



Clinical trial results:

A Randomized, Double-blind, Placebo-controlled, 2-Part Study of Orally Administered ALS-008176 to Evaluate the Safety, Tolerability, Pharmacokinetics and Pharmacodynamics of Single Ascending Dosing and Multiple Ascending Dosing in Infants Hospitalized with Respiratory Syncytial Virus (RSV) Infection

Summary

EudraCT number	2013-005104-33
Trial protocol	GB FR RO
Global end of trial date	15 February 2018

Results information

Result version number	v2 (current)
This version publication date	01 March 2019
First version publication date	01 December 2018
Version creation reason	

Trial information

Trial identification

Sponsor protocol code	ALS-8176-503
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02202356
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Alios BioPharma
Sponsor organisation address	260 E. Grand Ave, South San Francisco CA, United States, 94080
Public contact	Clinical Registry group, Alios BioPharma, GDeLaRos@its.jnj.com
Scientific contact	Clinical Registry group, Alios BioPharma, GDeLaRos@its.jnj.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMA-001758-PIP01-15
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	15 February 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	15 February 2018
Global end of trial reached?	Yes
Global end of trial date	15 February 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective of this study was to evaluate the safety and tolerability of single and multiple doses of ALS-008176.

Protection of trial subjects:

This study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki and that are consistent with good clinical practices and applicable regulatory requirements. Safety was evaluated throughout the study and included adverse events (AEs), vital signs, laboratory assessments (routine hematology, biochemistry, coagulation and urinalysis, 12-lead electrocardiogram (ECG), and physical examination.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	23 July 2014
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	Australia: 2
Country: Number of subjects enrolled	Chile: 12
Country: Number of subjects enrolled	Colombia: 7
Country: Number of subjects enrolled	France: 14
Country: Number of subjects enrolled	United Kingdom: 22
Country: Number of subjects enrolled	Japan: 38
Country: Number of subjects enrolled	New Zealand: 9
Country: Number of subjects enrolled	Panama: 25
Country: Number of subjects enrolled	Thailand: 27
Country: Number of subjects enrolled	Taiwan: 5
Country: Number of subjects enrolled	United States: 20
Worldwide total number of subjects	181
EEA total number of subjects	36

Notes:

Subjects enrolled per age group	
In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	1
Infants and toddlers (28 days-23 months)	180
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 181 subjects were randomized and received ALS-008176 or Placebo.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes
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Arm title	SAD: ALS-008176 (1.37 mg/kg)
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Arm description:

Subjects received single oral dose of 1.37 milligrams per kilogram (mg/kg) of ALS-008176.

Arm type	Experimental
Investigational medicinal product name	ALS-008176
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral suspension
Routes of administration	Oral use

Dosage and administration details:

Subjects received single dose of 1.37 mg/kg of ALS-8176 orally.

Arm title	SAD: ALS-008176 (4.1 mg/kg)
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Arm description:

Subjects received single oral dose of 4.1 mg/kg of ALS-008176.

Arm type	Experimental
Investigational medicinal product name	ALS-008176
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral suspension
Routes of administration	Oral use

Dosage and administration details:

Subjects received single dose of 4.1 mg/kg of ALS-008176 orally.

Arm title	SAD: ALS-008176 (12 mg/kg)
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Arm description:

Subjects received single oral dose of 12 mg/kg of ALS-008176.

Arm type	Experimental
Investigational medicinal product name	ALS-008176
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral suspension
Routes of administration	Oral use

Dosage and administration details:

Subjects received single dose of 12 mg/kg of ALS-008176 orally.

Arm title	SAD: ALS-008176 (25 mg/kg)
Arm description:	
Subjects received single oral dose of 25 mg/kg of ALS-008176.	
Arm type	Experimental
Investigational medicinal product name	ALS-008176
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral suspension
Routes of administration	Oral use
Dosage and administration details:	
Subjects received single dose of 25 mg/kg of ALS-008176 orally.	
Arm title	MAD: ALS-008176 (4.1/1.37 mg/kg)
Arm description:	
Subjects received 1 loading dose of 4.1 mg/kg of ALS-008176 for dose 1 on Day 1 followed by 9 doses of 1.37 mg/kg of ALS-008176 twice daily for 5 consecutive days.	
Arm type	Experimental
Investigational medicinal product name	ALS-008176
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral suspension
Routes of administration	Oral use
Dosage and administration details:	
Subjects received 1 loading dose of 4.1 mg/kg of ALS-008176 for dose 1 on Day 1 followed by 9 doses of 1.37 mg/kg of ALS-008176 twice daily for 5 consecutive days.	
Arm title	MAD: ALS-008176 (10/2 mg/kg)
Arm description:	
Subjects received loading dose of 10 mg/kg of ALS-008176 for dose 1 on Day 1 followed by 9 doses of 2 mg/kg of ALS-008176 twice daily for 5 consecutive days.	
Arm type	Experimental
Investigational medicinal product name	ALS-008176
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral suspension
Routes of administration	Oral use
Dosage and administration details:	
Subjects received loading dose of 10 mg/kg of ALS-008176 for dose 1 on Day 1 followed by 9 doses of 2 mg/kg of ALS-008176 twice daily for 5 consecutive days.	
Arm title	MAD: ALS-008176 (30/6 mg/kg)
Arm description:	
Subjects received loading dose of 30 mg/kg of ALS-008176 for dose 1 on Day 1 followed by 9 doses of 6 mg/kg of ALS-008176 twice daily for 5 consecutive days.	
Arm type	Experimental
Investigational medicinal product name	ALS-008176
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral suspension
Routes of administration	Oral use
Dosage and administration details:	
Subjects received loading dose of 30 mg/kg of ALS-008176 for dose 1 on Day 1 followed by 9 doses of 6 mg/kg of ALS-008176 twice daily for 5 consecutive days.	
Arm title	MAD: ALS-008176 (30/10 mg/kg)

Arm description:

Subjects received loading dose of 30 mg/kg of ALS-008176 for dose 1 on Day 1 followed by 9 doses of 10 mg/kg of ALS-008176 twice daily for 5 consecutive days.

Arm type	Experimental
Investigational medicinal product name	ALS-008176
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral suspension
Routes of administration	Oral use

Dosage and administration details:

Subjects received loading dose of 30 mg/kg of ALS-008176 for dose 1 on Day 1 followed by 9 doses of 10 mg/kg of ALS-008176 twice daily for 5 consecutive days.

Arm title	MAD: ALS-008176 (40/20 mg/kg)
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Arm description:

Subjects received loading dose of 40 mg/kg of ALS-008176 for dose 1 on Day 1 followed by 9 doses of 20 mg/kg of ALS-008176 twice daily for 5 consecutive days.

Arm type	Experimental
Investigational medicinal product name	ALS-008176
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral suspension
Routes of administration	Oral use

Dosage and administration details:

Subjects received loading dose of 40 mg/kg of ALS-008176 for dose 1 on Day 1 followed by 9 doses of 20 mg/kg of ALS-008176 twice daily for 5 consecutive days.

Arm title	MAD: ALS-008176 (60/40 mg/kg)
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Arm description:

Subjects received loading dose of 60 mg/kg of ALS-008176 for dose 1 on Day 1 followed by 9 doses of 40 mg/kg of ALS-008176 twice daily for 5 consecutive days.

Arm type	Experimental
Investigational medicinal product name	ALS-008176
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral suspension
Routes of administration	Oral use

Dosage and administration details:

Subjects received loading dose of 60 mg/kg of ALS-008176 for dose 1 on Day 1 followed by 9 doses of 40 mg/kg of ALS-008176 twice daily for 5 consecutive days.

Arm title	Placebo
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Arm description:

Subjects received Placebo orally in SAD and MAD part.

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

Dosage and administration details:

Subjects received Placebo orally in SAD and MAD part.

Number of subjects in period 1	SAD: ALS-008176 (1.37 mg/kg)	SAD: ALS-008176 (4.1 mg/kg)	SAD: ALS-008176 (12 mg/kg)
Started	18	18	14
Completed	18	17	14
Not completed	0	1	0
Adverse Event (Serious-Non Fatal)	-	-	-
Lost to follow-up	-	1	-
Withdrawal by subject	-	-	-

Number of subjects in period 1	SAD: ALS-008176 (25 mg/kg)	MAD: ALS-008176 (4.1/1.37 mg/kg)	MAD: ALS-008176 (10/2 mg/kg)
Started	3	5	14
Completed	2	5	14
Not completed	1	0	0
Adverse Event (Serious-Non Fatal)	-	-	-
Lost to follow-up	-	-	-
Withdrawal by subject	1	-	-

Number of subjects in period 1	MAD: ALS-008176 (30/6 mg/kg)	MAD: ALS-008176 (30/10 mg/kg)	MAD: ALS-008176 (40/20 mg/kg)
Started	8	17	18
Completed	8	17	15
Not completed	0	0	3
Adverse Event (Serious-Non Fatal)	-	-	1
Lost to follow-up	-	-	-
Withdrawal by subject	-	-	2

Number of subjects in period 1	MAD: ALS-008176 (60/40 mg/kg)	Placebo
Started	16	50
Completed	16	47
Not completed	0	3
Adverse Event (Serious-Non Fatal)	-	-
Lost to follow-up	-	1
Withdrawal by subject	-	2

Baseline characteristics

Reporting groups	
Reporting group title	SAD: ALS-008176 (1.37 mg/kg)
Reporting group description: Subjects received single oral dose of 1.37 milligrams per kilogram (mg/kg) of ALS-008176.	
Reporting group title	SAD: ALS-008176 (4.1 mg/kg)
Reporting group description: Subjects received single oral dose of 4.1 mg/kg of ALS-008176.	
Reporting group title	SAD: ALS-008176 (12 mg/kg)
Reporting group description: Subjects received single oral dose of 12 mg/kg of ALS-008176.	
Reporting group title	SAD: ALS-008176 (25 mg/kg)
Reporting group description: Subjects received single oral dose of 25 mg/kg of ALS-008176.	
Reporting group title	MAD: ALS-008176 (4.1/1.37 mg/kg)
Reporting group description: Subjects received 1 loading dose of 4.1 mg/kg of ALS-008176 for dose 1 on Day 1 followed by 9 doses of 1.37 mg/kg of ALS-008176 twice daily for 5 consecutive days.	
Reporting group title	MAD: ALS-008176 (10/2 mg/kg)
Reporting group description: Subjects received loading dose of 10 mg/kg of ALS-008176 for dose 1 on Day 1 followed by 9 doses of 2 mg/kg of ALS-008176 twice daily for 5 consecutive days.	
Reporting group title	MAD: ALS-008176 (30/6 mg/kg)
Reporting group description: Subjects received loading dose of 30 mg/kg of ALS-008176 for dose 1 on Day 1 followed by 9 doses of 6 mg/kg of ALS-008176 twice daily for 5 consecutive days.	
Reporting group title	MAD: ALS-008176 (30/10 mg/kg)
Reporting group description: Subjects received loading dose of 30 mg/kg of ALS-008176 for dose 1 on Day 1 followed by 9 doses of 10 mg/kg of ALS-008176 twice daily for 5 consecutive days.	
Reporting group title	MAD: ALS-008176 (40/20 mg/kg)
Reporting group description: Subjects received loading dose of 40 mg/kg of ALS-008176 for dose 1 on Day 1 followed by 9 doses of 20 mg/kg of ALS-008176 twice daily for 5 consecutive days.	
Reporting group title	MAD: ALS-008176 (60/40 mg/kg)
Reporting group description: Subjects received loading dose of 60 mg/kg of ALS-008176 for dose 1 on Day 1 followed by 9 doses of 40 mg/kg of ALS-008176 twice daily for 5 consecutive days.	
Reporting group title	Placebo
Reporting group description: Subjects received Placebo orally in SAD and MAD part.	

Reporting group values	SAD: ALS-008176 (1.37 mg/kg)	SAD: ALS-008176 (4.1 mg/kg)	SAD: ALS-008176 (12 mg/kg)
Number of subjects	18	18	14
Title for AgeCategorical Units: subjects			
Newborns (0-28 days)	0	0	0
Infants and toddlers (>28 days-12 months)	18	18	14

Title for AgeContinuous Units: months arithmetic mean standard deviation	4 ± 2.8	4.2 ± 2.66	5.7 ± 2.77
Title for Gender Units: subjects			
Female	9	8	3
Male	9	10	11

Reporting group values	SAD: ALS-008176 (25 mg/kg)	MAD: ALS-008176 (4.1/1.37 mg/kg)	MAD: ALS-008176 (10/2 mg/kg)
Number of subjects	3	5	14
Title for AgeCategorical Units: subjects			
Newborns (0-28 days)	0	0	1
Infants and toddlers (>28 days-12 months)	3	5	13
Title for AgeContinuous Units: months arithmetic mean standard deviation	5 ± 2.29	5 ± 3.32	3.2 ± 2.89
Title for Gender Units: subjects			
Female	1	3	4
Male	2	2	10

Reporting group values	MAD: ALS-008176 (30/6 mg/kg)	MAD: ALS-008176 (30/10 mg/kg)	MAD: ALS-008176 (40/20 mg/kg)
Number of subjects	8	17	18
Title for AgeCategorical Units: subjects			
Newborns (0-28 days)	0	0	0
Infants and toddlers (>28 days-12 months)	8	17	18
Title for AgeContinuous Units: months arithmetic mean standard deviation	2.3 ± 1.39	3.5 ± 2.62	4.2 ± 2.94
Title for Gender Units: subjects			
Female	3	6	4
Male	5	11	14

Reporting group values	MAD: ALS-008176 (60/40 mg/kg)	Placebo	Total
Number of subjects	16	50	181
Title for AgeCategorical Units: subjects			
Newborns (0-28 days)	0	0	1
Infants and toddlers (>28 days-12 months)	16	50	180
Title for AgeContinuous Units: months arithmetic mean	4.2	4.1	

standard deviation	± 3.39	± 3.23	-
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Title for Gender			
Units: subjects			
Female	6	23	70
Male	10	27	111

End points

End points reporting groups

Reporting group title	SAD: ALS-008176 (1.37 mg/kg)
Reporting group description: Subjects received single oral dose of 1.37 milligrams per kilogram (mg/kg) of ALS-008176.	
Reporting group title	SAD: ALS-008176 (4.1 mg/kg)
Reporting group description: Subjects received single oral dose of 4.1 mg/kg of ALS-008176.	
Reporting group title	SAD: ALS-008176 (12 mg/kg)
Reporting group description: Subjects received single oral dose of 12 mg/kg of ALS-008176.	
Reporting group title	SAD: ALS-008176 (25 mg/kg)
Reporting group description: Subjects received single oral dose of 25 mg/kg of ALS-008176.	
Reporting group title	MAD: ALS-008176 (4.1/1.37 mg/kg)
Reporting group description: Subjects received 1 loading dose of 4.1 mg/kg of ALS-008176 for dose 1 on Day 1 followed by 9 doses of 1.37 mg/kg of ALS-008176 twice daily for 5 consecutive days.	
Reporting group title	MAD: ALS-008176 (10/2 mg/kg)
Reporting group description: Subjects received loading dose of 10 mg/kg of ALS-008176 for dose 1 on Day 1 followed by 9 doses of 2 mg/kg of ALS-008176 twice daily for 5 consecutive days.	
Reporting group title	MAD: ALS-008176 (30/6 mg/kg)
Reporting group description: Subjects received loading dose of 30 mg/kg of ALS-008176 for dose 1 on Day 1 followed by 9 doses of 9 doses of 6 mg/kg of ALS-008176 twice daily for 5 consecutive days.	
Reporting group title	MAD: ALS-008176 (30/10 mg/kg)
Reporting group description: Subjects received loading dose of 30 mg/kg of ALS-008176 for dose 1 on Day 1 followed by 9 doses of 10 mg/kg of ALS-008176 twice daily for 5 consecutive days.	
Reporting group title	MAD: ALS-008176 (40/20 mg/kg)
Reporting group description: Subjects received loading dose of 40 mg/kg of ALS-008176 for dose 1 on Day 1 followed by 9 doses of 20 mg/kg of ALS-008176 twice daily for 5 consecutive days.	
Reporting group title	MAD: ALS-008176 (60/40 mg/kg)
Reporting group description: Subjects received loading dose of 60 mg/kg of ALS-008176 for dose 1 on Day 1 followed by 9 doses of 40 mg/kg of ALS-008176 twice daily for 5 consecutive days.	
Reporting group title	Placebo
Reporting group description: Subjects received Placebo orally in SAD and MAD part.	
Subject analysis set title	SAD: Placebo
Subject analysis set type	Safety analysis
Subject analysis set description: Subjects received Placebo orally in SAD part.	
Subject analysis set title	MAD: Placebo
Subject analysis set type	Safety analysis
Subject analysis set description: Subjects received Placebo orally in MAD part.	

Primary: SAD: Number of Subjects with Treatment Emergent Adverse Events (TEAEs)

End point title	SAD: Number of Subjects with Treatment Emergent Adverse Events (TEAEs) ^{[1][2]}
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End point description:

An adverse event is any untoward medical event that occurs in a subjects administered an investigational product, and it does not necessarily indicate only events with clear causal relationship with the relevant investigational product. Safety Analysis Set defined as all randomized subjects who received at least 1 dose of study medication.

End point type	Primary
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End point timeframe:

Approximately 4 years

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: Descriptive statistics were done, no inferential statistical analyses were performed.

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

Justification: Endpoint was planned to be reported for the specified arms only.

End point values	SAD: ALS-008176 (1.37 mg/kg)	SAD: ALS-008176 (4.1 mg/kg)	SAD: ALS-008176 (12 mg/kg)	SAD: ALS-008176 (25 mg/kg)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	18	18	14	3
Units: Subjects	14	8	6	2

End point values	MAD: ALS-008176 (4.1/1.37)	MAD: ALS-008176 (10/2 mg/kg)	MAD: ALS-008176 (30/6 mg/kg)	MAD: ALS-008176 (30/10 mg/kg)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	14	8	17
Units: Subjects	4	9	4	13

End point values	MAD: ALS-008176 (40/20 mg/kg)	MAD: ALS-008176 (60/40 mg/kg)	SAD: Placebo	MAD: Placebo
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	18	16	17	33
Units: Subjects	13	14	4	20

Statistical analyses

No statistical analyses for this end point

Primary: SAD: Change From Baseline in Physical Examination (Temperature)

End point title	SAD: Change From Baseline in Physical Examination (Temperature) ^{[3][4]}
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End point description:

Change from baseline in temperature was assessed. Safety analysis set defined as all randomized subjects who received at least 1 dose of study medication. Here "99999" indicates data was not evaluated at specified timepoint. Here "n" indicates number of subjects evaluated at specific timepoints.

End point type	Primary
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End point timeframe:

Baseline up to Day 7

Notes:

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

Justification: Descriptive statistics were done, no inferential statistical analyses were performed.

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

Justification: Endpoint was planned to be reported for the specified arms only.

End point values	SAD: ALS-008176 (1.37 mg/kg)	SAD: ALS-008176 (4.1 mg/kg)	SAD: ALS-008176 (12 mg/kg)	SAD: ALS-008176 (25 mg/kg)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	18	18	14	3
Units: Degree celsius				
arithmetic mean (standard deviation)				
Change at Day 1, 0.5-1h (n=18,18,14,3,15)	-0.1 (± 0.80)	-0.2 (± 0.56)	-0.3 (± 0.78)	0.3 (± 1.74)
Change at Day 2, 24h (n=18, 18, 14, 3, 17)	-0.0 (± 0.68)	-0.1 (± 0.64)	-0.5 (± 0.77)	-0.3 (± 1.07)
Change at Day 3 (n=15, 14, 11, 2, 8)	-0.1 (± 0.59)	0.0 (± 0.66)	-0.7 (± 0.76)	-1.3 (± 1.48)
Change at Day 4 (n=12, 6, 7, 1, 3)	-0.2 (± 0.64)	0.0 (± 0.58)	-0.6 (± 0.79)	0.7 (± 99999)
Change at Day 5 (n=6, 4, 6, 0, 2)	0.1 (± 0.57)	-0.0 (± 0.45)	-0.8 (± 0.71)	99999 (± 99999)
Change at Day 6 (n=1, 2, 2, 0, 5, 1)	0.2 (± 99999)	0.1 (± 0.28)	-0.4 (± 0.99)	99999 (± 99999)
Change at Day 7 (n=18, 17, 14, 2, 16)	-0.1 (± 0.74)	-0.1 (± 0.63)	-0.9 (± 0.87)	-1.2 (± 0.78)

End point values	SAD: Placebo			
Subject group type	Subject analysis set			
Number of subjects analysed	17			
Units: Degree celsius				
arithmetic mean (standard deviation)				
Change at Day 1, 0.5-1h (n=18,18,14,3,15)	-0.0 (± 0.74)			
Change at Day 2, 24h (n=18, 18, 14, 3, 17)	-0.1 (± 0.66)			
Change at Day 3 (n=15, 14, 11, 2, 8)	-0.0 (± 0.57)			
Change at Day 4 (n=12, 6, 7, 1, 3)	-0.5 (± 0.35)			
Change at Day 5 (n=6, 4, 6, 0, 2)	-0.4 (± 0.21)			
Change at Day 6 (n=1, 2, 2, 0, 5, 1)	-1.7 (± 99999)			
Change at Day 7 (n=18, 17, 14, 2, 16)	-0.2 (± 0.68)			

Statistical analyses

Primary: SAD: Change From Baseline for Physical Examination (Respiratory Rate)

End point title	SAD: Change From Baseline for Physical Examination (Respiratory Rate) ^{[5][6]}
End point description: Change from baseline in respiratory rate was assessed. Safety analysis set defined as all randomized subjects who received at least 1 dose of study medication. Here "99999" indicates data was not evaluated at specified timepoint. Here "n" indicates number of subjects evaluated at specific timepoints.	
End point type	Primary
End point timeframe: Baseline up to Day 7	

Notes:

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

Justification: Descriptive statistics were done, no inferential statistical analyses were performed.

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

Justification: Endpoint was planned to be reported for the specified arms only.

End point values	SAD: ALS-008176 (1.37 mg/kg)	SAD: ALS-008176 (4.1 mg/kg)	SAD: ALS-008176 (12 mg/kg)	SAD: ALS-008176 (25 mg/kg)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	18	18	14	3
Units: Breaths per minute				
arithmetic mean (standard deviation)				
Change at Day 1, (n=18,18,14,3,16)	1.7 (± 12.53)	1.8 (± 6.53)	-0.1 (± 5.88)	-1.3 (± 4.16)
Change at Day 2, (n=18, 18, 14, 3, 17)	-2.2 (± 13.17)	-2.4 (± 6.20)	-2.4 (± 8.49)	2.7 (± 1.53)
Change at Day 3 (n=15, 14, 10, 2, 8)	-2.3 (± 11.63)	-3.1 (± 8.34)	-7.6 (± 6.83)	3.0 (± 1.41)
Change at Day 4 (n=11, 6, 6, 1, 3)	-1.2 (± 16.77)	-3.3 (± 8.66)	-4.7 (± 7.76)	0.0 (± 99999)
Change at Day 5 (n=5, 4, 5, 0, 2)	-4.6 (± 14.62)	-4.0 (± 8.04)	-5.2 (± 6.10)	99999 (± 99999)
Change at Day 6 (n=1, 2, 2, 0, 1)	-10.0 (± 99999)	-6.0 (± 5.66)	2.0 (± 8.49)	99999 (± 99999)
Change at Day 7 (n=18, 17, 14, 2, 16)	-9.2 (± 12.50)	-3.0 (± 9.05)	-5.3 (± 6.76)	1.0 (± 1.41)

End point values	SAD: Placebo			
Subject group type	Subject analysis set			
Number of subjects analysed	17			
Units: Breaths per minute				
arithmetic mean (standard deviation)				
Change at Day 1, (n=18,18,14,3,16)	0.8 (± 12.31)			
Change at Day 2, (n=18, 18, 14, 3, 17)	-2.6 (± 12.56)			
Change at Day 3 (n=15, 14, 10, 2, 8)	-0.8 (± 16.99)			
Change at Day 4 (n=11, 6, 6, 1, 3)	2.7 (± 12.70)			
Change at Day 5 (n=5, 4, 5, 0, 2)	2.0 (± 2.83)			
Change at Day 6 (n=1, 2, 2, 0, 1)	0.0 (± 99999)			
Change at Day 7 (n=18, 17, 14, 2, 16)	-5.0 (± 12.77)			

Statistical analyses

No statistical analyses for this end point

Primary: SAD: Change From Baseline in Physical Examination (Heart Rate)

End point title	SAD: Change From Baseline in Physical Examination (Heart Rate) ^{[7][8]}
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End point description:

Change from baseline in Heart rate was assessed. Safety analysis set defined as all randomized subjects who received at least 1 dose of study medication. Here "99999" indicates data was not evaluated at specified timepoint. Here "n" indicates number of subjects evaluated at specific timepoints.

End point type	Primary
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End point timeframe:

Baseline up to Day 7

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: Descriptive statistics were done, no inferential statistical analyses were performed.

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

Justification: Endpoint was planned to be reported for the specified arms only.

End point values	SAD: ALS-008176 (1.37 mg/kg)	SAD: ALS-008176 (4.1 mg/kg)	SAD: ALS-008176 (12 mg/kg)	SAD: ALS-008176 (25 mg/kg)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	18	18	14	3
Units: Beats per minute				
arithmetic mean (standard deviation)				
Change at Day 1, 0.5-1h (n=18,18,14,3,16)	-4.8 (± 21.66)	-3.1 (± 25.99)	-12.7 (± 20.37)	-6.3 (± 19.09)
Change at Day 2, 24h (n=18,18,14,3,17)	-10.5 (± 26.83)	-3.9 (± 18.46)	-13.5 (± 29.85)	6.7 (± 23.18)
Change at Day 3 (n=15, 14, 11, 2, 8)	-5.0 (± 30.03)	-6.8 (± 22.95)	-11.6 (± 23.35)	10.0 (± 32.53)
Change at Day 4 (n=12, 6, 7, 1, 3)	-12.3 (± 26.70)	-6.8 (± 32.18)	-12.1 (± 19.68)	4.0 (± 99999)
Change at Day 5 (n=6, 4, 6, 0, 2)	-12.7 (± 23.73)	-0.3 (± 28.23)	-21.0 (± 19.46)	99999 (± 99999)
Change at Day 6 (n=1, 2, 2, 0, 1)	5.0 (± 99999)	-11.5 (± 48.79)	4.0 (± 29.70)	99999 (± 99999)
Change at Day 7 (n=18, 17, 14, 2, 16)	-17.2 (± 25.76)	-6.1 (± 26.30)	-10.7 (± 28.48)	8.0 (± 1.41)

End point values	SAD: Placebo			
Subject group type	Subject analysis set			
Number of subjects analysed	17			

Units: Beats per minute				
arithmetic mean (standard deviation)				
Change at Day 1, 0.5-1h (n=18,18,14,3,16)	-10.9 (± 20.58)			
Change at Day 2, 24h (n=18,18,14,3,17)	-13.9 (± 22.80)			
Change at Day 3 (n=15, 14, 11, 2, 8)	-11.3 (± 18.84)			
Change at Day 4 (n=12, 6, 7, 1, 3)	1.3 (± 2.31)			
Change at Day 5 (n=6, 4, 6, 0, 2)	0.0 (± 8.49)			
Change at Day 6 (n=1, 2, 2, 0, 1)	-48.0 (± 99999)			
Change at Day 7 (n=18, 17, 14, 2, 16)	-14.4 (± 18.86)			

Statistical analyses

No statistical analyses for this end point

Primary: SAD: Change From Baseline in Physical Examination (Weight)

End point title	SAD: Change From Baseline in Physical Examination
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End point description:

Change from Baseline in weight was assessed. Safety analysis set defined as all randomized subjects who received at least 1 dose of study medication. Here "n" indicates number of subjects evaluated at specified timepoints.

End point type	Primary
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End point timeframe:

Baseline, Day 2 and Day 7

Notes:

[9] - 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: Descriptive statistics were done, no inferential statistical analyses were performed.

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

Justification: Endpoint was planned to be reported for the specified arms only.

End point values	SAD: ALS-008176 (1.37 mg/kg)	SAD: ALS-008176 (4.1 mg/kg)	SAD: ALS-008176 (12 mg/kg)	SAD: ALS-008176 (25 mg/kg)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	18	18	14	3
Units: Kilogram (kg)				
arithmetic mean (standard deviation)				
Change at Day 2, 24h (n=18,17,13,3,12)	-0.0 (± 0.37)	-0.0 (± 0.08)	0.0 (± 0.21)	0.0 (± 0.22)
Change at Day 7 (n=18, 17, 14, 2, 16)	-0.1 (± 0.45)	-0.2 (± 0.45)	-0.1 (± 0.14)	0.2 (± 0.30)

End point values	SAD: Placebo			
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Subject group type	Subject analysis set			
Number of subjects analysed	17			
Units: Kilogram (kg)				
arithmetic mean (standard deviation)				
Change at Day 2, 24h (n=18,17,13,3,12)	-0.0 (± 0.10)			
Change at Day 7 (n=18, 17, 14, 2, 16)	-0.1 (± 0.27)			

Statistical analyses

No statistical analyses for this end point

Primary: SAD: Change From Baseline in Physical Examination (Body Mass Index [BMI])

End point title	SAD: Change From Baseline in Physical Examination (Body Mass Index [BMI])[¹¹][¹²]
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End point description:

Change from baseline in BMI was assessed and measured in kilogram per square meter (kg/m²). Safety analysis set defined as all randomized subjects who received at least 1 dose of study medication. Here "n" indicates number of subjects evaluated at specified timepoints.

End point type	Primary
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End point timeframe:

Baseline, Day 2 and Day 7

Notes:

[11] - 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: Descriptive statistics were done, no inferential statistical analyses were performed.

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

Justification: Endpoint was planned to be reported for the specified arms only.

End point values	SAD: ALS-008176 (1.37 mg/kg)	SAD: ALS-008176 (4.1 mg/kg)	SAD: ALS-008176 (12 mg/kg)	SAD: ALS-008176 (25 mg/kg)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	18	18	14	3
Units: kg/m ²				
arithmetic mean (standard deviation)				
Change at Day 2, 24h (n=17, 16, 13, 3, 12)	-0.2 (± 1.09)	-0.0 (± 0.24)	-0.0 (± 0.51)	0.1 (± 0.61)
Change at Day 7 (n=17, 16, 14, 2, 16)	-0.2 (± 1.25)	-0.5 (± 1.06)	-0.2 (± 0.35)	0.4 (± 0.65)

End point values	SAD: Placebo			
Subject group type	Subject analysis set			
Number of subjects analysed	17			
Units: kg/m ²				
arithmetic mean (standard deviation)				
Change at Day 2, 24h (n=17, 16, 13, 3, 12)	-0.1 (± 0.25)			

Change at Day 7 (n=17, 16, 14, 2, 16)	-0.1 (± 0.63)			
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Statistical analyses

No statistical analyses for this end point

Primary: SAD: Change From Baseline in Physical Examination (Blood Pressure: Systolic Blood Pressure [sBP] and Distolic Blood Pressure [dBP])

End point title	SAD: Change From Baseline in Physical Examination (Blood Pressure: Systolic Blood Pressure [sBP] and Distolic Blood Pressure [dBP])[13][14]
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End point description:

Change from baseline in Blood pressure: sBP and dBP was assessed. Safety analysis set defined as all randomized subjects who received at least 1 dose of study medication. Here "99999" indicates data was not evaluated at specified timepoint. Here "n" indicates number of subjects evaluated at specific timepoints.

End point type	Primary
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End point timeframe:

Baseline up to Day 7

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: Descriptive statistics were done, no inferential statistical analyses were performed.

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

Justification: Endpoint was planned to be reported for the specified arms only.

End point values	SAD: ALS-008176 (1.37 mg/kg)	SAD: ALS-008176 (4.1 mg/kg)	SAD: ALS-008176 (12 mg/kg)	SAD: ALS-008176 (25 mg/kg)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	18	18	14	3
Units: Millimeter of Mercury (mmHg)				
arithmetic mean (standard deviation)				
sBP:Change at Day 1, (n=17,18,12,3,14)	-2.5 (± 9.99)	-0.6 (± 9.22)	5.4 (± 23.05)	1.0 (± 9.64)
sBP:Change at Day 2, (n=17,18,13,3,13)	-5.4 (± 18.46)	-0.9 (± 8.16)	4.5 (± 18.21)	7.0 (± 7.94)
sBP:Change at Day 3 (n=14, 13, 10, 1, 7)	-5.1 (± 12.25)	1.5 (± 8.84)	0.0 (± 11.99)	-3.0 (± 99999)
sBP:Change at Day 4 (n=9, 6, 6, 0, 3)	-5.3 (± 14.10)	1.8 (± 16.73)	-0.2 (± 12.06)	99999 (± 99999)
sBP:Change at Day 5 (n=4, 4, 5, 0, 2)	-0.3 (± 3.69)	-9.5 (± 13.33)	3.2 (± 14.75)	99999 (± 99999)
sBP:Change at Day 6 (n=1, 1, 2, 0, 1)	-5.0 (± 99999)	5.0 (± 99999)	-7.5 (± 0.71)	99999 (± 99999)
sBP:Change at Day 7 (n=16, 16, 12, 2, 14)	-9.8 (± 14.80)	2.6 (± 21.07)	4.9 (± 31.61)	1.0 (± 12.73)
dBp:Change at Day 1 (n=17, 18, 12, 3, 14)	-3.4 (± 10.95)	5.1 (± 16.46)	3.7 (± 14.57)	1.0 (± 17.35)
dBp:Change at Day 2 (n=17, 18, 13, 3, 13)	-5.2 (± 12.20)	3.3 (± 11.65)	1.6 (± 16.19)	-1.3 (± 14.98)

dBP:Change at Day 3 (n=14, 13, 10, 1, 7)	-5.6 (± 10.02)	4.3 (± 14.29)	1.2 (± 8.23)	-11.0 (± 99999)
dBP:Change at Day 4 (n=9, 6, 6, 0, 3)	-4.3 (± 6.65)	-0.3 (± 10.91)	-10.8 (± 12.81)	99999 (± 99999)
dBP:Change at Day 5 (n=4, 4, 5, 0, 2)	2.5 (± 6.45)	-2.8 (± 9.91)	-3.6 (± 9.07)	99999 (± 99999)
dBP:Change at Day 6 (n=1, 1, 2, 0, 1)	15.0 (± 99999)	0.0 (± 99999)	-3.5 (± 6.36)	99999 (± 99999)
dBP:Change at Day 7 (n=16, 16, 12, 2, 14)	-3.7 (± 12.99)	2.1 (± 15.82)	-1.3 (± 14.28)	15.5 (± 0.71)

End point values	SAD: Placebo			
Subject group type	Subject analysis set			
Number of subjects analysed	17			
Units: Millimeter of Mercury (mmHg)				
arithmetic mean (standard deviation)				
sBP:Change at Day 1, (n=17,18,12,3,14)	5.6 (± 12.84)			
sBP:Change at Day 2, (n=17,18,13,3,13)	3.8 (± 17.82)			
sBP:Change at Day 3 (n=14, 13, 10, 1, 7)	5.9 (± 5.15)			
sBP:Change at Day 4 (n=9, 6, 6, 0, 3)	11.3 (± 14.47)			
sBP:Change at Day 5 (n=4, 4, 5, 0, 2)	5.0 (± 12.73)			
sBP:Change at Day 6 (n=1, 1, 2, 0, 1)	4.0 (± 99999)			
sBP:Change at Day 7 (n=16, 16, 12, 2, 14)	7.1 (± 13.95)			
dBP:Change at Day 1 (n=17, 18, 12, 3, 14)	0.5 (± 15.30)			
dBP:Change at Day 2 (n=17, 18, 13, 3, 13)	5.0 (± 14.66)			
dBP:Change at Day 3 (n=14, 13, 10, 1, 7)	-5.3 (± 8.94)			
dBP:Change at Day 4 (n=9, 6, 6, 0, 3)	-5.0 (± 17.78)			
dBP:Change at Day 5 (n=4, 4, 5, 0, 2)	-16.0 (± 5.66)			
dBP:Change at Day 6 (n=1, 1, 2, 0, 1)	1.0 (± 99999)			
dBP:Change at Day 7 (n=16, 16, 12, 2, 14)	6.4 (± 13.21)			

Statistical analyses

No statistical analyses for this end point

Primary: SAD: Change From Baseline for 12-lead Electrocardiogram (ECG) Parameters

End point title	SAD: Change From Baseline for 12-lead Electrocardiogram (ECG) Parameters ^{[15][16]}
End point description:	Change from Baseline in ECG (RR interval, PR interval, QRS interval, QT interval, QTcB interval, QTcF interval) was assessed. Safety analysis set defined as all randomized subjects who received at least 1 dose of study medication. Here "n" indicates number of subjects evaluated at specified timepoints.
End point type	Primary

End point timeframe:

Baseline up to Day 7

Notes:

[15] - 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: Descriptive statistics were done, no inferential statistical analyses were performed.

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

Justification: Endpoint was planned to be reported for the specified arms only.

End point values	SAD: ALS-008176 (1.37 mg/kg)	SAD: ALS-008176 (4.1 mg/kg)	SAD: ALS-008176 (12 mg/kg)	SAD: ALS-008176 (25 mg/kg)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	18	18	14	3
Units: millisecond (msec)				
arithmetic mean (standard deviation)				
RR interval: Change at Day 1(n=18, 16, 14, 3, 17)	5.7 (± 79.52)	26.6 (± 82.92)	38.0 (± 92.81)	5.3 (± 104.58)
RR interval: Change at Day 7(n=18, 16, 13, 2, 16)	10.7 (± 72.99)	2.7 (± 60.06)	36.5 (± 107.57)	61.5 (± 21.92)
PR interval: Change at Day 1(n=18, 16, 14, 3, 17)	0.3 (± 22.78)	0.4 (± 18.74)	-2.7 (± 15.48)	2.7 (± 7.02)
PR interval: Change at Day 7(n=18, 16, 13, 2, 16)	-6.2 (± 21.59)	-4.8 (± 21.86)	-5.9 (± 11.81)	-6.0 (± 16.97)
QRS interval:Change at Day 1(n=18, 16, 14, 3, 17)	-0.6 (± 24.77)	-1.6 (± 11.75)	-5.7 (± 11.66)	-1.0 (± 2.65)
QRS interval:Change at Day 7(n=18, 16, 13, 2, 16)	-4.3 (± 21.27)	1.8 (± 16.47)	-3.8 (± 12.43)	2.0 (± 5.66)
QT interval:Change at Day 1(n= 18, 16, 14, 3, 17)	0.9 (± 44.51)	1.8 (± 23.10)	-7.6 (± 66.76)	4.0 (± 30.27)
QT interval:Change at Day 7(n=18, 16, 13, 2, 16)	3.7 (± 49.72)	0.7 (± 26.66)	-3.5 (± 64.44)	43.5 (± 24.75)
QTcB interval:Change at Day 1(n=18,16,13,3,17)	-2.7 (± 65.31)	-9.2 (± 21.47)	-13.1 (± 44.88)	3.0 (± 5.29)
QTcB interval:Change at Day 7(n=18, 16,13,2,16)	-3.3 (± 68.45)	4.6 (± 40.58)	-2.4 (± 36.56)	36.5 (± 23.33)
QTcF interval:Change at Day 1(n=18, 16,14,3,17)	-0.4 (± 55.72)	-3.2 (± 16.70)	-4.6 (± 40.59)	3.3 (± 10.69)
QTcF interval:Change at Day 7(n=18,16,13,2,16)	1.3 (± 60.19)	5.1 (± 30.78)	1.9 (± 28.37)	40.5 (± 24.75)

End point values	SAD: Placebo			
Subject group type	Subject analysis set			
Number of subjects analysed	17			
Units: millisecond (msec)				
arithmetic mean (standard deviation)				
RR interval: Change at Day 1(n=18, 16, 14, 3, 17)	11.6 (± 54.87)			
RR interval: Change at Day 7(n=18, 16, 13, 2, 16)	38.6 (± 73.31)			
PR interval: Change at Day 1(n=18, 16, 14, 3, 17)	-2.4 (± 15.26)			
PR interval: Change at Day 7(n=18, 16, 13, 2, 16)	3.2 (± 13.18)			

QRS interval:Change at Day 1(n=18, 16, 14, 3, 17)	-0.4 (± 19.13)			
QRS interval:Change at Day 7(n=18, 16, 13, 2, 16)	-1.1 (± 17.37)			
QT interval:Change at Day 1(n= 18, 16, 14, 3, 17)	-3.5 (± 43.52)			
QT interval:Change at Day 7(n=18, 16, 13, 2, 16)	4.5 (± 38.97)			
QTcB interval:Change at Day 1(n=18,16,13,3,17)	-20.7 (± 72.59)			
QTcB interval:Change at Day 7(n=18, 16,13,2,16)	-17.8 (± 68.46)			
QTcF interval:Change at Day 1(n=18, 16,14,3,17)	-12.9 (± 82.87)			
QTcF interval:Change at Day 7(n=18,16,13,2,16)	-5.3 (± 52.04)			

Statistical analyses

No statistical analyses for this end point

Primary: SAD: Change From Baseline in Clinical Laboratory Parameter (Serum Chemistry-Alkaline Phosphatase [AP], Alanine Aminotransferase [ALA], Aspartate Aminotransferase [ASA], Creatine Kinase [CrK])

End point title	SAD: Change From Baseline in Clinical Laboratory Parameter (Serum Chemistry-Alkaline Phosphatase [AP], Alanine Aminotransferase [ALA], Aspartate Aminotransferase [ASA], Creatine Kinase [CrK])[¹⁷][¹⁸]
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End point description:

Change from baseline in Serum Chemistry-AP, ALA, ASA, CrK were assessed. Here "99999" indicates data was not evaluated at specified timepoint. Here "n" indicates number of subjects evaluated at specific timepoints.

End point type	Primary
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End point timeframe:

From Baseline, Day 1 and Day 7

Notes:

[17] - 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: Descriptive statistics were done, no inferential statistical analyses were performed.

[18] - 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: Endpoint was planned to be reported for the specified arms only.

End point values	SAD: ALS-008176 (1.37 mg/kg)	SAD: ALS-008176 (4.1 mg/kg)	SAD: ALS-008176 (12 mg/kg)	SAD: ALS-008176 (25 mg/kg)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	18	18	14	3
Units: Microkatal per liter				
arithmetic mean (standard deviation)				
AP:Change at Day 1, 3h (n=7, 7, 6, 1, 8)	-0.300 (± 0.4948)	-0.440 (± 1.3063)	-0.094 (± 0.1361)	-0.167 (± 99999)
AP:Change at Day 1, 7h (n=7, 8, 7, 2, 6)	-0.241 (± 0.2095)	-0.204 (± 0.5564)	-0.088 (± 0.4043)	0.208 (± 0.1061)

AP:Change at Day 7 (n=18, 16, 13, 2, 16)	0.172 (± 0.9051)	0.414 (± 0.8600)	0.012 (± 0.7169)	1.125 (± 0.2004)
ALA:Change at Day 1, 3h (n=7, 7, 7, 1, 7)	-0.009 (± 0.0841)	-0.008 (± 0.0337)	-0.012 (± 0.0826)	-0.017 (± 99999)
ALA:Change at Day 1, 7h (n=7, 8, 7, 2, 6)	-0.062 (± 0.0967)	0.060 (± 0.2745)	-0.002 (± 0.0619)	0.000 (± 0.0000)
ALA:Change at Day 7 (n=18, 17, 13, 2, 16)	0.040 (± 0.2101)	-0.376 (± 1.2695)	0.077 (± 0.3084)	0.000 (± 0.0707)
ASA:Change at Day 1, 3h (n=6, 7, 5, 0, 6)	-0.041 (± 0.0886)	0.022 (± 0.1012)	0.103 (± 0.1639)	99999 (± 99999)
ASA:Change at Day 1, 7h (n=5, 6, 6, 2, 5)	-0.004 (± 0.0766)	0.217 (± 0.4365)	-0.061 (± 0.1754)	0.092 (± 0.1061)
ASA:Change at Day 7 (n=15, 14, 12, 2, 12)	0.027 (± 0.2693)	-0.252 (± 0.7332)	0.032 (± 0.2700)	0.083 (± 0.0943)
CrK:Change at Day 1, 3h (n=7, 6, 6, 1, 8)	-0.100 (± 1.3554)	-0.967 (± 2.1592)	0.008 (± 0.4103)	0.033 (± 99999)
CrK:Change at Day 1, 7h (n=6, 7, 7, 2, 4)	-0.172 (± 0.4526)	-0.040 (± 0.6998)	-0.031 (± 0.4879)	0.108 (± 0.0589)
CrK:Change at Day 7 (n=17, 13, 13, 2, 13)	0.001 (± 1.9922)	-1.500 (± 4.0774)	2.958 (± 9.4720)	0.675 (± 0.1532)

End point values	SAD: Placebo			
Subject group type	Subject analysis set			
Number of subjects analysed	17			
Units: Microkatal per liter				
arithmetic mean (standard deviation)				
AP:Change at Day 1, 3h (n=7, 7, 6, 1, 8)	0.050 (± 0.2049)			
AP:Change at Day 1, 7h (n=7, 8, 7, 2, 6)	-0.119 (± 0.3383)			
AP:Change at Day 7 (n=18, 16, 13, 2, 16)	0.362 (± 1.1151)			
ALA:Change at Day 1, 3h (n=7, 7, 7, 1, 7)	0.000 (± 0.0491)			
ALA:Change at Day 1, 7h (n=7, 8, 7, 2, 6)	-0.025 (± 0.0673)			
ALA:Change at Day 7 (n=18, 17, 13, 2, 16)	0.020 (± 0.1564)			
ASA:Change at Day 1, 3h (n=6, 7, 5, 0, 6)	0.083 (± 0.0803)			
ASA:Change at Day 1, 7h (n=5, 6, 6, 2, 5)	0.200 (± 0.3156)			
ASA:Change at Day 7 (n=15, 14, 12, 2, 12)	-0.050 (± 0.2278)			
CrK:Change at Day 1, 3h (n=7, 6, 6, 1, 8)	-0.517 (± 0.8730)			
CrK:Change at Day 1, 7h (n=6, 7, 7, 2, 4)	-0.146 (± 0.7974)			
CrK:Change at Day 7 (n=17, 13, 13, 2, 13)	-0.044 (± 1.9820)			

Statistical analyses

Primary: SAD: Change From Baseline in Clinical Laboratory Parameter (Serum Chemistry-Bilirubin, Direct Bilirubin [DB], and Indirect Bilirubin [IB], Creatinine [Cr])

End point title	SAD: Change From Baseline in Clinical Laboratory Parameter (Serum Chemistry-Bilirubin, Direct Bilirubin [DB], and Indirect Bilirubin [IB], Creatinine [Cr])[¹⁹][²⁰]
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End point description:

Change From Baseline in Serum Chemistry-Bilirubin, Direct Bilirubin (DB), Indirect Bilirubin (IB), and Creatinine (Cr) were assessed. Safety analysis set defined as all randomized subjects who received at least 1 dose of study medication. Here "99999" indicates data was not evaluated at specified timepoint. Here "n" indicates number of subjects evaluated at specific timepoints.

End point type	Primary
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End point timeframe:

For DB and IB: From Baseline, Day 1, Day 3 and Day 7 and for Cr: From Baseline, Day 1, Day 3, Day 4 and Day 7

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: Descriptive statistics were done, no inferential statistical analyses were performed.

[20] - 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: Endpoint was planned to be reported for the specified arms only.

End point values	SAD: ALS-008176 (1.37 mg/kg)	SAD: ALS-008176 (4.1 mg/kg)	SAD: ALS-008176 (12 mg/kg)	SAD: ALS-008176 (25 mg/kg)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	18	18	14	3
Units: Micromoles per liter (mcmol/L)				
arithmetic mean (standard deviation)				
Bilirubin:Change at Day 1, 3h (n=7,6,7,1,8)	-2.178 (± 3.2316)	-0.599 (± 0.9288)	-0.942 (± 1.3241)	0.000 (± 99999)
Bilirubin:Change at Day 1, 7h (n=7,7,7,2,6)	-0.310 (± 0.4754)	-0.216 (± 2.1765)	-0.126 (± 1.5381)	-1.000 (± 1.4142)
Bilirubin:Change at Day 3 (n=1, 0, 0, 0, 0)	0.171 (± 99999)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)
Bilirubin: Change at Day 7 (n=18, 15, 13, 2, 16)	-1.809 (± 5.7567)	0.390 (± 3.7937)	0.155 (± 2.7809)	-0.500 (± 0.7071)
DB: Change at Day 1, 3h (n=5, 5, 4, 0, 6)	-1.626 (± 1.0669)	-0.039 (± 0.7201)	-0.385 (± 0.8872)	99999 (± 99999)
DB: Change at Day 1, 7h (n=4, 5, 5, 1, 3)	0.428 (± 0.8550)	0.000 (± 1.0747)	0.239 (± 0.2294)	0.000 (± 99999)
DB: Change at Day 3 (n=1, 0, 0, 0, 0)	0.171 (± 99999)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)
DB: Change at Day 7 (n=10, 10, 9, 1, 9)	0.117 (± 0.8729)	0.425 (± 1.7729)	-0.247 (± 1.3895)	0.000 (± 99999)
IB: Change at Day 1, 3h (n=3, 3, 1, 0, 4)	-1.430 (± 4.0490)	-0.570 (± 0.9873)	-0.342 (± 99999)	99999 (± 99999)
IB: Change at Day 1, 7h (n=3, 1, 3, 1, 2)	-0.627 (± 0.9418)	-1.710 (± 99999)	0.342 (± 2.2361)	0.000 (± 99999)
IB: Change as Day 3 (n=1, 0, 0, 0, 0)	0.000 (± 99999)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)
IB: Change at Day 7 (n=7, 4, 4, 1, 6)	0.081 (± 1.6524)	-2.693 (± 3.7681)	2.309 (± 3.2848)	0.000 (± 99999)
Cr: Change at Day 1, 3h (n=6, 7, 7, 1, 8)	-0.167 (± 1.6021)	-1.449 (± 3.8813)	-0.027 (± 4.2436)	0.000 (± 99999)

Cr: Change at Day 1, 7h (n=7, 8, 7, 2, 7)	-0.538 (± 5.8116)	-1.013 (± 3.8128)	-0.126 (± 7.1625)	-0.500 (± 0.7071)
Cr: Change at Day 3 (n=1, 0, 1, 0, 0)	-0.884 (± 99999)	99999 (± 99999)	0.000 (± 99999)	99999 (± 99999)
Cr: Change at Day 4 (n=0, 1, 0, 0, 0)	99999 (± 99999)	-6.000 (± 99999)	99999 (± 99999)	99999 (± 99999)
Cr: Change at Day 7 (n=18, 17, 13, 2, 16)	1.403 (± 2.3512)	2.024 (± 3.6523)	3.386 (± 11.6813)	1.500 (± 2.1213)

End point values	SAD: Placebo			
Subject group type	Subject analysis set			
Number of subjects analysed	17			
Units: Micromoles per liter (mcmol/L)				
arithmetic mean (standard deviation)				
Bilirubin:Change at Day 1, 3h (n=7,6,7,1,8)	-0.516 (± 1.8990)			
Bilirubin:Change at Day 1, 7h (n=7,7,7,2,6)	-2.594 (± 4.7885)			
Bilirubin:Change at Day 3 (n=1, 0, 0, 0, 0)	99999 (± 99999)			
Bilirubin: Change at Day 7 (n=18, 15, 13, 2, 16)	-0.142 (± 4.7240)			
DB: Change at Day 1, 3h (n=5, 5, 4, 0, 6)	-0.366 (± 0.8641)			
DB: Change at Day 1, 7h (n=4, 5, 5, 1, 3)	-0.570 (± 0.9873)			
DB: Change at Day 3 (n=1, 0, 0, 0, 0)	99999 (± 99999)			
DB: Change at Day 7 (n=10, 10, 9, 1, 9)	1.374 (± 4.2736)			
IB: Change at Day 1, 3h (n=3, 3, 1, 0, 4)	-0.770 (± 1.2527)			
IB: Change at Day 1, 7h (n=3, 1, 3, 1, 2)	-0.941 (± 1.0882)			
IB: Change as Day 3 (n=1, 0, 0, 0, 0)	99999 (± 99999)			
IB: Change at Day 7 (n=7, 4, 4, 1, 6)	1.254 (± 3.1728)			
Cr: Change at Day 1, 3h (n=6, 7, 7, 1, 8)	3.774 (± 9.3274)			
Cr: Change at Day 1, 7h (n=7, 8, 7, 2, 7)	-2.389 (± 3.8129)			
Cr: Change at Day 3 (n=1, 0, 1, 0, 0)	99999 (± 99999)			
Cr: Change at Day 4 (n=0, 1, 0, 0, 0)	99999 (± 99999)			
Cr: Change at Day 7 (n=18, 17, 13, 2, 16)	0.353 (± 6.7510)			

Statistical analyses

No statistical analyses for this end point

Primary: SAD: Change From Baseline in Clinical Laboratory Parameter (Serum Chemistry-Blood Urea Nitrogen [BUN], Derived Urea [DU], Chloride [Cl], Bicarbonate [BiC], Glucose [Glu], Potassium [K], Sodium[Na])

End point title	SAD: Change From Baseline in Clinical Laboratory Parameter (Serum Chemistry-Blood Urea Nitrogen [BUN], Derived Urea [DU], Chloride [Cl], Bicarbonate [BiC], Glucose [Glu], Potassium [K], Sodium[Na]) ^{[21][22]}
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End point description:

Change from baseline for clinical laboratory parameter (Serum chemistry- Blood Urea Nitrogen [BUN], Derived Urea [DU], Chloride [Cl], Bicarbonate [BiC], Glucose [Glu], Potassium [K], and Sodium [Na]) was assessed. Safety analysis set defined as all randomized subjects who received at least 1 dose of study medication. Here "99999" indicates data was not evaluated at specified timepoint. Here "n" indicates number of subjects evaluated at specific timepoints.

End point type	Primary
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End point timeframe:

For BUN and DU: From Baseline, Day 1, Day 3, Day 7; for Cl, K and Na: From baseline, Day 1, 3, 4, 6 and Day 7

Notes:

[21] - 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: Descriptive statistics were done, no inferential statistical analyses were performed.

[22] - 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: Endpoint was planned to be reported for the specified arms only.

End point values	SAD: ALS-008176 (1.37 mg/kg)	SAD: ALS-008176 (4.1 mg/kg)	SAD: ALS-008176 (12 mg/kg)	SAD: ALS-008176 (25 mg/kg)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	18	18	14	3
Units: Millimoles per liter (mmol/L)				
arithmetic mean (standard deviation)				
BUN: Change at Day 1, 3h Postdose(n=6, 6, 4, 0, 4)	0.075 (± 0.3764)	0.292 (± 0.6872)	-0.018 (± 0.5136)	99999 (± 99999)
BUN: Change at Day 1, 7h Postdose(n=4, 6, 5, 0, 4)	0.134 (± 0.5518)	-0.014 (± 0.7761)	-0.221 (± 0.5544)	99999 (± 99999)
BUN: Change at Day 3 (n=0, 0, 1, 0, 0)	99999 (± 99999)	99999 (± 99999)	0.678 (± 99999)	99999 (± 99999)
BUN: Change at Day 7 (n=10, 11, 9, 1, 8)	0.597 (± 0.7556)	0.831 (± 1.0460)	0.409 (± 0.7407)	1.071 (± 99999)
DU: Change at Day 1, 3h(n=6, 8, 7, 1, 8)	-0.261 (± 0.5504)	0.151 (± 0.6290)	-0.339 (± 0.6782)	0.000 (± 99999)
DU: Change at Day 1, 7h(n=7, 8, 7, 1, 7)	-0.038 (± 0.5881)	0.080 (± 0.6776)	-0.015 (± 0.6182)	0.200 (± 99999)
DU: Change at Day 3 (n=0, 0, 1, 0, 0)	99999 (± 99999)	99999 (± 99999)	0.678 (± 99999)	99999 (± 99999)
DU: Change at Day 7 (n=17, 17, 13, 2, 15)	0.217 (± 0.6580)	0.926 (± 1.0024)	0.652 (± 0.9884)	0.836 (± 0.3330)
Cl: Change at Day 1, 3h Postdose (n=6, 8, 6, 0 7)	-1.167 (± 2.1370)	-1.625 (± 2.0659)	0.400 (± 2.9933)	99999 (± 99999)
Cl: Change at Day 1; 7h Postdose(n=7, 8, 6, 2, 5)	-0.286 (± 1.7995)	-0.575 (± 2.3457)	-0.500 (± 3.1464)	0.000 (± 0.0000)
Cl: Change at Day 3 (n=0, 0, 1, 0, 1)	99999 (± 99999)	-6.300 (± 99999)	99999 (± 99999)	99999 (± 99999)
Cl: Change at Day 4 (n=0, 0, 0, 0, 1)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)
Cl: Change at Day 6 (n=0, 0, 0, 0, 1)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)

Cl: Change at Day 7 (n=17, 16, 13, 2, 13)	0.176 (± 3.5397)	-0.131 (± 3.3380)	0.015 (± 2.9274)	3.000 (± 0.0000)
BiC: Change at Day 1, 3h Postdose (n=6, 7, 6, 0, 7)	0.367 (± 1.7500)	1.771 (± 2.8929)	0.667 (± 2.4312)	99999 (± 99999)
BiC: Change at Day 1; 7h Postdose (n=7, 8, 7, 2, 5)	-0.614 (± 2.6143)	0.325 (± 2.1881)	0.157 (± 2.3999)	-0.050 (± 0.3536)
BiC: Change at Day 3 (n=0, 0, 1, 0, 1)	99999 (± 99999)	99999 (± 99999)	-1.100 (± 99999)	99999 (± 99999)
BiC: Change at Day 4 (n=0, 0, 0, 0, 1)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)
BiC: Change at Day 6 (n=0, 0, 0, 0, 1)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)
BiC: Change at Day 7 (n=16, 14, 13, 2, 11)	-2.463 (± 4.5964)	-2.486 (± 2.5792)	-1.015 (± 3.2761)	-3.200 (± 0.0000)
Glu: Change at Day 1, 3h(n=6, 6, 6, 0, 7)	-0.559 (± 1.0626)	-1.638 (± 3.1932)	0.348 (± 0.5935)	99999 (± 99999)
Glu: Change at Day 1, 7h(n=7, 8, 6, 2, 5)	-0.370 (± 0.7408)	-0.468 (± 1.0589)	6.510 (± 13.7761)	-0.244 (± 0.2040)
Glu: Change at Day 7 (n=16, 17, 12, 2, 14)	-0.973 (± 1.1516)	-1.020 (± 1.8882)	-0.455 (± 0.6583)	-1.239 (± 0.6526)
K: Change at Day 1, 3h Postdose(n=7, 8, 7, 1, 8)	-0.029 (± 0.3450)	-0.083 (± 0.6207)	-0.069 (± 0.3458)	0.800 (± 99999)
K: Change at Day 1, 7h Postdose(n=7, 8, 6, 2, 6)	-0.416 (± 0.4176)	-0.063 (± 0.5208)	-0.143 (± 0.6191)	0.750 (± 0.7778)
K: Change at Day 3 (n=0, 0, 1, 0, 1)	99999 (± 99999)	99999 (± 99999)	0.480 (± 99999)	99999 (± 99999)
K: Change at Day 4 (n=0, 1, 0, 0, 1)	99999 (± 99999)	0.300 (± 99999)	99999 (± 99999)	99999 (± 99999)
K: Change at Day 6 (n=0, 0, 0, 0, 1)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)
K: Change at Day 7 (n=18, 17, 13, 2, 16)	0.281 (± 0.7417)	0.324 (± 0.8241)	0.437 (± 1.2304)	0.400 (± 0.2828)
Na: Change at Day 1, 3h(n=7, 8, 7, 1, 8)	-1.143 (± 0.9163)	-0.988 (± 2.9406)	1.143 (± 3.5322)	0.000 (± 99999)
Na: Change at Day 1, 7h(n=7, 8, 6, 2, 7)	-0.543 (± 2.9563)	-0.500 (± 2.7255)	-1.833 (± 4.8339)	0.000 (± 0.0000)
Na: Change at Day 3 (n=0, 0, 1, 0, 1)	99999 (± 99999)	99999 (± 99999)	-1.000 (± 99999)	99999 (± 99999)
Na: Change at Day 4 (n=0, 1, 0, 0, 1)	99999 (± 99999)	3.000 (± 99999)	99999 (± 99999)	99999 (± 99999)
Na: Change at Day 6 (n=0, 0, 0, 0, 1)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)
Na: Change at Day 7 (n=18, 17, 13, 2, 16)	-0.761 (± 2.2968)	-0.818 (± 2.9394)	0.154 (± 2.8532)	0.500 (± 0.7071)

End point values	SAD: Placebo			
Subject group type	Subject analysis set			
Number of subjects analysed	17			
Units: Millimoles per liter (mmol/L)				
arithmetic mean (standard deviation)				
BUN: Change at Day 1, 3h Postdose(n=6, 6, 4, 0, 4)	0.062 (± 0.3969)			
BUN: Change at Day 1, 7h Postdose(n=4, 6, 5, 0, 4)	-0.687 (± 0.5884)			
BUN: Change at Day 3 (n=0, 0, 1, 0, 0)	99999 (± 99999)			

BUN: Change at Day 7 (n=10, 11, 9, 1, 8)	0.228 (± 1.4166)			
DU: Change at Day 1, 3h(n=6, 8, 7, 1, 8)	-0.106 (± 0.3757)			
DU: Change at Day 1, 7h(n=7, 8, 7, 1, 7)	-0.393 (± 0.9118)			
DU: Change at Day 3 (n=0, 0, 1, 0, 0)	99999 (± 99999)			
DU: Change at Day 7 (n=17, 17, 13, 2, 15)	0.368 (± 1.1038)			
Cl: Change at Day 1, 3h Postdose (n=6, 8, 6, 0 7)	-0.643 (± 1.9730)			
Cl: Change at Day 1; 7h Postdose(n=7, 8, 6, 2, 5)	-0.560 (± 2.9846)			
Cl: Change at Day 3 (n=0, 0, 1, 0, 1)	-3.800 (± 99999)			
Cl: Change at Day 4 (n=0, 0, 0, 0, 1)	-1.100 (± 99999)			
Cl: Change at Day 6 (n=0, 0, 0, 0, 1)	-4.300 (± 99999)			
Cl: Change at Day 7 (n=17, 16, 13, 2, 13)	0.469 (± 2.8238)			
BiC:Change at Day 1, 3h Postdose (n=6, 7, 6, 0, 7)	-2.686 (± 4.7355)			
BiC:Change at Day 1; 7h Postdose (n=7, 8, 7, 2, 5)	-1.440 (± 2.7181)			
BiC: Change at Day 3 (n=0, 0, 1, 0, 1)	1.600 (± 99999)			
BiC: Change at Day 4 (n=0, 0, 0, 0, 1)	-2.500 (± 99999)			
BiC: Change at Day 6 (n=0, 0, 0, 0, 1)	2.200 (± 99999)			
BiC: Change at Day 7 (n=16, 14, 13, 2, 11)	-2.073 (± 3.5508)			
Glu: Change at Day 1, 3h(n=6, 6, 6, 0, 7)	0.144 (± 0.6468)			
Glu: Change at Day 1, 7h(n=7, 8, 6, 2, 5)	-0.418 (± 0.9007)			
Glu: Change at Day 7 (n=16, 17, 12, 2, 14)	-0.636 (± 1.2004)			
K: Change at Day 1, 3h Postdose(n=7, 8, 7, 1, 8)	0.200 (± 0.5555)			
K: Change at Day 1, 7h Postdose(n=7, 8, 6, 2, 6)	0.592 (± 1.0754)			
K: Change at Day 3 (n=0, 0, 1, 0, 1)	0.350 (± 99999)			
K: Change at Day 4 (n=0, 1, 0, 0, 1)	0.620 (± 99999)			
K: Change at Day 6 (n=0, 0, 0, 0, 1)	0.840 (± 99999)			
K: Change at Day 7 (n=18, 17, 13, 2, 16)	0.312 (± 0.7808)			
Na: Change at Day 1, 3h(n=7, 8, 7, 1, 8)	-1.000 (± 3.0706)			
Na: Change at Day 1, 7h(n=7, 8, 6, 2, 7)	0.000 (± 2.8868)			
Na: Change at Day 3 (n=0, 0, 1, 0, 1)	-1.000 (± 99999)			
Na: Change at Day 4 (n=0, 1, 0, 0, 1)	-2.000 (± 99999)			
Na: Change at Day 6 (n=0, 0, 0, 0, 1)	-3.000 (± 99999)			

Na: Change at Day 7 (n=18, 17, 13, 2, 16)	-0.063 ($\pm$ 2.5682)			
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Statistical analyses

No statistical analyses for this end point

Primary: SAD: Change From Baseline in Clinical laboratory Parameter (Hematology-Reticulocyte Absolute [RA], Platelets [PI], Leukocytes [LU], Monocytes [MO], Neutrophils [NE])

End point title	SAD: Change From Baseline in Clinical laboratory Parameter (Hematology-Reticulocyte Absolute [RA], Platelets [PI], Leukocytes [LU], Monocytes [MO], Neutrophils [NE])[²³][²⁴]
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End point description:

Change from baseline in Hematology- reticulocyte, Absolute (RA), Platelets (PI), Leukocytes (LU), Monocytes (MO) and Neutrophils (NE) were assessed. Safety analysis set defined as all randomized subjects who received at least 1 dose of study medication. Here "99999" indicates data was not evaluated at specified timepoint. Here "n" indicates number of subjects evaluated at specific timepoints.

End point type	Primary
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End point timeframe:

For RA, MO, NE: From Baseline, Day 1 and Day 7; For PI, LU: From Baseline, Day 1, Day 3, Day 6 and Day 7

Notes:

[23] - 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: Descriptive statistics were done, no inferential statistical analyses were performed.

[24] - 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: Endpoint was planned to be reported for the specified arms only.

End point values	SAD: ALS-008176 (1.37 mg/kg)	SAD: ALS-008176 (4.1 mg/kg)	SAD: ALS-008176 (12 mg/kg)	SAD: ALS-008176 (25 mg/kg)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	18	18	14	3
Units: 10 ⁹ per liter				
arithmetic mean (standard deviation)				
RA: Change at Day, 3h (n=1, 1, 2, 1, 2)	-3.200 ($\pm$ 99999)	-0.200 ($\pm$ 99999)	-2.250 ($\pm$ 2.4749)	-0.200 ($\pm$ 99999)
RA: Change at Day 1, 7h (n=3, 3, 1, 1, 1)	3.333 ($\pm$ 6.1101)	2.873 ($\pm$ 5.2253)	33.000 ($\pm$ 99999)	5.300 ($\pm$ 99999)
RA: Change at Day 7 (n=5, 5, 3, 0, 6)	18.920 ($\pm$ 14.0901)	45.500 ($\pm$ 28.2952)	83.533 ($\pm$ 28.3285)	99999 ($\pm$ 99999)
PI: Change at Day 1, 3h (n=7, 8, 7, 1, 7)	15.429 ($\pm$ 51.6135)	-11.500 ($\pm$ 104.8768)	17.143 ($\pm$ 83.8718)	52.000 ($\pm$ 99999)
PI: Change at Day 1, 7h (n=7, 8, 6, 2, 5)	4.286 ($\pm$ 58.9992)	81.375 ($\pm$ 147.4807)	-13.667 ($\pm$ 73.7500)	17.500 ($\pm$ 10.6066)
PI: Change at Day 3 (n=0, 0, 1, 0, 1)	99999 ($\pm$ 99999)	99999 ($\pm$ 99999)	77.000 ($\pm$ 99999)	99999 ($\pm$ 99999)
PI: Change at Day 6 (n=0, 0, 0, 0, 1)	99999 ($\pm$ 99999)	99999 ($\pm$ 99999)	99999 ($\pm$ 99999)	99999 ($\pm$ 99999)
PI: Change at Day 7 (n=17, 16, 12, 0, 16)	239.765 ($\pm$ 250.8260)	214.438 ($\pm$ 204.2335)	226.750 ($\pm$ 181.5404)	99999 ($\pm$ 99999)

LU: Change at Day 1, 3h (n=7, 8, 7, 1, 7)	-1.194 (± 3.1878)	-2.008 (± 2.9722)	1.864 (± 6.7045)	1.470 (± 99999)
LU: Change at Day 1, 7h (n=7, 8, 6, 2, 6)	-1.730 (± 3.6807)	1.366 (± 2.3019)	1.073 (± 2.3062)	0.210 (± 0.1273)
LU: Change at Day 3 (n=0, 0, 1, 0, 1)	99999 (± 99999)	99999 (± 99999)	5.500 (± 99999)	99999 (± 99999)
LU: Change at Day 6 (n=0, 0, 0, 0, 1)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)
LU: Change at Day 7 (n=17, 16, 12, 0, 16)	0.549 (± 3.5909)	2.682 (± 4.6478)	3.398 (± 4.6757)	99999 (± 99999)
MO: Change at Day 1, 3h (n=4, 7, 5, 1, 7)	-0.4108 (± 0.34710)	-0.5242 (± 1.18012)	-0.0629 (± 0.75397)	0.4300 (± 99999)
MO: Change at Day 1, 7h (n=5, 5, 4, 1, 5)	-0.2473 (± 0.74147)	0.2852 (± 0.66781)	-0.1637 (± 0.14324)	0.0300 (± 99999)
MO: Change at Day 7 (n=12, 12, 8, 0, 15)	-0.5250 (± 1.00177)	-0.0051 (± 0.97576)	-0.0045 (± 0.75931)	99999 (± 99999)
NE: Change at Day 1, 3h (n=4, 7, 5, 1, 7)	-1.0579 (± 1.81701)	-1.0449 (± 1.77922)	0.3576 (± 4.94630)	-0.7800 (± 99999)
NE: Change at Day 1, 7h (n=5, 6, 4, 2, 5)	-1.3340 (± 1.49913)	1.0500 (± 0.83268)	0.6315 (± 1.01518)	-1.1300 (± 0.38184)
NE: Change at Day 7 (n=12, 13, 8, 0, 15)	-1.3650 (± 3.59894)	0.8115 (± 2.57739)	0.3376 (± 3.02596)	99999 (± 99999)

End point values	SAD: Placebo			
Subject group type	Subject analysis set			
Number of subjects analysed	17			
Units: 10 ⁹ per liter				
arithmetic mean (standard deviation)				
RA: Change at Day, 3h (n=1, 1, 2, 1, 2)	3.750 (± 0.4950)			
RA: Change at Day 1, 7h (n=3, 3, 1, 1, 1)	38.640 (± 99999)			
RA: Change at Day 7 (n=5, 5, 3, 0, 6)	48.710 (± 32.0216)			
PI: Change at Day 1, 3h (n=7, 8, 7, 1, 7)	28.000 (± 57.2655)			
PI: Change at Day 1, 7h (n=7, 8, 6, 2, 5)	-21.400 (± 246.0616)			
PI: Change at Day 3 (n=0, 0, 1, 0, 1)	-95.000 (± 99999)			
PI: Change at Day 6 (n=0, 0, 0, 0, 1)	45.000 (± 99999)			
PI: Change at Day 7 (n=17, 16, 12, 0, 16)	188.375 (± 144.8916)			
LU: Change at Day 1, 3h (n=7, 8, 7, 1, 7)	0.254 (± 2.0285)			
LU: Change at Day 1, 7h (n=7, 8, 6, 2, 6)	-0.523 (± 6.4347)			
LU: Change at Day 3 (n=0, 0, 1, 0, 1)	-12.900 (± 99999)			
LU: Change at Day 6 (n=0, 0, 0, 0, 1)	-6.800 (± 99999)			
LU: Change at Day 7 (n=17, 16, 12, 0, 16)	0.431 (± 4.6811)			
MO: Change at Day 1, 3h (n=4, 7, 5, 1, 7)	-0.0325 (± 0.36931)			

MO: Change at Day 1, 7h (n=5, 5, 4, 1, 5)	0.1278 ($\pm$ 0.52287)			
MO: Change at Day 7 (n=12, 12, 8, 0, 15)	-0.0492 ($\pm$ 0.48357)			
NE: Change at Day 1, 3h (n=4, 7, 5, 1, 7)	-0.2936 ($\pm$ 1.39078)			
NE: Change at Day 1, 7h (n=5, 6, 4, 2, 5)	-0.3760 ($\pm$ 1.51896)			
NE: Change at Day 7 (n=12, 13, 8, 0, 15)	0.0527 ($\pm$ 2.17787)			

Statistical analyses

No statistical analyses for this end point

Primary: SAD: Change From Baseline in Reticulocyte Percent, Hematocrit, Basophils/Leukocytes, Eosinophils/Leukocytes, Monocytes/Leukocytes, Neutrophils/Leukocytes, and Lymphocytes/Leukocytes

End point title	SAD: Change From Baseline in Reticulocyte Percent, Hematocrit, Basophils/Leukocytes, Eosinophils/Leukocytes, Monocytes/Leukocytes, Neutrophils/Leukocytes, and Lymphocytes/Leukocytes ^{[25][26]}
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End point description:

Change from baseline in hematology- Reticulocyte Percent (RE), Hematocrit (HeT), Basophils/Leukocytes (B/LU), Eosinophils/Leukocytes (E/LU), Monocytes/Leukocytes (MO/LU), Neutrophils/Leukocytes (N/LU), and Lymphocytes/Leukocytes (Ly/LU) were assessed. Safety analysis set defined as all randomized subjects who received at least 1 dose of study medication. Here "99999" indicates data was not evaluated at specified timepoint in respective arm. Here "n" indicates number of subjects evaluated at specific timepoints.

End point type	Primary
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End point timeframe:

For RE: From Baseline to Day 1 and Day 7; For HeT, B/LU, E/LU, Ly/LU, MO/LU and N/LU: From Baseline to Day 1, 3, 6 and Day 7

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: Descriptive statistics were done, no inferential statistical analyses were performed.

[26] - 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: Endpoint was planned to be reported for the specified arms only.

End point values	SAD: ALS-008176 (1.37 mg/kg)	SAD: ALS-008176 (4.1 mg/kg)	SAD: ALS-008176 (12 mg/kg)	SAD: ALS-008176 (25 mg/kg)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	18	18	14	3
Units: Fraction of 1				
arithmetic mean (standard deviation)				
RE: Change at Day 1 3h (n=5, 7, 4, 0, 4)	0.00138 ($\pm$ 0.002318)	0.00157 ($\pm$ 0.012323)	-0.00143 ($\pm$ 0.000960)	99999 ($\pm$ 99999)
RE: Change at Day 1, 7h (n=4, 4, 5, 1, 2)	0.00505 ($\pm$ 0.013516)	0.00212 ($\pm$ 0.003115)	-0.00326 ($\pm$ 0.005209)	0.00600 ($\pm$ 99999)
RE: Change at Day 7 (n=8, 9, 9, 0, 6)	0.00935 ($\pm$ 0.010193)	0.00739 ($\pm$ 0.005278)	0.00460 ($\pm$ 0.002929)	99999 ($\pm$ 99999)
HeT: Change at Day 1, 3h (n=7, 8, 6, 1, 7)	-0.0080 ($\pm$ 0.02867)	-0.0174 ($\pm$ 0.02573)	-0.0080 ($\pm$ 0.01694)	0.0000 ($\pm$ 99999)

HeT: Change at Day 1, 7h (n=7, 8, 6, 2, 6)	-0.0011 (± 0.01935)	0.0011 (± 0.01618)	-0.0113 (± 0.04131)	0.0215 (± 0.02616)
HeT: Change at Day 3 (n=0, 0, 1, 0, 1)	99999 (± 99999)	99999 (± 99999)	0.0460 (± 99999)	99999 (± 99999)
HeT: Change at Day 6 (n=0, 0, 0, 0, 1)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)
HeT: Change at Day 7 (n=17, 16, 12, 0, 16)	0.0144 (± 0.02895)	0.0079 (± 0.02734)	0.0241 (± 0.01695)	99999 (± 99999)
B/LU: Change at Day 1, 3h (n=5, 6, 4, 0, 4)	-0.0002 (± 0.00383)	-0.0015 (± 0.01131)	0.0030 (± 0.00469)	99999 (± 99999)
B/LU: Change at Day 1, 7h (n=4, 5, 5, 1, 3)	-0.0012 (± 0.00660)	0.0018 (± 0.00349)	-0.0014 (± 0.00488)	0.0019 (± 99999)
B/LU: Change at Day 3 (n=0, 0, 1, 0, 1)	99999 (± 99999)	99999 (± 99999)	0.0000 (± 99999)	99999 (± 99999)
B/LU: Change at Day 6 (n=0, 0, 0, 0, 1)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)
B/LU: Change at Day 7 (n=9, 10, 9, 1, 7)	-0.0012 (± 0.00891)	-0.0006 (± 0.01015)	-0.0003 (± 0.00819)	99999 (± 99999)
E/LU: Change at Day 1, 3h (n=5, 6, 4, 0, 4)	0.0016 (± 0.00568)	-0.0046 (± 0.01604)	-0.0030 (± 0.00476)	99999 (± 99999)
E/LU: Change at Day 1, 7h (n=4, 5, 5, 1, 3)	0.0055 (± 0.00971)	-0.0022 (± 0.01291)	-0.0008 (± 0.00719)	0.0040 (± 99999)
E/LU: Change at Day 3 (n=0, 0, 1, 0, 1)	99999 (± 99999)	99999 (± 99999)	-0.0100 (± 99999)	99999 (± 99999)
E/LU: Change at Day 6 (n=0, 0, 0, 0, 1)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)
E/LU: Change at Day 7 (n=9, 10, 9, 0, 7)	0.0296 (± 0.02785)	0.0198 (± 0.01600)	0.0186 (± 0.01388)	99999 (± 99999)
MO/LU: Change at Day 1, 3h (n=5, 6, 4, 0, 4)	-0.0156 (± 0.02907)	-0.0075 (± 0.02661)	-0.0573 (± 0.07671)	99999 (± 99999)
MO/LU: Change at Day 1, 7h (n=4, 5, 5, 1, 3)	-0.0320 (± 0.05655)	-0.0122 (± 0.00907)	-0.0314 (± 0.04378)	0.0020 (± 99999)
MO/LU: Change at Day 3 (n=0, 0, 1, 0, 1)	99999 (± 99999)	99999 (± 99999)	-0.1200 (± 99999)	99999 (± 99999)
MO/LU: Change at Day 6 (n=0, 0, 0, 0, 1)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)
MO/LU: Change at Day 7 (n=9, 10, 9, 0, 7)	-0.0197 (± 0.04803)	-0.0067 (± 0.03467)	-0.0504 (± 0.05563)	99999 (± 99999)
N/LU: Change at Day 1, 3h (n=5, 6, 4, 0, 4)	-0.0396 (± 0.12380)	-0.0355 (± 0.06897)	0.0120 (± 0.08459)	99999 (± 99999)
N/LU: Change at Day 1 7h (n=4, 5, 5, 1, 3)	-0.0568 (± 0.10584)	0.0664 (± 0.06183)	-0.0208 (± 0.07854)	-0.0940 (± 99999)
N/LU: Change at Day 3 (n=0, 0, 1, 0, 1)	99999 (± 99999)	99999 (± 99999)	0.1800 (± 99999)	99999 (± 99999)
N/LU: Change at Day 6 (n=0, 0, 0, 0, 1)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)
N/LU: Change at Day 7 (n=9, 10, 9, 0, 7)	-0.1278 (± 0.19019)	-0.0833 (± 0.14232)	-0.0551 (± 0.15450)	99999 (± 99999)
Ly/LU: Change at Day 1, 3h (n=5, 6, 4, 0, 4)	0.0858 (± 0.12152)	0.0668 (± 0.07582)	0.052 (± 0.04582)	99999 (± 99999)
Ly/LU: Change at Day, 7h (n=4, 5, 5, 1, 3)	0.0945 (± 0.05695)	-0.0500 (± 0.03889)	0.052 (± 0.07604)	0.0870 (± 99999)
Ly/LU: Change at Day 3 (n=0, 0, 1, 0, 1)	99999 (± 99999)	99999 (± 99999)	-0.0500 (± 99999)	99999 (± 99999)
Ly/LU: Change at Day 6 (n=0, 0, 0, 0, 1)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)
Ly/LU: Change at Day 7 (n=9, 10, 9, 0, 7)	0.1458 (± 0.17418)	0.0731 (± 0.12663)	0.0856 (± 0.19524)	99999 (± 99999)

End point values	SAD: Placebo			
Subject group type	Subject analysis set			
Number of subjects analysed	17			
Units: Fraction of 1				
arithmetic mean (standard deviation)				
RE: Change at Day 1 3h (n=5, 7, 4, 0, 4)	0.00158 (± 0.003021)			
RE: Change at Day 1, 7h (n=4, 4, 5, 1, 2)	0.00100 (± 0.002828)			
RE: Change at Day 7 (n=8, 9, 9, 0, 6)	0.06128 (± 0.133660)			
HeT: Change at Day 1, 3h (n=7, 8, 6, 1, 7)	0.0093 (± 0.01129)			
HeT: Change at Day 1, 7h (n=7, 8, 6, 2, 6)	-0.0418 (± 0.10265)			
HeT: Change at Day 3 (n=0, 0, 1, 0, 1)	0.0060 (± 99999)			
HeT: Change at Day 6 (n=0, 0, 0, 0, 1)	-0.0450 (± 99999)			
HeT: Change at Day 7 (n=17, 16, 12, 0, 16)	-0.0079 (± 0.06638)			
B/LU: Change at Day 1, 3h (n=5, 6, 4, 0, 4)	0.0020 (± 0.00542)			
B/LU: Change at Day 1, 7h (n=4, 5, 5, 1, 3)	-0.0047 (± 0.00503)			
B/LU: Change at Day 3 (n=0, 0, 1, 0, 1)	0.0000 (± 99999)			
B/LU: Change at Day 6 (n=0, 0, 0, 0, 1)	0.0030 (± 99999)			
B/LU: Change at Day 7 (n=9, 10, 9, 1, 7)	-0.0020 (± 0.00693)			
E/LU: Change at Day 1, 3h (n=5, 6, 4, 0, 4)	0.0038 (± 0.01377)			
E/LU: Change at Day 1, 7h (n=4, 5, 5, 1, 3)	-0.0080 (± 0.00721)			
E/LU: Change at Day 3 (n=0, 0, 1, 0, 1)	0.0000 (± 99999)			
E/LU: Change at Day 6 (n=0, 0, 0, 0, 1)	0.0240 (± 99999)			
E/LU: Change at Day 7 (n=9, 10, 9, 0, 7)	0.0209 (± 0.02014)			
MO/LU: Change at Day 1, 3h (n=5, 6, 4, 0, 4)	0.0065 (± 0.05313)			
MO/LU: Change at Day 1, 7h (n=4, 5, 5, 1, 3)	-0.0070 (± 0.02858)			
MO/LU: Change at Day 3 (n=0, 0, 1, 0, 1)	0.0600 (± 99999)			
MO/LU: Change at Day 6 (n=0, 0, 0, 0, 1)	-0.0310 (± 99999)			
MO/LU: Change at Day 7 (n=9, 10, 9, 0, 7)	0.0036 (± 0.04837)			
N/LU: Change at Day 1, 3h (n=5, 6, 4, 0, 4)	-0.0460 (± 0.14651)			
N/LU: Change at Day 1 7h (n=4, 5, 5, 1, 3)	-0.0400 (± 0.01732)			
N/LU: Change at Day 3 (n=0, 0, 1, 0, 1)	0.0300 (± 99999)			
N/LU: Change at Day 6 (n=0, 0, 0, 0, 1)	-0.0910 (± 99999)			
N/LU: Change at Day 7 (n=9, 10, 9, 0, 7)	-0.0284 (± 0.19168)			

Ly/LU: Change at Day 1, 3h (n=5, 6, 4, 0, 4)	0.0363 (± 0.10796)			
Ly/LU: Change at Day, 7h (n=4, 5, 5, 1, 3)	0.0997 (± 0.06603)			
Ly/LU: Change at Day 3 (n=0, 0, 1, 0, 1)	0.0900 (± 99999)			
Ly/LU: Change at Day 6 (n=0, 0, 0, 0, 1)	0.3050 (± 99999)			
Ly/LU: Change at Day 7 (n=9, 10, 9, 0, 7)	-0.0611 (± 0.29588)			

Statistical analyses

No statistical analyses for this end point

Primary: SAD: Change From Baseline in Clinical Laboratory Parameter (Hematology-Erythrocytes Mean Corpuscular Hemoglobin)

End point title	SAD: Change From Baseline in Clinical Laboratory Parameter (Hematology- Erythrocytes Mean Corpuscular Hemoglobin) ^{[27][28]}
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End point description:

Change from baseline for hematology- Erythrocytes Mean Corpuscular Hemoglobin was assessed. Safety analysis set defined as all randomized subjects who received at least 1 dose of study medication. Here "99999" indicates data was not evaluated at specified timepoint. Here "n" indicates number of subjects evaluated at specific timepoints.

End point type	Primary
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End point timeframe:

From Baseline to Day 1, 3, 6 and Day 7

Notes:

[27] - 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: Descriptive statistics were done, no inferential statistical analyses were performed.

[28] - 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: Endpoint was planned to be reported for the specified arms only.

End point values	SAD: ALS-008176 (1.37 mg/kg)	SAD: ALS-008176 (4.1 mg/kg)	SAD: ALS-008176 (12 mg/kg)	SAD: ALS-008176 (25 mg/kg)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	18	18	14	3
Units: Picogram (pg)				
arithmetic mean (standard deviation)				
Change at Day 1, 3h Postdose(n=7, 8, 7, 1, 7)	-0.286 (± 0.3934)	-0.175 (± 0.5800)	0.200 (± 0.3786)	-0.400 (± 99999)
Change at Day 1, 7h postdose(n=7, 8, 6, 2, 6)	0.000 (± 0.5715)	-0.137 (± 0.7050)	0.017 (± 0.8377)	-0.100 (± 0.1414)
Change at Day 3 (n=0, 0, 1, 0, 1)	99999 (± 99999)	99999 (± 99999)	0.000 (± 99999)	99999 (± 99999)
Change at Day 6 (n=0, 0, 0, 0, 1)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)
Change at Day 7 (n=17, 16, 12, 0, 16)	-0.347 (± 0.6829)	-0.531 (± 0.7319)	-0.233 (± 0.4979)	99999 (± 99999)

End point values	SAD: Placebo			
Subject group type	Subject analysis set			
Number of subjects analysed	17			
Units: Picogram (pg)				
arithmetic mean (standard deviation)				
Change at Day 1, 3h Postdose(n=7, 8, 7, 1, 7)	-0.300 (± 0.5000)			
Change at Day 1, 7h postdose(n=7, 8, 6, 2, 6)	0.067 (± 0.7633)			
Change at Day 3 (n=0, 0, 1, 0, 1)	-0.700 (± 99999)			
Change at Day 6 (n=0, 0, 0, 0, 1)	-0.500 (± 99999)			
Change at Day 7 (n=17, 16, 12, 0, 16)	-0.269 (± 0.5606)			

Statistical analyses

No statistical analyses for this end point

Primary: SAD: Change From Baseline in Clinical Laboratory Parameter (Hematology-Erythrocytes Mean Corpuscular Hemoglobin (HGB) Concentration)

End point title	SAD: Change From Baseline in Clinical Laboratory Parameter (Hematology- Erythrocytes Mean Corpuscular Hemoglobin (HGB) Concentration) ^{[29][30]}
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End point description:

Change from baseline in Hematology- Erythrocytes mean corpuscular HGB concentration was assessed. Safety analysis set defined as all randomized subjects who received at least 1 dose of study medication. Here "99999" indicates data was not evaluated at specified timepoint. Here "n" indicates number of subjects evaluated at specific timepoints.

End point type	Primary
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End point timeframe:

Baseline, Day 1, 3, 6 and Day 7

Notes:

[29] - 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: Descriptive statistics were done, no inferential statistical analyses were performed.

[30] - 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: Endpoint was planned to be reported for the specified arms only.

End point values	SAD: ALS-008176 (1.37 mg/kg)	SAD: ALS-008176 (4.1 mg/kg)	SAD: ALS-008176 (12 mg/kg)	SAD: ALS-008176 (25 mg/kg)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	18	18	14	3
Units: Gram per liter (g/L)				
arithmetic mean (standard deviation)				

Change at Day 1, 3h Postdose (n=6, 8, 7, 1, 6)	-1.000 (± 4.1952)	1.500 (± 7.7275)	6.571 (± 10.3418)	8.000 (± 99999)
Change at Day 1 7h, Postdose (n=5, 6, 6, 1, 5)	4.600 (± 11.6533)	0.167 (± 6.1455)	4.167 (± 10.9985)	0.000 (± 99999)
Change at Day 3 (n=0, 0, 1, 0, 1)	99999 (± 99999)	99999 (± 99999)	-3.000 (± 99999)	99999 (± 99999)
Change at Day 6 (n=0, 0, 0, 0, 1)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)
Change at Day 7 (15, 13, 12, 0, 13)	1.533 (± 10.7562)	2.462 (± 10.6819)	1.417 (± 10.3173)	99999 (± 99999)

End point values	SAD: Placebo			
Subject group type	Subject analysis set			
Number of subjects analysed	17			
Units: Gram per liter (g/L)				
arithmetic mean (standard deviation)				
Change at Day 1, 3h Postdose (n=6, 8, 7, 1, 6)	-2.333 (± 8.9815)			
Change at Day 1 7h, Postdose (n=5, 6, 6, 1, 5)	-0.200 (± 7.8867)			
Change at Day 3 (n=0, 0, 1, 0, 1)	-7.000 (± 99999)			
Change at Day 6 (n=0, 0, 0, 0, 1)	-6.000 (± 99999)			
Change at Day 7 (15, 13, 12, 0, 13)	-0.769 (± 7.9073)			

Statistical analyses

No statistical analyses for this end point

Primary: SAD: Change From Baseline in Clinical Laboratory Parameter (Hematology: Erythrocytes Mean Corpuscular Volume [e-MCV] and Mean Platelet Volume [MPV])

End point title	SAD: Change From Baseline in Clinical Laboratory Parameter (Hematology: Erythrocytes Mean Corpuscular Volume [e-MCV] and Mean Platelet Volume [MPV])[³¹][³²]
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End point description:

Change from baseline in hematology: e-MCV and MPV were assessed. Safety analysis set defined as all randomized subjects who received at least 1 dose of study medication. Safety analysis set defined as all randomized subjects who received at least 1 dose of study medication. Here "99999" indicates data was not evaluated at specified timepoint. Here "n" indicates number of subjects evaluated at specific timepoints.

End point type	Primary
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End point timeframe:

From Baseline to Day 1, 3, 6 and Day 7

Notes:

[31] - 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: Descriptive statistics were done, no inferential statistical analyses were performed.

[32] - 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: Endpoint was planned to be reported for the specified arms only.

End point values	SAD: ALS-008176 (1.37 mg/kg)	SAD: ALS-008176 (4.1 mg/kg)	SAD: ALS-008176 (12 mg/kg)	SAD: ALS-008176 (25 mg/kg)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	18	18	14	3
Units: femtolitre (fL)				
arithmetic mean (standard deviation)				
e-MCV:Change at Day 1, 3h Postdose(n=7,8,6,1,7)	-0.357 (± 1.5306)	-0.862 (± 0.7210)	-0.717 (± 1.3091)	0.700 (± 99999)
e-MCV:Change at Day 1, 7h Postdose(n=7,8,6,2,6)	-0.529 (± 2.4150)	-0.875 (± 1.0320)	-1.017 (± 1.2906)	0.000 (± 0.0000)
e-MCV: Change at Day 3 (n=0, 0, 1, 0, 1)	99999 (± 99999)	99999 (± 99999)	0.600 (± 99999)	99999 (± 99999)
e-MCV: Change at Day 6 (n=0, 0, 0, 0, 1)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)
e-MCV: Change at Day 7 (n=17, 16, 11, 0, 16)	-1.229 (± 1.7054)	-2.213 (± 2.0803)	-0.582 (± 1.4925)	99999 (± 99999)
MPV: Change at Day 1, 3h Postdose(n=5, 5, 5, 0, 4)	0.080 (± 0.4324)	-0.110 (± 0.2302)	-1.020 (± 2.7022)	99999 (± 99999)
MPV: Change at Day 1, 7h Postdose(n=5, 4, 6, 2, 3)	-0.246 (± 1.0581)	0.125 (± 0.8016)	0.117 (± 0.7468)	0.755 (± 0.3606)
MPV: Change at Day 3 (n=0, 0, 1, 0, 1)	99999 (± 99999)	99999 (± 99999)	0.400 (± 99999)	99999 (± 99999)
MPV: Change at Day 6 (n=0, 0, 0, 0, 1)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)
MPV: Change at Day 7 (n=12, 9, 11, 0, 9)	-0.078 (± 0.8480)	0.168 (± 0.7649)	-0.509 (± 1.6202)	99999 (± 99999)

End point values	SAD: Placebo			
Subject group type	Subject analysis set			
Number of subjects analysed	17			
Units: femtolitre (fL)				
arithmetic mean (standard deviation)				
e-MCV:Change at Day 1, 3h Postdose(n=7,8,6,1,7)	-0.271 (± 0.8180)			
e-MCV:Change at Day 1, 7h Postdose(n=7,8,6,2,6)	-0.250 (± 0.7369)			
e-MCV: Change at Day 3 (n=0, 0, 1, 0, 1)	-0.600 (± 99999)			
e-MCV: Change at Day 6 (n=0, 0, 0, 0, 1)	0.000 (± 99999)			
e-MCV: Change at Day 7 (n=17, 16, 11, 0, 16)	-0.669 (± 1.7895)			
MPV: Change at Day 1, 3h Postdose(n=5, 5, 5, 0, 4)	0.025 (± 0.7805)			
MPV: Change at Day 1, 7h Postdose(n=5, 4, 6, 2, 3)	-0.140 (± 1.2770)			
MPV: Change at Day 3 (n=0, 0, 1, 0, 1)	-0.400 (± 99999)			
MPV: Change at Day 6 (n=0, 0, 0, 0, 1)	-0.600 (± 99999)			
MPV: Change at Day 7 (n=12, 9, 11, 0, 9)	-0.212 (± 0.5398)			

Statistical analyses

No statistical analyses for this end point

Primary: SAD: Change From Baseline in Clinical Laboratory Parameter (Hematology: Erythrocytes Distribution Width)

End point title	SAD: Change From Baseline in Clinical Laboratory Parameter (Hematology: Erythrocytes Distribution Width) ^{[33][34]}
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End point description:

Change from baseline for hematology: erythrocytes distribution width was assessed. Safety analysis set defined as all randomized subjects who received at least 1 dose of study medication. Here "99999" indicates data was not evaluated at specified timepoint. Here "n" indicates number of subjects evaluated at specific timepoints.

End point type	Primary
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End point timeframe:

From Baseline to Day 1, 3, 6 and Day 7

Notes:

[33] - 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: Descriptive statistics were done, no inferential statistical analyses were performed.

[34] - 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: Endpoint was planned to be reported for the specified arms only.

End point values	SAD: ALS-008176 (1.37 mg/kg)	SAD: ALS-008176 (4.1 mg/kg)	SAD: ALS-008176 (12 mg/kg)	SAD: ALS-008176 (25 mg/kg)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	18	18	14	3
Units: Percentage (%)				
arithmetic mean (standard deviation)				
Change at Day 1, 3h Postdose(n=5, 7, 4, 0, 4)	0.020 (± 0.1095)	0.100 (± 0.2309)	0.350 (± 1.1030)	99999 (± 99999)
Change at Day 1, 7h Postdose(n=5, 5, 6, 1, 3)	0.700 (± 0.6595)	0.180 (± 0.4919)	0.700 (± 1.1243)	0.800 (± 99999)
Change at Day 3 (n=0, 0, 1, 0, 1)	99999 (± 99999)	99999 (± 99999)	0.300 (± 99999)	99999 (± 99999)
Change at Day 6 (n=0, 0, 0, 0, 1)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)
Change at Day 7 (n=12, 11, 10, 0, 9)	0.325 (± 0.6621)	0.145 (± 0.5298)	0.640 (± 1.0906)	99999 (± 99999)

End point values	SAD: Placebo			
Subject group type	Subject analysis set			
Number of subjects analysed	17			
Units: Percentage (%)				

arithmetic mean (standard deviation)				
Change at Day 1, 3h Postdose(n=5, 7, 4, 0, 4)	0.450 (± 0.3697)			
Change at Day 1, 7h Postdose(n=5, 5, 6, 1, 3)	0.333 (± 0.5774)			
Change at Day 3 (n=0, 0, 1, 0, 1)	0.200 (± 99999)			
Change at Day 6 (n=0, 0, 0, 0, 1)	0.800 (± 99999)			
Change at Day 7 (n=12, 11, 10, 0, 9)	0.233 (± 0.4873)			

Statistical analyses

No statistical analyses for this end point

Primary: MAD: Change From Baseline in Physical Examination (Temperature)

End point title	MAD: Change From Baseline in Physical Examination (Temperature) ^{[35][36]}
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End point description:

Change from baseline in temperature was assessed. Safety analysis set defined as all randomized subjects who received at least 1 dose of study medication. Here "99999" indicates data was not evaluated at specified timepoint. Here "n" indicates number of subjects evaluated at specific timepoints.

End point type	Primary
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End point timeframe:

From Baseline up to Day 28

Notes:

[35] - 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: Descriptive statistics were done, no inferential statistical analyses were performed.

[36] - 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: Endpoint was planned to be reported for the specified arms only.

End point values	MAD: ALS-008176 (4.1/1.37)	MAD: ALS-008176 (10/2 mg/kg)	MAD: ALS-008176 (30/6 mg/kg)	MAD: ALS-008176 (30/10 mg/kg)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	14	8	17
Units: Degree Celsius				
arithmetic mean (standard deviation)				
Change at Day 1 (n=5,14,6,16,17,16,33)	-0.4 (± 1.35)	-0.1 (± 0.81)	-0.0 (± 0.37)	-0.2 (± 0.86)
Change at Day 2 (n=5 14, 6, 16, 16, 16, 33)	-0.8 (± 1.33)	-0.1 (± 0.80)	-0.3 (± 0.39)	-0.0 (± 0.65)
Change at Day 3 (n=5, 12, 6, 13, 14, 13, 27)	-0.4 (± 1.46)	-0.1 (± 0.50)	-0.5 (± 0.60)	-0.2 (± 0.75)
Change at Day 4 (n=5, 9, 4, 10, 8, 10, 22)	-0.2 (± 1.34)	-0.1 (± 0.62)	-0.6 (± 0.57)	-0.5 (± 0.63)
Change at Day 5 (n=5, 14, 6, 16, 15, 16, 31)	-0.8 (± 1.28)	-0.4 (± 0.95)	-0.4 (± 0.58)	-0.4 (± 0.59)
Change at Day 6 (n=3, 6, 4, 7, 5, 4, 8)	-0.5 (± 1.12)	0.0 (± 0.64)	-0.7 (± 0.43)	-0.4 (± 0.61)
Change at Day 7 (n=3, 4, 1, 5, 2, 2, 3)	-0.5 (± 0.59)	0.1 (± 0.87)	-0.5 (± 99999)	-0.2 (± 0.65)

Change at Day 8 (n=2, 3, 0, 3, 2, 0, 1)	-0.8 (± 1.06)	-0.3 (± 0.36)	99999 (± 99999)	-1.2 (± 1.70)
Change at Day 9 (n=2, 2, 0, 1, 0, 0, 1)	-1.0 (± 0.78)	-0.0 (± 0.07)	99999 (± 99999)	-0.2 (± 99999)
Change at Day 10 (n=1, 1, 0, 0, 0, 0, 0)	-0.2 (± 99999)	-0.2 (± 99999)	99999 (± 99999)	99999 (± 99999)
Change at Day 11 (n=5, 14, 5, 16, 18, 15, 32)	-0.8 (± 0.93)	-0.3 (± 0.79)	-0.4 (± 0.33)	-0.6 (± 0.60)
Change at Day 28 (n=4, 5, 1, 10, 10, 13, 17)	-1.2 (± 1.04)	-0.1 (± 0.43)	-0.2 (± 99999)	-0.4 (± 0.54)

End point values	MAD: ALS-008176 (40/20 mg/kg)	MAD: ALS-008176 (60/40 mg/kg)	MAD: Placebo	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	18	16	33	
Units: Degree Celsius				
arithmetic mean (standard deviation)				
Change at Day 1 (n=5,14,6,16,17,16,33)	-0.3 (± 0.74)	-0.3 (± 0.84)	-0.2 (± 0.66)	
Change at Day 2 (n=5 14, 6, 16, 16, 16, 33)	-0.5 (± 0.82)	-0.3 (± 0.86)	-0.2 (± 0.74)	
Change at Day 3 (n=5, 12, 6, 13, 14, 13, 27)	-0.6 (± 0.78)	-0.7 (± 0.89)	-0.4 (± 0.66)	
Change at Day 4 (n=5, 9, 4, 10, 8, 10, 22)	-0.7 (± 0.53)	-0.8 (± 0.74)	-0.4 (± 0.68)	
Change at Day 5 (n=5, 14, 6, 16, 15, 16, 31)	-0.6 (± 1.01)	-0.6 (± 0.74)	-0.3 (± 0.69)	
Change at Day 6 (n=3, 6, 4, 7, 5, 4, 8)	-0.8 (± 0.94)	-0.6 (± 0.56)	-0.4 (± 0.41)	
Change at Day 7 (n=3, 4, 1, 5, 2, 2, 3)	-0.8 (± 0.64)	-1.0 (± 0.71)	-0.5 (± 0.55)	
Change at Day 8 (n=2, 3, 0, 3, 2, 0, 1)	-0.7 (± 0.42)	99999 (± 99999)	0.2 (± 99999)	
Change at Day 9 (n=2, 2, 0, 1, 0, 0, 1)	99999 (± 99999)	99999 (± 99999)	0.2 (± 99999)	
Change at Day 10 (n=1, 1, 0, 0, 0, 0, 0)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	
Change at Day 11 (n=5, 14, 5, 16, 18, 15, 32)	-0.7 (± 0.75)	-0.8 (± 1.01)	-0.4 (± 0.51)	
Change at Day 28 (n=4, 5, 1, 10, 10, 13, 17)	-0.4 (± 0.65)	-0.4 (± 0.98)	-0.4 (± 0.74)	

Statistical analyses

No statistical analyses for this end point

Primary: MAD: Change From Baseline in Physical Examination (Respiratory Rate)

End point title	MAD: Change From Baseline in Physical Examination (Respiratory Rate) ^{[37][38]}
End point description:	Change from baseline in respiratory rate was assessed. Safety analysis set defined as all randomized subjects who received at least 1 dose of study medication. Here "99999" indicates data was not evaluated at specified timepoint. Here "n" indicates number of subjects evaluated at specific timepoints.
End point type	Primary

End point timeframe:

From Baseline up to Day 28

Notes:

[37] - 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: Descriptive statistics were done, no inferential statistical analyses were performed.

[38] - 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: Endpoint was planned to be reported for the specified arms only.

End point values	MAD: ALS-008176 (4.1/1.37)	MAD: ALS-008176 (10/2 mg/kg)	MAD: ALS-008176 (30/6 mg/kg)	MAD: ALS-008176 (30/10 mg/kg)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	14	8	17
Units: Breadth per minute				
arithmetic mean (standard deviation)				
Change at Day 1 (n=5,14,7,17,17,16,33)	-0.6 (± 21.02)	0.7 (± 7.52)	-7.6 (± 7.72)	0.4 (± 10.07)
Change at Day 2 (n=5, 14, 7, 17, 16, 16, 33)	-6.2 (± 9.76)	-3.1 (± 12.09)	-9.0 (± 8.04)	-1.3 (± 7.95)
Change at Day 3 (n=5, 12, 6, 13, 14, 13, 27)	-5.4 (± 11.22)	-5.8 (± 11.36)	-9.7 (± 11.04)	-1.7 (± 9.10)
Change at Day 4 (n=5, 8, 5, 10, 7, 10, 22)	-9.8 (± 5.12)	-12.0 (± 16.65)	-8.0 (± 8.22)	-2.6 (± 12.92)
Change at Day 5 (n=5, 13, 7, 17, 15, 16, 32)	-8.2 (± 11.63)	-8.9 (± 15.39)	-8.1 (± 7.90)	-3.6 (± 12.90)
Change at Day 6 (n=3, 5, 4, 7, 4, 4, 8)	-3.7 (± 7.23)	3.0 (± 6.60)	-9.3 (± 16.72)	-1.1 (± 3.98)
Change at Day 7 (n=3, 3, 1, 5, 2, 2, 4)	-9.7 (± 11.68)	-5.7 (± 21.55)	10.0 (± 99999)	-7.0 (± 3.16)
Change at Day 8 (n=2, 3, 0, 3, 2, 0, 1)	-6.5 (± 7.78)	-5.0 (± 16.52)	99999 (± 99999)	-2.0 (± 19.29)
Change at Day 9 (n=2, 2, 0, 1, 0, 0, 1)	-7.5 (± 14.85)	-2.5 (± 2.12)	99999 (± 99999)	-20.0 (± 99999)
Change at Day 10 (1, 1, 0, 0, 0, 0, 0)	15.0 (± 99999)	-4.0 (± 99999)	99999 (± 99999)	99999 (± 99999)
Change at Day 11 (n=5, 14, 7, 17, 18, 15, 32)	-6.2 (± 9.15)	-8.7 (± 17.98)	-2.1 (± 13.06)	-2.1 (± 12.64)
Change at Day 28 (n= 3, 4, 2, 11, 10, 12, 20)	1.3 (± 4.73)	2.8 (± 17.25)	-0.5 (± 9.19)	-4.3 (± 14.40)

End point values	MAD: ALS-008176 (40/20 mg/kg)	MAD: ALS-008176 (60/40 mg/kg)	MAD: Placebo	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	18	16	33	
Units: Breadth per minute				
arithmetic mean (standard deviation)				
Change at Day 1 (n=5,14,7,17,17,16,33)	-0.1 (± 9.80)	-3.1 (± 13.02)	-1.4 (± 11.16)	
Change at Day 2 (n=5, 14, 7, 17, 16, 16, 33)	-4.1 (± 14.01)	-0.6 (± 15.84)	0.7 (± 11.93)	
Change at Day 3 (n=5, 12, 6, 13, 14, 13, 27)	-6.4 (± 10.51)	-6.7 (± 16.07)	-4.0 (± 9.62)	
Change at Day 4 (n=5, 8, 5, 10, 7, 10, 22)	-6.9 (± 11.13)	-10.6 (± 10.71)	-4.9 (± 9.20)	

Change at Day 5 (n=5, 13, 7, 17, 15, 16, 32)	-4.5 (± 13.31)	-6.9 (± 10.83)	-0.8 (± 11.25)	
Change at Day 6 (n=3, 5, 4, 7, 4, 4, 8)	-11.3 (± 7.09)	-8.5 (± 9.57)	-4.1 (± 8.59)	
Change at Day 7 (n=3, 3, 1, 5, 2, 2, 4)	-7.0 (± 18.38)	-1.0 (± 9.90)	3.3 (± 8.81)	
Change at Day 8 (n=2, 3, 0, 3, 2, 0, 1)	-8.0 (± 16.97)	99999 (± 99999)	2.0 (± 99999)	
Change at Day 9 (n=2, 2, 0, 1, 0, 0, 1)	99999 (± 99999)	99999 (± 99999)	0.0 (± 99999)	
Change at Day 10 (1, 1, 0, 0, 0, 0, 0)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	
Change at Day 11 (n=5, 14, 7, 17, 18, 15, 32)	-5.8 (± 12.24)	-7.9 (± 13.53)	-4.3 (± 12.60)	
Change at Day 28 (n= 3, 4, 2, 11, 10, 12, 20)	-8.4 (± 11.54)	-9.7 (± 15.82)	-3.9 (± 11.32)	

Statistical analyses

No statistical analyses for this end point

Primary: MAD: Change From Baseline in Physical Examination (Heart Rate)

End point title	MAD: Change From Baseline in Physical Examination (Heart Rate) ^{[39][40]}
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End point description:

Change from baseline in Heart rate was assessed. Safety analysis set defined as all randomized subjects who received at least 1 dose of study medication. Here "99999" indicates data was not evaluated at specified timepoint. Here "n" indicates number of subjects evaluated at specific timepoints.

End point type	Primary
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End point timeframe:

From Baseline up to Day 28

Notes:

[39] - 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: Descriptive statistics were done, no inferential statistical analyses were performed.

[40] - 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: Endpoint was planned to be reported for the specified arms only.

End point values	MAD: ALS-008176 (4.1/1.37)	MAD: ALS-008176 (10/2 mg/kg)	MAD: ALS-008176 (30/6 mg/kg)	MAD: ALS-008176 (30/10 mg/kg)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	14	8	17
Units: Beats per minute				
arithmetic mean (standard deviation)				
Change at Day 1 (n=5,14,8,17,17,16,33)	-10.6 (± 21.03)	-0.9 (± 21.63)	-2.0 (± 14.80)	8.2 (± 16.70)
Change at Day 2 (n=5, 14, 8, 17, 16, 16, 33)	-12.2 (± 24.41)	-2.3 (± 24.41)	0.4 (± 26.09)	2.0 (± 19.94)
Change at Day 3 (n=5, 12, 7, 13, 14, 13, 27)	0.4 (± 23.42)	-5.2 (± 12.26)	-19.3 (± 31.49)	-1.7 (± 19.55)
Change at Day 4 (n=5, 9, 5, 10, 8, 10, 22)	-15.4 (± 35.51)	-4.9 (± 23.12)	-5.2 (± 29.08)	-10.2 (± 34.27)
Change at Day 5 (n=5, 14, 8, 17, 15, 16, 32)	-19.0 (± 23.46)	-2.8 (± 24.45)	-1.1 (± 24.17)	-6.5 (± 21.95)

Change at Day 6 (n=3, 6, 4, 7, 4, 4, 8)	-21.0 (± 26.23)	4.7 (± 25.33)	-13.3 (± 18.86)	-8.0 (± 20.29)
Change at Day 7 (n=3, 4, 1, 5, 2, 2, 4)	-17.0 (± 20.22)	11.8 (± 16.64)	-9.0 (± 99999)	-14.2 (± 12.70)
Change at Day 8 (n=2, 4, 0, 3, 2, 0, 1)	-24.5 (± 2.12)	2.5 (± 20.50)	99999 (± 99999)	-10.3 (± 22.14)
Change at Day 9 (n=2, 2, 0, 1, 0, 0, 1)	-6.5 (± 16.26)	-8.0 (± 5.66)	99999 (± 99999)	14.0 (± 99999)
Change at Day 10 (n=1, 1, 0, 0, 0, 0, 0)	-13.0 (± 99999)	3.0 (± 99999)	99999 (± 99999)	99999 (± 99999)
Change at Day 11 (n=5, 14, 8, 17, 18, 15, 32)	-20.0 (± 23.19)	-5.2 (± 24.71)	6.3 (± 24.42)	-6.9 (± 27.88)
Change at Day 28 (n=4, 5, 2, 11, 11, 12, 20)	-17.5 (± 22.58)	7.6 (± 23.04)	-27.0 (± 22.63)	-8.5 (± 23.75)

End point values	MAD: ALS-008176 (40/20 mg/kg)	MAD: ALS-008176 (60/40 mg/kg)	MAD: Placebo	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	18	16	33	
Units: Beats per minute				
arithmetic mean (standard deviation)				
Change at Day 1 (n=5,14,8,17,17,16,33)	-1.4 (± 21.03)	-6.4 (± 27.97)	-0.6 (± 21.36)	
Change at Day 2 (n=5, 14, 8, 17, 16, 16, 33)	-5.8 (± 23.41)	-4.2 (± 28.11)	-6.2 (± 24.92)	
Change at Day 3 (n=5, 12, 7, 13, 14, 13, 27)	-5.7 (± 22.28)	-20.4 (± 24.80)	-11.0 (± 31.19)	
Change at Day 4 (n=5, 9, 5, 10, 8, 10, 22)	-3.5 (± 14.49)	-22.8 (± 25.12)	-13.2 (± 19.49)	
Change at Day 5 (n=5, 14, 8, 17, 15, 16, 32)	-7.1 (± 27.62)	-11.6 (± 27.46)	-8.2 (± 27.01)	
Change at Day 6 (n=3, 6, 4, 7, 4, 4, 8)	-30.0 (± 16.25)	-7.0 (± 11.60)	-15.3 (± 17.30)	
Change at Day 7 (n=3, 4, 1, 5, 2, 2, 4)	-2.0 (± 2.83)	-15.0 (± 9.90)	-4.0 (± 33.85)	
Change at Day 8 (n=2, 4, 0, 3, 2, 0, 1)	-32.0 (± 5.66)	99999 (± 99999)	-18.0 (± 99999)	
Change at Day 9 (n=2, 2, 0, 1, 0, 0, 1)	99999 (± 99999)	99999 (± 99999)	-26.0 (± 99999)	
Change at Day 10 (n=1, 1, 0, 0, 0, 0, 0)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	
Change at Day 11 (n=5, 14, 8, 17, 18, 15, 32)	-1.3 (± 21.37)	-17.3 (± 29.39)	-6.8 (± 22.46)	
Change at Day 28 (n=4, 5, 2, 11, 11, 12, 20)	-13.2 (± 21.61)	-30.1 (± 30.53)	-11.0 (± 26.38)	

Statistical analyses

No statistical analyses for this end point

Primary: MAD: Change From Baseline in Physical Examination (Weight)

End point title	MAD: Change From Baseline in Physical Examination
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End point description:

Change from Baseline in weight was assessed. Safety analysis set defined as all randomized subjects who received at least 1 dose of study medication. Here "99999" indicates data was not evaluated at specified timepoint. Here "n" indicates number of subjects evaluated at specific timepoints.

End point type	Primary
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End point timeframe:

From Baseline, Day 2, 5 and Day 28

Notes:

[41] - 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: Descriptive statistics were done, no inferential statistical analyses were performed.

[42] - 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: Endpoint was planned to be reported for the specified arms only.

End point values	MAD: ALS-008176 (4.1/1.37)	MAD: ALS-008176 (10/2 mg/kg)	MAD: ALS-008176 (30/6 mg/kg)	MAD: ALS-008176 (30/10 mg/kg)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	14	8	17
Units: Kilogram (kg)				
arithmetic mean (standard deviation)				
Change at Day 2 12h (n=5, 13, 7, 17, 15, 14 ,31)	0.1 (± 0.28)	0.0 (± 0.25)	0.1 (± 0.11)	-0.1 (± 0.23)
Change at Day 5 (n=5, 14, 6, 15, 15, 15, 30)	0.1 (± 0.31)	0.0 (± 0.22)	0.0 (± 0.10)	-0.0 (± 0.28)
Change at Day 28 (n=5, 14, 8, 16, 16, 15, 31)	0.6 (± 0.32)	0.5 (± 0.44)	0.8 (± 0.31)	0.6 (± 0.44)

End point values	MAD: ALS-008176 (40/20 mg/kg)	MAD: ALS-008176 (60/40 mg/kg)	MAD: Placebo	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	18	16	33	
Units: Kilogram (kg)				
arithmetic mean (standard deviation)				
Change at Day 2 12h (n=5, 13, 7, 17, 15, 14 ,31)	0.2 (± 0.29)	0.0 (± 0.18)	0.1 (± 0.39)	
Change at Day 5 (n=5, 14, 6, 15, 15, 15, 30)	0.0 (± 0.21)	-0.0 (± 0.38)	0.0 (± 0.18)	
Change at Day 28 (n=5, 14, 8, 16, 16, 15, 31)	0.7 (± 0.34)	0.7 (± 0.40)	0.6 (± 0.40)	

Statistical analyses

No statistical analyses for this end point

Primary: MAD: Change From Baseline in Physical Examination (BMI)

End point title	MAD: Change From Baseline in Physical Examination
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End point description:

Change from baseline in BMI was assessed. Safety analysis set defined as all randomized subjects who received at least 1 dose of study medication. Here "99999" indicates data was not evaluated at specified timepoint. Here "n" indicates number of subjects evaluated at specific timepoints.

End point type Primary

End point timeframe:

From Baseline, Day 2, 5 and Day 28

Notes:

[43] - 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: Descriptive statistics were done, no inferential statistical analyses were performed.

[44] - 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: Endpoint was planned to be reported for the specified arms only.

End point values	MAD: ALS-008176 (4.1/1.37)	MAD: ALS-008176 (10/2 mg/kg)	MAD: ALS-008176 (30/6 mg/kg)	MAD: ALS-008176 (30/10 mg/kg)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	14	8	17
Units: kg/m ²				
arithmetic mean (standard deviation)				
Change at Day 2 12h (n=5, 12, 7, 17, 15, 14 ,31)	0.4 (± 0.61)	0.1 (± 0.67)	0.2 (± 0.29)	-0.2 (± 0.68)
Change at Day 5 (n=5, 13, 6, 15, 15, 14, 30)	0.3 (± 0.67)	0.1 (± 0.72)	0.0 (± 0.26)	-0.1 (± 0.84)
Change at Day 28 (n=5, 13, 8, 16, 16, 14, 31)	1.5 (± 0.94)	1.6 (± 1.54)	2.4 (± 1.27)	1.6 (± 1.35)

End point values	MAD: ALS-008176 (40/20 mg/kg)	MAD: ALS-008176 (60/40 mg/kg)	MAD: Placebo	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	18	16	33	
Units: kg/m ²				
arithmetic mean (standard deviation)				
Change at Day 2 12h (n=5, 12, 7, 17, 15, 14 ,31)	0.4 (± 0.64)	0.1 (± 0.45)	0.4 (± 1.39)	
Change at Day 5 (n=5, 13, 6, 15, 15, 14, 30)	0.1 (± 0.46)	-0.0 (± 0.82)	0.2 (± 0.64)	
Change at Day 28 (n=5, 13, 8, 16, 16, 14, 31)	1.7 (± 1.00)	1.9 (± 1.22)	2.0 (± 1.44)	

Statistical analyses

No statistical analyses for this end point

Primary: MAD: Change From Baseline for Vital signs (Blood Pressure: sBP and dBP)

End point title MAD: Change From Baseline for Vital signs (Blood Pressure: sBP and dBP)^{[45][46]}

End point description:

Change from Baseline in Blood pressure: sBP and dBP was assessed. Safety analysis set defined as all randomized subjects who received at least 1 dose of study medication. Here "99999" indicates data was not evaluated at specified timepoint. Here "n" indicates number of subjects evaluated at specific timepoints.

End point type Primary

End point timeframe:

From Baseline to Day 28

Notes:

[45] - 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: Descriptive statistics were done, no inferential statistical analyses were performed.

[46] - 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: Endpoint was planned to be reported for the specified arms only.

End point values	MAD: ALS-008176 (4.1/1.37)	MAD: ALS-008176 (10/2 mg/kg)	MAD: ALS-008176 (30/6 mg/kg)	MAD: ALS-008176 (30/10 mg/kg)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	14	8	17
Units: mmHg				
arithmetic mean (standard deviation)				
sBP: Change at Day 1 (n=5,5,3,2,6,6,11)	1.6 (± 12.62)	0.6 (± 19.46)	6.0 (± 8.72)	5.0 (± 7.07)
sBP: Change at Day 2 (n=5, 5, 3, 2, 5, 6, 11)	8.8 (± 9.09)	-2.0 (± 13.84)	11.3 (± 6.43)	9.0 (± 9.90)
sBP: Change at Day 3 (n= 5, 5, 3, 2, 3, 6, 11)	3.8 (± 8.23)	3.6 (± 18.51)	6.3 (± 12.66)	19.5 (± 6.36)
sBP: Change at Day 4 (n=5, 5, 3, 2, 5, 6, 11)	14.0 (± 30.14)	-4.0 (± 19.71)	10.7 (± 17.47)	11.0 (± 12.73)
sBP: Change at Day 5 (n=5, 5, 3, 2, 5, 6, 11)	7.8 (± 7.98)	7.4 (± 20.27)	13.7 (± 20.40)	16.5 (± 17.68)
sBP: Change at Day 6 (n=3, 4, 3, 1, 2, 3, 6)	-0.3 (± 9.50)	-1.0 (± 12.27)	6.7 (± 9.24)	5.0 (± 99999)
sBP: Change at Day 7 (n=3, 2, 0, 0, 1, 1, 2)	3.0 (± 13.00)	-13.0 (± 21.21)	99999 (± 99999)	99999 (± 99999)
sBP: Change at Day 8 (n=2, 2, 0, 0, 1, 0, 1)	-5.5 (± 19.09)	6.0 (± 22.63)	99999 (± 99999)	99999 (± 99999)
sBP: Change at Day 9 (n=2, 2, 0, 0, 0, 0, 1)	1.5 (± 0.71)	-0.5 (± 10.61)	99999 (± 99999)	99999 (± 99999)
sBP: Change at Day 10 (n=1, 1, 0, 0, 0, 0, 0)	0.0 (± 99999)	21.0 (± 99999)	99999 (± 99999)	99999 (± 99999)
sBP: Change at Day 11 (n=5, 5, 3, 2, 6, 6, 11)	1.2 (± 17.91)	8.0 (± 23.32)	1.0 (± 29.60)	18.5 (± 14.85)
sBP: Change at Day 28 (n=4, 1, 0, 1, 1, 2, 5)	6.0 (± 19.20)	-4.0 (± 99999)	99999 (± 99999)	14.0 (± 99999)
dBP: Change at Day 1 (n=5,5,3,2,6,6,11)	-2.8 (± 14.27)	-4.8 (± 14.18)	6.7 (± 13.32)	-1.5 (± 19.09)
dBP: Change at Day 2 (n=5, 5, 3, 2, 5, 6, 10)	-2.6 (± 15.26)	-3.2 (± 11.19)	3.3 (± 11.37)	-8.0 (± 8.49)
dBP: Change at Day 3 (n= 5, 5, 3, 2, 5, 6, 11)	-5.2 (± 9.78)	0.6 (± 22.53)	-6.0 (± 5.29)	13.0 (± 7.07)
dBP: Change at Day 4 (n=5, 5, 3, 2, 3, 6, 10)	-7.8 (± 24.20)	-7.6 (± 10.92)	6.0 (± 5.29)	3.0 (± 15.56)
dBP: Change at Day 5 (n=5, 5, 3, 2, 5, 6, 10)	-8.0 (± 16.00)	7.4 (± 14.38)	7.3 (± 9.87)	4.0 (± 8.49)
dBP: Change at Day 6 (n=3, 4, 3, 1, 2, 3, 6)	-2.7 (± 8.33)	-10.0 (± 11.34)	4.7 (± 6.11)	2.0 (± 99999)

dBP: Change at Day 7 (n=3, 2, 0, 0, 1, 1, 2)	-12.7 (± 11.02)	-15.5 (± 3.54)	99999 (± 99999)	99999 (± 99999)
dBP: Change at Day 8 (n=2, 2, 0, 0, 1, 0, 1)	-6.0 (± 2.83)	-7.0 (± 43.84)	99999 (± 99999)	99999 (± 99999)
dBP: Change at Day 9 (n=2, 2, 0, 0, 0, 0, 1)	-4.0 (± 11.31)	-8.5 (± 0.71)	99999 (± 99999)	99999 (± 99999)
dBP: Change at Day 10 (n=1, 1, 0, 0, 0, 0, 0)	-4.0 (± 99999)	-7.0 (± 99999)	99999 (± 99999)	99999 (± 99999)
dBP: Change at Day 11 (n=5, 5, 3, 2, 6, 6, 10)	-3.8 (± 9.63)	11.8 (± 27.58)	-9.0 (± 10.82)	7.5 (± 6.36)
dBP: Change at Day 28 (n=4, 1, 0, 1, 1, 2, 4)	-6.3 (± 9.81)	-19.0 (± 99999)	99999 (± 99999)	-7.0 (± 99999)

End point values	MAD: ALS-008176 (40/20 mg/kg)	MAD: ALS-008176 (60/40 mg/kg)	MAD: Placebo	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	18	16	33	
Units: mmHg				
arithmetic mean (standard deviation)				
sBP: Change at Day 1 (n=5,5,3,2,6,6,11)	0.8 (± 7.60)	8.0 (± 15.38)	-3.1 (± 16.20)	
sBP: Change at Day 2 (n=5, 5, 3, 2, 5, 6, 11)	-3.0 (± 11.51)	7.5 (± 12.50)	1.8 (± 18.15)	
sBP: Change at Day 3 (n= 5, 5, 3, 2, 3, 6, 11)	3.4 (± 23.31)	4.7 (± 13.65)	6.5 (± 16.11)	
sBP: Change at Day 4 (n=5, 5, 3, 2, 5, 6, 11)	-3.3 (± 12.10)	4.5 (± 15.67)	-3.6 (± 14.81)	
sBP: Change at Day 5 (n=5, 5, 3, 2, 5, 6, 11)	7.0 (± 17.65)	-0.3 (± 20.16)	3.5 (± 16.59)	
sBP: Change at Day 6 (n=3, 4, 3, 1, 2, 3, 6)	1.5 (± 10.61)	-4.7 (± 14.36)	1.5 (± 21.71)	
sBP: Change at Day 7 (n=3, 2, 0, 0, 1, 1, 2)	-7.0 (± 99999)	-10.0 (± 99999)	6.5 (± 12.02)	
sBP: Change at Day 8 (n=2, 2, 0, 0, 1, 0, 1)	13.0 (± 99999)	99999 (± 99999)	-2.0 (± 99999)	
sBP: Change at Day 9 (n=2, 2, 0, 0, 0, 0, 1)	99999 (± 99999)	99999 (± 99999)	2.0 (± 99999)	
sBP: Change at Day 10 (n=1, 1, 0, 0, 0, 0, 0)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	
sBP: Change at Day 11 (n=5, 5, 3, 2, 6, 6, 11)	-2.5 (± 22.90)	-2.0 (± 9.59)	3.7 (± 10.87)	
sBP: Change at Day 28 (n=4, 1, 0, 1, 1, 2, 5)	15.0 (± 99999)	2.0 (± 16.97)	9.0 (± 17.52)	
dBP: Change at Day 1 (n=5,5,3,2,6,6,11)	-2.7 (± 12.89)	8.2 (± 14.96)	-3.7 (± 8.20)	
dBP: Change at Day 2 (n=5, 5, 3, 2, 5, 6, 10)	-2.6 (± 13.41)	9.2 (± 9.04)	-0.1 (± 10.04)	
dBP: Change at Day 3 (n= 5, 5, 3, 2, 5, 6, 11)	2.0 (± 14.42)	7.0 (± 10.22)	3.5 (± 9.35)	
dBP: Change at Day 4 (n=5, 5, 3, 2, 3, 6, 10)	4.3 (± 10.02)	9.2 (± 19.92)	0.1 (± 11.31)	
dBP: Change at Day 5 (n=5, 5, 3, 2, 5, 6, 10)	-1.8 (± 14.87)	5.0 (± 22.61)	3.0 (± 14.61)	
dBP: Change at Day 6 (n=3, 4, 3, 1, 2, 3, 6)	-6.5 (± 13.44)	-15.7 (± 9.61)	2.8 (± 8.47)	
dBP: Change at Day 7 (n=3, 2, 0, 0, 1, 1, 2)	12.0 (± 99999)	4.0 (± 99999)	-4.0 (± 4.24)	

dBP: Change at Day 8 (n=2, 2, 0, 0, 1, 0, 1)	4.0 (± 99999)	99999 (± 99999)	0.0 (± 99999)	
dBP: Change at Day 9 (n=2, 2, 0, 0, 0, 0, 1)	99999 (± 99999)	99999 (± 99999)	9.0 (± 99999)	
dBP: Change at Day 10 (n=1, 1, 0, 0, 0, 0, 0)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	
dBP: Change at Day 11 (n=5, 5, 3, 2, 6, 6, 10)	3.2 (± 13.17)	11.2 (± 17.13)	2.7 (± 10.58)	
dBP: Change at Day 28 (n=4, 1, 0, 1, 1, 2, 4)	-27.0 (± 99999)	5.0 (± 25.46)	16.5 (± 10.41)	

Statistical analyses

No statistical analyses for this end point

Primary: MAD: Change From Baseline in ECG Parameters

End point title	MAD: Change From Baseline in ECG Parameters ^{[47][48]}
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End point description:

Change from Baseline in ECG parameters (RR interval, PR interval, QRS interval, QT interval, QTcB interval, QTcF interval) was assessed. Safety analysis set defined as all randomized subjects who received at least 1 dose of study medication. Here "99999" indicates data was not evaluated at specified timepoint. Here "n" indicates number of subjects evaluated at specific timepoints.

End point type	Primary
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End point timeframe:

From Baseline, Day 1, 5, 11 and Day 28

Notes:

[47] - 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: Descriptive statistics were done, no inferential statistical analyses were performed.

[48] - 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: Endpoint was planned to be reported for the specified arms only.

End point values	MAD: ALS-008176 (4.1/1.37)	MAD: ALS-008176 (10/2 mg/kg)	MAD: ALS-008176 (30/6 mg/kg)	MAD: ALS-008176 (30/10 mg/kg)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	14	8	17
Units: msec				
arithmetic mean (standard deviation)				
RR:Change at Day 1 (n=5,13,8,17,17,16,32)	-34.4 (± 95.16)	11.6 (± 58.91)	-12.3 (± 77.26)	-12.6 (± 54.18)
RR:Change at Day 5 (n=5, 14, 8, 16, 15, 15, 33)	37.2 (± 91.58)	-15.8 (± 110.61)	-32.0 (± 93.81)	-0.2 (± 80.67)
RR:Change at Day 11 (n=5, 14, 8, 16, 17, 15, 32)	-10.0 (± 51.79)	13.7 (± 65.29)	-23.1 (± 62.18)	-18.0 (± 114.64)
RR:Change at Day 28 (n=2, 3, 0, 3, 0, 1, 3)	1.0 (± 43.84)	-3.3 (± 68.16)	99999 (± 99999)	32.0 (± 30.41)
PR:Change at Day 1 (n=5,14,8,15,17,15,31)	12.0 (± 14.70)	3.3 (± 8.41)	-12.1 (± 41.51)	7.0 (± 33.16)
PR:Change at Day 5 (n=5, 12, 8, 16, 15, 14, 32)	-4.4 (± 21.00)	4.2 (± 6.69)	-15.6 (± 35.96)	5.3 (± 30.86)
PR:Change at Day 11 (n=5, 14, 8, 15, 16, 14, 31)	-5.6 (± 14.38)	-1.1 (± 15.21)	-14.9 (± 35.69)	-2.6 (± 19.59)

PR:Change at Day 28 (n=2, 3, 0, 3, 0, 1, 3)	-1.0 (± 7.07)	0.0 (± 24.25)	99999 (± 99999)	-6.3 (± 15.50)
QRS:Change at Day 1 (n=5,14,8,17,17,16,32)	3.6 (± 4.10)	-1.0 (± 5.31)	-0.8 (± 3.41)	-4.5 (± 28.49)
QRS:Change at Day 5 (n=5, 14, 8, 16, 15, 15, 33)	4.4 (± 3.29)	-0.3 (± 4.21)	-0.5 (± 5.01)	-5.5 (± 29.01)
QRS:Change at Day 11 (n=5, 14, 8, 16, 17, 15, 32)	7.2 (± 4.60)	0.5 (± 7.22)	-1.9 (± 3.72)	-5.6 (± 24.57)
QRS:Change at Day 28 (n=2, 3, 0, 3, 0, 1, 3)	7.0 (± 4.24)	1.3 (± 3.06)	99999 (± 99999)	-56.0 (± 55.03)
QT: Change at Day 1 (n=5,14,8,17,17,16,32)	-12.4 (± 35.76)	-0.2 (± 14.62)	-4.0 (± 20.26)	4.8 (± 29.09)
QT:Change at Day 5 (n=5, 14, 8, 16, 15, 15, 33)	27.2 (± 43.14)	4.1 (± 27.13)	-19.3 (± 22.52)	1.2 (± 29.00)
QT:Change at Day 11 (n=5, 14, 8, 16, 17, 15, 32)	16.8 (± 34.43)	1.9 (± 22.62)	-11.8 (± 11.47)	6.6 (± 36.29)
QT:Change at Day 28 (n=2, 3, 0, 3, 0, 1, 3)	10.0 (± 14.14)	0.7 (± 34.49)	99999 (± 99999)	84.3 (± 89.61)
QTcB:Change at Day 1 (n=5,14,8,17,17,16,32)	-1.6 (± 12.40)	-6.1 (± 21.58)	-4.4 (± 22.08)	17.9 (± 25.50)
QTcB:Change at Day 5 (n=5, 14, 8, 16, 15, 15, 33)	23.6 (± 64.75)	-5.7 (± 21.79)	-15.4 (± 34.21)	4.3 (± 26.53)
QTcB:Change at Day 11 (n=5, 14, 8, 16, 17, 15, 32)	32.4 (± 51.49)	-4.6 (± 27.31)	-7.3 (± 40.56)	5.9 (± 33.87)
QTcB:Change at Day 28 (n=2, 3, 0, 3, 0, 1, 3)	12.0 (± 0.00)	2.3 (± 38.19)	99999 (± 99999)	34.3 (± 32.15)
QTcF:Change at Day 1 (n=5,14,8,17,17,16,32)	-6.8 (± 21.04)	-6.6 (± 23.23)	-4.3 (± 16.99)	12.5 (± 24.98)
QTcF:Change at Day 5 (n=5, 14, 8, 16, 15, 15, 33)	25.2 (± 53.02)	-5.4 (± 19.29)	-17.6 (± 22.33)	2.4 (± 25.08)
QTcF:Change at Day 11 (n=5, 14, 8, 16, 17, 15, 32)	25.8 (± 43.59)	-3.8 (± 28.90)	-10.3 (± 28.62)	5.6 (± 33.59)
QTcF:Change at Day 28 (n=2, 3, 0, 3, 0, 1, 3)	11.5 (± 6.36)	-12.7 (± 52.63)	99999 (± 99999)	26.3 (± 37.17)

End point values	MAD: ALS-008176 (40/20 mg/kg)	MAD: ALS-008176 (60/40 mg/kg)	MAD: Placebo	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	18	16	33	
Units: msec				
arithmetic mean (standard deviation)				
RR:Change at Day 1 (n=5,13,8,17,17,16,32)	-8.9 (± 70.07)	8.3 (± 57.33)	4.8 (± 51.96)	
RR:Change at Day 5 (n=5, 14, 8, 16, 15, 15, 33)	29.3 (± 64.02)	23.9 (± 74.62)	5.9 (± 79.53)	
RR:Change at Day 11 (n=5, 14, 8, 16, 17, 15, 32)	30.9 (± 72.50)	32.6 (± 64.66)	9.0 (± 78.18)	
RR:Change at Day 28 (n=2, 3, 0, 3, 0, 1, 3)	99999 (± 99999)	0.0 (± 99999)	68.3 (± 84.24)	
PR:Change at Day 1 (n=5,14,8,15,17,15,31)	-4.6 (± 11.23)	2.9 (± 12.59)	0.2 (± 17.89)	
PR:Change at Day 5 (n=5, 12, 8, 16, 15, 14, 32)	6.2 (± 14.17)	6.3 (± 19.72)	-2.0 (± 13.74)	
PR:Change at Day 11 (n=5, 14, 8, 15, 16, 14, 31)	-1.3 (± 13.58)	-2.4 (± 15.72)	-4.0 (± 17.13)	
PR:Change at Day 28 (n=2, 3, 0, 3, 0, 1, 3)	99999 (± 99999)	0.0 (± 99999)	19.0 (± 12.77)	

QRS:Change at Day 1 (n=5,14,8,17,17,16,32)	0.6 (± 2.45)	-2.6 (± 13.03)	-0.5 (± 5.87)
QRS:Change at Day 5 (n=5, 14, 8, 16, 15, 15, 33)	-2.6 (± 6.76)	-1.8 (± 11.81)	-1.0 (± 6.07)
QRS:Change at Day 11 (n=5, 14, 8, 16, 17, 15, 32)	0.5 (± 6.94)	-2.8 (± 14.85)	0.9 (± 8.50)
QRS:Change at Day 28 (n=2, 3, 0, 3, 0, 1, 3)	99999 (± 99999)	-40.0 (± 99999)	4.3 (± 2.08)
QT: Change at Day 1 (n=5,14,8,17,17,16,32)	7.8 (± 24.57)	7.4 (± 35.45)	-8.4 (± 33.65)
QT:Change at Day 5 (n=5, 14, 8, 16, 15, 15, 33)	2.3 (± 29.47)	10.9 (± 40.16)	3.9 (± 48.75)
QT:Change at Day 11 (n=5, 14, 8, 16, 17, 15, 32)	10.2 (± 31.61)	16.0 (± 41.38)	-1.7 (± 34.84)
QT:Change at Day 28 (n=2, 3, 0, 3, 0, 1, 3)	99999 (± 99999)	-20.0 (± 99999)	33.7 (± 29.87)
QTcB:Change at Day 1 (n=5,14,8,17,17,16,32)	16.9 (± 48.69)	8.1 (± 59.41)	-15.9 (± 39.99)
QTcB:Change at Day 5 (n=5, 14, 8, 16, 15, 15, 33)	-13.8 (± 48.84)	3.3 (± 51.19)	-5.1 (± 35.99)
QTcB:Change at Day 11 (n=5, 14, 8, 16, 17, 15, 32)	1.3 (± 38.42)	7.6 (± 51.09)	-8.2 (± 46.59)
QTcB:Change at Day 28 (n=2, 3, 0, 3, 0, 1, 3)	99999 (± 99999)	-31.0 (± 99999)	16.0 (± 7.00)
QTcF:Change at Day 1 (n=5,14,8,17,17,16,32)	12.2 (± 34.86)	8.5 (± 48.11)	-12.8 (± 36.53)
QTcF:Change at Day 5 (n=5, 14, 8, 16, 15, 15, 33)	-6.9 (± 39.59)	7.3 (± 44.38)	-3.4 (± 34.16)
QTcF:Change at Day 11 (n=5, 14, 8, 16, 17, 15, 32)	5.4 (± 33.35)	21.7 (± 57.05)	-5.4 (± 39.06)
QTcF:Change at Day 28 (n=2, 3, 0, 3, 0, 1, 3)	99999 (± 99999)	-20.0 (± 99999)	24.3 (± 15.89)

Statistical analyses

No statistical analyses for this end point

Primary: MAD: Change From Baseline in Clinical Laboratory Parameter: Serum Chemistry-Alkaline Phosphatase (AP), Alanine Aminotransferase (ALA), Aspartate Aminotransferase (ASA), Creatine Kinase (CrK)

End point title	MAD: Change From Baseline in Clinical Laboratory Parameter: Serum Chemistry-Alkaline Phosphatase (AP), Alanine Aminotransferase (ALA), Aspartate Aminotransferase (ASA), Creatine Kinase (CrK) ^{[49][50]}
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End point description:

Change From Baseline in Clinical Laboratory Parameter (Serum Chemistry-AP, ALA, ASA, CrK) was assessed. Safety analysis set defined as all randomized subjects who received at least 1 dose of study medication. Here "99999" indicates data was not evaluated at specified timepoint. Here "n" indicates number of subjects evaluated at specific timepoints.

End point type	Primary
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End point timeframe:

From Baseline, Day 1, 3, 4, 5, 6, 7, 11 and 28

Notes:

[49] - 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: Descriptive statistics were done, no inferential statistical analyses were performed.

[50] - 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: Endpoint was planned to be reported for the specified arms only.

End point values	MAD: ALS-008176 (4.1/1.37)	MAD: ALS-008176 (10/2 mg/kg)	MAD: ALS-008176 (30/6 mg/kg)	MAD: ALS-008176 (30/10 mg/kg)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	14	8	17
Units: ukat/L				
arithmetic mean (standard deviation)				
AP: Change at Day 1 (n=3,6,5,9,8,8,15)	-1.678 (± 3.5728)	-0.564 (± 0.9252)	-0.050 (± 0.8050)	-0.219 (± 0.8755)
AP: Change at Day 1 7h (n=2, 8, 2, 7, 8, 7, 15)	-0.008 (± 1.3320)	-0.438 (± 0.6512)	-1.367 (± 2.2160)	-0.402 (± 0.8138)
AP: Change at Day 3 (n=0, 1, 1, 0, 0, 0, 1)	99999 (± 99999)	-0.267 (± 99999)	-0.133 (± 99999)	99999 (± 99999)
AP: Change at Day 4 (n=0, 1, 0, 0, 0, 1, 1)	99999 (± 99999)	-0.233 (± 99999)	99999 (± 99999)	99999 (± 99999)
AP: Change at Day 5 (n=5, 14, 7, 15, 14, 15, 29)	0.333 (± 3.2360)	0.120 (± 0.3483)	0.414 (± 0.9106)	-0.045 (± 0.5638)
AP: Change at Day 6 (n=0, 0, 0, 1, 0, 0, 0)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	0.333 (± 99999)
AP: Change at Day 7 (n=1, 0, 0, 0, 0, 0, 0)	-1.200 (± 99999)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)
AP: Change at Day 11 (n=5, 14, 6, 15, 18, 15, 28)	2.934 (± 3.1704)	0.805 (± 1.3344)	0.856 (± 0.8769)	0.396 (± 0.9444)
AP: Change at Day 28 (n=4, 2, 2, 3, 1, 3, 3)	6.218 (± 2.9955)	0.867 (± 0.2829)	3.101 (± 2.7818)	0.272 (± 0.2710)
ALA: Change at Day 1 (n=3,6,5,9,8,8,15)	0.128 (± 0.2111)	-0.056 (± 0.0880)	0.007 (± 0.0325)	0.016 (± 0.1814)
ALA: Change at Day 1 7h (n=2,8,3,7,8,8,15)	0.283 (± 0.3536)	0.079 (± 0.3680)	-0.006 (± 0.0822)	-0.012 (± 0.0865)
ALA: Change at Day 3 (n=0, 1, 1, 0, 0, 0, 1)	99999 (± 99999)	-0.117 (± 99999)	-0.050 (± 99999)	99999 (± 99999)
ALA: Change at Day 4 (n=0, 1, 0, 0, 0, 1, 1)	99999 (± 99999)	-0.117 (± 99999)	99999 (± 99999)	99999 (± 99999)
ALA: Change at Day 5 (n=5, 14, 8, 16, 13, 15, 29)	0.273 (± 0.4086)	0.057 (± 0.2540)	0.113 (± 0.1195)	0.021 (± 0.3011)
ALA: Change at Day 6 (n=0, 0, 0, 1, 0, 0, 0)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	0.083 (± 99999)
ALA: Change at Day 7 (n=1, 0, 0, 0, 0, 0, 0)	0.167 (± 99999)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)
ALA: Change at Day 11 (n=5, 14, 7, 15, 18, 15, 29)	0.113 (± 0.2637)	0.163 (± 0.4496)	0.167 (± 0.3535)	-0.037 (± 0.2464)
ALA: Change at Day 28 (n=4, 2, 2, 3, 2, 4, 4)	0.075 (± 0.0739)	0.017 (± 0.0236)	0.292 (± 0.0354)	-0.411 (± 0.4016)
ASA: Change at Day 1 (n=3,4,5,9,8,8,13)	0.211 (± 0.2937)	0.013 (± 0.1258)	0.110 (± 0.1251)	-0.074 (± 0.4793)
ASA: Change at Day 1 7h (n=2,8,3,7,8,8,15)	0.400 (± 0.6129)	0.138 (± 0.4543)	-0.022 (± 0.0347)	-0.043 (± 0.2400)
ASA: Change at Day 3 (n=0, 1, 1, 0, 0, 0, 1)	99999 (± 99999)	-0.100 (± 99999)	0.000 (± 99999)	99999 (± 99999)
ASA: Change at Day 4 (n=0, 1, 0, 0, 0, 1, 1)	99999 (± 99999)	-0.183 (± 99999)	99999 (± 99999)	99999 (± 99999)
ASA: Change at Day 5 (n=5, 12, 8, 16, 14, 15, 28)	0.137 (± 0.1891)	0.089 (± 0.1865)	0.113 (± 0.1558)	-0.186 (± 0.3501)
ASA: Change at Day 6 (n=0, 0, 0, 1, 0, 0, 0)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	0.250 (± 99999)

ASA: Change at Day 7 (n=1, 0, 0, 0, 0, 0, 0)	0.033 (± 99999)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)
ASA: Change at Day 11 (n=5, 11, 7, 14, 18, 15, 26)	0.077 (± 0.0384)	0.188 (± 0.3124)	0.186 (± 0.1230)	-0.092 (± 0.4864)
ASA: Change at Day 28 (n=4, 2, 2, 3, 3, 4, 4)	0.142 (± 0.1190)	0.008 (± 0.0589)	0.233 (± 0.0000)	-0.706 (± 0.7171)
CrK: Change at Day 1 0.5-1h (n=3,6,5,6,6,8,16)	0.478 (± 0.7057)	0.067 (± 0.4563)	-0.173 (± 0.2965)	1.147 (± 1.4385)
CrK: Change at Day 1 7h (n=2,8,3,7,8,7,15)	-1.309 (± 2.3693)	-0.394 (± 0.9921)	-0.161 (± 0.2811)	-0.619 (± 0.7937)
CrK: Change at Day 3 (n=0, 1, 1, 0, 0, 0, 0)	99999 (± 99999)	-0.017 (± 99999)	0.350 (± 99999)	99999 (± 99999)
CrK: Change at Day 4 (n=0, 1, 0, 0, 0, 0, 1)	99999 (± 99999)	-0.400 (± 99999)	99999 (± 99999)	99999 (± 99999)
CrK: Change at Day 5 (n=5, 14, 8, 13, 13, 15, 30)	-0.820 (± 1.8541)	-0.201 (± 0.7061)	-0.006 (± 0.4932)	-0.126 (± 5.4970)
CrK: Change at Day 6 (n=0, 0, 0, 1, 0, 0, 0)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	-1.867 (± 99999)
CrK: Change at Day 7 (n=1, 0, 0, 0, 0, 0, 0)	1.084 (± 99999)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)
CrK: Change at Day 11 (n=5, 14, 7, 13, 17, 15, 29)	0.160 (± 2.5623)	0.418 (± 1.5535)	0.445 (± 0.9954)	-1.121 (± 3.3099)
CrK: Change at Day 28 (n=4, 2, 2, 3, 2, 4, 5)	2.192 (± 1.2596)	-0.142 (± 0.5304)	1.234 (± 0.7072)	0.111 (± 1.3676)

End point values	MAD: ALS-008176 (40/20 mg/kg)	MAD: ALS-008176 (60/40 mg/kg)	MAD: Placebo	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	18	16	33	
Units: ukat/L				
arithmetic mean (standard deviation)				
AP: Change at Day 1 (n=3,6,5,9,8,8,15)	-0.656 (± 1.5735)	-1.386 (± 1.1609)	-0.961 (± 1.2125)	
AP: Change at Day 1 7h (n=2, 8, 2, 7, 8, 7, 15)	-0.208 (± 0.4361)	-0.143 (± 0.2834)	-0.412 (± 0.8993)	
AP: Change at Day 3 (n=0, 1, 1, 0, 0, 0, 1)	99999 (± 99999)	99999 (± 99999)	0.250 (± 99999)	
AP: Change at Day 4 (n=0, 1, 0, 0, 0, 1, 1)	99999 (± 99999)	-0.800 (± 99999)	0.383 (± 99999)	
AP: Change at Day 5 (n=5, 14, 7, 15, 14, 15, 29)	0.643 (± 1.1915)	0.837 (± 1.8684)	0.240 (± 1.3498)	
AP: Change at Day 6 (n=0, 0, 0, 1, 0, 0, 0)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	
AP: Change at Day 7 (n=1, 0, 0, 0, 0, 0, 0)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	
AP: Change at Day 11 (n=5, 14, 6, 15, 18, 15, 28)	1.335 (± 2.0936)	2.153 (± 2.1544)	1.294 (± 1.8375)	
AP: Change at Day 28 (n=4, 2, 2, 3, 1, 3, 3)	6.718 (± 99999)	1.022 (± 1.1542)	0.600 (± 0.1093)	
ALA: Change at Day 1 (n=3,6,5,9,8,8,15)	0.044 (± 0.1324)	-0.056 (± 0.0597)	0.004 (± 0.0722)	
ALA: Change at Day 1 7h (n=2,8,3,7,8,8,15)	0.063 (± 0.0755)	0.190 (± 0.2042)	-0.038 (± 0.0803)	
ALA: Change at Day 3 (n=0, 1, 1, 0, 0, 0, 1)	99999 (± 99999)	99999 (± 99999)	0.033 (± 99999)	
ALA: Change at Day 4 (n=0, 1, 0, 0, 0, 1, 1)	99999 (± 99999)	0.000 (± 99999)	0.117 (± 99999)	

ALA: Change at Day 5 (n=5, 14, 8, 16, 13, 15, 29)	0.210 (± 0.2255)	0.248 (± 0.2658)	0.039 (± 0.1429)
ALA: Change at Day 6 (n=0, 0, 0, 1, 0, 0, 0)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)
ALA: Change at Day 7 (n=1, 0, 0, 0, 0, 0, 0)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)
ALA: Change at Day 11(n=5, 14, 7, 15, 18, 15, 29)	0.146 (± 0.2115)	0.039 (± 0.2169)	0.006 (± 0.2091)
ALA: Change at Day 28 (n=4, 2, 2, 3, 2, 4, 4)	0.142 (± 0.2947)	0.179 (± 0.3211)	0.050 (± 0.0943)
ASA: Change at Day 1 (n=3,4,5,9,8,8,13)	0.104 (± 0.2739)	-0.085 (± 0.0721)	0.005 (± 0.0846)
ASA: Change at Day 1 7h (n=2,8,3,7,8,8,15)	0.150 (± 0.2118)	0.402 (± 0.4497)	-0.122 (± 0.5006)
ASA: Change at Day 3 (n=0, 1, 1, 0, 0, 0, 1)	99999 (± 99999)	99999 (± 99999)	-0.167 (± 99999)
ASA: Change at Day 4 (n=0, 1, 0, 0, 0, 1, 1)	99999 (± 99999)	0.017 (± 99999)	-0.133 (± 99999)
ASA: Change at Day 5 (n=5, 12, 8, 16, 14, 15, 28)	0.176 (± 0.2563)	0.295 (± 0.3749)	0.044 (± 0.5127)
ASA: Change at Day 6 (n=0, 0, 0, 1, 0, 0, 0)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)
ASA: Change at Day 7 (n=1, 0, 0, 0, 0, 0, 0)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)
ASA: Change at Day 11 (n=5, 11, 7, 14, 18, 15, 26)	0.184 (± 0.3527)	0.120 (± 0.2835)	-0.021 (± 0.5298)
ASA: Change at Day 28 (n=4, 2, 2, 3, 3, 4, 4)	0.267 (± 0.2892)	0.142 (± 0.2197)	-0.033 (± 0.1587)
CrK: Change at Day 1 0.5-1h (n=3,6,5,6,6,8,16)	-0.314 (± 0.8019)	0.271 (± 1.7412)	-0.058 (± 0.7089)
CrK: Change at Day 1 7h (n=2,8,3,7,8,7,15)	0.381 (± 1.5252)	0.257 (± 0.6124)	0.190 (± 0.8554)
CrK: Change at Day 3 (n=0, 1, 1, 0, 0, 0, 0)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)
CrK: Change at Day 4 (n=0, 1, 0, 0, 0, 0, 1)	99999 (± 99999)	99999 (± 99999)	0.583 (± 99999)
CrK: Change at Day 5 (n=5, 14, 8, 13, 13, 15, 30)	0.276 (± 1.5585)	-0.442 (± 0.7528)	-0.251 (± 0.8541)
CrK: Change at Day 6 (n=0, 0, 0, 1, 0, 0, 0)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)
CrK: Change at Day 7 (n=1, 0, 0, 0, 0, 0, 0)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)
CrK: Change at Day 11(n=5, 14, 7, 13, 17, 15, 29)	0.478 (± 1.5865)	0.069 (± 0.9801)	0.155 (± 1.0566)
CrK: Change at Day 28 (n=4, 2, 2, 3, 2, 4, 5)	-0.592 (± 0.4833)	0.554 (± 0.8134)	-0.200 (± 1.1625)

Statistical analyses

No statistical analyses for this end point

Primary: MAD: Change From Baseline in Clinical Laboratory Parameter (Serum Chemistry-Bilirubin, Direct [DB], Indirect bilirubin [IB], and Creatinine [Cr])

End point title	MAD: Change From Baseline in Clinical Laboratory Parameter (Serum Chemistry-Bilirubin, Direct [DB], Indirect bilirubin [IB], and Creatinine [Cr])[51][52]
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End point description:

Change from baseline in serum chemistry-bilirubin, DB, IB, and Cr were assessed. Safety analysis set

defined as all randomized subjects who received at least 1 dose of study medication. Here "99999" indicates data was not evaluated at specified timepoint. Here "n" indicates number of subjects evaluated at specific timepoints.

End point type	Primary
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End point timeframe:

For Bilirubin, DB and Cr: From Baseline, Day 1, 3, 4, 5, 6, 7, 11 and Day 28; For IB: From Baseline, Day 1, 5, 6, 11 and Day 28

Notes:

[51] - 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: Descriptive statistics were done, no inferential statistical analyses were performed.

[52] - 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: Endpoint was planned to be reported for the specified arms only.

End point values	MAD: ALS-008176 (4.1/1.37)	MAD: ALS-008176 (10/2 mg/kg)	MAD: ALS-008176 (30/6 mg/kg)	MAD: ALS-008176 (30/10 mg/kg)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	14	8	17
Units: mcmol/L				
arithmetic mean (standard deviation)				
BI: Change at Day 1 (n=3,5,5,9,8,8,15)	-1.140 (± 3.3217)	0.342 (± 1.4307)	-3.078 (± 9.1609)	3.227 (± 7.9231)
BI: Change at Day 1, 7h (n=2,6,3,6,8,8,14)	0.086 (± 2.2974)	-11.681 (± 15.9198)	-3.990 (± 0.9873)	-0.570 (± 1.4334)
BI: Change at Day 3 (n=0, 1, 1, 0, 0, 0, 1)	99999 (± 99999)	-32.490 (± 99999)	99999 (± 0.000)	99999 (± 99999)
BI: Change at Day 4 (n=0, 1, 0, 0, 0, 1, 1)	99999 (± 99999)	-32.490 (± 99999)	99999 (± 99999)	99999 (± 99999)
BI: Change at Day 5 (n=5, 11, 8, 15, 14, 15, 28)	-5.917 (± 18.2360)	-7.604 (± 15.6519)	-6.840 (± 17.3185)	0.371 (± 2.1723)
BI: Change at Day 6 (n=0, 0, 0, 1, 0, 0, 0)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	-1.710 (± 99999)
BI: Change at Day 7 (n=1, 0, 0, 0, 0, 0, 0)	-5.130 (± 99999)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)
BI: Change at Day 11 (n=5,11,7,14,18,15,27)	-3.762 (± 16.0544)	-9.749 (± 20.9100)	-9.039 (± 23.1896)	1.049 (± 3.0559)
BI: Change at Day 28 (n=4, 2, 2, 3, 2, 4, 3)	1.325 (± 4.3403)	-29.412 (± 23.6994)	-35.055 (± 47.1570)	-0.473 (± 2.1420)
DB: Change at Day 1 (n=3,2,4,6,7,7,14)	-0.456 (± 0.5224)	0.000 (± 0.0000)	-1.282 (± 5.6499)	-0.627 (± 2.2418)
DB: Change at Day 1 7h (n=1,3,2,4,7,5,13)	0.000 (± 99999)	-3.534 (± 6.8514)	0.000 (± 0.0000)	0.299 (± 1.5191)
DB: Change at Day 3 (n=0, 1, 0, 0, 0, 0, 1)	99999 (± 99999)	0.000 (± 99999)	99999 (± 99999)	99999 (± 99999)
DB: Change at Day 4 (n=0, 1, 0, 0, 0, 1, 1)	99999 (± 99999)	0.000 (± 99999)	99999 (± 99999)	99999 (± 99999)
DB: Change at Day 5 (n=5, 5, 5, 11, 13, 12, 25)	0.239 (± 1.9482)	-2.804 (± 5.2825)	-4.104 (± 8.2542)	-0.171 (± 1.9765)
DB: Change at Day 6 (n=0, 0, 0, 1, 0, 0, 0)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	0.000 (± 99999)
DB: Change at Day 11 (n=5, 5, 5, 12, 15, 12, 24)	-0.376 (± 1.3913)	-4.104 (± 8.0787)	-4.104 (± 10.1598)	0.128 (± 1.9252)
DB: Change at Day 28 (n=4, 2, 2, 2, 2, 4, 3)	0.000 (± 1.3098)	-1.197 (± 1.6928)	-11.970 (± 16.9281)	0.000 (± 0.0000)
IB: Change at Day 1 (n=2,1,2,3,3,5,7)	-1.881 (± 2.6601)	1.710 (± 99999)	0.855 (± 1.2092)	7.752 (± 14.2252)
IB: Change at Day 1 7h (n=0,2,0,3,4,2,6)	99999 (± 99999)	-14.279 (± 15.1144)	99999 (± 99999)	-0.627 (± 1.3927)

IB: Change at Day 5 (n=3, 3, 2, 7, 7, 7, 13)	-1.710 (± 1.3356)	-10.887 (± 16.5140)	0.855 (± 1.2092)	-0.489 (± 1.7197)
IB: Change at Day 6 (n=0, 0, 0, 1, 0, 0, 0)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	-1.710 (± 99999)
IB: Change at Day 11 (n=3, 3, 2, 8, 7, 7, 13)	-1.083 (± 1.8758)	-15.219 (± 24.4638)	0.000 (± 2.4183)	0.641 (± 3.0256)
IB: Change at Day 28 (n=3, 1, 0, 0, 2, 4, 1)	0.057 (± 2.1517)	-10.260 (± 99999)	99999 (± 99999)	99999 (± 99999)
Cr: Change at Day 1 (n=3,6,5,9,8,8,16)	-0.589 (± 1.0208)	0.609 (± 1.6200)	-1.414 (± 2.3884)	-0.295 (± 6.0649)
Cr: Change at Day 1 7h (n=2,8,3,7,8,8,16)	0.442 (± 4.3756)	-1.341 (± 1.6999)	-4.420 (± 7.6557)	1.894 (± 6.4443)
Cr: Change at Day 3 (n=0, 1, 1, 0, 0, 0, 1)	99999 (± 99999)	-7.956 (± 99999)	-3.536 (± 99999)	99999 (± 99999)
Cr: Change at Day 4 (n=0, 1, 0, 0, 0, 1, 1)	99999 (± 99999)	-3.536 (± 99999)	99999 (± 99999)	99999 (± 99999)
Cr: Change at Day 5 (n=5, 14, 8, 16, 14, 15, 32)	0.354 (± 1.4792)	0.294 (± 4.1295)	-0.331 (± 7.6620)	0.077 (± 6.7179)
Cr: Change at Day 6 (n=0, 0, 0, 1, 0, 0, 0)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	0.884 (± 99999)
Cr: Change at Day 7 (n=1, 0, 0, 0, 0, 0, 0)	0.000 (± 99999)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)
Cr: Change at Day 11 (n=5, 13, 7, 14, 18, 15, 31)	-0.354 (± 2.3884)	0.331 (± 2.8039)	-2.526 (± 5.0892)	-0.522 (± 7.4052)
Cr: Change at Day 28 (n=4,2,2,4,2,4,4)	0.000 (± 2.9760)	-5.746 (± 6.8759)	-1.768 (± 5.0007)	1.960 (± 8.4423)

End point values	MAD: ALS-008176 (40/20 mg/kg)	MAD: ALS-008176 (60/40 mg/kg)	MAD: Placebo	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	18	16	33	
Units: mcmol/L				
arithmetic mean (standard deviation)				
BI: Change at Day 1 (n=3,5,5,9,8,8,15)	-1.774 (± 4.8641)	-4.147 (± 11.4866)	-3.306 (± 7.5812)	
BI: Change at Day 1, 7h (n=2,6,3,6,8,8,14)	-1.664 (± 1.8058)	-0.792 (± 1.7033)	-1.083 (± 2.5768)	
BI: Change at Day 3 (n=0, 1, 1, 0, 0, 0, 1)	99999 (± 99999)	99999 (± 99999)	0.000 (± 99999)	
BI: Change at Day 4 (n=0, 1, 0, 0, 0, 1, 1)	99999 (± 99999)	0.000 (± 99999)	-1.710 (± 99999)	
BI: Change at Day 5 (n=5, 11, 8, 15, 14, 15, 28)	-0.020 (± 5.3325)	-0.401 (± 9.9071)	-4.395 (± 9.4563)	
BI: Change at Day 6 (n=0, 0, 0, 1, 0, 0, 0)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	
BI: Change at Day 7 (n=1, 0, 0, 0, 0, 0, 0)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	
BI: Change at Day 11 (n=5,11,7,14,18,15,27)	-4.482 (± 16.4250)	-2.601 (± 13.6963)	-3.483 (± 13.4190)	
BI: Change at Day 28 (n=4, 2, 2, 3, 2, 4, 3)	-1.539 (± 0.2418)	-56.644 (± 115.0046)	-3.990 (± 3.5596)	
DB: Change at Day 1 (n=3,2,4,6,7,7,14)	-1.026 (± 1.9144)	-0.318 (± 1.0468)	-0.794 (± 1.5551)	
DB: Change at Day 1 7h (n=1,3,2,4,7,5,13)	-1.221 (± 1.1987)	-0.068 (± 0.9413)	-0.105 (± 1.2769)	
DB: Change at Day 3 (n=0, 1, 0, 0, 0, 0, 1)	99999 (± 99999)	99999 (± 99999)	1.710 (± 99999)	

DB: Change at Day 4 (n=0, 1, 0, 0, 0, 1, 1)	99999 (± 99999)	99999 (± 99999)	0.000 (± 99999)	
DB: Change at Day 5 (n=5, 5, 5, 11, 13, 12, 25)	-0.460 (± 1.9775)	0.114 (± 1.2186)	-0.705 (± 1.7173)	
DB: Change at Day 6 (n=0, 0, 0, 1, 0, 0, 0)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	
DB: Change at Day 11 (n=5, 5, 5, 12, 15, 12, 24)	0.091 (± 4.1060)	-0.242 (± 1.3996)	-0.477 (± 1.9627)	
DB: Change at Day 28 (n=4, 2, 2, 2, 2, 4, 3)	-1.026 (± 0.9673)	0.256 (± 1.2051)	-1.140 (± 0.9873)	
IB: Change at Day 1 (n=2,1,2,3,3,5,7)	0.513 (± 0.4524)	-6.532 (± 14.5141)	-3.469 (± 9.1623)	
IB: Change at Day 1 7h (n=0,2,0,3,4,2,6)	0.342 (± 1.1513)	-0.940 (± 3.7484)	-0.940 (± 1.1933)	
IB: Change at Day 5 (n=3, 3, 2, 7, 7, 7, 13)	2.028 (± 3.4078)	-2.565 (± 13.5328)	-3.065 (± 8.0289)	
IB: Change at Day 6 (n=0, 0, 0, 1, 0, 0, 0)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	
IB: Change at Day 11 (n=3, 3, 2, 8, 7, 7, 13)	1.344 (± 1.2466)	-5.667 (± 19.5016)	-2.451 (± 10.6977)	
IB: Change at Day 28 (n=3, 1, 0, 0, 2, 4, 1)	-0.513 (± 0.7255)	-56.772 (± 114.9225)	0.000 (± 99999)	
Cr: Change at Day 1 (n=3,6,5,9,8,8,16)	1.989 (± 4.7193)	-2.431 (± 2.5773)	-1.602 (± 3.4042)	
Cr: Change at Day 1 7h (n=2,8,3,7,8,8,16)	1.303 (± 6.5106)	1.475 (± 6.9183)	-2.438 (± 8.0003)	
Cr: Change at Day 3 (n=0, 1, 1, 0, 0, 0, 1)	99999 (± 99999)	99999 (± 99999)	2.652 (± 99999)	
Cr: Change at Day 4 (n=0, 1, 0, 0, 0, 1, 1)	99999 (± 99999)	-1.768 (± 99999)	0.884 (± 99999)	
Cr: Change at Day 5 (n=5, 14, 8, 16, 14, 15, 32)	1.439 (± 4.0210)	-0.825 (± 4.1927)	-1.005 (± 6.2223)	
Cr: Change at Day 6 (n=0, 0, 0, 1, 0, 0, 0)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	
Cr: Change at Day 7 (n=1, 0, 0, 0, 0, 0, 0)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	
Cr: Change at Day 11 (n=5, 13, 7, 14, 18, 15, 31)	0.376 (± 5.0890)	-1.002 (± 4.1445)	-0.128 (± 6.5873)	
Cr: Change at Day 28 (n=4,2,2,4,2,4,4)	-1.326 (± 1.8752)	3.978 (± 11.6942)	3.757 (± 3.5635)	

Statistical analyses

No statistical analyses for this end point

Primary: MAD: Change From Baseline in Clinical Laboratory Parameter (Serum Chemistry-Blood Urea nitrogen [BUN], Derived Urea [DU], Chloride [Cl], Bicarbonate [BiC], Glucose [Glu], Potassium [K], Sodium [Na])

End point title	MAD: Change From Baseline in Clinical Laboratory Parameter (Serum Chemistry-Blood Urea nitrogen [BUN], Derived Urea [DU], Chloride [Cl], Bicarbonate [BiC], Glucose [Glu], Potassium [K], Sodium [Na]) ^{[53][54]}
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End point description:

Change From Baseline for Clinical Laboratory Parameter (Serum Chemistry-BUN, DU, Cl, BiC, Glu, K, and Na) was assessed. HeSafety analysis set defined as all randomized subjects who received at least 1 dose of study medication. Here "99999" indicates data was not evaluated at specified timepoint. Here "n" indicates number of subjects evaluated at specific timepoints.

End point type	Primary
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End point timeframe:

For BUN, DU, Cl, Glu, K and Na: From Baseline Day 1, 3, 4, 5, 6, 7, 11 and Day 28; For BiC: From Baseline, Day 1, 3, 4, 5, 11 and Day 28

Notes:

[53] - 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: Descriptive statistics were done, no inferential statistical analyses were performed.

[54] - 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: Endpoint was planned to be reported for the specified arms only.

End point values	MAD: ALS-008176 (4.1/1.37)	MAD: ALS-008176 (10/2 mg/kg)	MAD: ALS-008176 (30/6 mg/kg)	MAD: ALS-008176 (30/10 mg/kg)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	14	8	17
Units: mmol/L				
arithmetic mean (standard deviation)				
BUN: Change at Day 1, (n=3,4,5,7,8,8,16)	-0.464 (± 1.3674)	-0.295 (± 0.8288)	-0.143 (± 0.7403)	-0.525 (± 0.7442)
BUN: Change at Day 1, 7h (n=2,5,3,7,7,6,13)	-0.286 (± 0.4039)	-0.750 (± 0.5143)	-0.952 (± 1.3516)	0.092 (± 0.6537)
BUN: Change at Day 3 (n=0, 1, 1, 0, 0, 0, 1)	99999 (± 99999)	-0.536 (± 99999)	1.071 (± 99999)	99999 (± 99999)
BUN: Change at Day 4 (n=0, 1, 0, 0, 0, 1, 0)	99999 (± 99999)	-0.428 (± 99999)	99999 (± 99999)	99999 (± 99999)
BUN: Change at Day 5 (n=5, 9, 8, 13, 13, 15, 29)	0.086 (± 0.9876)	-0.258 (± 0.9709)	0.223 (± 1.6846)	-0.014 (± 1.0222)
BUN: Change at Day 6 (n=0, 0, 0, 1, 0, 0, 0)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	0.643 (± 99999)
BUN: Change at Day 7 (n=1, 0, 0, 0, 0, 0, 0)	-0.500 (± 99999)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)
BUN: Change at Day 11 (n=5, 8, 7, 13, 16, 15, 28)	0.307 (± 0.3494)	0.884 (± 2.2140)	0.408 (± 1.5066)	0.719 (± 1.3786)
BUN: Change at Day 28 (n=4, 2, 2, 3, 1, 4, 4)	0.598 (± 1.0962)	0.196 (± 0.536)	0.2524 (± 0.428)	0.2574 (± 1.071)
DU: Change at Day 1 (n=3,6,5,9,8,8,16)	-0.464 (± 1.3674)	-0.263 (± 0.6438)	-0.143 (± 0.7403)	-0.331 (± 0.7714)
DU: Change at Day 1 7h (n=2,7,3,7,8,7,15)	-0.286 (± 0.4039)	-0.578 (± 0.6023)	-0.952 (± 1.3516)	0.092 (± 0.6537)
DU: Change at Day 3 (n=0, 1, 1, 0, 0, 0, 1)	99999 (± 99999)	-0.536 (± 99999)	1.071 (± 99999)	99999 (± 99999)
DU: Change at Day 4 (n=0, 1, 0, 0, 0, 1, 1)	99999 (± 99999)	-0.428 (± 99999)	99999 (± 99999)	99999 (± 99999)
DU: Change at Day 5 (n=5, 13, 8, 14, 14, 15, 32)	0.086 (± 0.9876)	-0.048 (± 0.8651)	0.223 (± 1.6846)	0.052 (± 1.0120)
DU: Change at Day 6 (n=0, 0, 0, 1, 0, 0, 0)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	0.643 (± 99999)
DU: Change at Day 7 (n=1, 0, 0, 0, 0, 0, 0)	-0.500 (± 99999)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)
DU: Change at Day 11 (n=5, 12, 7, 14, 18, 15, 31)	0.307 (± 0.3494)	0.481 (± 1.9201)	0.408 (± 1.5066)	1.429 (± 3.1244)
DU: Change at Day 28 (n=4, 2, 2, 4, 1, 4, 4)	0.598 (± 1.0962)	0.196 (± 0.1767)	0.536 (± 0.2524)	0.221 (± 0.4645)
Cl: Change at Day 1 (n=3,6,4,7,8,8,16)	4.000 (± 2.6458)	0.167 (± 3.6560)	-1.000 (± 1.4142)	1.000 (± 2.5166)
Cl: Change at Day 1 7h (n=2,8,3,6,7,8,16)	-0.500 (± 6.3640)	0.125 (± 1.4577)	-0.667 (± 7.3711)	0.300 (± 3.0033)
Cl: Change at Day 3 (n=0, 1, 1, 0, 0, 0, 1)	99999 (± 99999)	-4.000 (± 99999)	0.000 (± 99999)	99999 (± 99999)

CI: Change at Day 4 (n=0, 1, 0, 0, 0, 1, 1)	99999 (± 99999)	-3.000 (± 99999)	99999 (± 99999)	99999 (± 99999)
CI: Change at Day 5 (n=5, 13, 7, 14, 14, 15, 30)	3.000 (± 1.8708)	-0.462 (± 2.8465)	-1.000 (± 4.2426)	0.871 (± 2.2293)
CI: Change at Day 6 (n=0, 0, 0, 1, 0, 0, 0)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	4.000 (± 99999)
CI: Change at Day 7 (n=1, 0, 0, 0, 0, 0, 0)	8.000 (± 99999)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)
CI: Change at Day 11 (n=5, 12, 6, 14, 18, 15, 28)	3.600 (± 2.6077)	0.500 (± 3.3166)	1.167 (± 3.7103)	1.079 (± 2.2723)
CI: Change at Day 28 (n=4, 2, 2, 2, 2, 4, 4)	3.750 (± 2.9861)	-2.500 (± 0.7071)	1.000 (± 1.4142)	2.000 (± 2.8284)
BiC: Change at Day 1 (n=1,5,4,5,6,5,12)	-4.400 (± 99999)	0.840 (± 2.0959)	1.250 (± 1.3699)	-3.220 (± 3.4347)
BiC: Change at Day 1 7h (n=1,4,3,5,5,8,14)	1.600 (± 99999)	0.200 (± 0.9092)	0.667 (± 0.5774)	1.240 (± 1.7126)
BiC: Change at Day 3 (n=0,1,1,0,0,0,1)	99999 (± 99999)	3.200 (± 99999)	0.000 (± 99999)	99999 (± 99999)
BiC: Change at Day 4 (n=0,1,0,0,0,0,0)	99999 (± 99999)	1.500 (± 99999)	99999 (± 99999)	99999 (± 99999)
BiC: Change at Day 5 (n=2,11,7,12,11,12,27)	-0.600 (± 2.9698)	0.918 (± 2.3142)	-0.457 (± 2.3853)	-0.883 (± 4.6910)
BiC: Change at Day 11 (n=1,10,6,11,15,12,25)	-7.200 (± 99999)	-1.470 (± 2.2696)	-2.217 (± 2.9856)	-0.282 (± 2.7239)
BiC: Change at Day 28 (n=1,1,2,2,1,2,3)	-0.100 (± 99999)	-2.100 (± 99999)	-6.850 (± 3.4648)	0.950 (± 0.0707)
Glu: Change at Day 1 (n=3,5,5,9,8,8,16)	0.574 (± 0.1784)	0.027 (± 0.3211)	0.022 (± 1.0456)	0.394 (± 0.9391)
Glu: Change at Day 1 7h (n=2,8,3,7,8,8,16)	-0.944 (± 0.3140)	0.524 (± 2.0440)	0.444 (± 0.4441)	-0.936 (± 1.8798)
Glu: Change at Day 3 (n=0, 1, 1, 0, 0, 0, 1)	99999 (± 99999)	4.774 (± 99999)	-0.222 (± 99999)	99999 (± 99999)
Glu: Change at Day 4 (n=0, 1, 0, 0, 0, 0, 1)	99999 (± 99999)	-2.220 (± 99999)	99999 (± 99999)	99999 (± 99999)
Glu: Change at Day 5 (n=5, 13, 8, 16, 14, 15, 31)	-0.455 (± 1.1627)	-0.589 (± 0.9103)	0.056 (± 1.1074)	-0.529 (± 1.4839)
Glu: Change at Day 11 (n=5, 12, 7, 15, 17, 15, 29)	-0.377 (± 0.7441)	-0.735 (± 1.2051)	-0.254 (± 0.7960)	-0.540 (± 1.4190)
Glu: Change at Day 28 (n=3, 2, 2, 3, 1, 3, 3)	-0.259 (± 0.6941)	-1.055 (± 1.0205)	0.250 (± 0.5888)	-0.403 (± 0.8107)
K: Change at Day 1 (n=3,6,5,8,8,8,16)	-0.367 (± 0.7371)	-0.217 (± 0.5776)	-0.100 (± 0.4743)	0.446 (± 0.7071)
K: Change at Day 1 7h (n=2,8,3,7,8,8,16)	0.000 (± 0.2828)	-0.025 (± 0.6585)	0.833 (± 0.8505)	-0.35 (± 0.7678)
K: Change at Day 3 (n=0, 1, 1, 0, 0, 0, 1)	99999 (± 99999)	0.500 (± 99999)	-0.100 (± 99999)	99999 (± 99999)
K: Change at Day 4 (n=0, 1, 0, 0, 0, 1, 1)	99999 (± 99999)	-0.300 (± 99999)	99999 (± 99999)	99999 (± 99999)
K: Change at Day 5 (n=5, 14, 8, 16, 14, 15, 31)	-0.080 (± 0.5630)	0.383 (± 0.4422)	0.225 (± 0.7046)	0.123 (± 0.7766)
K: Change at Day 6 (n=0, 0, 0, 1, 0, 0, 0)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	0.800 (± 99999)
K: Change at Day 7 (n=1, 0, 0, 0, 0, 0, 0)	-0.800 (± 99999)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)
K: Change at Day 11 (n=5, 12, 7, 15, 18, 15, 30)	-0.180 (± 0.2683)	0.367 (± 1.0008)	0.386 (± 0.8214)	0.019 (± 0.7057)
K: Change at Day 28 (n=4, 2, 2, 4, 2, 4, 5)	-0.450 (± 0.3416)	0.150 (± 0.9192)	0.350 (± 0.4950)	-0.200 (± 0.3367)
Na: Change at Day 1 (n=3,6,5,8,8,8,17)	1.333 (± 3.2146)	1.500 (± 1.6432)	-0.600 (± 1.1402)	-1.513 (± 3.3702)
Na: Change at Day 1 7h (n=2,8,3,7,8,8,16)	-0.500 (± 6.3640)	-0.250 (± 1.7525)	-1.333 (± 4.9329)	1.429 (± 4.1173)

Na: Change at Day 3 (n=0, 1, 1, 0, 0, 0, 1)	99999 (± 99999)	-5.000 (± 99999)	1.000 (± 99999)	99999 (± 99999)
Na: Change at Day 4 (n=0, 1, 0, 0, 0, 1, 1)	99999 (± 99999)	-4.000 (± 99999)	99999 (± 99999)	99999 (± 99999)
Na: Change at Day 5 (n=5, 14, 8, 16, 14, 15, 32)	2.000 (± 2.7386)	1.286 (± 2.2336)	0.125 (± 3.6815)	0.050 (± 3.6715)
Na: Change at Day 6 (n=0, 0, 0, 1, 0, 0, 0)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	2.000 (± 99999)
Na: Change at Day 7 (n=1, 0, 0, 0, 0, 0, 0)	6.000 (± 99999)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)
Na: Change at Day 11 (n=5, 12, 7, 15, 18, 15, 29)	1.000 (± 2.8284)	0.462 (± 1.8081)	0.286 (± 4.1115)	0.273 (± 2.6497)
Na: Change at Day 28 (n=4, 2, 2, 4, 2, 4, 4)	1.500 (± 1.7321)	-5.500 (± 0.7071)	1.000 (± 0.0000)	-0.667 (± 1.5275)

End point values	MAD: ALS-008176 (40/20 mg/kg)	MAD: ALS-008176 (60/40 mg/kg)	MAD: Placebo	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	18	16	33	
Units: mmol/L				
arithmetic mean (standard deviation)				
BUN: Change at Day 1, (n=3,4,5,7,8,8,16)	-0.469 (± 1.3102)	-0.927 (± 1.4263)	-0.512 (± 0.6770)	
BUN: Change at Day 1, 7h (n=2,5,3,7,7,6,13)	-0.719 (± 1.4030)	-0.286 (± 0.7147)	-0.637 (± 0.8280)	
BUN: Change at Day 3 (n=0, 1, 1, 0, 0, 0, 1)	99999 (± 99999)	99999 (± 99999)	0.964 (± 99999)	
BUN: Change at Day 4 (n=0, 1, 0, 0, 0, 1, 0)	99999 (± 99999)	99999 (± 99999)	0.714 (± 99999)	
BUN: Change at Day 5 (n=5, 9, 8, 13, 13, 15, 29)	0.232 (± 1.2653)	0.322 (± 1.4978)	0.057 (± 0.7834)	
BUN: Change at Day 6 (n=0, 0, 0, 1, 0, 0, 0)	99999 (± 99999)	0.643 (± 99999)	99999 (± 99999)	
BUN: Change at Day 7 (n=1, 0, 0, 0, 0, 0, 0)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	
BUN: Change at Day 11 (n=5, 8, 7, 13, 16, 15, 28)	0.364 (± 1.3144)	0.501 (± 1.2024)	0.395 (± 0.8645)	
BUN: Change at Day 28 (n=4, 2, 2, 3, 1, 4, 4)	99999 (± 1.011)	1.3398 (± 99999)	0.446 (± 0.6262)	
DU: Change at Day 1 (n=3,6,5,9,8,8,16)	-0.674 (± 1.4148)	-0.927 (± 1.4263)	-0.574 (± 0.6728)	
DU: Change at Day 1 7h (n=2,7,3,7,8,7,15)	-0.642 (± 1.3172)	-0.331 (± 0.6632)	-0.369 (± 1.4107)	
DU: Change at Day 3 (n=0, 1, 1, 0, 0, 0, 1)	99999 (± 99999)	99999 (± 99999)	0.964 (± 99999)	
DU: Change at Day 4 (n=0, 1, 0, 0, 0, 1, 1)	99999 (± 99999)	-1.714 (± 99999)	0.714 (± 99999)	
DU: Change at Day 5 (n=5, 13, 8, 14, 14, 15, 32)	0.859 (± 2.8693)	0.322 (± 1.4978)	0.007 (± 1.1992)	
DU: Change at Day 6 (n=0, 0, 0, 1, 0, 0, 0)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	
DU: Change at Day 7 (n=1, 0, 0, 0, 0, 0, 0)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	
DU: Change at Day 11 (n=5, 12, 7, 14, 18, 15, 31)	0.664 (± 1.6573)	0.501 (± 1.2024)	0.668 (± 1.8060)	
DU: Change at Day 28 (n=4, 2, 2, 4, 1, 4, 4)	1.071 (± 99999)	1.011 (± 1.3398)	0.446 (± 0.6262)	

CI: Change at Day 1 (n=3,6,4,7,8,8,16)	0.625 (± 1.6850)	0.875 (± 3.3991)	1.181 (± 2.6240)	
CI: Change at Day 1 7h (n=2,8,3,6,7,8,16)	0.286 (± 3.1472)	1.250 (± 3.4538)	1.625 (± 2.5000)	
CI: Change at Day 3 (n=0, 1, 1, 0, 0, 0, 1)	99999 (± 99999)	99999 (± 99999)	-3.000 (± 99999)	
CI: Change at Day 4 (n=0, 1, 0, 0, 0, 1, 1)	99999 (± 99999)	0.000 (± 99999)	4.000 (± 99999)	
CI: Change at Day 5 (n=5, 13, 7, 14, 14, 15, 30)	0.143 (± 3.3936)	0.667 (± 5.8269)	0.617 (± 3.9950)	
CI: Change at Day 6 (n=0, 0, 0, 1, 0, 0, 0)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	
CI: Change at Day 7 (n=1, 0, 0, 0, 0, 0, 0)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	
CI: Change at Day 11 (n=5, 12, 6, 14, 18, 15, 28)	0.500 (± 2.7279)	0.467 (± 2.5317)	1.471 (± 3.0841)	
CI: Change at Day 28 (n=4, 2, 2, 2, 2, 4, 4)	-1.000 (± 2.8284)	2.000 (± 2.9439)	1.000 (± 2.1602)	
BiC: Change at Day 1 (n=1,5,4,5,6,5,12)	-0.967 (± 4.0805)	2.220 (± 2.2786)	-0.100 (± 2.0596)	
BiC: Change at Day 1 7h (n=1,4,3,5,5,8,14)	1.600 (± 4.7518)	0.425 (± 3.4446)	0.100 (± 2.8914)	
BiC: Change at Day 3 (n=0,1,1,0,0,0,1)	99999 (± 99999)	99999 (± 99999)	-0.700 (± 99999)	
BiC: Change at Day 4 (n=0,1,0,0,0,0,0)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	
BiC: Change at Day 5 (n=2,11,7,12,11,12,27)	-1.045 (± 3.1986)	-0.700 (± 1.8650)	-1.674 (± 3.8609)	
BiC: Change at Day 11 (n=1,10,6,11,15,12,25)	-0.680 (± 3.3830)	-1.342 (± 4.0514)	-2.024 (± 3.3589)	
BiC: Change at Day 28 (n=1,1,2,2,1,2,3)	-1.000 (± 99999)	-2.000 (± 2.8284)	-1.033 (± 4.0253)	
Glu: Change at Day 1 (n=3,5,5,9,8,8,16)	-1.131 (± 1.3339)	0.118 (± 1.1405)	-0.144 (± 1.0466)	
Glu: Change at Day 1 7h (n=2,8,3,7,8,8,16)	-0.180 (± 0.8312)	-1.610 (± 1.7419)	-0.200 (± 1.0311)	
Glu: Change at Day 3 (n=0, 1, 1, 0, 0, 0, 1)	99999 (± 99999)	99999 (± 99999)	-1.443 (± 99999)	
Glu: Change at Day 4 (n=0, 1, 0, 0, 0, 0, 1)	99999 (± 99999)	99999 (± 99999)	-0.389 (± 99999)	
Glu: Change at Day 5 (n=5, 13, 8, 16, 14, 15, 31)	-1.321 (± 1.2549)	-0.981 (± 1.1512)	-0.597 (± 0.8138)	
Glu: Change at Day 11 (n=5, 12, 7, 15, 17, 15, 29)	-1.118 (± 1.2295)	-0.855 (± 1.0013)	-0.602 (± 0.8924)	
Glu: Change at Day 28 (n=3, 2, 2, 3, 1, 3, 3)	-3.997 (± 99999)	-2.368 (± 2.4198)	-0.907 (± 0.3899)	
K: Change at Day 1 (n=3,6,5,8,8,8,16)	0.663 (± 0.8667)	-0.538 (± 0.4241)	-0.158 (± 0.4367)	
K: Change at Day 1 7h (n=2,8,3,7,8,8,16)	0.163 (± 0.4138)	0.166 (± 0.7890)	-0.042 (± 0.4909)	
K: Change at Day 3 (n=0, 1, 1, 0, 0, 0, 1)	99999 (± 99999)	99999 (± 99999)	0.400 (± 99999)	
K: Change at Day 4 (n=0, 1, 0, 0, 0, 1, 1)	99999 (± 99999)	-0.400 (± 99999)	0.100 (± 99999)	
K: Change at Day 5 (n=5, 14, 8, 16, 14, 15, 31)	0.529 (± 0.4177)	0.327 (± 0.6606)	0.446 (± 0.7510)	
K: Change at Day 6 (n=0, 0, 0, 1, 0, 0, 0)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	
K: Change at Day 7 (n=1, 0, 0, 0, 0, 0, 0)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	
K: Change at Day 11 (n=5, 12, 7, 15, 18, 15, 30)	0.328 (± 0.5154)	0.207 (± 0.9098)	0.296 (± 0.7519)	

K: Change at Day 28 (n=4, 2, 2, 4, 2, 4, 5)	0.650 (± 0.0707)	0.250 (± 0.8583)	0.000 (± 0.5148)	
Na: Change at Day 1 (n=3,6,5,8,8,8,17)	0.000 (± 1.8516)	0.875 (± 2.2321)	0.529 (± 2.7640)	
Na: Change at Day 1 7h (n=2,8,3,7,8,8,16)	-0.250 (± 3.1510)	1.000 (± 1.4142)	0.188 (± 2.1360)	
Na: Change at Day 3 (n=0, 1, 1, 0, 0, 0, 1)	99999 (± 99999)	99999 (± 99999)	-2.000 (± 99999)	
Na: Change at Day 4 (n=0, 1, 0, 0, 0, 1, 1)	99999 (± 99999)	1.000 (± 99999)	0.000 (± 99999)	
Na: Change at Day 5 (n=5, 14, 8, 16, 14, 15, 32)	0.500 (± 3.1805)	-1.400 (± 2.4437)	0.344 (± 2.1192)	
Na: Change at Day 6 (n=0, 0, 0, 1, 0, 0, 0)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	
Na: Change at Day 7 (n=1, 0, 0, 0, 0, 0, 0)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	
Na: Change at Day 11 (n=5, 12, 7, 15, 18, 15, 29)	0.111 (± 2.6097)	-0.867 (± 2.2318)	-0.517 (± 2.2775)	
Na: Change at Day 28 (n=4, 2, 2, 4, 2, 4, 4)	0.500 (± 2.1213)	-1.250 (± 2.0616)	0.750 (± 2.8723)	

Statistical analyses

No statistical analyses for this end point

Primary: MAD: Change From Baseline in Clinical laboratory Parameter (Hematology-Reticulocyte Absolute [RA], Platelets [PI], Leukocytes [LU], Monocytes [MO], Neutrophils [NE])

End point title	MAD: Change From Baseline in Clinical laboratory Parameter (Hematology-Reticulocyte Absolute [RA], Platelets [PI], Leukocytes [LU], Monocytes [MO], Neutrophils [NE]) ^{[55][56]}
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End point description:

Change from baseline in Hematology-RA, PI, LU, MO, NE were assessed. Safety analysis set defined as all randomized subjects who received at least 1 dose of study medication. Here "99999" indicates data was not evaluated at specified timepoint. Here "n" indicates number of subjects evaluated at specific timepoints.

End point type	Primary
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End point timeframe:

From Baseline, Day 1, 5, 11 and Day 28

Notes:

[55] - 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: Descriptive statistics were done, no inferential statistical analyses were performed.

[56] - 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: Endpoint was planned to be reported for the specified arms only.

End point values	MAD: ALS-008176 (4.1/1.37)	MAD: ALS-008176 (10/2 mg/kg)	MAD: ALS-008176 (30/6 mg/kg)	MAD: ALS-008176 (30/10 mg/kg)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	14	8	17
Units: 10 ⁹ /L				
arithmetic mean (standard deviation)				

RA: Change at Day 1 (n=0,1,1,3,0,0,2)	99999 (± 99999)	12.300 (± 99999)	0.700 (± 99999)	-1.867 (± 7.7861)
RA: Change at Day 1 7h (n=0,1,0,1,1,1,2)	99999 (± 99999)	-16.000 (± 99999)	99999 (± 99999)	174.000 (± 99999)
RA: Change at Day 5 (n=0,2,1,4,2,0,6)	99999 (± 99999)	22.600 (± 4.8083)	25.000 (± 99999)	21.433 (± 23.1768)
RA: Change at Day 11 (n=0, 2, 1, 4, 2, 0, 6)	99999 (± 99999)	29.100 (± 28.1428)	20.100 (± 99999)	33.550 (± 32.7856)
RA: Change at Day 28 (n=0, 0, 0, 2, 1, 0, 2)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	-7.400 (± 10.4652)
PI: Change at Day 1 (n=3,6,5,7,8,7,16)	55.333 (± 139.2204)	-69.833 (± 127.8928)	15.000 (± 36.4211)	30.143 (± 49.7475)
PI: Change at Day 1 7h (n=2,8,3,7,8,8,15)	102.000 (± 45.2548)	-26.125 (± 79.3013)	2.333 (± 65.2482)	14.429 (± 118.0408)
PI: Change at Day 3 (n=0, 1, 0, 0, 0, 0, 1)	99999 (± 99999)	14.000 (± 99999)	99999 (± 99999)	99999 (± 99999)
PI: Change at Day 4 (n=0, 1, 0, 1, 1, 1, 1)	99999 (± 99999)	-4.000 (± 99999)	99999 (± 99999)	187.000 (± 99999)
PI: Change at Day 5 (n=5, 13, 7, 16, 14, 14, 30)	176.200 (± 147.7031)	85.538 (± 80.9852)	116.571 (± 77.5411)	126.000 (± 173.6241)
PI: Change at Day 6 (n=0, 0, 0, 1, 0, 0, 0)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	33.000 (± 99999)
PI: Change at Day 7 (n=1, 0, 0, 0, 0, 0, 0)	246.000 (± 99999)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)
PI: Change at Day 11 (n=5, 14, 7, 16, 18, 14, 30)	224.400 (± 187.1692)	184.143 (± 161.7576)	146.000 (± 139.5087)	161.563 (± 143.9111)
PI: Change at Day 28 (n=4, 2, 3, 4, 7, 5, 5)	-1.250 (± 77.3235)	53.500 (± 187.3833)	51.667 (± 46.1988)	90.250 (± 114.7123)
LU: Change at Day 1 (n=3,6,5,8,8,8,16)	-0.947 (± 4.2824)	-0.458 (± 4.6275)	1.496 (± 1.5027)	2.224 (± 5.2023)
LU: Change at Day 1 7h (n=2,8,3,7,8,8,16)	4.105 (± 1.5344)	-0.026 (± 2.2113)	1.830 (± 4.4559)	0.779 (± 3.0700)
LU: Change at Day 3 (n=0, 1, 0, 0, 0, 0, 1)	99999 (± 99999)	3.700 (± 99999)	99999 (± 99999)	99999 (± 99999)
LU: Change at Day 4 (n=0, 1, 0, 1, 1, 1, 1)	99999 (± 99999)	2.600 (± 99999)	99999 (± 99999)	2.900 (± 99999)
LU: Change at Day 5 (n=5, 14, 7, 16, 14, 15, 30)	4.658 (± 4.0670)	2.899 (± 4.1105)	2.617 (± 2.8576)	1.919 (± 4.1434)
LU: Change at Day 6 (n=0, 0, 0, 1, 0, 0, 0)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	1.700 (± 99999)
LU: Change at Day 7 (n=1, 0, 0, 0, 0, 0, 0)	-5.200 (± 99999)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)
LU: Change at Day 11 (n=5, 14, 7, 16, 18, 15, 30)	2.202 (± 4.2067)	1.343 (± 3.4003)	1.560 (± 6.3322)	1.051 (± 3.7508)
LU: Change at Day 28 (n=4, 2, 3, 4, 7, 5, 5)	0.990 (± 3.8787)	2.350 (± 5.4447)	2.340 (± 3.7843)	1.305 (± 5.8319)
MO: Change at Day 1 (n=0,2,5,6,7,4,8)	99999 (± 99999)	0.5400 (± 1.47078)	0.4060 (± 0.77797)	0.1517 (± 1.29711)
MO: Change at Day 1 7h (n=2,3,3,5,5,6,10)	0.3300 (± 0.12728)	-0.4700 (± 0.68088)	-0.8033 (± 1.62254)	0.4122 (± 0.71410)
MO: Change at Day 4 (n=0, 0, 0, 1, 0, 1, 0)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	0.3000 (± 99999)
MO: Change at Day 5 (n=2, 6, 7, 12, 10, 9, 18)	-0.0850 (± 0.19092)	0.3633 (± 0.82553)	-0.5700 (± 1.47410)	-0.0713 (± 0.59409)
MO: Change at Day 11 (n=2, 6, 7, 1`2, 14, 9, 19)	-0.2300 (± 0.25456)	-0.6133 (± 0.23763)	-0.5600 (± 1.40801)	-0.3043 (± 0.98092)
MO: Change at Day 28 (n=2, 0, 3, 2, 6, 4, 1)	-0.2800 (± 0.31113)	99999 (± 99999)	0.0700 (± 0.72794)	-0.1850 (± 0.54447)
NE: Change at Day 1 (n=0,3,5,6,7,4,8)	99999 (± 99999)	-0.1500 (± 2.11714)	-0.1040 (± 0.94664)	-0.1117 (± 2.67649)
NE: Change at Day 1 7h (n=2,5,3,5,5,6,11)	-0.3000 (± 0.42426)	-0.7100 (± 2.05825)	0.7323 (± 0.81159)	0.0688 (± 1.92003)

NE: Change at Day 4 (n=0, 0, 0, 1, 0, 1, 0)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	5.3000 (± 99999)
NE: Change at Day 5 (n=2, 8, 7, 12, 14, 9, 19)	0.1800 (± 1.32936)	-0.6150 (± 1.99115)	0.7381 (± 1.94822)	0.6671 (± 2.26738)
NE: Change at Day 11 (n=2, 8, 7, 12, 14, 9, 19)	0.2200 (± 1.15966)	-0.6350 (± 2.62318)	-0.2574 (± 1.89726)	-0.1292 (± 2.35877)
NE: Change at Day 28 (n=2, 0, 3, 2, 6, 4, 1)	-0.7350 (± 0.36062)	99999 (± 99999)	0.8800 (± 0.45133)	2.5500 (± 4.73762)

End point values	MAD: ALS-008176 (40/20 mg/kg)	MAD: ALS-008176 (60/40 mg/kg)	MAD: Placebo	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	18	16	33	
Units: 10 ⁹ /L				
arithmetic mean (standard deviation)				
RA: Change at Day 1 (n=0,1,1,3,0,0,2)	99999 (± 99999)	99999 (± 99999)	-7.750 (± 13.3643)	
RA: Change at Day 1 7h (n=0,1,0,1,1,2)	16.000 (± 99999)	4.000 (± 99999)	1.500 (± 2.1213)	
RA: Change at Day 5 (n=0,2,1,4,2,0,6)	20.000 (± 99999)	99999 (± 99999)	19.050 (± 38.6507)	
RA: Change at Day 11 (n=0, 2, 1, 4, 2, 0, 6)	15.050 (± 1.3435)	99999 (± 99999)	74.250 (± 75.8861)	
RA: Change at Day 28 (n=0, 0, 0, 2, 1, 0, 2)	-1.700 (± 99999)	99999 (± 99999)	11.950 (± 11.2430)	
PI: Change at Day 1 (n=3,6,5,7,8,7,16)	21.125 (± 38.0768)	13.286 (± 102.5032)	-9.375 (± 83.1199)	
PI: Change at Day 1 7h (n=2,8,3,7,8,8,15)	1.625 (± 51.1411)	28.000 (± 49.7106)	30.200 (± 96.7207)	
PI: Change at Day 3 (n=0, 1, 0, 0, 0, 0, 1)	99999 (± 99999)	99999 (± 99999)	220.000 (± 99999)	
PI: Change at Day 4 (n=0, 1, 0, 1, 1, 1, 1)	25.000 (± 99999)	8.000 (± 99999)	266.000 (± 99999)	
PI: Change at Day 5 (n=5, 13, 7, 16, 14, 14, 30)	51.429 (± 127.6279)	93.214 (± 105.2866)	148.467 (± 131.1471)	
PI: Change at Day 6 (n=0, 0, 0, 1, 0, 0, 0)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	
PI: Change at Day 7 (n=1, 0, 0, 0, 0, 0, 0)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	
PI: Change at Day 11 (n=5, 14, 7, 16, 18, 14, 30)	97.056 (± 135.6741)	62.857 (± 152.4996)	189.067 (± 199.0547)	
PI: Change at Day 28 (n=4, 2, 3, 4, 7, 5, 5)	64.857 (± 80.6090)	90.000 (± 82.5530)	105.200 (± 93.8840)	
LU: Change at Day 1 (n=3,6,5,8,8,8,16)	-0.109 (± 1.8526)	-1.759 (± 2.4622)	-0.646 (± 2.8928)	
LU: Change at Day 1 7h (n=2,8,3,7,8,8,16)	1.449 (± 5.0896)	1.004 (± 3.1465)	0.737 (± 2.9601)	
LU: Change at Day 3 (n=0, 1, 0, 0, 0, 0, 1)	99999 (± 99999)	99999 (± 99999)	3.500 (± 99999)	
LU: Change at Day 4 (n=0, 1, 0, 1, 1, 1, 1)	1.800 (± 99999)	-2.410 (± 99999)	10.600 (± 99999)	
LU: Change at Day 5 (n=5, 14, 7, 16, 14, 15, 30)	1.018 (± 3.5099)	-1.158 (± 4.8667)	2.047 (± 3.6648)	
LU: Change at Day 6 (n=0, 0, 0, 1, 0, 0, 0)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	
LU: Change at Day 7 (n=1, 0, 0, 0, 0, 0, 0)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	

LU: Change at Day 11 (n=5, 14, 7, 16, 18, 15, 30)	0.966 (± 3.1490)	-1.252 (± 5.3719)	1.596 (± 3.9254)	
LU: Change at Day 28 (n=4, 2, 3, 4, 7, 5, 5)	2.131 (± 2.2922)	-0.232 (± 1.2545)	1.734 (± 2.8677)	
MO: Change at Day 1 (n=0,2,5,6,7,4,8)	-0.1277 (± 0.37158)	-0.4441 (± 0.59779)	-0.3081 (± 0.96999)	
MO: Change at Day 1 7h (n=2,3,3,5,5,6,10)	0.2389 (± 0.43763)	-0.2541 (± 0.35293)	-0.3696 (± 0.74369)	
MO: Change at Day 4 (n=0, 0, 0, 1, 0, 1, 0)	99999 (± 99999)	-0.6900 (± 99999)	99999 (± 99999)	
MO: Change at Day 5 (n=2, 6, 7, 12, 10, 9, 18)	-0.3018 (± 0.45398)	-0.9631 (± 0.78187)	-0.2382 (± 0.73679)	
MO: Change at Day 11 (n=2, 6, 7, 1`2, 14, 9, 19)	-0.2959 (± 0.52460)	-0.7158 (± 0.80561)	-0.5811 (± 0.74793)	
MO: Change at Day 28 (n=2, 0, 3, 2, 6, 4, 1)	0.2202 (± 0.61356)	-0.5366 (± 0.47212)	0.0000 (± 99999)	
NE: Change at Day 1 (n=0,3,5,6,7,4,8)	-1.1420 (± 1.36427)	-1.3210 (± 1.38441)	-1.7673 (± 2.27238)	
NE: Change at Day 1 7h (n=2,5,3,5,5,6,11)	-0.2506 (± 0.94318)	-0.4207 (± 1.81599)	-0.0937 (± 1.63375)	
NE: Change at Day 4 (n=0, 0, 0, 1, 0, 1, 0)	99999 (± 99999)	-1.4800 (± 99999)	99999 (± 99999)	
NE: Change at Day 5 (n=2, 8, 7, 12, 14, 9, 19)	-0.9553 (± 1.06988)	-2.1604 (± 4.01227)	-0.5921 (± 2.92195)	
NE: Change at Day 11 (n=2, 8, 7, 12, 14, 9, 19)	-1.0729 (± 1.47713)	-2.8000 (± 3.77919)	-0.7321 (± 3.54809)	
NE: Change at Day 28 (n=2, 0, 3, 2, 6, 4, 1)	-0.6352 (± 0.67595)	-2.3981 (± 1.49300)	-0.7000 (± 99999)	

Statistical analyses

No statistical analyses for this end point

Primary: MAD: Change From Baseline in Reticulocyte Percent, Hematocrit, Basophils/Leukocytes, Eosinophils/Leukocytes, Monocytes/Leukocytes, Neutrophils/Leukocytes, and Lymphocytes/Leukocytes

End point title	MAD: Change From Baseline in Reticulocyte Percent, Hematocrit, Basophils/Leukocytes, Eosinophils/Leukocytes, Monocytes/Leukocytes, Neutrophils/Leukocytes, and Lymphocytes/Leukocytes ^[57] ^[58]
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End point description:

Change from baseline in Hematology- RE, HeT, B/LU, E/LU, Ly/LU, N/LU and MO/LU were assessed. Safety analysis set defined as all randomized subjects who received at least 1 dose of study medication. Here "99999" indicates data was not evaluated at specified timepoint. in respective arm. Here "n" indicates number of subjects evaluated at specific timepoints.

End point type	Primary
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End point timeframe:

From Baseline, Day 1, 3, 4, 5, 11 and Day 28

Notes:

[57] - 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: Descriptive statistics were done, no inferential statistical analyses were performed.

[58] - 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: Endpoint was planned to be reported for the specified arms only.

End point values	MAD: ALS-008176 (4.1/1.37)	MAD: ALS-008176 (10/2 mg/kg)	MAD: ALS-008176 (30/6 mg/kg)	MAD: ALS-008176 (30/10 mg/kg)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	14	8	17
Units: Fraction of 1				
arithmetic mean (standard deviation)				
RE: Change at Day 1 (n=3,3,3,3,6,8,12)	-0.00100 ($\pm$ 0.001000)	-0.00033 ($\pm$ 0.000577)	0.00210 ($\pm$ 0.002152)	0.00033 ($\pm$ 0.002517)
RE:Change at Day 1 7h (n=2,5,2,6,5,7,11)	0.00255 ($\pm$ 0.006293)	-0.00364 ($\pm$ 0.004219)	0.00140 ($\pm$ 0.003394)	0.00330 ($\pm$ 0.006239)
RE:Change at Day 3 (n=0, 1, 0, 0, 0, 0, 1)	99999 ($\pm$ 99999)	0 ($\pm$ 99999)	99999 ($\pm$ 99999)	99999 ($\pm$ 99999)
RE:Change at Day 4 (n=0, 1, 0, 0, 1, 0, 1)	99999 ($\pm$ 99999)	0.00100 ($\pm$ 99999)	99999 ($\pm$ 99999)	99999 ($\pm$ 99999)
RE:Change at Day 5 (n=5, 8, 4, 9, 11, 15, 21)	0.00650 ($\pm$ 0.002373)	0.00093 ($\pm$ 0.007055)	0.00020 ($\pm$ 0.002903)	0.00253 ($\pm$ 0.006009)
RE:Change at Day 7 (n=1, 0, 0, 0, 0, 0, 0)	0.01220 ($\pm$ 99999)	99999 ($\pm$ 99999)	99999 ($\pm$ 99999)	99999 ($\pm$ 99999)
RE: Change at Day 11 (n=5, 8, 5, 9, 13, 15, 21)	0.00458 ($\pm$ 0.007345)	0.00671 ($\pm$ 0.007802)	0.01088 ($\pm$ 0.005876)	0.00759 ($\pm$ 0.012458)
RE:Change at Day 28 (n=4, 2, 1, 1, 3, 5, 2)	-0.00045 ($\pm$ 0.007967)	0.00310 ($\pm$ 0.015415)	-0.00200 ($\pm$ 99999)	0.00200 ($\pm$ 99999)
HeT:Change at Day 1 (n=3,6,5,8,8,8,15)	-0.0103 ($\pm$ 0.04636)	-0.0067 ($\pm$ 0.02911)	0.0002 ($\pm$ 0.01472)	0.0021 ($\pm$ 0.01802)
HeT:Change at Day 1 7h (n=2,8,3,7,8,8,16)	0.0145 ($\pm$ 0.02616)	-0.0162 ($\pm$ 0.03420)	-0.0127 ($\pm$ 0.02969)	-0.0170 ($\pm$ 0.03645)
HeT:Change at Day 3 (n=0, 1, 0, 0, 0, 0, 1)	99999 ($\pm$ 99999)	-0.0500 ($\pm$ 99999)	99999 ($\pm$ 99999)	99999 ($\pm$ 99999)
HeT:Change at Day 4 (n=0, 1, 0, 1, 1, 1, 1)	99999 ($\pm$ 99999)	-0.0830 ($\pm$ 99999)	99999 ($\pm$ 99999)	-0.0460 ($\pm$ 99999)
HeT: Change at Day 5 (n=5, 14, 7, 16, 14, 15, 29)	0.0114 ($\pm$ 0.03206)	0.0052 ($\pm$ 0.03671)	0.0213 ($\pm$ 0.02721)	-0.0049 ($\pm$ 0.04071)
HeT:Change at Day 6 (n=0, 0, 0, 1, 0, 0, 0)	99999 ($\pm$ 99999)	99999 ($\pm$ 99999)	99999 ($\pm$ 99999)	0.0280 ($\pm$ 99999)
HeT:Change at Day 7 (n=1, 0, 0, 0, 0, 0, 0)	-0.0380 ($\pm$ 99999)	99999 ($\pm$ 99999)	99999 ($\pm$ 99999)	99999 ($\pm$ 99999)
HeT:Change at Day 11 (n=5, 14, 7, 16, 18, 15, 29)	0.0104 ($\pm$ 0.03093)	-0.0006 ($\pm$ 0.03947)	0.0130 ($\pm$ 0.05371)	-0.0021 ($\pm$ 0.03684)
HeT:Change at Day 28 (n=4, 2, 3, 4, 7, 5, 4)	0.0255 ($\pm$ 0.02947)	-0.0585 ($\pm$ 0.11384)	0.0563 ($\pm$ 0.04649)	0.0233 ($\pm$ 0.04339)
B/LU:Change at Day 1 (n=3,6,4,6,8,7,12)	-0.0007 ($\pm$ 0.00115)	-0.0005 ($\pm$ 0.00071)	0 ($\pm$ 0.00316)	0.0030 ($\pm$ 0.00548)
B/LU:Change at Day 1 7h (n=2,4,3,7,7,6,12)	0.0020 ($\pm$ 0.00424)	-0.0018 ($\pm$ 0.00556)	-0.0040 ($\pm$ 0.00600)	0 ($\pm$ 0)
B/LU:Change at Day 3 (n=0, 1, 0, 0, 0, 0, 1)	99999 ($\pm$ 99999)	0 ($\pm$ 99999)	99999 ($\pm$ 99999)	99999 ($\pm$ 99999)
B/LU:Change at Day 4 (n=0, 1, 0, 1, 1, 1, 1)	99999 ($\pm$ 99999)	0 ($\pm$ 99999)	99999 ($\pm$ 99999)	-0.0030 ($\pm$ 99999)
B/LU:Change at Day 5 (n=5, 7, 6, 14, 13, 13, 22)	-0.0002 ($\pm$ 0.00179)	-0.0029 ($\pm$ 0.00426)	-0.0033 ($\pm$ 0.00333)	0.0011 ($\pm$ 0.00388)
B/LU:Change at Day 6 (n=0, 0, 0, 1, 0, 0, 0)	99999 ($\pm$ 99999)	99999 ($\pm$ 99999)	99999 ($\pm$ 99999)	0.0020 ($\pm$ 99999)
B/LU:Change at Day 7 (n=1, 0, 0, 0, 0, 0, 0)	0.0100 ($\pm$ 99999)	99999 ($\pm$ 99999)	99999 ($\pm$ 99999)	99999 ($\pm$ 99999)
B/LU:Change at Day 11 (n=5, 7, 5, 13, 16, 13, 22)	0.0004 ($\pm$ 0.00297)	-0.0003 ($\pm$ 0.00585)	-0.0032 ($\pm$ 0.00349)	0.0026 ($\pm$ 0.00441)
B/LU:Change at Day 28 (n=4, 2, 3, 3, 6, 5, 4)	-0.0005 ($\pm$ 0.00129)	0 ($\pm$ 0.01414)	-0.0010 ($\pm$ 0.00100)	0.0033 ($\pm$ 0.00577)
E/LU:Change at Day 1 (n=3,3,4,6,8,7,12)	0.0170 ($\pm$ 0.01480)	-0.0140 ($\pm$ 0.01400)	0.0108 ($\pm$ 0.01190)	-0.0033 ($\pm$ 0.02069)

E/LU:Change at Day 1 7h (n=22,5,2,7,7,6,11)	0.0040 (± 0.00424)	0.0130 (± 0.03655)	0.0150 (± 0.00849)	-0.0064 (± 0.01796)
E/LU:Change at Day 3 (n=0, 1, 0, 0, 0, 0, 1)	99999 (± 99999)	0.0300 (± 99999)	99999 (± 99999)	99999 (± 99999)
E/LU:Change at Day 4 (n=0, 1, 0, 1, 1, 1, 1)	99999 (± 99999)	0.0600 (± 99999)	99999 (± 99999)	-0.0080 (± 99999)
E/LU:Change at Day 5 (n=5, 8, 5, 14, 13, 13, 21)	0.0218 (± 0.01388)	0.0050 (± 0.01996)	0.0220 (± 0.01190)	0.0047 (± 0.01722)
E/LU:Change at Day 6 (n=0, 0, 0, 1, 0, 0, 0)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	0.0210 (± 99999)
E/LU:Change at Day 7 (n=1, 0, 0, 0, 0, 0, 0)	0.0600 (± 99999)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)
E/LU:Change at Day 11 (n=5, 7, 5, 13, 16, 13, 22)	0.0210 (± 0.01725)	0.0019 (± 0.02660)	0.0124 (± 0.00814)	0.0057 (± 0.02356)
E/LU:Change at Day 28 (n=4, 2, 3, 3, 6, 5, 4)	0.0393 (± 0.02254)	0 (± 0.01414)	0.0400 (± 0.00265)	0.0263 (± 0.01518)
Ly/LU:Change at Day 1 (n=3,3,4,6,8,7,12)	0.0647 (± 0.15279)	0.0053 (± 0.06795)	0.0313 (± 0.12570)	0.1023 (± 0.11833)
Ly/LU:Change at Day 1 7h (n=2,6,3,7,7,6,12)	0.1900 (± 0.05091)	0.1003 (± 0.11078)	0.0043 (± 0.03550)	0.0114 (± 0.13422)
Ly/LU:Change at Day 3 (n=0, 1, 0, 0, 0, 0, 1)	99999 (± 99999)	-0.1000 (± 99999)	99999 (± 99999)	99999 (± 99999)
Ly/LU:Change at Day 4 (n=0, 1, 0, 1, 1, 1, 1)	99999 (± 99999)	-0.1400 (± 99999)	99999 (± 99999)	-0.4180 (± 99999)
Ly/LU:Change at Day 5 (n=5, 9, 6, 14, 13, 13, 22)	0.0436 (± 0.16829)	0.0973 (± 0.14759)	-0.0207 (± 0.06181)	0.0243 (± 0.14084)
Ly/LU:Change at Day 6 (n=0, 0, 0, 1, 0, 0, 0)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	0.1740 (± 99999)
Ly/LU:Change at Day 7 (n=1,0,0,0,0,0,0)	0.1700 (± 99999)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)
Ly/LU:Change at Day 11(n=5,9,6,13,16,13,22)	0.0802 (± 0.13331)	0.0914 (± 0.15882)	0.1217 (± 0.13303)	0.0528 (± 0.18947)
Ly/LU:Change at Day 28(n=4,2,3,3,6,5,4)	0.1740 (± 0.18472)	0.1850 (± 0.00707)	-0.0527 (± 0.05065)	-0.1037 (± 0.19995)
NE/LU:Change at Day 1(n=3,3,4,6,8,7,12)	-0.0487 (± 0.14075)	-0.0217 (± 0.03731)	-0.0315 (± 0.12331)	-0.0817 (± 0.15243)
NE/LU:Change at Day 1 7h (n=2,6,3,7,7,6,12)	-0.1835 (± 0.03323)	-0.1087 (± 0.07159)	0.0167 (± 0.00666)	-0.0107 (± 0.17936)
NE/LU:Change at Day 3(n=0,1,0,0, 0,0,1)	99999 (± 99999)	0.0500 (± 99999)	99999 (± 99999)	99999 (± 99999)
NE/LU:Change at Day 4(n=0,1,0,1, 1,1,1)	99999 (± 99999)	0.0700 (± 99999)	99999 (± 99999)	0.4260 (± 99999)
NE/LU:Change at Day 5(n=5,9,6,14, 13,13,22)	-0.0304 (± 0.15891)	-0.0728 (± 0.13749)	0.0617 (± 0.06439)	0.0050 (± 0.15536)
NE/LU: Change at Day 6 (n=0, 0, 0, 1, 0, 0, 0)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	-0.1590 (± 99999)
NE/LU:Change at Day 7(n=1,0,0,0, 0,0,0)	-0.2000 (± 99999)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)
N/L:Change at Day 11(n=5,9,6,13,16,13,22)	-0.0432 (± 0.12650)	-0.0607 (± 0.14905)	-0.0408 (± 0.11622)	-0.0230 (± 0.21813)
NE/LU:Change at Day 28(n=4,2,3,3,6,5,4)	-0.1605 (± 0.13847)	-0.1300 (± 0)	0.0447 (± 0.02442)	0.1287 (± 0.20146)
MO/LU:Change at Day 1(n=3,3,4,6,8,7,12)	-0.0257 (± 0.03707)	0.0273 (± 0.03855)	-0.0115 (± 0.00645)	-0.0223 (± 0.06961)
MO/LU:Change at Day 1, 7h(n= 2, 6, 3, 7, 7, 6, 12)	-0.0125 (± 0.01768)	-0.0018 (± 0.04649)	-0.0797 (± 0.11327)	0 (± 0.05292)
MO/LU: Change at Day 3 (n=0, 1, 0, 0, 0, 0, 1)	99999 (± 99999)	0.0200 (± 99999)	99999 (± 99999)	99999 (± 99999)
MO/LU: Change at Day 4 (n=0, 1, 0, 1, 1, 1, 1)	99999 (± 99999)	-0.0200 (± 99999)	99999 (± 99999)	-0.0010 (± 99999)
MO/LU: Change at Day 5 (n=5, 9, 6, 14, 13, 13, 22)	-0.0348 (± 0.01645)	-0.0296 (± 0.03387)	-0.0953 (± 0.08841)	-0.0347 (± 0.04417)

MO/LU: Change at Day 6 (n=0, 0, 0, 1, 0, 0, 0)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	-0.0380 (± 99999)
MO/LU: Change at Day 7 (n=1, 0, 0, 0, 0, 0, 0)	-0.0300 (± 99999)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)
MO/LU: Change at Day 11 (n=5, 9, 6, 13, 16, 13, 22)	-0.0524 (± 0.03692)	-0.0353 (± 0.04317)	-0.0870 (± 0.06773)	-0.0299 (± 0.05849)
MO/LU: Change at Day 28 (n=4, 2, 2, 3, 6, 5, 4)	-0.0448 (± 0.03924)	-0.050 (± 0.02828)	-0.0445 (± 0.04313)	-0.0547 (± 0.02335)

End point values	MAD: ALS-008176 (40/20 mg/kg)	MAD: ALS-008176 (60/40 mg/kg)	MAD: Placebo	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	18	16	33	
Units: Fraction of 1				
arithmetic mean (standard deviation)				
RE: Change at Day 1 (n=3, 3, 3, 3, 6, 8, 12)	0.00052 (± 0.001443)	-0.00114 (± 0.003794)	0.00038 (± 0.002702)	
RE: Change at Day 1 7h (n=2, 5, 2, 6, 5, 7, 11)	-0.00110 (± 0.00258)	0.00010 (± 0.00296)	0.00499 (± 0.011443)	
RE: Change at Day 3 (n=0, 1, 0, 0, 0, 0, 1)	99999 (± 99999)	99999 (± 99999)	0.03000 (± 99999)	
RE: Change at Day 4 (n=0, 1, 0, 0, 1, 0, 1)	-0.00200 (± 99999)	99999 (± 99999)	0.01000 (± 99999)	
RE: Change at Day 5 (n=5, 8, 4, 9, 11, 15, 21)	-0.00118 (± 0.003986)	-0.00591 (± 0.006861)	0.00515 (± 0.008977)	
RE: Change at Day 7 (n=1, 0, 0, 0, 0, 0, 0)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	
RE: Change at Day 11 (n=5, 8, 5, 9, 13, 15, 21)	0.00936 (± 0.008564)	0.01654 (± 0.028015)	0.00694 (± 0.005788)	
RE: Change at Day 28 (n=4, 2, 1, 1, 3, 5, 2)	0.00480 (± 0.006702)	0.00484 (± 0.005498)	0.00300 (± 0)	
HeT: Change at Day 1 (n=3, 6, 5, 8, 8, 8, 15)	-0.0026 (± 0.01160)	-0.0330 (± 0.02734)	-0.0084 (± 0.02084)	
HeT: Change at Day 1 7h (n=2, 8, 3, 7, 8, 8, 16)	-0.0009 (± 0.02047)	-0.0006 (± 0.01862)	-0.0104 (± 0.02869)	
HeT: Change at Day 3 (n=0, 1, 0, 0, 0, 0, 1)	99999 (± 99999)	99999 (± 99999)	-0.0010 (± 99999)	
HeT: Change at Day 4 (n=0, 1, 0, 1, 1, 1, 1)	0.0210 (± 99999)	-0.0060 (± 99999)	0.0240 (± 99999)	
HeT: Change at Day 5 (n=5, 14, 7, 16, 14, 15, 29)	0.0036 (± 0.02690)	-0.0070 (± 0.03210)	0.0019 (± 0.02624)	
HeT: Change at Day 6 (n=0, 0, 0, 1, 0, 0, 0)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	
HeT: Change at Day 7 (n=1, 0, 0, 0, 0, 0, 0)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	
HeT: Change at Day 11 (n=5, 14, 7, 16, 18, 15, 29)	-0.0080 (± 0.02276)	-0.0247 (± 0.02871)	-0.0020 (± 0.02726)	
HeT: Change at Day 28 (n=4, 2, 3, 4, 7, 5, 4)	0.0279 (± 0.03936)	0.0008 (± 0.01829)	0.0080 (± 0.03429)	
B/LU: Change at Day 1 (n=3, 6, 4, 6, 8, 7, 12)	-0.0038 (± 0.00787)	0.0021 (± 0.00353)	-0.0001 (± 0.00360)	
B/LU: Change at Day 1 7h (n=2, 4, 3, 7, 7, 6, 12)	-0.0003 (± 0.01098)	-0.0012 (± 0.00440)	0.0006 (± 0.00491)	
B/LU: Change at Day 3 (n=0, 1, 0, 0, 0, 0, 1)	99999 (± 99999)	99999 (± 99999)	-0.0040 (± 99999)	
B/LU: Change at Day 4 (n=0, 1, 0, 1, 1, 1, 1)	0.0050 (± 99999)	0.0020 (± 99999)	0 (± 99999)	

B/LU:Change at Day 5 (n=5, 7, 6, 14, 13, 13, 22)	-0.0001 (± 0.00971)	-0.0002 (± 0.00424)	0.0010 (± 0.00501)
B/LU:Change at Day 6 (n=0, 0, 0, 1, 0, 0, 0)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)
B/LU:Change at Day 7 (n=1, 0, 0, 0, 0, 0, 0)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)
B/LU:Change at Day 11 (n=5, 7, 5, 13, 16, 13, 22)	-0.0024 (± 0.00896)	-0.0007 (± 0.00563)	-0.0003 (± 0.00372)
B/LU:Change at Day 28 (n=4, 2, 3, 3, 6, 5, 4)	-0.0023 (± 0.00622)	-0.0012 (± 0.00507)	0.0025 (± 0.00574)
E/LU:Change at Day 1 (n=3,3,4,6,8,7,12)	0.0139 (± 0.00919)	0.0016 (± 0.00969)	0.0027 (± 0.01069)
E/LU:Change at Day 1 7h (n=22,5,2,7,7,6,11)	0.0027 (± 0.00663)	0.0110 (± 0.01515)	0.0135 (± 0.02070)
E/LU:Change at Day 3 (n=0, 1, 0, 0, 0, 0, 1)	99999 (± 99999)	99999 (± 99999)	0.0160 (± 99999)
E/LU:Change at Day 4 (n=0, 1, 0, 1, 1, 1, 1)	0.0220 (± 99999)	0.0020 (± 99999)	0.0100 (± 99999)
E/LU:Change at Day 5 (n=5, 8, 5, 14, 13, 13, 21)	0.0226 (± 0.01823)	0.0130 (± 0.01194)	0.0219 (± 0.02104)
E/LU:Change at Day 6 (n=0, 0, 0, 1, 0, 0, 0)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)
E/LU:Change at Day 7 (n=1, 0, 0, 0, 0, 0, 0)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)
E/LU:Change at Day 11 (n=5, 7, 5, 13, 16, 13, 22)	0.0226 (± 0.01821)	0.0048 (± 0.00826)	0.0125 (± 0.01627)
E/LU:Change at Day 28 (n=4, 2, 3, 3, 6, 5, 4)	0.0313 (± 0.01715)	0.0334 (± 0.02924)	0.0248 (± 0.03362)
Ly/LU:Change at Day 1 (n=3,3,4,6,8,7,12)	0.1145 (± 0.13475)	0.0309 (± 0.12500)	0.0216 (± 0.13094)
Ly/LU:Change at Day 1 7h (n=2,6,3,7,7,6,12)	0.1856 (± 0.10153)	0.1557 (± 0.13484)	0.1263 (± 0.15505)
Ly/LU:Change at Day 3 (n=0, 1, 0, 0, 0, 0, 1)	99999 (± 99999)	99999 (± 99999)	0.2770 (± 99999)
Ly/LU:Change at Day 4 (n=0, 1, 0, 1, 1, 1, 1)	0.3010 (± 99999)	0.0590 (± 99999)	0.0500 (± 99999)
Ly/LU:Change at Day 5 (n=5, 9, 6, 14, 13, 13, 22)	0.2381 (± 0.13613)	0.1698 (± 0.17056)	0.0719 (± 0.13371)
Ly/LU:Change at Day 6 (n=0, 0, 0, 1, 0, 0, 0)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)
Ly/LU:Change at Day 7 (n=1,0,0,0,0,0,0)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)
Ly/LU:Change at Day 11(n=5,9,6,13,16,13,22)	0.1951 (± 0.17741)	0.2074 (± 0.17816)	0.0785 (± 0.15841)
Ly/LU:Change at Day 28(n=4,2,3,3,6,5,4)	0.1642 (± 0.16080)	0.2072 (± 0.20963)	0.1443 (± 0.03622)
NE/LU:Change at Day 1(n=3,3,4,6,8,7,12)	-0.1073 (± 0.12579)	-0.0257 (± 0.13069)	-0.3081 (± 0.96999)
NE/LU:Change at Day 1 7h (n=2,6,3,7,7,6,12)	-0.1730 (± 0.08578)	-0.1290 (± 0.13407)	-0.0077 (± 0.13576)
NE/LU:Change at Day 3(n=0,1,0,0,0,0,1)	99999 (± 99999)	99999 (± 99999)	-0.1172 (± 0.12884)
NE/LU:Change at Day 4(n=0,1,0,1,1,1,1)	-0.3010 (± 99999)	-0.0350 (± 99999)	-0.0600 (± 99999)
NE/LU:Change at Day 5(n=5,9,6,14,13,13,22)	-0.2025 (± 0.12148)	-0.1022 (± 0.16801)	-0.0815 (± 99999)
NE/LU: Change at Day 6 (n=0, 0, 0, 1, 0, 0, 0)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)
NE/LU:Change at Day 7(n=1,0,0,0,0,0,0)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)
N/L:Change at Day 11(n=5,9,6,13,16,13,22)	-0.1760 (± 0.15354)	-0.1668 (± 0.18456)	-0.0465 (± 0.16944)

NE/LU: Change at Day 28 (n=4,2,3,3,6,5,4)	-0.1763 (± 0.08492)	-0.1830 (± 0.24943)	-0.1225 (± 0.08685)	
MO/LU: Change at Day 1 (n=3,3,4,6,8,7,12)	-0.0057 (± 0.03163)	-0.0201 (± 0.02559)	-0.0148 (± 0.05153)	
MO/LU: Change at Day 1, 7h (n= 2, 6, 3, 7, 7, 6, 12)	-0.0176 (± 0.03777)	-0.0277 (± 0.01461)	-0.0215 (± 0.05408)	
MO/LU: Change at Day 3 (n=0, 1, 0, 0, 0, 0, 1)	99999 (± 99999)	99999 (± 99999)	-0.0190 (± 99999)	
MO/LU: Change at Day 4 (n=0, 1, 0, 1, 1, 1, 1)	-0.0170 (± 99999)	-0.0280 (± 99999)	-0.0100 (± 99999)	
MO/LU: Change at Day 5 (n=5, 9, 6, 14, 13, 13, 22)	-0.0448 (± 0.04020)	-0.0763 (± 0.03677)	-0.0287 (± 0.04721)	
MO/LU: Change at Day 6 (n=0, 0, 0, 1, 0, 0, 0)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	
MO/LU: Change at Day 7 (n=1, 0, 0, 0, 0, 0, 0)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	
MO/LU: Change at Day 11 (n=5,9, 6,13,16,13,22)	-0.0236 (± 0.04057)	-0.0448 (± 0.03341)	-0.0405 (± 0.03295)	
MO/LU: Change at Day 28 (n=4, 2, 2, 3, 6, 5, 4)	0.0110 (± 0.03289)	-0.0546 (± 0.03049)	-0.0415 (± 0.04273)	

Statistical analyses

No statistical analyses for this end point

Primary: MAD: Change From Baseline in Clinical Laboratory Parameter (Hematology-Erythrocytes Mean Corpuscular Hemoglobin)

End point title	MAD: Change From Baseline in Clinical Laboratory Parameter (Hematology- Erythrocytes Mean Corpuscular Hemoglobin) ^{[59][60]}
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End point description:

Change From Baseline in Clinical Laboratory Parameter (Hematology- Erythrocytes Mean Corpuscular Hemoglobin) was assessed. Safety analysis set defined as all randomized subjects who received at least 1 dose of study medication. Here "99999" indicates data was not evaluated at specified timepoint. Here "n" indicates number of subjects evaluated at specific timepoints.

End point type	Primary
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End point timeframe:

From Baseline, Day 1, 3, 4, 5, 6, 7, 11 and Day 28

Notes:

[59] - 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: Descriptive statistics were done, no inferential statistical analyses were performed.

[60] - 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: Endpoint was planned to be reported for the specified arms only.

End point values	MAD: ALS-008176 (4.1/1.37)	MAD: ALS-008176 (10/2 mg/kg)	MAD: ALS-008176 (30/6 mg/kg)	MAD: ALS-008176 (30/10 mg/kg)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	14	8	17
Units: pg				
arithmetic mean (standard deviation)				
Change at Day 1 (n=3, 6, 5, 8, 8, 8, 8, 16)	-0.033 (± 0.7572)	-0.467 (± 0.4719)	-0.020 (± 0.5119)	0.587 (± 1.0921)

Change at Day 1 7h (n=2, 8, 3, 7, 8, 8, 16)	-0.200 (± 0.8485)	0.100 (± 0.4957)	0.167 (± 0.4619)	-0.600 (± 0.7234)
Change at Day 3 (n=0, 1, 0, 0, 0, 0, 1)	99999 (± 99999)	-0.500 (± 99999)	99999 (± 99999)	99999 (± 99999)
Change at Day 4 (n=0, 1, 0, 1, 1, 1, 1)	99999 (± 99999)	-0.200 (± 99999)	99999 (± 99999)	99999 (± 99999)
Change at Day 5 (n=5, 14, 7, 16, 14, 15, 30)	-0.300 (± 0.4472)	-0.236 (± 0.5624)	-0.371 (± 0.5376)	0.250 (± 1.7084)
Change at Day 6 (n=0, 0, 0, 1, 0, 0, 0)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	-0.500 (± 99999)
Change at Day 7 (n=1, 0, 0, 0, 0, 0, 0)	-0.500 (± 99999)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)
Change at Day 11 (n=5, 14, 7, 16, 18, 15, 30)	-0.460 (± 0.8142)	-0.443 (± 0.5019)	-0.129 (± 0.5936)	-0.138 (± 1.2010)
Change at Day 28 (n=4, 2, 3, 4, 7, 5, 5)	-0.050 (± 0.6807)	-1.800 (± 0.2828)	-1.133 (± 1.6166)	-0.550 (± 1.1958)

End point values	MAD: ALS-008176 (40/20 mg/kg)	MAD: ALS-008176 (60/40 mg/kg)	MAD: Placebo	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	18	16	33	
Units: pg				
arithmetic mean (standard deviation)				
Change at Day 1 (n=3, 6, 5, 8, 8, 8, 8, 16)	-0.162 (± 0.3249)	0.062 (± 0.8400)	-0.050 (± 0.5279)	
Change at Day 1 7h (n=2, 8, 3, 7, 8, 8, 16)	0.225 (± 0.5175)	-0.112 (± 0.4190)	-0.175 (± 1.1072)	
Change at Day 3 (n=0, 1, 0, 0, 0, 0, 1)	99999 (± 99999)	99999 (± 99999)	-0.400 (± 99999)	
Change at Day 4 (n=0, 1, 0, 1, 1, 1, 1)	99999 (± 99999)	99999 (± 99999)	0.100 (± 99999)	
Change at Day 5 (n=5, 14, 7, 16, 14, 15, 30)	0.000 (± 0.7565)	0.087 (± 0.9180)	-0.173 (± 0.8068)	
Change at Day 6 (n=0, 0, 0, 1, 0, 0, 0)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	
Change at Day 7 (n=1, 0, 0, 0, 0, 0, 0)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	
Change at Day 11 (n=5, 14, 7, 16, 18, 15, 30)	-0.111 (± 0.6970)	0.073 (± 1.0229)	-0.533 (± 0.5868)	
Change at Day 28 (n=4, 2, 3, 4, 7, 5, 5)	0.343 (± 0.9235)	0.320 (± 3.0425)	-1.180 (± 1.4025)	

Statistical analyses

No statistical analyses for this end point

Primary: MAD: Change From Baseline in Clinical Laboratory Parameter (Hematology-Erythrocytes Mean Corpuscular HGB Concentration)

End point title	MAD: Change From Baseline in Clinical Laboratory Parameter (Hematology- Erythrocytes Mean Corpuscular HGB Concentration) ^{[61][62]}
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End point description:

Change from baseline in clinical laboratory parameter (Hematology- erythrocytes mean corpuscular HGB

concentration) was assessed. Safety analysis set defined as all randomized subjects who received at least 1 dose of study medication. Here "99999" indicates data was not evaluated at specified timepoint. Here "n" indicates number of subjects evaluated at specific timepoints.

End point type	Primary
End point timeframe:	
From Baseline to Day 1, 3, 4, 5, 6, 7, 11 and Day 28	

Notes:

[61] - 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: Descriptive statistics were done, no inferential statistical analyses were performed.

[62] - 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: Endpoint was planned to be reported for the specified arms only.

End point values	MAD: ALS-008176 (4.1/1.37)	MAD: ALS-008176 (10/2 mg/kg)	MAD: ALS-008176 (30/6 mg/kg)	MAD: ALS-008176 (30/10 mg/kg)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	14	8	17
Units: g/L				
arithmetic mean (standard deviation)				
Change at Day 1 (n=3, 6, 5, 8, 8, 8, 8, 16)	-0.667 (± 6.6583)	0.000 (± 4.5607)	-3.600 (± 6.1887)	0.500 (± 8.1670)
Change at Day 1 7h (n=2, 8, 3, 7, 8, 8, 16)	1.000 (± 11.3137)	2.875 (± 4.6733)	5.333 (± 10.0167)	-6.714 (± 6.3957)
Change at Day 3 (n=0, 1, 0, 0, 0, 0, 1)	99999 (± 99999)	-2.000 (± 99999)	99999 (± 99999)	99999 (± 99999)
Change at Day 4 (n=0, 1, 0, 1, 1, 1, 1)	99999 (± 99999)	1.000 (± 99999)	99999 (± 99999)	10.000 (± 99999)
Change at Day 5 (n=5, 14, 7, 14, 13, 15, 30)	1.600 (± 8.0187)	2.000 (± 6.8388)	0.857 (± 4.4508)	0.857 (± 11.4518)
Change at Day 6 (n=0, 0, 0, 1, 0, 0, 0)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	-2.000 (± 99999)
Change at Day 7 (n=1, 0, 0, 0, 0, 0, 0)	-3.000 (± 99999)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)
Change at Day 11 (n=5, 14, 7, 14, 17, 15, 30)	-1.000 (± 8.6891)	3.143 (± 9.3138)	-2.571 (± 8.1416)	-1.000 (± 10.2582)
Change at Day 28 (n=4, 2, 3, 3, 7, 5, 5)	6.750 (± 6.2383)	-8.500 (± 13.4350)	4.667 (± 8.5049)	2.000 (± 7.0000)

End point values	MAD: ALS-008176 (40/20 mg/kg)	MAD: ALS-008176 (60/40 mg/kg)	MAD: Placebo	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	18	16	33	
Units: g/L				
arithmetic mean (standard deviation)				
Change at Day 1 (n=3, 6, 5, 8, 8, 8, 8, 16)	-0.375 (± 6.6103)	-1.500 (± 11.0454)	-1.750 (± 6.8069)	
Change at Day 1 7h (n=2, 8, 3, 7, 8, 8, 16)	2.429 (± 9.2711)	-0.375 (± 9.1486)	-0.063 (± 14.5349)	
Change at Day 3 (n=0, 1, 0, 0, 0, 0, 1)	99999 (± 99999)	99999 (± 99999)	1.000 (± 99999)	
Change at Day 4 (n=0, 1, 0, 1, 1, 1, 1)	12.000 (± 99999)	-6.000 (± 99999)	-1.000 (± 99999)	

Change at Day 5 (n=5, 14, 7, 14, 13, 15, 30)	5.154 (± 14.3169)	4.333 (± 9.6115)	3.233 (± 9.8250)	
Change at Day 6 (n=0, 0, 0, 1, 0, 0, 0)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	
Change at Day 7 (n=1, 0, 0, 0, 0, 0, 0)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	
Change at Day 11 (n=5, 14, 7, 14, 17, 15, 30)	2.176 (± 8.8898)	7.400 (± 13.5320)	1.800 (± 8.2144)	
Change at Day 28 (n=4, 2, 3, 3, 7, 5, 5)	0.714 (± 14.9634)	-4.600 (± 18.2975)	-1.000 (± 7.8740)	

Statistical analyses

No statistical analyses for this end point

Primary: MAD: Change From Baseline in Clinical Laboratory Parameter (Erythrocytes Mean Corpuscular Volume [e-MCV] and Mean Platelet Volume [MPV])

End point title	MAD: Change From Baseline in Clinical Laboratory Parameter (Erythrocytes Mean Corpuscular Volume [e-MCV] and Mean Platelet Volume [MPV])[⁶³][⁶⁴]
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End point description:

Change from Baseline in Clinical Laboratory Parameter (e-MCV and MPV) was assessed. Safety analysis set defined as all randomized subjects who received at least 1 dose of study medication. Here "99999" indicates data was not evaluated at specified timepoint. Here "n" indicates number of subjects evaluated at specific timepoints.

End point type	Primary
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End point timeframe:

From Baseline, Day 1, 3, 4, 5, 6, 7, 11 and Day 28

Notes:

[63] - 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: Descriptive statistics were done, no inferential statistical analyses were performed.

[64] - 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: Endpoint was planned to be reported for the specified arms only.

End point values	MAD: ALS-008176 (4.1/1.37)	MAD: ALS-008176 (10/2 mg/kg)	MAD: ALS-008176 (30/6 mg/kg)	MAD: ALS-008176 (30/10 mg/kg)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	14	8	17
Units: FL				
arithmetic mean (standard deviation)				
e-MCV: Change at Day 1 (n=3,6,5,8,8,16)	0.167 (± 0.7234)	-1.300 (± 0.8649)	0.760 (± 0.9940)	1.325 (± 5.1917)
e-MCV: Change at Day 1 7h (n=2, 8, 3, 7, 8, 8, 16)	-0.850 (± 0.4950)	-0.500 (± 1.3690)	-1.033 (± 1.8502)	0.043 (± 1.4954)
e-MCV: Change at Day 3 (n=0, 1, 0, 0, 0, 0, 1)	99999 (± 99999)	-0.700 (± 99999)	99999 (± 99999)	99999 (± 99999)
e-MCV: Change at Day 4 (n=0, 1, 0, 1, 1, 1, 1)	99999 (± 99999)	-0.700 (± 99999)	99999 (± 99999)	-0.100 (± 99999)
e-MCV: Change at Day 5 (n=5, 13, 7, 16, 14, 15, 30)	-1.320 (± 1.6022)	-1.177 (± 1.5034)	-1.429 (± 1.0095)	0.281 (± 3.4582)
e-MCV: Change at Day 6 (n=0, 0, 0, 1, 0, 0, 0)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	-1.300 (± 99999)

e-MCV: Change at Day 7 (n=1, 0, 0, 0, 0, 0, 0)	-0.900 (± 99999)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)
e-MCV: Change at Day 11 (n=5,13,7,16,18,15,30)	-1.140 (± 1.7925)	-2.138 (± 1.9410)	0.386 (± 2.1567)	0.017 (± 3.7913)
e-MCV: Change at Day 28 (n=4, 2, 3, 4, 7, 5, 5)	-1.775 (± 2.0549)	-3.050 (± 4.4548)	-4.533 (± 2.9738)	-1.925 (± 2.3543)
MPV: Change at Day 1 (n=3,4,5,8,7,13)	-0.400 (± 0.6557)	0.050 (± 0.3697)	0.200 (± 0.3391)	1.220 (± 1.2317)
MPV: Change at Day 1 7h (n=2, 7, 2, 6, 7, 8, 12)	0.250 (± 0.2121)	0.171 (± 0.4071)	-0.050 (± 0.6364)	-0.233 (± 0.5750)
MPV: Change at Day 4 (n=0, 0, 0, 0, 1, 1, 0)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)
MPV: Change at Day 5 (n=5, 10, 6, 11, 13, 14, 24)	0.220 (± 0.1643)	-0.200 (± 0.3830)	-0.100 (± 0.2828)	0.045 (± 0.7815)
MPV: Change at Day 6 (n=0, 0, 0, 1, 0, 0, 0)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	-0.200 (± 99999)
MPV: Change at Day 7 (n=1, 0, 0, 0, 0, 0, 0)	-0.100 (± 99999)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)
MPV: Change at Day 11 (n=5,11,6,11,16,14,23)	-0.460 (± 0.8019)	-0.091 (± 0.6236)	0.383 (± 0.5193)	0.282 (± 0.7795)
MPV: Change at Day 28 (n=4, 1, 3, 1, 6, 3, 2)	0.025 (± 0.2986)	-0.200 (± 99999)	0.267 (± 0.4041)	0.800 (± 99999)

End point values	MAD: ALS-008176 (40/20 mg/kg)	MAD: ALS-008176 (60/40 mg/kg)	MAD: Placebo	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	18	16	33	
Units: FL				
arithmetic mean (standard deviation)				
e-MCV: Change at Day 1 (n=3,6,5,8,8,8,16)	-0.213 (± 1.1344)	0.188 (± 1.0480)	0.237 (± 1.7258)	
e-MCV: Change at Day 1 7h (n=2, 8, 3, 7, 8, 8, 16)	-0.225 (± 1.8584)	-0.412 (± 1.2287)	-0.375 (± 2.6532)	
e-MCV: Change at Day 3 (n=0, 1, 0, 0, 0, 0, 1)	99999 (± 99999)	99999 (± 99999)	-1.700 (± 99999)	
e-MCV: Change at Day 4 (n=0, 1, 0, 1, 1, 1, 1)	-0.600 (± 99999)	0.200 (± 99999)	0.400 (± 99999)	
e-MCV: Change at Day 5 (n=5, 13, 7, 16, 14, 15, 30)	-1.236 (± 2.9014)	-1.107 (± 1.5121)	-1.240 (± 2.0346)	
e-MCV: Change at Day 6 (n=0, 0, 0, 1, 0, 0, 0)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	
e-MCV: Change at Day 7 (n=1, 0, 0, 0, 0, 0, 0)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	
e-MCV: Change at Day 11 (n=5,13,7,16,18,15,30)	-0.861 (± 2.3722)	-1.980 (± 2.3373)	-2.053 (± 2.1800)	
e-MCV: Change at Day 28 (n=4, 2, 3, 4, 7, 5, 5)	0.571 (± 3.3678)	0.820 (± 4.7457)	-3.180 (± 3.1364)	
MPV: Change at Day 1 (n=3,4,5,8,7,13)	-0.075 (± 0.5175)	0.286 (± 0.8375)	0.069 (± 0.5105)	
MPV: Change at Day 1 7h (n=2, 7, 2, 6, 7, 8, 12)	-0.029 (± 0.3302)	-0.075 (± 0.9051)	0.183 (± 0.9272)	
MPV: Change at Day 4 (n=0, 0, 0, 0, 1, 1, 0)	0.100 (± 99999)	0.000 (± 99999)	99999 (± 99999)	
MPV: Change at Day 5 (n=5, 10, 6, 11, 13, 14, 24)	0.115 (± 0.7777)	0.350 (± 0.8707)	0.021 (± 0.5517)	
MPV: Change at Day 6 (n=0, 0, 0, 1, 0, 0, 0)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	

MPV: Change at Day 7 (n=1, 0, 0, 0, 0, 0, 0)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	
MPV: Change at Day 11 (n=5,11,6,11,16,14,23)	0.038 (± 0.4064)	0.507 (± 0.7405)	-0.087 (± 0.5480)	
MPV: Change at Day 28 (n=4, 1, 3, 1, 6, 3, 2)	-0.017 (± 0.8280)	-0.367 (± 0.8327)	0.050 (± 0.2121)	

Statistical analyses

No statistical analyses for this end point

Primary: MAD: Change From Baseline in Clinical Laboratory Parameter (Erythrocytes Distribution Width)

End point title	MAD: Change From Baseline in Clinical Laboratory Parameter (Erythrocytes Distribution Width) ^{[65][66]}
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End point description:

Change From Baseline in Hematology-Erythrocytes Distribution Width was assessed. Safety analysis set defined as all randomized subjects who received at least 1 dose of study medication. Here "99999" indicates data was not evaluated at specified timepoint. Here "n" indicates number of subjects evaluated at specific timepoints.

End point type	Primary
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End point timeframe:

From Baseline to Day 1, 3, 4, 5, 6, 7, 11 and Day 28

Notes:

[65] - 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: Descriptive statistics were done, no inferential statistical analyses were performed.

[66] - 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: Endpoint was planned to be reported for the specified arms only.

End point values	MAD: ALS-008176 (4.1/1.37)	MAD: ALS-008176 (10/2 mg/kg)	MAD: ALS-008176 (30/6 mg/kg)	MAD: ALS-008176 (30/10 mg/kg)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	14	8	17
Units: Percentage (%)				
arithmetic mean (standard deviation)				
Change at Day 1 (n=3,4,5,5,8,8,13)	-0.133 (± 0.4726)	-0.025 (± 0.0500)	-0.100 (± 0.2550)	-0.020 (± 0.2775)
Change at Day 1 7h (n=2, 8, 3, 7, 7, 8, 15)	-0.100 (± 0.2828)	-0.087 (± 0.3091)	-0.033 (± 0.1528)	0.043 (± 0.3735)
Change at Day 3 (n=0, 1, 0, 0, 0, 0, 1)	99999 (± 99999)	0.000 (± 99999)	99999 (± 99999)	99999 (± 99999)
Change at Day 4 (n=0, 1, 0, 1, 1, 1, 0)	99999 (± 99999)	0.000 (± 99999)	99999 (± 99999)	99999 (± 99999)
Change at Day 5 (n=5, 12, 7, 13, 13, 15, 27)	-0.160 (± 0.5413)	-0.083 (± 0.3271)	3.271 (± 8.7007)	0.031 (± 0.3987)
Change at Day 6 (n=0, 0, 0, 1, 0, 0, 0)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	0.100 (± 99999)
Change at Day 7 (n=1, 0, 0, 0, 0, 0, 0)	-1.000 (± 99999)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)
Change at Day 11 (n=5,12,7,13,16,15,26)	0.280 (± 0.4324)	0.350 (± 0.5351)	1.286 (± 0.5273)	0.646 (± 0.7655)

Change at Day 28 (n=4, 2, 3, 2, 6, 5, 3)	0.150 (± 0.3697)	-0.900 (± 1.2728)	0.533 (± 0.9609)	1.400 (± 0.9899)
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End point values	MAD: ALS-008176 (40/20 mg/kg)	MAD: ALS-008176 (60/40 mg/kg)	MAD: Placebo	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	18	16	33	
Units: Percentage (%)				
arithmetic mean (standard deviation)				
Change at Day 1 (n=3,4,5,5,8,8,13)	-0.150 (± 0.2449)	0.138 (± 0.4719)	0.131 (± 0.4461)	
Change at Day 1 7h (n=2, 8, 3, 7, 7, 8, 15)	0.014 (± 0.2795)	0.162 (± 0.4069)	0.173 (± 0.3990)	
Change at Day 3 (n=0, 1, 0, 0, 0, 0, 1)	99999 (± 99999)	99999 (± 99999)	0.400 (± 99999)	
Change at Day 4 (n=0, 1, 0, 1, 1, 1, 0)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	
Change at Day 5 (n=5, 12, 7, 13, 13, 15, 27)	-0.108 (± 0.4699)	-0.213 (± 0.5222)	0.081 (± 0.4715)	
Change at Day 6 (n=0, 0, 0, 1, 0, 0, 0)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	
Change at Day 7 (n=1, 0, 0, 0, 0, 0, 0)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	
Change at Day 11 (n=5,12,7,13,16,15,26)	0.406 (± 1.7883)	0.007 (± 1.1068)	0.281 (± 0.4373)	
Change at Day 28 (n=4, 2, 3, 2, 6, 5, 3)	2.883 (± 1.0797)	3.620 (± 1.9690)	0.500 (± 0.5292)	

Statistical analyses

No statistical analyses for this end point

Secondary: SAD: Respiratory Syncytial Virus (RSV) viral Ribonucleic Acid (RNA) Concentrations in Nasal Swabs or Aspirates - FAS Infected: Virology Set

End point title	SAD: Respiratory Syncytial Virus (RSV) viral Ribonucleic Acid (RNA) Concentrations in Nasal Swabs or Aspirates - FAS Infected: Virology Set ^[67]
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End point description:

RSV viral RNA concentration in nasal swabs or aspirates was assessed by quantitative RT-PCR in Log 10 Plaque forming units per millilitre (PFUe/mL). The Full Analysis Set-Infected Virology (FAS-IV) population is defined to include all FAS-I subjects who have sufficient virology data for analysis. Subjects were considered not have sufficient virology data for analysis and will be removed from the FAS-IV population if any of the conditions were met-baseline viral load is less than (<) 2 log10 PFUe/mL; missing baseline viral load; percent of intended volume administered is < 50% for the loading dose or total maintenance dose or < 3 viral load observations during the first 120 hours. Here, 'n' signifies the number of subjects analyzed at specified time point. Here "99999" indicates data was not evaluated at specified timepoint.

End point type	Secondary
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End point timeframe:

Baseline to Day 7

Notes:

[67] - 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: Endpoint was planned to be reported for the specified arms only.

End point values	SAD: ALS-008176 (1.37 mg/kg)	SAD: ALS-008176 (4.1 mg/kg)	SAD: ALS-008176 (12 mg/kg)	SAD: ALS-008176 (25 mg/kg)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	15	17	14	3
Units: Log 10 PFUe/mL				
arithmetic mean (standard deviation)				
Baseline (n=15, 17, 14, 3, 16)	4.933 (± 1.3126)	5.567 (± 1.3314)	6.188 (± 0.7897)	4.700 (± 1.3604)
Day 1 (n=13, 17, 14, 3, 16)	4.417 (± 1.8042)	5.170 (± 1.4124)	5.875 (± 1.4416)	4.667 (± 0.4924)
Day 2 (n=14, 14, 13, 3, 15)	4.154 (± 1.8270)	4.503 (± 1.2868)	5.376 (± 1.2581)	4.477 (± 0.4879)
Day 3 (n=2, 2, 2, 0, 0)	4.785 (± 1.3364)	5.338 (± 2.6269)	5.625 (± 0.2192)	99999 (± 99999)
Day 4 (n=1, 0, 2, 0, 0)	4.940 (± 99999)	99999 (± 99999)	6.055 (± 1.1526)	99999 (± 99999)
Day 5 (n=0, 0, 2, 0, 0)	99999 (± 99999)	99999 (± 99999)	4.665 (± 0.1344)	99999 (± 99999)
Day 6 (n=0, 0, 1, 0, 0)	99999 (± 99999)	99999 (± 99999)	4.890 (± 99999)	99999 (± 99999)
day 7 (n=14, 15, 12, 2, 15)	2.189 (± 1.4523)	2.469 (± 1.5193)	3.808 (± 1.5745)	2.756 (± 2.2688)

End point values	Placebo			
Subject group type	Reporting group			
Number of subjects analysed	16			
Units: Log 10 PFUe/mL				
arithmetic mean (standard deviation)				
Baseline (n=15, 17, 14, 3, 16)	5.123 (± 1.6435)			
Day 1 (n=13, 17, 14, 3, 16)	5.114 (± 1.6727)			
Day 2 (n=14, 14, 13, 3, 15)	4.531 (± 2.2140)			
Day 3 (n=2, 2, 2, 0, 0)	99999 (± 99999)			
Day 4 (n=1, 0, 2, 0, 0)	99999 (± 99999)			
Day 5 (n=0, 0, 2, 0, 0)	99999 (± 99999)			
Day 6 (n=0, 0, 1, 0, 0)	99999 (± 99999)			
day 7 (n=14, 15, 12, 2, 15)	2.751 (± 1.9724)			

Statistical analyses

No statistical analyses for this end point

Secondary: SAD: RSV viral RNA Concentrations in Nasal Swabs or Aspirates - FAS: Infected

End point title	SAD: RSV viral RNA Concentrations in Nasal Swabs or Aspirates - FAS: Infected ^[68]
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End point description:

RSV viral RNA concentrations in nasal swabs or aspirates was assessed by quantitative RT-PCR. The Full Analysis Set-Infected (FAS-I) is defined to include all FAS subjects who were confirmed PCR positive for RSV viral RNA. Here, 'n' signifies the number of subjects analyzed at specified time point. Here "99999" indicates data was not evaluated at specified timepoint.

End point type	Secondary
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End point timeframe:

Baseline to Day 7

Notes:

[68] - 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: Endpoint was planned to be reported for the specified arms only.

End point values	SAD: ALS-008176 (1.37 mg/kg)	SAD: ALS-008176 (4.1 mg/kg)	SAD: ALS-008176 (12 mg/kg)	SAD: ALS-008176 (25 mg/kg)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	18	17	14	3
Units: log10 PFUe/mL				
arithmetic mean (standard deviation)				
Baseline (n=16, 17, 14, 3, 16)	4.858 (± 1.3027)	5.567 (± 1.3314)	6.188 (± 0.7897)	4.700 (± 1.3604)
Day 1 (n=16, 17, 14, 3, 17)	4.385 (± 1.6393)	5.170 (± 1.4124)	5.875 (± 1.4416)	4.667 (± 0.4924)
Day 2 (n=17, 14, 13, 3, 15)	4.184 (± 1.7204)	4.503 (± 1.2868)	5.376 (± 1.2581)	4.477 (± 0.4879)
Day 3 (n=2, 2, 2, 0, 0)	4.785 (± 1.3364)	5.338 (± 2.6269)	5.625 (± 0.2192)	99999 (± 99999)
Day 4 (n=1, 0, 2, 0, 0)	4.940 (± 99999)	99999 (± 99999)	6.055 (± 1.1526)	99999 (± 99999)
Day 5 (n=0, 0, 2, 0, 0)	99999 (± 99999)	99999 (± 99999)	4.665 (± 0.1344)	99999 (± 99999)
Day 6 (n=0, 0, 1, 0, 0)	99999 (± 99999)	99999 (± 99999)	4.890 (± 99999)	99999 (± 99999)
Day 7 (n=17, 15, 12, 2, 15)	2.134 (± 1.4451)	2.469 (± 1.5193)	3.808 (± 1.5745)	2.756 (± 2.2688)

End point values	SAD: Placebo			
Subject group type	Subject analysis set			
Number of subjects analysed	17			
Units: log10 PFUe/mL				
arithmetic mean (standard deviation)				
Baseline (n=16, 17, 14, 3, 16)	5.123 (± 1.6435)			
Day 1 (n=16, 17, 14, 3, 17)	5.184 (± 1.6450)			

Day 2 (n=17, 14, 13, 3, 15)	4.531 (± 2.2140)			
Day 3 (n=2, 2, 2, 0, 0)	99999 (± 99999)			
Day 4 (n=1, 0, 2, 0, 0)	99999 (± 99999)			
Day 5 (n=0, 0, 2, 0, 0)	99999 (± 99999)			
Day 6 (n=0, 0, 1, 0, 0)	99999 (± 99999)			
Day 7 (n=17, 15, 12, 2, 15)	2.751 (± 1.9724)			

Statistical analyses

No statistical analyses for this end point

Secondary: MAD: RSV viral RNA Concentrations in Nasal Swabs or Aspirates - FAS: Infected: Virology set

End point title	MAD: RSV viral RNA Concentrations in Nasal Swabs or Aspirates - FAS: Infected: Virology set ^[69]
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End point description:

RSV viral RNA Concentrations in Nasal Swabs or Aspirates was assessed by quantitative RT-PCR. The FAS-IV population is defined to include all FAS-I subjects who have sufficient virology data for analysis. Subjects will be considered to not have sufficient virology data for analysis and will be removed from the FAS-IV population if Baseline viral load is <2 log₁₀ PFUe/mL; Missing baseline viral load; Percent of intended volume administered is <50% for the loading dose or total maintenance dose or <3 viral load observations during the first 120 hours. Here, 'n' signifies the number of subjects analyzed at specified time point. Here "99999" indicates data was not evaluated at specified timepoint.

End point type	Secondary
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End point timeframe:

Baseline up to Day 28

Notes:

[69] - 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: Endpoint was planned to be reported for the specified arms only.

End point values	MAD: ALS-008176 (4.1/1.37)	MAD: ALS-008176 (10/2 mg/kg)	MAD: ALS-008176 (30/6 mg/kg)	MAD: ALS-008176 (30/10 mg/kg)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	12	5	13
Units: Log 10 PFUe/mL				
arithmetic mean (standard deviation)				
Baseline (n=5, 12, 5, 13, 12, 13, 25)	5.176 (± 1.0939)	5.534 (± 1.6926)	6.584 (± 0.9639)	5.578 (± 1.3815)
Day 1 (n=5, 12, 5, 13, 12, 13, 24)	4.528 (± 1.0248)	5.386 (± 1.2769)	5.760 (± 1.5262)	4.668 (± 1.5975)
Day 2 (5, 12, 5, 13, 10, 12, 25)	4.098 (± 1.2297)	4.838 (± 1.6102)	5.052 (± 1.5155)	4.522 (± 1.4690)
Day 3 (n=0, 2, 0, 1, 12, 11, 13)	99999 (± 99999)	3.595 (± 1.9445)	99999 (± 99999)	6.460 (± 99999)
Day 4 (0, 1, 0, 1, 7, 8, 11)	99999 (± 99999)	2.900 (± 99999)	99999 (± 99999)	3.200 (± 99999)

Day 5 (n=5, 12, 5, 13, 11, 13, 24)	2.658 (± 1.4290)	3.807 (± 1.8995)	4.408 (± 1.1502)	3.514 (± 1.7953)
Day 6 (n=0, 0, 0, 0, 6, 5, 2)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)
Day 7 (n=0, 0, 0, 0, 2, 1, 1)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)
Day 8 (n=0, 0, 0, 0, 2, 1, 1)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)
Day 11 (n=5, 12, 4, 12, 12, 12, 24)	1.570 (± 1.2253)	1.737 (± 1.5841)	2.075 (± 1.6607)	1.031 (± 1.2529)
Day 28 (n=1, 1, 0, 7, 7, 5, 3)	5.230 (± 99999)	0.020 (± 99999)	99999 (± 99999)	0.793 (± 1.0111)

End point values	MAD: ALS-008176 (40/20 mg/kg)	MAD: ALS-008176 (60/40 mg/kg)	MAD: Placebo	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	12	13	25	
Units: Log 10 PFUe/mL				
arithmetic mean (standard deviation)				
Baseline (n=5, 12, 5, 13, 12, 13, 25)	4.671 (± 1.1396)	4.768 (± 0.8777)	4.743 (± 1.3366)	
Day 1 (n=5, 12, 5, 13, 12, 13, 24)	4.051 (± 1.5294)	4.079 (± 1.3464)	4.348 (± 1.3836)	
Day 2 (5, 12, 5, 13, 10, 12, 25)	3.960 (± 1.9010)	3.737 (± 0.8746)	4.071 (± 1.5695)	
Day 3 (n=0, 2, 0, 1, 12, 11, 13)	3.118 (± 1.9139)	3.129 (± 1.0418)	3.000 (± 1.6639)	
Day 4 (0, 1, 0, 1, 7, 8, 11)	1.883 (± 1.3612)	2.661 (± 1.3573)	2.741 (± 1.5524)	
Day 5 (n=5, 12, 5, 13, 11, 13, 24)	1.646 (± 1.4766)	2.608 (± 1.1903)	2.598 (± 1.7806)	
Day 6 (n=0, 0, 0, 0, 6, 5, 2)	1.062 (± 1.2809)	2.452 (± 1.0368)	1.355 (± 0.0212)	
Day 7 (n=0, 0, 0, 0, 2, 1, 1)	1.535 (± 0.2899)	2.900 (± 99999)	0.300 (± 99999)	
Day 8 (n=0, 0, 0, 0, 2, 1, 1)	0.930 (± 1.3152)	1.790 (± 99999)	2.720 (± 99999)	
Day 11 (n=5, 12, 4, 12, 12, 12, 24)	0.294 (± 0.6004)	1.001 (± 1.7687)	1.304 (± 1.4359)	
Day 28 (n=1, 1, 0, 7, 7, 5, 3)	1.347 (± 1.8556)	1.942 (± 2.6602)	0.087 (± 0.1501)	

Statistical analyses

No statistical analyses for this end point

Secondary: MAD: RSV viral RNA Concentrations in Nasal Swabs or Aspirates - FAS: Infected

End point title	MAD: RSV viral RNA Concentrations in Nasal Swabs or Aspirates - FAS: Infected ^[70]
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End point description:

RSV viral RNA Concentrations in Nasal Swabs or Aspirates was assessed by quantitative RT-PCR. FAS-I is defined to include all FAS subjects who are confirmed PCR positive for RSV viral RNA. Here, 'n'

signifies the number of subjects analyzed at specified time point. Here "99999" indicates data was not evaluated at specified timepoint.

End point type	Secondary
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End point timeframe:

Baseline to Day 28

Notes:

[70] - 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: Endpoint was planned to be reported for the specified arms only.

End point values	MAD: ALS-008176 (4.1/1.37)	MAD: ALS-008176 (10/2 mg/kg)	MAD: ALS-008176 (30/6 mg/kg)	MAD: ALS-008176 (30/10 mg/kg)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	13	8	16
Units: Log 10 PFUe/mL				
arithmetic mean (standard deviation)				
Baseline (n=5, 13, 6, 16, 18, 16, 31)	5.176 (± 1.0939)	5.212 (± 1.9932)	5.765 (± 2.1835)	5.120 (± 1.9784)
Day 1 (n=5, 13, 8, 16, 17, 16, 28)	4.528 (± 1.0248)	5.013 (± 1.8168)	4.060 (± 2.8505)	4.481 (± 1.7503)
Day 2 (n=5, 13, 7, 15, 12, 15, 30)	4.098 (± 1.2297)	4.556 (± 1.8455)	4.326 (± 2.2737)	4.113 (± 1.7465)
Day 3 (n=0, 2, 0, 2, 14, 13, 14)	99999 (± 99999)	3.595 (± 1.9445)	99999 (± 99999)	3.545 (± 4.1224)
Day 4 (n=0, 1, 0, 2, 8, 11, 13)	99999 (± 99999)	2.900 (± 99999)	99999 (± 99999)	2.620 (± 0.8202)
Day 5 (n=5, 13, 8, 16, 14, 16, 29)	2.658 (± 1.4290)	3.514 (± 2.1028)	2.755 (± 2.4414)	3.254 (± 1.8680)
Day 6 (n=0, 0, 0, 1, 7, 6, 2)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	0.720 (± 99999)
Day 7 (n=0, 0, 0, 1, 3, 2, 1)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	1.880 (± 99999)
Day 8 (n=0, 0, 0, 0, 3, 1, 1)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)
Day 9 (n=0, 0, 0, 0, 1, 0, 0)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)
Day 11 (n=5, 13, 7, 15, 17, 15, 29)	1.570 (± 1.2253)	1.822 (± 1.5478)	1.891 (± 1.4589)	1.003 (± 1.1193)
Day 28 (n=1, 1, 0, 8, 10, 7, 5)	5.230 (± 99999)	0.020 (± 99999)	99999 (± 99999)	1.210 (± 1.5060)

End point values	MAD: ALS-008176 (40/20 mg/kg)	MAD: ALS-008176 (60/40 mg/kg)	MAD: Placebo	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	18	16	31	
Units: Log 10 PFUe/mL				
arithmetic mean (standard deviation)				
Baseline (n=5, 13, 6, 16, 18, 16, 31)	4.676 (± 1.3800)	4.743 (± 0.9484)	4.460 (± 1.7332)	
Day 1 (n=5, 13, 8, 16, 17, 16, 28)	4.195 (± 1.4386)	4.064 (± 1.3392)	4.272 (± 1.5434)	
Day 2 (n=5, 13, 7, 15, 12, 15, 30)	3.971 (± 1.7865)	3.709 (± 1.0221)	4.034 (± 1.5983)	

Day 3 (n=0, 2, 0, 2, 14, 13, 14)	3.271 (± 1.8706)	2.998 (± 1.1195)	3.029 (± 1.6024)	
Day 4 (n=0, 1, 0, 2, 8, 11, 13)	2.054 (± 1.3498)	2.685 (± 1.5268)	2.670 (± 1.7043)	
Day 5 (n=5, 13, 8, 16, 14, 16, 29)	1.864 (± 1.7632)	2.416 (± 1.2001)	2.762 (± 1.9417)	
Day 6 (n=0, 0, 0, 1, 7, 6, 2)	1.357 (± 1.4065)	2.043 (± 1.3645)	1.355 (± 0.0212)	
Day 7 (n=0, 0, 0, 1, 3, 2, 1)	2.023 (± 0.8703)	1.945 (± 1.3506)	0.300 (± 99999)	
Day 8 (n=0, 0, 0, 0, 3, 1, 1)	0.620 (± 1.0739)	1.790 (± 99999)	2.720 (± 99999)	
Day 9 (n=0, 0, 0, 0, 1, 0, 0)	0.000 (± 99999)	99999 (± 99999)	99999 (± 99999)	
Day 11 (n=5, 13, 7, 15, 17, 15, 29)	0.726 (± 1.5087)	0.801 (± 1.6216)	1.345 (± 1.4458)	
Day 28 (n=1, 1, 0, 8, 10, 7, 5)	0.974 (± 1.6320)	1.387 (± 2.3698)	0.638 (± 1.2862)	

Statistical analyses

No statistical analyses for this end point

Secondary: SAD: Maximum Plasma Observed Concentration (Cmax) of ALS-008112 (JNJ-63549109)

End point title	SAD: Maximum Plasma Observed Concentration (Cmax) of ALS-008112 (JNJ-63549109) ^[71]
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End point description:

Cmax is the maximum observed plasma concentration. Pharmacokinetics (PK) population was defined as all subjects that received one or more doses of ALS-008176 and with 1 quantifiable blood concentration.

End point type	Secondary
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End point timeframe:

On Day 1

Notes:

[71] - 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: Endpoint was planned to be reported for the specified arms only.

End point values	SAD: ALS-008176 (1.37 mg/kg)	SAD: ALS-008176 (4.1 mg/kg)	SAD: ALS-008176 (12 mg/kg)	SAD: ALS-008176 (25 mg/kg)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	18	17	13	3
Units: nano-gram/milliliter (ng/ml)				
arithmetic mean (geometric coefficient of variation)	129.5 (± 43.19)	404.3 (± 63)	1269 (± 55.86)	1909 (± 20.91)

Statistical analyses

No statistical analyses for this end point

Secondary: SAD: Area Under Curve (AUC) of ALS-008112 (JNJ-63549109)

End point title	SAD: Area Under Curve (AUC) of ALS-008112 (JNJ-
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End point description:

AUC is the area under plasma concentration curve. PK population was defined as all subjects that received one or more doses of ALS-008176 and with 1 quantifiable blood concentration.

End point type	Secondary
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End point timeframe:

On Day 1

Notes:

[72] - 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: Endpoint was planned to be reported for the specified arms only.

End point values	SAD: ALS-008176 (1.37 mg/kg)	SAD: ALS-008176 (4.1 mg/kg)	SAD: ALS-008176 (12 mg/kg)	SAD: ALS-008176 (25 mg/kg)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	18	17	13	3
Units: nanogram*hour/milliliter (ng*h/ml)				
arithmetic mean (geometric coefficient of variation)	350.9 (± 14.89)	959.9 (± 15.02)	2574 (± 10.09)	5122 (± 12.73)

Statistical analyses

No statistical analyses for this end point

Secondary: MAD: Cmax of ALS-008112 (JNJ-63549109)

End point title	MAD: Cmax of ALS-008112 (JNJ-63549109) ^[73]
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End point description:

Cmax is the maximum observed plasma concentration. PK population was defined as all subjects that received one or more doses of ALS-008176 and with 1 quantifiable blood concentration. Here 'n' signifies the number of subjects analyzed at specified time point.

End point type	Secondary
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End point timeframe:

Day 1 and Day 5

Notes:

[73] - 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: Endpoint was planned to be reported for the specified arms only.

End point values	MAD: ALS-008176 (4.1/1.37)	MAD: ALS-008176 (10/2 mg/kg)	MAD: ALS-008176 (30/6 mg/kg)	MAD: ALS-008176 (30/10 mg/kg)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	14	8	17
Units: ng/ml				
arithmetic mean (geometric coefficient of variation)				
Day 1 (n=5, 14, 8, 17, 17, 16)	285 (± 25.81)	867 (± 49.66)	2431 (± 34.45)	1895 (± 44.08)

Day 5 (n=5, 14, 7, 16, 14, 16)	172.1 (± 29.09)	211.8 (± 41.02)	591.2 (± 44.23)	991.3 (± 46.18)
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End point values	MAD: ALS-008176 (40/20 mg/kg)	MAD: ALS-008176 (60/40 mg/kg)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	18	16		
Units: ng/ml				
arithmetic mean (geometric coefficient of variation)				
Day 1 (n=5, 14, 8, 17, 17, 16)	3142 (± 38.26)	4653 (± 51.44)		
Day 5 (n=5, 14, 7, 16, 14, 16)	1867 (± 41.22)	3380 (± 46.85)		

Statistical analyses

No statistical analyses for this end point

Secondary: MAD: AUC of ALS-008112 (JNJ-63549109)

End point title	MAD: AUC of ALS-008112 (JNJ-63549109) ^[74]
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End point description:

AUC is area under plasma under curve. PK population was defined as all subjects that received one or more doses of ALS-008176 and with 1 quantifiable blood concentration. Here, 'n' signifies the number of subjects analyzed at specified time point.

End point type	Secondary
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End point timeframe:

On Day 1 and Day 5

Notes:

[74] - 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: Endpoint was planned to be reported for the specified arms only.

End point values	MAD: ALS-008176 (4.1/1.37)	MAD: ALS-008176 (10/2 mg/kg)	MAD: ALS-008176 (30/6 mg/kg)	MAD: ALS-008176 (30/10 mg/kg)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	14	8	17
Units: ng*h/ml				
arithmetic mean (geometric coefficient of variation)				
Day 1 (5, 14, 8, 17, 17, 16)	1305 (± 10.04)	2466 (± 11.34)	6508 (± 8.843)	7459 (± 15.62)
Day 5 (n=5, 14, 7, 16, 14, 16)	1114 (± 7.467)	1529 (± 8.405)	3912 (± 8.483)	6117 (± 7.843)

End point values	MAD: ALS-008176 (40/20 mg/kg)	MAD: ALS-008176 (60/40 mg/kg)		
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Subject group type	Reporting group	Reporting group		
Number of subjects analysed	18	16		
Units: ng*h/ml				
arithmetic mean (geometric coefficient of variation)				
Day 1 (5, 14, 8, 17, 17, 16)	10940 ($\pm$ 11.88)	16770 ($\pm$ 10.28)		
Day 5 (n=5, 14, 7, 16, 14, 16)	10820 ($\pm$ 13.76)	18790 ($\pm$ 9.45)		

Statistical analyses

No statistical analyses for this end point

Secondary: MAD: Number of Subjects with Emerging Genetic Variations in the RSV L Gene Considering the 4 Positions of Interest at the Last Evaluable On-treatment Time Point

End point title	MAD: Number of Subjects with Emerging Genetic Variations in the RSV L Gene Considering the 4 Positions of Interest at the Last Evaluable On-treatment Time Point ^[75]
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End point description:

The emergence of genetic variations at RSV L amino acid positions 628, 789, 795, and 796 was evaluated. An emerging genetic variation is defined as a genetic variation (amino acid substitution, insertion or deletion) that is absent, that is with next-generation sequencing (NGS) read frequency <3%, at baseline but present with an NGS read frequency $\geq$ 15% at a later post-baseline time point. Safety Analysis Set defined as all randomized subjects who received at least 1 dose of study medication. Evaluable subjects for the secondary endpoint are subjects in the MAD Part with baseline and post-baseline RSV sequencing data available.

End point type	Secondary
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End point timeframe:

From Baseline to Day 28

Notes:

[75] - 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: Endpoint was planned to be reported for the specified arms only.

End point values	MAD: ALS-008176 (4.1/1.37)	MAD: ALS-008176 (10/2 mg/kg)	MAD: ALS-008176 (30/6 mg/kg)	MAD: ALS-008176 (30/10 mg/kg)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	8	3	4
Units: Subjects				
number (not applicable)	0	0	0	0

End point values	MAD: ALS-008176 (40/20 mg/kg)	MAD: ALS-008176 (60/40 mg/kg)	MAD: Placebo	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	13	9	13	
Units: Subjects				
number (not applicable)	0	0	0	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Approximately 4 years

Adverse event reporting additional description:

Safety Analysis Set defined as all randomized subjects who received at least 1 dose of study medication. Some grade 3 and grade 4 low neutrophil counts were not reported as Adverse Events.

Assessment type	Non-systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	16.1
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Reporting groups

Reporting group title	Single dose of ALS-008176 (1.37 mg/kg)
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Reporting group description:

Subjects received single oral dose of 1.37 milligrams per kilogram (mg/kg) of ALS-008176.

Reporting group title	Single dose of ALS-008176 (4.1 mg/kg)
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Reporting group description:

Subjects received single oral dose of 4.1 mg/kg of ALS-008176.

Reporting group title	Single dose of ALS-008176 (12 mg/kg)
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Reporting group description:

Subjects received single oral dose of 12 mg/kg of ALS-008176.

Reporting group title	Single dose of ALS-008176 (25 mg/kg)
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Reporting group description:

Subjects received single oral dose of 25 mg/kg of ALS-008176.

Reporting group title	Multiple dose of ALS-008176 (4.1/1.37 mg/kg)
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Reporting group description:

Subjects received 1 loading dose of 4.1 mg/kg of ALS-008176 for dose 1 on Day 1 followed by 9 doses of 1.37 mg/kg of ALS-008176 twice daily for 5 consecutive days.

Reporting group title	Multiple dose of ALS-008176 (10/2 mg/kg)
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Reporting group description:

Subjects received loading dose of 10 mg/kg of ALS-008176 for dose 1 on Day 1 followed by 9 doses of 2 mg/kg of ALS-008176 twice daily for 5 consecutive days.

Reporting group title	Multiple dose of ALS-008176 (30/6 mg/kg)
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Reporting group description:

Subjects received loading dose of 30 mg/kg of ALS-008176 for dose 1 on Day 1 followed by 9 doses of 6 mg/kg of ALS-008176 twice daily for 5 consecutive days.

Reporting group title	Multiple dose of ALS-008176 (30/10 mg/kg)
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Reporting group description:

Subjects received loading dose of 30 mg/kg of ALS-008176 for dose 1 on Day 1 followed by 9 doses of 10 mg/kg of ALS-008176 twice daily for 5 consecutive days.

Reporting group title	Multiple dose of ALS-008176 (40/20 mg/kg)
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Reporting group description:

Subjects received loading dose of 40 mg/kg of ALS-008176 for dose 1 on Day 1 followed by 9 doses of 20 mg/kg of ALS-008176 twice daily for 5 consecutive days.

Reporting group title	Multiple dose of ALS-008176 (60/40 mg/kg)
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Reporting group description:

Subjects received loading dose of 60 mg/kg of ALS-008176 for dose 1 on Day 1 followed by 9 doses of 40 mg/kg of ALS-008176 twice daily for 5 consecutive days.

Reporting group title	Placebo
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Reporting group description:

Subjects received single and multiple doses of Placebo orally.

Serious adverse events	Single dose of ALS-008176 (1.37 mg/kg)	Single dose of ALS-008176 (4.1 mg/kg)	Single dose of ALS-008176 (12 mg/kg)
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 18 (5.56%)	0 / 18 (0.00%)	0 / 14 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Vascular disorders			
Phlebitis			
subjects affected / exposed	1 / 18 (5.56%)	0 / 18 (0.00%)	0 / 14 (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
Cardiac disorders			
Sinus Tachycardia			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (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
Blood and lymphatic system disorders			
Lymphadenitis			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (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
Neutropenia			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (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, thoracic and mediastinal disorders			
Respiratory Failure			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (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 Bacterial			

subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (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 Bronchiolitis			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (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

Serious adverse events	Single dose of ALS-008176 (25 mg/kg)	Multiple dose of ALS-008176 (4.1/1.37 mg/kg)	Multiple dose of ALS-008176 (10/2 mg/kg)
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 3 (33.33%)	0 / 5 (0.00%)	0 / 14 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Vascular disorders			
Phlebitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (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
Cardiac disorders			
Sinus Tachycardia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 5 (0.00%)	0 / 14 (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
Blood and lymphatic system disorders			
Lymphadenitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (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
Neutropenia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (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, thoracic and mediastinal disorders			
Respiratory Failure			

subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (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 Bacterial			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (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 Bronchiolitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (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

Serious adverse events	Multiple dose of ALS-008176 (30/6 mg/kg)	Multiple dose of ALS-008176 (30/10 mg/kg)	Multiple dose of ALS-008176 (40/20 mg/kg)
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 8 (0.00%)	1 / 17 (5.88%)	2 / 18 (11.11%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Vascular disorders			
Phlebitis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	0 / 18 (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			
Sinus Tachycardia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	0 / 18 (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			
Lymphadenitis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	0 / 18 (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
Neutropenia			

subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	1 / 18 (5.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Respiratory Failure			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	1 / 18 (5.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Pneumonia Bacterial			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	0 / 18 (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 Bronchiolitis			
subjects affected / exposed	0 / 8 (0.00%)	1 / 17 (5.88%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Multiple dose of ALS-008176 (60/40 mg/kg)	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 16 (0.00%)	2 / 50 (4.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			
Vascular disorders			
Phlebitis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 50 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Sinus Tachycardia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 50 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			

Lymphadenitis			
subjects affected / exposed	0 / 16 (0.00%)	1 / 50 (2.00%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 50 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Respiratory Failure			
subjects affected / exposed	0 / 16 (0.00%)	0 / 50 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Pneumonia Bacterial			
subjects affected / exposed	0 / 16 (0.00%)	1 / 50 (2.00%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory Syncytial Virus Bronchiolitis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 50 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Single dose of ALS-008176 (1.37 mg/kg)	Single dose of ALS-008176 (4.1 mg/kg)	Single dose of ALS-008176 (12 mg/kg)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	13 / 18 (72.22%)	8 / 18 (44.44%)	6 / 14 (42.86%)
Investigations			
Alanine Aminotransferase Increased			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Aspartate Aminotransferase Increased			

subjects affected / exposed	1 / 18 (5.56%)	0 / 18 (0.00%)	1 / 14 (7.14%)
occurrences (all)	1	0	1
Bilirubin Conjugated Increased			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Blood Alkaline Phosphatase Increased			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Blood Bicarbonate Decreased			
subjects affected / exposed	1 / 18 (5.56%)	0 / 18 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Blood Bilirubin Increased			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Blood Creatine Phosphokinase Increased			
subjects affected / exposed	1 / 18 (5.56%)	0 / 18 (0.00%)	1 / 14 (7.14%)
occurrences (all)	1	0	1
Blood Potassium Increased			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Blood Pressure Diastolic Increased			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Blood Pressure Systolic Increased			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Cardiac Murmur			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Electrocardiogram QT Prolonged			
subjects affected / exposed	1 / 18 (5.56%)	0 / 18 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Hepatic Enzyme Increased			

subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0	0 / 18 (0.00%) 0	1 / 14 (7.14%) 1
Lymphocyte Count Increased subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1	0 / 18 (0.00%) 0	0 / 14 (0.00%) 0
Monocyte Count Increased subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1	0 / 18 (0.00%) 0	0 / 14 (0.00%) 0
Neutrophil Count Decreased subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0	0 / 18 (0.00%) 0	0 / 14 (0.00%) 0
Platelet Count Increased subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1	0 / 18 (0.00%) 0	0 / 14 (0.00%) 0
Reticulocyte Count Increased subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0	0 / 18 (0.00%) 0	0 / 14 (0.00%) 0
Weight Decreased subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0	1 / 18 (5.56%) 1	0 / 14 (0.00%) 0
White Blood Cell Count Increased subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1	0 / 18 (0.00%) 0	0 / 14 (0.00%) 0
Injury, poisoning and procedural complications Contusion subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0	0 / 18 (0.00%) 0	0 / 14 (0.00%) 0
Cardiac disorders Bradycardia subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1	0 / 18 (0.00%) 0	0 / 14 (0.00%) 0
Sinus Tachycardia subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0	1 / 18 (5.56%) 1	0 / 14 (0.00%) 0
Tachycardia			

subjects affected / exposed	0 / 18 (0.00%)	1 / 18 (5.56%)	0 / 14 (0.00%)
occurrences (all)	0	1	0
Ventricular Extrasystoles			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Hyperleukocytosis			
subjects affected / exposed	1 / 18 (5.56%)	0 / 18 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Leukocytosis			
subjects affected / exposed	0 / 18 (0.00%)	1 / 18 (5.56%)	0 / 14 (0.00%)
occurrences (all)	0	1	0
Neutropenia			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Thrombocytosis			
subjects affected / exposed	4 / 18 (22.22%)	1 / 18 (5.56%)	1 / 14 (7.14%)
occurrences (all)	4	1	1
General disorders and administration site conditions			
Instillation Site Swelling			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Pyrexia			
subjects affected / exposed	1 / 18 (5.56%)	0 / 18 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Eye disorders			
Periorbital Oedema			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Abnormal Faeces			
subjects affected / exposed	1 / 18 (5.56%)	0 / 18 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0

Aphthous Ulcer subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0	0 / 18 (0.00%) 0	0 / 14 (0.00%) 0
Constipation subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0	1 / 18 (5.56%) 1	0 / 14 (0.00%) 0
Diarrhoea subjects affected / exposed occurrences (all)	2 / 18 (11.11%) 2	0 / 18 (0.00%) 0	1 / 14 (7.14%) 1
Vomiting subjects affected / exposed occurrences (all)	2 / 18 (11.11%) 3	1 / 18 (5.56%) 1	0 / 14 (0.00%) 0
Hepatobiliary disorders Hepatocellular Injury subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0	0 / 18 (0.00%) 0	0 / 14 (0.00%) 0
Respiratory, thoracic and mediastinal disorders Epistaxis subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0	0 / 18 (0.00%) 0	0 / 14 (0.00%) 0
Rhinorrhoea subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0	0 / 18 (0.00%) 0	0 / 14 (0.00%) 0
Upper Respiratory Tract Inflammation subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0	0 / 18 (0.00%) 0	0 / 14 (0.00%) 0
Skin and subcutaneous tissue disorders Dermatitis Contact subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0	0 / 18 (0.00%) 0	0 / 14 (0.00%) 0
Dermatitis Diaper subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0	1 / 18 (5.56%) 1	0 / 14 (0.00%) 0
Dry Skin subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1	0 / 18 (0.00%) 0	0 / 14 (0.00%) 0

Eczema			
subjects affected / exposed	1 / 18 (5.56%)	0 / 18 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Eczema Infantile			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Erythema			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Miliaria			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Rash			
subjects affected / exposed	1 / 18 (5.56%)	0 / 18 (0.00%)	1 / 14 (7.14%)
occurrences (all)	1	0	1
Rash Erythematous			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Rash Macular			
subjects affected / exposed	1 / 18 (5.56%)	0 / 18 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Rash Papular			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Seborrhoeic Dermatitis			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Skin Lesion			
subjects affected / exposed	1 / 18 (5.56%)	0 / 18 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Skin Reaction			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Adenovirus Infection			

subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Bronchitis			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Candida Infection			
subjects affected / exposed	0 / 18 (0.00%)	1 / 18 (5.56%)	0 / 14 (0.00%)
occurrences (all)	0	1	0
Conjunctivitis			
subjects affected / exposed	1 / 18 (5.56%)	1 / 18 (5.56%)	0 / 14 (0.00%)
occurrences (all)	1	1	0
Eye Infection Bacterial			
subjects affected / exposed	0 / 18 (0.00%)	1 / 18 (5.56%)	0 / 14 (0.00%)
occurrences (all)	0	1	0
Nasopharyngitis			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Otitis Media Acute			
subjects affected / exposed	0 / 18 (0.00%)	1 / 18 (5.56%)	0 / 14 (0.00%)
occurrences (all)	0	1	0
Otitis Media Viral			
subjects affected / exposed	0 / 18 (0.00%)	1 / 18 (5.56%)	0 / 14 (0.00%)
occurrences (all)	0	1	0
Pneumonia Bacterial			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Respiratory Syncytial Virus Bronchiolitis			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Tinea Infection			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Tonsillitis			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0

Upper Respiratory Tract Infection subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0	0 / 18 (0.00%) 0	0 / 14 (0.00%) 0
Urinary Tract Infection subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0	0 / 18 (0.00%) 0	0 / 14 (0.00%) 0
Viral Rash subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0	0 / 18 (0.00%) 0	0 / 14 (0.00%) 0
Viral Upper Respiratory Tract Infection subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0	0 / 18 (0.00%) 0	0 / 14 (0.00%) 0
Metabolism and nutrition disorders			
Fluid Overload subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0	0 / 18 (0.00%) 0	0 / 14 (0.00%) 0
Hyperglycaemia subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0	0 / 18 (0.00%) 0	0 / 14 (0.00%) 0
Hypokalaemia subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0	0 / 18 (0.00%) 0	0 / 14 (0.00%) 0
Hypomagnesaemia subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0	0 / 18 (0.00%) 0	0 / 14 (0.00%) 0

Non-serious adverse events	Single dose of ALS-008176 (25 mg/kg)	Multiple dose of ALS-008176 (4.1/1.37 mg/kg)	Multiple dose of ALS-008176 (10/2 mg/kg)
Total subjects affected by non-serious adverse events subjects affected / exposed	2 / 3 (66.67%)	4 / 5 (80.00%)	9 / 14 (64.29%)
Investigations			
Alanine Aminotransferase Increased subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	1 / 5 (20.00%) 1	1 / 14 (7.14%) 1
Aspartate Aminotransferase Increased			

subjects affected / exposed	0 / 3 (0.00%)	1 / 5 (20.00%)	2 / 14 (14.29%)
occurrences (all)	0	1	2
Bilirubin Conjugated Increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Blood Alkaline Phosphatase Increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Blood Bicarbonate Decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Blood Bilirubin Increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Blood Creatine Phosphokinase Increased			
subjects affected / exposed	0 / 3 (0.00%)	1 / 5 (20.00%)	0 / 14 (0.00%)
occurrences (all)	0	1	0
Blood Potassium Increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Blood Pressure Diastolic Increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Blood Pressure Systolic Increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Cardiac Murmur			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Electrocardiogram QT Prolonged			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Hepatic Enzyme Increased			

subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 5 (0.00%) 0	0 / 14 (0.00%) 0
Lymphocyte Count Increased subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 5 (0.00%) 0	0 / 14 (0.00%) 0
Monocyte Count Increased subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 5 (0.00%) 0	0 / 14 (0.00%) 0
Neutrophil Count Decreased subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 5 (0.00%) 0	0 / 14 (0.00%) 0
Platelet Count Increased subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 5 (0.00%) 0	0 / 14 (0.00%) 0
Reticulocyte Count Increased subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 5 (0.00%) 0	0 / 14 (0.00%) 0
Weight Decreased subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 5 (0.00%) 0	0 / 14 (0.00%) 0
White Blood Cell Count Increased subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	1 / 5 (20.00%) 1	0 / 14 (0.00%) 0
Injury, poisoning and procedural complications Contusion subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 5 (0.00%) 0	1 / 14 (7.14%) 1
Cardiac disorders Bradycardia subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 5 (0.00%) 0	0 / 14 (0.00%) 0
Sinus Tachycardia subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 5 (0.00%) 0	0 / 14 (0.00%) 0
Tachycardia			

subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 5 (0.00%) 0	0 / 14 (0.00%) 0
Ventricular Extrasystoles subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 5 (0.00%) 0	0 / 14 (0.00%) 0
Blood and lymphatic system disorders			
Anaemia subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 5 (0.00%) 0	0 / 14 (0.00%) 0
Hyperleukocytosis subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 5 (0.00%) 0	0 / 14 (0.00%) 0
Leukocytosis subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 5 (0.00%) 0	0 / 14 (0.00%) 0
Neutropenia subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 5 (0.00%) 0	0 / 14 (0.00%) 0
Thrombocytosis subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	1 / 5 (20.00%) 1	1 / 14 (7.14%) 1
General disorders and administration site conditions			
Instillation Site Swelling subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 5 (0.00%) 0	0 / 14 (0.00%) 0
Pyrexia subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 5 (0.00%) 0	0 / 14 (0.00%) 0
Eye disorders			
Periorbital Oedema subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 5 (0.00%) 0	0 / 14 (0.00%) 0
Gastrointestinal disorders			
Abnormal Faeces subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 5 (0.00%) 0	0 / 14 (0.00%) 0

Aphthous Ulcer subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 5 (0.00%) 0	0 / 14 (0.00%) 0
Constipation subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 5 (0.00%) 0	0 / 14 (0.00%) 0
Diarrhoea subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1	2 / 5 (40.00%) 2	2 / 14 (14.29%) 2
Vomiting subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1	0 / 5 (0.00%) 0	1 / 14 (7.14%) 1
Hepatobiliary disorders Hepatocellular Injury subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 5 (0.00%) 0	1 / 14 (7.14%) 1
Respiratory, thoracic and mediastinal disorders Epistaxis subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 5 (0.00%) 0	1 / 14 (7.14%) 2
Rhinorrhoea subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 5 (0.00%) 0	0 / 14 (0.00%) 0
Upper Respiratory Tract Inflammation subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 5 (0.00%) 0	0 / 14 (0.00%) 0
Skin and subcutaneous tissue disorders Dermatitis Contact subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 5 (0.00%) 0	1 / 14 (7.14%) 1
Dermatitis Diaper subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	2 / 5 (40.00%) 2	2 / 14 (14.29%) 2
Dry Skin subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 5 (0.00%) 0	0 / 14 (0.00%) 0

Eczema			
subjects affected / exposed	0 / 3 (0.00%)	2 / 5 (40.00%)	1 / 14 (7.14%)
occurrences (all)	0	2	1
Eczema Infantile			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Erythema			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Miliaria			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Rash			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Rash Erythematous			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Rash Macular			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Rash Papular			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Seborrhoeic Dermatitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Skin Lesion			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Skin Reaction			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Adenovirus Infection			

subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Bronchitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Candida Infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Conjunctivitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Eye Infection Bacterial			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Otitis Media Acute			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Otitis Media Viral			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Pneumonia Bacterial			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Respiratory Syncytial Virus Bronchiolitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Tinea Infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Tonsillitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 5 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0

Upper Respiratory Tract Infection subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 5 (0.00%) 0	1 / 14 (7.14%) 1
Urinary Tract Infection subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 5 (0.00%) 0	0 / 14 (0.00%) 0
Viral Rash subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 5 (0.00%) 0	0 / 14 (0.00%) 0
Viral Upper Respiratory Tract Infection subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 5 (0.00%) 0	0 / 14 (0.00%) 0
Metabolism and nutrition disorders			
Fluid Overload subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 5 (0.00%) 0	0 / 14 (0.00%) 0
Hyperglycaemia subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 5 (0.00%) 0	1 / 14 (7.14%) 1
Hypokalaemia subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 5 (0.00%) 0	0 / 14 (0.00%) 0
Hypomagnesaemia subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 5 (0.00%) 0	0 / 14 (0.00%) 0

Non-serious adverse events	Multiple dose of ALS-008176 (30/6 mg/kg)	Multiple dose of ALS-008176 (30/10 mg/kg)	Multiple dose of ALS-008176 (40/20 mg/kg)
Total subjects affected by non-serious adverse events subjects affected / exposed	4 / 8 (50.00%)	12 / 17 (70.59%)	12 / 18 (66.67%)
Investigations			
Alanine Aminotransferase Increased subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	0 / 17 (0.00%) 0	1 / 18 (5.56%) 1
Aspartate Aminotransferase Increased			

subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	3 / 18 (16.67%)
occurrences (all)	0	0	3
Bilirubin Conjugated Increased			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Blood Alkaline Phosphatase Increased			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Blood Bicarbonate Decreased			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Blood Bilirubin Increased			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Blood Creatine Phosphokinase Increased			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Blood Potassium Increased			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Blood Pressure Diastolic Increased			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Blood Pressure Systolic Increased			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Cardiac Murmur			
subjects affected / exposed	1 / 8 (12.50%)	0 / 17 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Electrocardiogram QT Prolonged			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Hepatic Enzyme Increased			

subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Lymphocyte Count Increased			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Monocyte Count Increased			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Neutrophil Count Decreased			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Platelet Count Increased			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Reticulocyte Count Increased			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Weight Decreased			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
White Blood Cell Count Increased			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Bradycardia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Sinus Tachycardia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Tachycardia			

subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Ventricular Extrasystoles			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 8 (0.00%)	1 / 17 (5.88%)	0 / 18 (0.00%)
occurrences (all)	0	3	0
Hyperleukocytosis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Leukocytosis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Neutropenia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	2 / 18 (11.11%)
occurrences (all)	0	0	2
Thrombocytosis			
subjects affected / exposed	1 / 8 (12.50%)	0 / 17 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
General disorders and administration site conditions			
Instillation Site Swelling			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	2 / 18 (11.11%)
occurrences (all)	0	0	2
Pyrexia			
subjects affected / exposed	0 / 8 (0.00%)	1 / 17 (5.88%)	1 / 18 (5.56%)
occurrences (all)	0	3	1
Eye disorders			
Periorbital Oedema			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Gastrointestinal disorders			
Abnormal Faeces			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0

Aphthous Ulcer subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	1 / 17 (5.88%) 1	0 / 18 (0.00%) 0
Constipation subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	0 / 17 (0.00%) 0	0 / 18 (0.00%) 0
Diarrhoea subjects affected / exposed occurrences (all)	1 / 8 (12.50%) 1	1 / 17 (5.88%) 2	2 / 18 (11.11%) 2
Vomiting subjects affected / exposed occurrences (all)	1 / 8 (12.50%) 1	3 / 17 (17.65%) 5	2 / 18 (11.11%) 3
Hepatobiliary disorders Hepatocellular Injury subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	0 / 17 (0.00%) 0	0 / 18 (0.00%) 0
Respiratory, thoracic and mediastinal disorders Epistaxis subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	0 / 17 (0.00%) 0	0 / 18 (0.00%) 0
Rhinorrhoea subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	0 / 17 (0.00%) 0	1 / 18 (5.56%) 1
Upper Respiratory Tract Inflammation subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	0 / 17 (0.00%) 0	0 / 18 (0.00%) 0
Skin and subcutaneous tissue disorders Dermatitis Contact subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	0 / 17 (0.00%) 0	0 / 18 (0.00%) 0
Dermatitis Diaper subjects affected / exposed occurrences (all)	1 / 8 (12.50%) 1	1 / 17 (5.88%) 1	0 / 18 (0.00%) 0
Dry Skin subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	0 / 17 (0.00%) 0	0 / 18 (0.00%) 0

Eczema			
subjects affected / exposed	0 / 8 (0.00%)	1 / 17 (5.88%)	1 / 18 (5.56%)
occurrences (all)	0	1	1
Eczema Infantile			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Erythema			
subjects affected / exposed	0 / 8 (0.00%)	2 / 17 (11.76%)	1 / 18 (5.56%)
occurrences (all)	0	2	2
Miliaria			
subjects affected / exposed	0 / 8 (0.00%)	1 / 17 (5.88%)	1 / 18 (5.56%)
occurrences (all)	0	1	1
Rash			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Rash Erythematous			
subjects affected / exposed	0 / 8 (0.00%)	1 / 17 (5.88%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Rash Macular			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Rash Papular			
subjects affected / exposed	1 / 8 (12.50%)	0 / 17 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Seborrhoeic Dermatitis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Skin Lesion			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Skin Reaction			
subjects affected / exposed	0 / 8 (0.00%)	1 / 17 (5.88%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Infections and infestations			
Adenovirus Infection			

subjects affected / exposed	0 / 8 (0.00%)	1 / 17 (5.88%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Bronchitis			
subjects affected / exposed	0 / 8 (0.00%)	1 / 17 (5.88%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Candida Infection			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Conjunctivitis			
subjects affected / exposed	1 / 8 (12.50%)	0 / 17 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Eye Infection Bacterial			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Otitis Media Acute			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Otitis Media Viral			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Pneumonia Bacterial			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Respiratory Syncytial Virus Bronchiolitis			
subjects affected / exposed	0 / 8 (0.00%)	1 / 17 (5.88%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Tinea Infection			
subjects affected / exposed	0 / 8 (0.00%)	0 / 17 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Tonsillitis			
subjects affected / exposed	0 / 8 (0.00%)	1 / 17 (5.88%)	0 / 18 (0.00%)
occurrences (all)	0	1	0

Upper Respiratory Tract Infection subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	1 / 17 (5.88%) 1	0 / 18 (0.00%) 0
Urinary Tract Infection subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	1 / 17 (5.88%) 1	0 / 18 (0.00%) 0
Viral Rash subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	0 / 17 (0.00%) 0	1 / 18 (5.56%) 1
Viral Upper Respiratory Tract Infection subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	1 / 17 (5.88%) 1	0 / 18 (0.00%) 0
Metabolism and nutrition disorders			
Fluid Overload subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	0 / 17 (0.00%) 0	1 / 18 (5.56%) 1
Hyperglycaemia subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	0 / 17 (0.00%) 0	0 / 18 (0.00%) 0
Hypokalaemia subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	0 / 17 (0.00%) 0	1 / 18 (5.56%) 1
Hypomagnesaemia subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0	0 / 17 (0.00%) 0	1 / 18 (5.56%) 1

Non-serious adverse events	Multiple dose of ALS-008176 (60/40 mg/kg)	Placebo	
Total subjects affected by non-serious adverse events subjects affected / exposed	14 / 16 (87.50%)	22 / 50 (44.00%)	
Investigations			
Alanine Aminotransferase Increased subjects affected / exposed occurrences (all)	3 / 16 (18.75%) 3	0 / 50 (0.00%) 0	
Aspartate Aminotransferase Increased			

subjects affected / exposed	3 / 16 (18.75%)	2 / 50 (4.00%)	
occurrences (all)	3	2	
Bilirubin Conjugated Increased			
subjects affected / exposed	1 / 16 (6.25%)	0 / 50 (0.00%)	
occurrences (all)	1	0	
Blood Alkaline Phosphatase Increased			
subjects affected / exposed	1 / 16 (6.25%)	0 / 50 (0.00%)	
occurrences (all)	1	0	
Blood Bicarbonate Decreased			
subjects affected / exposed	0 / 16 (0.00%)	0 / 50 (0.00%)	
occurrences (all)	0	0	
Blood Bilirubin Increased			
subjects affected / exposed	1 / 16 (6.25%)	0 / 50 (0.00%)	
occurrences (all)	1	0	
Blood Creatine Phosphokinase Increased			
subjects affected / exposed	0 / 16 (0.00%)	1 / 50 (2.00%)	
occurrences (all)	0	1	
Blood Potassium Increased			
subjects affected / exposed	0 / 16 (0.00%)	0 / 50 (0.00%)	
occurrences (all)	0	0	
Blood Pressure Diastolic Increased			
subjects affected / exposed	0 / 16 (0.00%)	0 / 50 (0.00%)	
occurrences (all)	0	0	
Blood Pressure Systolic Increased			
subjects affected / exposed	0 / 16 (0.00%)	0 / 50 (0.00%)	
occurrences (all)	0	0	
Cardiac Murmur			
subjects affected / exposed	0 / 16 (0.00%)	0 / 50 (0.00%)	
occurrences (all)	0	0	
Electrocardiogram QT Prolonged			
subjects affected / exposed	0 / 16 (0.00%)	0 / 50 (0.00%)	
occurrences (all)	0	0	
Hepatic Enzyme Increased			

subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	0 / 50 (0.00%) 0	
Lymphocyte Count Increased subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	0 / 50 (0.00%) 0	
Monocyte Count Increased subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	0 / 50 (0.00%) 0	
Neutrophil Count Decreased subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	0 / 50 (0.00%) 0	
Platelet Count Increased subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	2 / 50 (4.00%) 2	
Reticulocyte Count Increased subjects affected / exposed occurrences (all)	2 / 16 (12.50%) 2	1 / 50 (2.00%) 1	
Weight Decreased subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	0 / 50 (0.00%) 0	
White Blood Cell Count Increased subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	1 / 50 (2.00%) 1	
Injury, poisoning and procedural complications Contusion subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	0 / 50 (0.00%) 0	
Cardiac disorders Bradycardia subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	0 / 50 (0.00%) 0	
Sinus Tachycardia subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	0 / 50 (0.00%) 0	
Tachycardia			

subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	0 / 50 (0.00%) 0	
Ventricular Extrasystoles subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	0 / 50 (0.00%) 0	
Blood and lymphatic system disorders			
Anaemia subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	1 / 50 (2.00%) 1	
Hyperleukocytosis subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	0 / 50 (0.00%) 0	
Leukocytosis subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1	0 / 50 (0.00%) 0	
Neutropenia subjects affected / exposed occurrences (all)	3 / 16 (18.75%) 3	1 / 50 (2.00%) 1	
Thrombocytosis subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1	1 / 50 (2.00%) 1	
General disorders and administration site conditions			
Instillation Site Swelling subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	0 / 50 (0.00%) 0	
Pyrexia subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1	1 / 50 (2.00%) 2	
Eye disorders			
Periorbital Oedema subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	0 / 50 (0.00%) 0	
Gastrointestinal disorders			
Abnormal Faeces subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	0 / 50 (0.00%) 0	

Aphthous Ulcer subjects affected / exposed occurrences (all)	0 / 16 (0.00%)	0 / 50 (0.00%)	
	0	0	
Constipation subjects affected / exposed occurrences (all)	0 / 16 (0.00%)	0 / 50 (0.00%)	
	0	0	
Diarrhoea subjects affected / exposed occurrences (all)	3 / 16 (18.75%)	5 / 50 (10.00%)	
	3	5	
Vomiting subjects affected / exposed occurrences (all)	5 / 16 (31.25%)	2 / 50 (4.00%)	
	9	2	
Hepatobiliary disorders Hepatocellular Injury subjects affected / exposed occurrences (all)	0 / 16 (0.00%)	0 / 50 (0.00%)	
	0	0	
Respiratory, thoracic and mediastinal disorders Epistaxis subjects affected / exposed occurrences (all)	0 / 16 (0.00%)	1 / 50 (2.00%)	
	0	3	
Skin and subcutaneous tissue disorders Dermatitis Contact subjects affected / exposed occurrences (all)	1 / 16 (6.25%)	0 / 50 (0.00%)	
	1	0	
Dermatitis Diaper subjects affected / exposed occurrences (all)	3 / 16 (18.75%)	4 / 50 (8.00%)	
	3	4	
Dry Skin subjects affected / exposed occurrences (all)	1 / 16 (6.25%)	0 / 50 (0.00%)	
	1	0	

Eczema			
subjects affected / exposed	1 / 16 (6.25%)	1 / 50 (2.00%)	
occurrences (all)	1	1	
Eczema Infantile			
subjects affected / exposed	1 / 16 (6.25%)	0 / 50 (0.00%)	
occurrences (all)	1	0	
Erythema			
subjects affected / exposed	0 / 16 (0.00%)	1 / 50 (2.00%)	
occurrences (all)	0	1	
Miliaria			
subjects affected / exposed	0 / 16 (0.00%)	0 / 50 (0.00%)	
occurrences (all)	0	0	
Rash			
subjects affected / exposed	1 / 16 (6.25%)	2 / 50 (4.00%)	
occurrences (all)	1	2	
Rash Erythematous			
subjects affected / exposed	0 / 16 (0.00%)	0 / 50 (0.00%)	
occurrences (all)	0	0	
Rash Macular			
subjects affected / exposed	0 / 16 (0.00%)	0 / 50 (0.00%)	
occurrences (all)	0	0	
Rash Papular			
subjects affected / exposed	0 / 16 (0.00%)	0 / 50 (0.00%)	
occurrences (all)	0	0	
Seborrhoeic Dermatitis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 50 (0.00%)	
occurrences (all)	0	0	
Skin Lesion			
subjects affected / exposed	0 / 16 (0.00%)	0 / 50 (0.00%)	
occurrences (all)	0	0	
Skin Reaction			
subjects affected / exposed	0 / 16 (0.00%)	1 / 50 (2.00%)	
occurrences (all)	0	1	
Infections and infestations			
Adenovirus Infection			

subjects affected / exposed	0 / 16 (0.00%)	0 / 50 (0.00%)
occurrences (all)	0	0
Bronchitis		
subjects affected / exposed	0 / 16 (0.00%)	1 / 50 (2.00%)
occurrences (all)	0	1
Candida Infection		
subjects affected / exposed	0 / 16 (0.00%)	0 / 50 (0.00%)
occurrences (all)	0	0
Conjunctivitis		
subjects affected / exposed	1 / 16 (6.25%)	1 / 50 (2.00%)
occurrences (all)	1	1
Eye Infection Bacterial		
subjects affected / exposed	0 / 16 (0.00%)	0 / 50 (0.00%)
occurrences (all)	0	0
Nasopharyngitis		
subjects affected / exposed	1 / 16 (6.25%)	4 / 50 (8.00%)
occurrences (all)	1	5
Otitis Media Acute		
subjects affected / exposed	0 / 16 (0.00%)	0 / 50 (0.00%)
occurrences (all)	0	0
Otitis Media Viral		
subjects affected / exposed	0 / 16 (0.00%)	0 / 50 (0.00%)
occurrences (all)	0	0
Pneumonia Bacterial		
subjects affected / exposed	0 / 16 (0.00%)	1 / 50 (2.00%)
occurrences (all)	0	1
Respiratory Syncytial Virus Bronchiolitis		
subjects affected / exposed	0 / 16 (0.00%)	0 / 50 (0.00%)
occurrences (all)	0	0
Tinea Infection		
subjects affected / exposed	0 / 16 (0.00%)	0 / 50 (0.00%)
occurrences (all)	0	0
Tonsillitis		
subjects affected / exposed	0 / 16 (0.00%)	0 / 50 (0.00%)
occurrences (all)	0	0

Upper Respiratory Tract Infection subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	2 / 50 (4.00%) 2	
Urinary Tract Infection subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	0 / 50 (0.00%) 0	
Viral Rash subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	0 / 50 (0.00%) 0	
Viral Upper Respiratory Tract Infection subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	0 / 50 (0.00%) 0	
Metabolism and nutrition disorders			
Fluid Overload subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	0 / 50 (0.00%) 0	
Hyperglycaemia subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	0 / 50 (0.00%) 0	
Hypokalaemia subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	0 / 50 (0.00%) 0	
Hypomagnesaemia subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	0 / 50 (0.00%) 0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
19 December 2013	Instituted sentinel groups and age de-escalation; refined age strata.
17 December 2014	Independent Data Monitoring Committee (IDMC) authorized to change doses to be studied within defined limits; eligibility criteria related to hospitalization duration, Respiratory syncytial virus (RSV) symptoms duration, and concomitant medications updated.
24 August 2015	Follow up Day 28 visit added; initial Japanese Multiple ascending dose (MAD) cohort will be a lower dose than subjects in rest of world; RSV diagnosis for eligibility can be performed using any RSV assay; allowance of corticosteroids clarified; IDMC authorized to determine appropriate timing for transition from single ascending dose (SAD) to MAD part of study.
22 January 2016	Added cohort of neonate subjects; allow every 12 hours or twice daily dosing; disallow substrates for Organic Anion Transporter 3 (OAT3) transporter and RSV prophylactic medications.
13 September 2016	Potential additional cohorts added; further defined IDMC authority for decision making within defined limits; Japanese subjects will now be dosed at same dose levels as subjects in rest of world; Nasal aspirate changed to nasal swab procedure; updated eligibility criteria related to RSV symptoms duration; study drug can be administered without regard to food.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
10 December 2016	Enrollment paused for evaluation of neutropenia	12 May 2017

Notes:

Limitations and caveats

None reported