposed	0 / 12 (0.00%)	1 / 27 (3.70%)	0 / 14 (0.00%)
occurrences (all)	0	1	0
Deep vein thrombosis			
subjects affected / exposed	2 / 12 (16.67%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	2	0	0
Thrombophlebitis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Phlebitis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Venous thrombosis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Arterial thrombosis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Circulatory collapse			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Extremity necrosis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Haematoma			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Hypoperfusion			
subjects affected / exposed	1 / 12 (8.33%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Jugular vein thrombosis			
subjects affected / exposed	0 / 12 (0.00%)	1 / 27 (3.70%)	0 / 14 (0.00%)
occurrences (all)	0	1	0
Poor peripheral circulation			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Venous thrombosis limb			

subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 27 (0.00%) 0	0 / 14 (0.00%) 0
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	1 / 12 (8.33%)	4 / 27 (14.81%)	1 / 14 (7.14%)
occurrences (all)	1	4	1
Oedema			
subjects affected / exposed	1 / 12 (8.33%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Asthenia			
subjects affected / exposed	0 / 12 (0.00%)	1 / 27 (3.70%)	1 / 14 (7.14%)
occurrences (all)	0	1	1
Pain			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Drug withdrawal syndrome			
subjects affected / exposed	1 / 12 (8.33%)	2 / 27 (7.41%)	0 / 14 (0.00%)
occurrences (all)	1	2	0
Chest pain			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Generalised oedema			
subjects affected / exposed	0 / 12 (0.00%)	1 / 27 (3.70%)	0 / 14 (0.00%)
occurrences (all)	0	1	0
Infusion site extravasation			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Catheter site haemorrhage			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Device occlusion			
subjects affected / exposed	0 / 12 (0.00%)	1 / 27 (3.70%)	0 / 14 (0.00%)
occurrences (all)	0	1	0
Facial pain			

subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Hypothermia			
subjects affected / exposed	1 / 12 (8.33%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Injection site reaction			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Multi-organ failure			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Oedema peripheral			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Thrombosis in device			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Unintentional medical device removal			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Reproductive system and breast disorders			
Perineal rash			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Pleural effusion			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Dyspnoea			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Bronchospasm			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Pneumothorax			

subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Pulmonary oedema			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Respiratory distress			
subjects affected / exposed	0 / 12 (0.00%)	1 / 27 (3.70%)	0 / 14 (0.00%)
occurrences (all)	0	1	0
Respiratory failure			
subjects affected / exposed	1 / 12 (8.33%)	0 / 27 (0.00%)	1 / 14 (7.14%)
occurrences (all)	1	0	1
Stridor			
subjects affected / exposed	0 / 12 (0.00%)	1 / 27 (3.70%)	0 / 14 (0.00%)
occurrences (all)	0	1	0
Cough			
subjects affected / exposed	1 / 12 (8.33%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Epistaxis			
subjects affected / exposed	1 / 12 (8.33%)	1 / 27 (3.70%)	0 / 14 (0.00%)
occurrences (all)	1	1	0
Acute pulmonary oedema			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Acute respiratory distress syndrome			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Acute respiratory failure			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Adenoidal hypertrophy			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Dysphonia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Dyspnoea exertional			

subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Haemoptysis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Interstitial lung disease			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Lung disorder			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Nasal congestion			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Nasal dryness			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Pneumonia aspiration			
subjects affected / exposed	0 / 12 (0.00%)	1 / 27 (3.70%)	0 / 14 (0.00%)
occurrences (all)	0	1	0
Pulmonary congestion			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Pulmonary hypertension			
subjects affected / exposed	0 / 12 (0.00%)	1 / 27 (3.70%)	0 / 14 (0.00%)
occurrences (all)	0	1	0
Rhinorrhoea			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Tachypnoea			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Thoracic haemorrhage			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Wheezing			

subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 27 (0.00%) 0	1 / 14 (7.14%) 1
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 12 (0.00%)	1 / 27 (3.70%)	0 / 14 (0.00%)
occurrences (all)	0	1	0
Insomnia			
subjects affected / exposed	0 / 12 (0.00%)	1 / 27 (3.70%)	0 / 14 (0.00%)
occurrences (all)	0	1	0
Mental status changes			
subjects affected / exposed	1 / 12 (8.33%)	0 / 27 (0.00%)	1 / 14 (7.14%)
occurrences (all)	1	0	1
Agitation			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Delirium			
subjects affected / exposed	0 / 12 (0.00%)	1 / 27 (3.70%)	0 / 14 (0.00%)
occurrences (all)	0	1	0
Conduct disorder			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Confusional state			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Drug dependence			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Withdrawal syndrome			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Aspartate aminotransferase increased			

subjects affected / exposed	0 / 12 (0.00%)	1 / 27 (3.70%)	0 / 14 (0.00%)
occurrences (all)	0	1	0
Blood creatinine phosphokinase increased			
subjects affected / exposed	0 / 12 (0.00%)	1 / 27 (3.70%)	0 / 14 (0.00%)
occurrences (all)	0	1	0
Hepatic enzyme increased			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Activated partial thromboplastin time prolonged			
subjects affected / exposed	0 / 12 (0.00%)	1 / 27 (3.70%)	0 / 14 (0.00%)
occurrences (all)	0	1	0
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Blood creatinine increased			
subjects affected / exposed	0 / 12 (0.00%)	1 / 27 (3.70%)	0 / 14 (0.00%)
occurrences (all)	0	1	0
Electrocardiogram QT prolonged			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Oxygen saturation decreased			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Transaminases increased			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Blood glucose increased			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Blood pressure increased			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Blood sodium increased			

subjects affected / exposed	0 / 12 (0.00%)	1 / 27 (3.70%)	0 / 14 (0.00%)
occurrences (all)	0	1	0
Blood triglycerides increased			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Chest X-ray abnormal			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Gastric occult blood positive			
subjects affected / exposed	1 / 12 (8.33%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Haematocrit decreased			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Haemoglobin decreased			
subjects affected / exposed	1 / 12 (8.33%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
International normalised ratio increased			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Liver function test abnormal			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Occult blood positive			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Prothrombin time prolonged			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Pseudomonas test positive			

subjects affected / exposed	0 / 12 (0.00%)	1 / 27 (3.70%)	0 / 14 (0.00%)
occurrences (all)	0	1	0
Troponin I increased			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Injury, poisoning and procedural complications			
Excoriation			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Contusion			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Endotracheal intubation complication			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Foot fracture			
subjects affected / exposed	0 / 12 (0.00%)	1 / 27 (3.70%)	0 / 14 (0.00%)
occurrences (all)	0	1	0
Overdose			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Procedural pain			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Tachycardia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Arrhythmia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Bundle branch block right			

subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Aortic valve incompetence			
subjects affected / exposed	0 / 12 (0.00%)	1 / 27 (3.70%)	0 / 14 (0.00%)
occurrences (all)	0	1	0
Bradycardia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Bundle branch block left			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Cardiac failure congestive			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Dilatation ventricular			
subjects affected / exposed	0 / 12 (0.00%)	1 / 27 (3.70%)	0 / 14 (0.00%)
occurrences (all)	0	1	0
Left ventricular dysfunction			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Left ventricular hypertrophy			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Mitral valve incompetence			
subjects affected / exposed	0 / 12 (0.00%)	1 / 27 (3.70%)	0 / 14 (0.00%)
occurrences (all)	0	1	0
Right atrial dilatation			
subjects affected / exposed	0 / 12 (0.00%)	1 / 27 (3.70%)	0 / 14 (0.00%)
occurrences (all)	0	1	0
Tricuspid valve incompetence			
subjects affected / exposed	0 / 12 (0.00%)	1 / 27 (3.70%)	0 / 14 (0.00%)
occurrences (all)	0	1	0
Ventricular arrhythmia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			

Headache			
subjects affected / exposed	0 / 12 (0.00%)	1 / 27 (3.70%)	0 / 14 (0.00%)
occurrences (all)	0	1	0
Critical illness polyneuropathy			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Dizziness			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Neuromyopathy			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Neuropathy peripheral			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Aphasia			
subjects affected / exposed	1 / 12 (8.33%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Apraxia			
subjects affected / exposed	0 / 12 (0.00%)	1 / 27 (3.70%)	0 / 14 (0.00%)
occurrences (all)	0	1	0
Brain injury			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Brain oedema			
subjects affected / exposed	0 / 12 (0.00%)	1 / 27 (3.70%)	0 / 14 (0.00%)
occurrences (all)	0	1	0
Dizziness exertional			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Epilepsy			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Migraine			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0

Polyneuropathy			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Psychomotor hyperactivity			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Tremor			
subjects affected / exposed	1 / 12 (8.33%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 12 (0.00%)	3 / 27 (11.11%)	1 / 14 (7.14%)
occurrences (all)	0	3	1
Neutropenia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Thrombocytopenia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Leukocytosis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Leukopenia			
subjects affected / exposed	0 / 12 (0.00%)	1 / 27 (3.70%)	0 / 14 (0.00%)
occurrences (all)	0	1	0
Thrombocytosis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Coagulopathy			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Agranulocytosis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Bandaemia			

subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Eosinophilia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Haemolytic anaemia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Lymphopenia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Normochromic normocytic anaemia			
subjects affected / exposed	0 / 12 (0.00%)	1 / 27 (3.70%)	0 / 14 (0.00%)
occurrences (all)	0	1	0
Eye disorders			
Conjunctival haemorrhage			
subjects affected / exposed	0 / 12 (0.00%)	1 / 27 (3.70%)	0 / 14 (0.00%)
occurrences (all)	0	1	0
Conjunctival oedema			
subjects affected / exposed	0 / 12 (0.00%)	1 / 27 (3.70%)	0 / 14 (0.00%)
occurrences (all)	0	1	0
Diplopia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Dry eye			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Keratopathy			
subjects affected / exposed	0 / 12 (0.00%)	1 / 27 (3.70%)	0 / 14 (0.00%)
occurrences (all)	0	1	0
Pupillary disorder			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Gastrointestinal disorders			
Constipation			

subjects affected / exposed	0 / 12 (0.00%)	3 / 27 (11.11%)	0 / 14 (0.00%)
occurrences (all)	0	3	0
Diarrhoea			
subjects affected / exposed	1 / 12 (8.33%)	0 / 27 (0.00%)	1 / 14 (7.14%)
occurrences (all)	1	0	1
Vomiting			
subjects affected / exposed	1 / 12 (8.33%)	2 / 27 (7.41%)	1 / 14 (7.14%)
occurrences (all)	1	2	1
Nausea			
subjects affected / exposed	0 / 12 (0.00%)	1 / 27 (3.70%)	0 / 14 (0.00%)
occurrences (all)	0	1	0
Abdominal pain			
subjects affected / exposed	0 / 12 (0.00%)	1 / 27 (3.70%)	0 / 14 (0.00%)
occurrences (all)	0	1	0
Dyspepsia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Abdominal compartment syndrome			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Abdominal discomfort			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Abdominal distension			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Gastritis erosive			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal haemorrhage			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Ileus			

subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Impaired gastric emptying			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Mouth haemorrhage			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Oral disorder			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Rectal haemorrhage			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Volvulus			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Hepatobiliary disorders			
Hyperbilirubinaemia			
subjects affected / exposed	0 / 12 (0.00%)	1 / 27 (3.70%)	1 / 14 (7.14%)
occurrences (all)	0	1	1
Hepatocellular injury			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Cholestasis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Cholelithiasis			
subjects affected / exposed	0 / 12 (0.00%)	1 / 27 (3.70%)	0 / 14 (0.00%)
occurrences (all)	0	1	0
Hepatomegaly			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Rash			

subjects affected / exposed	1 / 12 (8.33%)	1 / 27 (3.70%)	0 / 14 (0.00%)
occurrences (all)	2	1	0
Decubitus ulcer			
subjects affected / exposed	0 / 12 (0.00%)	2 / 27 (7.41%)	0 / 14 (0.00%)
occurrences (all)	0	2	0
Skin disorder			
subjects affected / exposed	0 / 12 (0.00%)	2 / 27 (7.41%)	0 / 14 (0.00%)
occurrences (all)	0	5	0
Dermatitis diaper			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Drug eruption			
subjects affected / exposed	0 / 12 (0.00%)	1 / 27 (3.70%)	0 / 14 (0.00%)
occurrences (all)	0	1	0
Blister			
subjects affected / exposed	0 / 12 (0.00%)	1 / 27 (3.70%)	0 / 14 (0.00%)
occurrences (all)	0	1	0
Prurigo			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Pruritus			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Rash erythematous			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Rash macular			
subjects affected / exposed	0 / 12 (0.00%)	1 / 27 (3.70%)	0 / 14 (0.00%)
occurrences (all)	0	1	0
Rash vesicular			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Skin discolouration			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Skin exfoliation			

subjects affected / exposed	1 / 12 (8.33%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Subcutaneous emphysema			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Urticaria			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Renal failure			
subjects affected / exposed	1 / 12 (8.33%)	0 / 27 (0.00%)	1 / 14 (7.14%)
occurrences (all)	1	0	2
Renal failure acute			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Dysuria			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Glycosuria			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Polyuria			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Renal impairment			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Renal tubular necrosis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Endocrine disorders			
Adrenal insufficiency			
subjects affected / exposed	0 / 12 (0.00%)	1 / 27 (3.70%)	1 / 14 (7.14%)
occurrences (all)	0	1	1
Hyperparathyroidism secondary			

subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 27 (0.00%) 0	0 / 14 (0.00%) 0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Muscle atrophy			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Muscle spasms			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Muscular weakness			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal stiffness			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Myalgia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Myositis ossificans			
subjects affected / exposed	0 / 12 (0.00%)	1 / 27 (3.70%)	0 / 14 (0.00%)
occurrences (all)	0	1	0
Neck pain			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Rhabdomyolysis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Pneumonia			
subjects affected / exposed	0 / 12 (0.00%)	1 / 27 (3.70%)	0 / 14 (0.00%)
occurrences (all)	0	1	0
Urinary tract infection			

subjects affected / exposed	0 / 12 (0.00%)	1 / 27 (3.70%)	0 / 14 (0.00%)
occurrences (all)	0	1	0
Oral herpes			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Bronchitis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Candida infection			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Oral candidiasis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Bronchopneumonia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Fungal skin infection			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Lung infection			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Pneumonia bacterial			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Sepsis			
subjects affected / exposed	1 / 12 (8.33%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Sinusitis			
subjects affected / exposed	0 / 12 (0.00%)	1 / 27 (3.70%)	0 / 14 (0.00%)
occurrences (all)	0	1	0
Bacterial disease carrier			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Bronchiolitis			

subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Clostridium difficile colitis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Clostridium difficile infection			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Croup infectious			
subjects affected / exposed	1 / 12 (8.33%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Device related infection			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Emphyema			
subjects affected / exposed	0 / 12 (0.00%)	1 / 27 (3.70%)	0 / 14 (0.00%)
occurrences (all)	0	1	0
Enterococcal infection			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Genital herpes			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Hordeolum			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Oesophageal candidiasis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Ophthalmic herpes simplex			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Otitis media			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Otitis media acute			

subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Penile infection			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Pneumonia haemophilus			
subjects affected / exposed	0 / 12 (0.00%)	1 / 27 (3.70%)	0 / 14 (0.00%)
occurrences (all)	0	1	0
Pneumonia necrotising			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Pneumonia staphylococcal			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Pneumonia viral			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Pseudomonas bronchitis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Respiratory moniliasis			
subjects affected / exposed	0 / 12 (0.00%)	1 / 27 (3.70%)	0 / 14 (0.00%)
occurrences (all)	0	1	0
Rhinitis			
subjects affected / exposed	1 / 12 (8.33%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Staphylococcal sepsis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Tracheitis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Upper respiratory tract infection			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Vulvovaginal mycotic infection			

subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 27 (0.00%) 0	0 / 14 (0.00%) 0
Metabolism and nutrition disorders			
Hypokalaemia			
subjects affected / exposed	1 / 12 (8.33%)	1 / 27 (3.70%)	0 / 14 (0.00%)
occurrences (all)	1	1	0
Hypoalbuminaemia			
subjects affected / exposed	1 / 12 (8.33%)	1 / 27 (3.70%)	0 / 14 (0.00%)
occurrences (all)	1	1	0
Hypophosphataemia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Hyperglycaemia			
subjects affected / exposed	0 / 12 (0.00%)	1 / 27 (3.70%)	1 / 14 (7.14%)
occurrences (all)	0	1	1
Hypocalcaemia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Hyperkalaemia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Hypernatraemia			
subjects affected / exposed	0 / 12 (0.00%)	1 / 27 (3.70%)	1 / 14 (7.14%)
occurrences (all)	0	1	1
Acidosis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Hypoglycaemia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Hypomagnesaemia			
subjects affected / exposed	1 / 12 (8.33%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Hyponatraemia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0

Metabolic acidosis			
subjects affected / exposed	1 / 12 (8.33%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Metabolic alkalosis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Food intolerance			
subjects affected / exposed	0 / 12 (0.00%)	2 / 27 (7.41%)	0 / 14 (0.00%)
occurrences (all)	0	2	0
Hyperphosphataemia			
subjects affected / exposed	0 / 12 (0.00%)	1 / 27 (3.70%)	0 / 14 (0.00%)
occurrences (all)	0	1	0
Hypochloraemia			
subjects affected / exposed	1 / 12 (8.33%)	1 / 27 (3.70%)	0 / 14 (0.00%)
occurrences (all)	1	1	0
Lactic acidosis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Fluid overload			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Fluid retention			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Hyperchloraemia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Hypophagia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Malnutrition			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Vitamin B12 deficiency			
subjects affected / exposed	0 / 12 (0.00%)	0 / 27 (0.00%)	0 / 14 (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
17 February 2010	Protocol Amendment 03 was written to i) modify pediatric/adolescent dose selection in response to recommendations from EU regulators, ii) add an inclusion criterion to include only subjects who have severe or progressive influenza illness on approved (fully licensed) influenza antiviral agents or who are considered unsuitable or inappropriate for treatment with approved influenza antivirals.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

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

Two participants who withdrew consent prior to receiving intravenous zanamivir have not been captured in any of the tables.

Notes: