Clinical trial results:
An open-label, adaptive design study in patients with amyotrophic lateral sclerosis (ALS) to characterize safety, tolerability and brain microglia response, as measured by TSPO binding, following multiple doses of BLZ945 using positron emission tomography (PET) with the radioligand[11C]-PBR28

Summary

EudraCT number	2019-000826-22
Trial protocol	SE FI
Global end of trial date	01 February 2024

Results information

Result version number	v1
This version publication date	13 February 2025
First version publication date	13 February 2025

Trial information

Trial identification

Sponsor protocol code	CBLZ945C12201

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04066244
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Novartis Pharma AG
Sponsor organisation address	Novartis Campus, Basel, Switzerland,
Public contact	Clinical Disclosure Office, Novartis Pharma AG, 41 613241111, Novartis.email@Novartis.com
Scientific contact	Clinical Disclosure Office, Novartis Pharma AG, 41 613241111, Novartis.email@Novartis.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	01 February 2024
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	01 February 2024
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

•Cohorts 1-4 and Cohort 5 (PET Sub-study): To evaluate brain microglial reduction, as measured by reduction in TSPO binding, following treatment with BLZ945 in ALS participants by using PET imaging with [11C]-PBR28

•Cohort 5: To assess safety-related effects on ECM accumulation under BLZ945 treatment

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and the International Conference on Harmonization (ICH) Good Clinical Practice (GCP) guidelines. All the local regulatory requirements pertinent to safety of trial subjects were also followed during the conduct of the trial.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	30 December 2019
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	United States: 8
Country: Number of subjects enrolled	Finland: 8
Country: Number of subjects enrolled	Sweden: 12
Worldwide total number of subjects	28
EEA total number of subjects	20

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0

Adults (18-64 years)	20
From 65 to 84 years	8
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

There was a screening and baseline period of up to 42 days for part 1 (Cohorts1-4) and of 6 weeks for part 2 (Cohort 5)

Period 1

Period 1 title	Overall study (Part 1 + Part 2) (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	BLZ945 300mg - Cohort 1 (Part 1)

Arm description:

BLZ945 300mg

Arm type	Experimental
Investigational medicinal product name	Sotuletinib
Investigational medicinal product code	BLZ945
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

300mg/day for 4 days

Arm title	BLZ945 600mg - Cohort 2 (Part 1)

Arm description:

BLZ945 600mg

Arm type	Experimental
Investigational medicinal product name	Sotuletinib
Investigational medicinal product code	BLZ945
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

600mg/day for 4 days

Arm title	BLZ945 800mg - Cohort 4 (Part 1)

Arm description:

BLZ945 800mg

Arm type	Experimental
Investigational medicinal product name	Sotuletinib
Investigational medicinal product code	BLZ945
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

800mg/day for 4 days

Arm title	BLZ945 1200mg - Cohort 3 (Part 1)
Arm description: BLZ945 1200mg	
Arm type	Experimental
Investigational medicinal product name	Sotuletinib
Investigational medicinal product code	BLZ945
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use
Dosage and administration details: 1200mg/day for 4 days	
Arm title	BLZ945 800mg - Cohort 5 Arm #1 (Part 2)
Arm description: BLZ945 800mg (4 days on/10 days off)	
Arm type	Experimental
Investigational medicinal product name	Sotuletinib
Investigational medicinal product code	BLZ945
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use, Enteral use
Dosage and administration details: 800mg in repeated cycles of 4 days on treatment followed by 10 days off for 12 weeks	
Arm title	BLZ945 800mg - Cohort 5 Arm #2 (Part 2)
Arm description: BLZ945 800mg (once weekly)	
Arm type	Experimental
Investigational medicinal product name	Sotuletinib
Investigational medicinal product code	BLZ945
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use, Enteral use
Dosage and administration details: 800mg once weekly for 12 weeks	

Number of subjects in period 1	BLZ945 300mg - Cohort 1 (Part 1)	BLZ945 600mg - Cohort 2 (Part 1)	BLZ945 800mg - Cohort 4 (Part 1)
Started	4	4	4
Completed	4	4	4
Not completed	0	0	0
Consent withdrawn by subject	-	-	-
Adverse Event	-	-	-
Death	-	-	-
Study terminated by sponsor	-	-	-

Number of subjects in period 1	BLZ945 1200mg - Cohort 3 (Part 1)	BLZ945 800mg - Cohort 5 Arm #1 (Part 2)	BLZ945 800mg - Cohort 5 Arm #2 (Part 2)

Started	4	6	6
Completed	4	5	2
Not completed	0	1	4
Consent withdrawn by subject	-	1	-
Adverse Event	-	-	1
Death	-	-	2
Study terminated by sponsor	-	-	1

Baseline characteristics

Reporting groups	
Reporting group title	BLZ945 300mg - Cohort 1 (Part 1)
Reporting group description: BLZ945 300mg	
Reporting group title	BLZ945 600mg - Cohort 2 (Part 1)
Reporting group description: BLZ945 600mg	
Reporting group title	BLZ945 800mg - Cohort 4 (Part 1)
Reporting group description: BLZ945 800mg	
Reporting group title	BLZ945 1200mg - Cohort 3 (Part 1)
Reporting group description: BLZ945 1200mg	
Reporting group title	BLZ945 800mg - Cohort 5 Arm #1 (Part 2)
Reporting group description: BLZ945 800mg (4 days on/10 days off)	
Reporting group title	BLZ945 800mg - Cohort 5 Arm #2 (Part 2)
Reporting group description: BLZ945 800mg (once weekly)	

Reporting group values	BLZ945 300mg - Cohort 1 (Part 1)	BLZ945 600mg - Cohort 2 (Part 1)	BLZ945 800mg - Cohort 4 (Part 1)
Number of subjects	4	4	4
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	4	3	2
From 65-84 years	0	1	2
85 years and over	0	0	0
Age Continuous Units: years			
median	50.5	59.5	65.5
full range (min-max)	46 to 58	33 to 76	56 to 68
Sex: Female, Male Units: Participants			
Female	2	2	1
Male	2	2	3
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	0	0	0

Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	0	0
White	4	3	4
More than one race	0	0	0
Unknown or Not Reported	0	1	0

Reporting group values	BLZ945 1200mg - Cohort 3 (Part 1)	BLZ945 800mg - Cohort 5 Arm #1 (Part 2)	BLZ945 800mg - Cohort 5 Arm #2 (Part 2)
Number of subjects	4	6	6
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	1	5	5
From 65-84 years	3	1	1
85 years and over	0	0	0
Age Continuous Units: years			
median	64	55.5	62.5
full range (min-max)	62 to 68	52 to 74	32 to 67
Sex: Female, Male Units: Participants			
Female	2	1	2
Male	2	5	4
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	0	0
White	4	6	6
More than one race	0	0	0
Unknown or Not Reported	0	0	0

Reporting group values	Total		
Number of subjects	28		
Age categorical Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	0		
Newborns (0-27 days)	0		
Infants and toddlers (28 days-23 months)	0		
Children (2-11 years)	0		

Adolescents (12-17 years)	0		
Adults (18-64 years)	20		
From 65-84 years	8		
85 years and over	0		
Age Continuous Units: years median full range (min-max)	 -		
Sex: Female, Male Units: Participants			
Female	10		
Male	18		
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0		
Asian	0		
Native Hawaiian or Other Pacific Islander	0		
Black or African American	0		
White	27		
More than one race	0		
Unknown or Not Reported	1		

End points

End points reporting groups

Reporting group title	BLZ945 300mg - Cohort 1 (Part 1)
Reporting group description: BLZ945 300mg	
Reporting group title	BLZ945 600mg - Cohort 2 (Part 1)
Reporting group description: BLZ945 600mg	
Reporting group title	BLZ945 800mg - Cohort 4 (Part 1)
Reporting group description: BLZ945 800mg	
Reporting group title	BLZ945 1200mg - Cohort 3 (Part 1)
Reporting group description: BLZ945 1200mg	
Reporting group title	BLZ945 800mg - Cohort 5 Arm #1 (Part 2)
Reporting group description: BLZ945 800mg (4 days on/10 days off)	
Reporting group title	BLZ945 800mg - Cohort 5 Arm #2 (Part 2)
Reporting group description: BLZ945 800mg (once weekly)	

Primary: Cohorts 1-4 : Change from baseline in volume of distribution (Vt) in different brain regions for [11C]-PBR28 PET scan

End point title	Cohorts 1-4 : Change from baseline in volume of distribution (Vt) in different brain regions for [11C]-PBR28 PET scan[1][2]

End point description:

[11C]-PBR28 is a positron emission tomography (PET) radiotracer for the 18 kDa translocator protein (TSPO) that is used to image neuroinflammation in vivo. [11C]PBR28 imaging was used to measure microglial activation at baseline and after BLZ945 treatment in ALS participants.

Relative % change from baseline in volume of distribution (Vt) of [11C]-PBR28 in different brain regions after BLZ945 treatment.

No statistical analysis was planned for this primary outcome.

End point type	Primary

End point timeframe:

Baseline, day 5

Notes:

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

[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: This endpoint was planned to be applicable only to cohorts 1-4

End point values	BLZ945 300mg - Cohort 1 (Part 1)	BLZ945 600mg - Cohort 2 (Part 1)	BLZ945 800mg - Cohort 4 (Part 1)	BLZ945 1200mg - Cohort 3 (Part 1)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	3	4	2
Units: Percent change from baseline				
arithmetic mean (standard deviation)				
Precentral gyrus - day 5	0.67 (± 33.825)	-20.33 (± 16.458)	9.90 (± 31.570)	-9.63 (± 1.516)
Basal Ganglia - day 5	-3.70 (± 22.729)	-15.18 (± 16.343)	13.27 (± 35.504)	-10.73 (± 5.872)
Brain Stem - day 5	-7.10 (± 20.890)	-10.00 (± 13.464)	50.56 (± 100.838)	-16.69 (± 61.674)
Cerebellar White Matter - day 5	-4.41 (± 20.678)	-14.11 (± 11.904)	27.65 (± 60.112)	-16.87 (± 4.874)
Cerebellum - day 5	-3.53 (± 20.459)	-10.06 (± 8.365)	17.52 (± 44.628)	-11.78 (± 3.854)
Frontal Lobe - day 5	1.33 (± 30.101)	-18.67 (± 15.881)	9.10 (± 29.745)	-9.70 (± 0.224)
Occipital Lobe - day 5	-3.01 (± 23.217)	-11.50 (± 10.457)	14.18 (± 36.595)	-5.87 (± 0.292)
Thalamus - day 5	-8.00 (± 22.581)	-14.85 (± 13.466)	13.89 (± 42.938)	-14.14 (± 3.521)
Whole Brain - day 5	-0.95 (± 26.606)	-15.59 (± 14.716)	12.22 (± 34.922)	-7.72 (± 0.326)

Statistical analyses

No statistical analyses for this end point

Primary: Cohort 5 (PET sub-study): Change from baseline in volume of distribution (Vt) in different brain regions for [11C]-PBR28 PET scan

End point title	Cohort 5 (PET sub-study): Change from baseline in volume of distribution (Vt) in different brain regions for [11C]-PBR28 PET scan[3][4]

End point description:

[11C]-PBR28 is a positron emission tomography (PET) radiotracer for the 18 kDa translocator protein (TSPO) that is used to image neuroinflammation in vivo. [11C]PBR28 imaging was used to measure microglial activation at baseline and after BLZ945 treatment in ALS participants.

Relative % change from baseline in volume of distribution (Vt) of [11C]-PBR28 in different brain regions after BLZ945 treatment.

No statistical analysis was planned for this primary outcome.

End point type	Primary

End point timeframe:

Baseline, day 84

Notes:

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

[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: This endpoint was planned to be applicable only to cohort 5

End point values	BLZ945 800mg - Cohort 5 Arm #1 (Part 2)	BLZ945 800mg - Cohort 5 Arm #2 (Part 2)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1	0[5]		
Units: Percent change from baseline				
arithmetic mean (standard deviation)				
Precentral gyrus - day 84	-21.95 (± 999)	()		
Basal Ganglia - day 84	-17.18 (± 999)	()		
Brain Stem - day 84	-26.10 (± 999)	()		
Cerebellar White Matter - day 84	-22.40 (± 999)	()		
Cerebellum - day 84	-19.40 (± 999)	()		
Frontal Lobe - day 84	-21.53 (± 999)	()		
Occipital Lobe - day 84	-17.76 (± 999)	()		
Thalamus - day 84	-29.39 (± 999)	()		
Whole Brain - day 84	-20.51 (± 999)	()		

Notes:

[5] - 0 participants with a valid assessment of the outcome measure.

Statistical analyses

No statistical analyses for this end point

Primary: Cohort 5: Change from baseline in esophageal wall thickness

End point title	Cohort 5: Change from baseline in esophageal wall

End point description:

Mean change from baseline in esophageal wall thickness measured in mm.

No statistical analysis was planned for this primary outcome.

End point type	Primary

End point timeframe:

Baseline, Day 84

Notes:

[6] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analysis was planned for this primary outcome.

[7] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was planned to be applicable only to cohort 5

End point values	BLZ945 800mg - Cohort 5 Arm #1 (Part 2)	BLZ945 800mg - Cohort 5 Arm #2 (Part 2)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	2		
Units: mm				
arithmetic mean (standard deviation)				
Wall thickness average	0.258 (± 0.7990)	0.758 (± 2.1708)		
Lower third Wall Thickness	0.040 (± 0.9475)	-1.400 (± 2.9981)		
Middle third Wall Thickness	0.235 (± 0.0212)	2.795 (± 2.6234)		
Upper third Wall Thickness	0.500 (± 1.4284)	0.880 (± 0.8910)		

Statistical analyses

No statistical analyses for this end point

Primary: Cohort 5: Cardiac valve thickness at day 84 compared to baseline

End point title	Cohort 5: Cardiac valve thickness at day 84 compared to baseline[8][9]

End point description:

Cardiac valve thickness on a three point ordinal scale. Categorized by imaging vendor into three semiquantitative (normal, mild-moderate and severe) categories. Cardiac valves evaluated are aortic valve (AV), mitral valve (MV), Pulmonary valve (PV) and Tricuspid valve (TV).

No statistical analysis was planned for this primary outcome.

End point type	Primary

End point timeframe:

Baseline, Day 84

Notes:

[8] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analysis was planned for this primary outcome.

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

End point values	BLZ945 800mg - Cohort 5 Arm #1 (Part 2)	BLZ945 800mg - Cohort 5 Arm #2 (Part 2)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	6		
Units: Participants				
Baseline AV thickness - Normal	6	6		
Day 84 AV thickness - Normal (n=2)	2	2		
Baseline MV thickness - Normal	6	5		
Baseline MV thickness - Mild-Moderate	0	1		
Day 84 MV thickness - Normal (n=2)	2	2		
Baseline PV thickness - Normal	6	6		
Day 84 PV thickness - Normal (n=2)	2	2		
Baseline TV thickness - Normal	6	6		
Day 84 TV thickness - Normal (n=2)	2	2		

Statistical analyses

No statistical analyses for this end point

Primary: Cohort 5: Cardiac valve stenosis at day 84 compared to baseline

End point title	Cohort 5: Cardiac valve stenosis at day 84 compared to baseline[10][11]

End point description:

Cardiac valve stenosis on a four point ordinal scale. Categorized by imaging vendor into four semiquantitative (normal, mild, moderate and severe) categories. ardiac valves evaluated are aortic valve (AV), mitral valve (MV), Pulmonary valve (PV) and Tricuspid valve (TV).

No statistical analysis was planned for this primary outcome.

End point type	Primary

End point timeframe:

Baseline, Day 84

Notes:

[10] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analysis was planned for this primary outcome.

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

End point values	BLZ945 800mg - Cohort 5 Arm #1 (Part 2)	BLZ945 800mg - Cohort 5 Arm #2 (Part 2)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	6		
Units: Participants				
Baseline AV stenosis - Normal	6	6		
Day 84 AV stenosis - Normal (n=2)	2	2		
Baseline MV stenosis - Normal	6	6		
Day 84 MV stenosis - Normal (n=2)	2	2		
Baseline PV stenosis - Normal	6	6		
Day 84 PV stenosis - Normal (n=2)	2	2		
Baseline TV stenosis - Normal	6	6		
Day 84 TV stenosis - Normal (n=2)	2	2		

Statistical analyses

No statistical analyses for this end point

Primary: Cohort 5: Cardiac valve regurgitation severity at day 84 compared to baseline

End point title	Cohort 5: Cardiac valve regurgitation severity at day 84 compared to baseline[12][13]

End point description:

Cardiac valve regurgitation severity on a four point ordinal scale. Categorized by imaging vendor into four semiquantitative (normal, mild, moderate and severe) categories. ardiac valves evaluated are aortic valve (AV), mitral valve (MV), Pulmonary valve (PV) and Tricuspid valve (TV).

No statistical analysis was planned for this primary outcome.

End point type	Primary

End point timeframe:

Baseline, Day 84

Notes:

[12] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analysis was planned for this primary outcome.

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

End point values	BLZ945 800mg - Cohort 5 Arm #1 (Part 2)	BLZ945 800mg - Cohort 5 Arm #2 (Part 2)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	6		
Units: Participants				
Baseline AV regurgitation - Normal	5	6		
Baseline AV regurgitation - Mild	1	0		
Day 84 AV regurgitation - Normal	2	2		
Day 84 AV regurgitation - Mild	0	0		
Baseline MV regurgitation - Normal	3	3		
Baseline MV regurgitation - mild	3	3		
Day 84 MV regurgitation - Normal	0	1		
Day 84 MV regurgitation - Mild	2	1		
Baseline PV regurgitation - Normal	3	4		
Baseline PV regurgitation - Mild	3	2		
Day 84 PV regurgitation - Normal	2	1		
Day 84 PV regurgitation - Mild	0	1		
Baseline TV regurgitation - Normal	3	2		
Baseline TV regurgitation - Mild	3	4		
Day 84 TV regurgitation - Normal	1	1		
Day 84 TV regurgitation - Mild	1	1		

Statistical analyses

No statistical analyses for this end point

Primary: Cohort 5: Adverse events related to Extracellular matrix (ECM) accumulation

End point title	Cohort 5: Adverse events related to Extracellular matrix (ECM) accumulation[14][15]

End point description:

Number of patients with adverse events related to ECM accumulation.

No statistical analysis was planned for this primary outcome.

End point type	Primary

End point timeframe:

Up to Day 84

Notes:

[14] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analysis was planned for this primary outcome.

[15] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was planned to be applicable only to cohort 5

End point values	BLZ945 800mg - Cohort 5 Arm #1 (Part 2)	BLZ945 800mg - Cohort 5 Arm #2 (Part 2)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	6		
Units: Participants	2	2		

Statistical analyses

No statistical analyses for this end point

Primary: Cohort 5: Change from baseline in Left Ventricular Ejection Fraction (LVEF).

End point title	Cohort 5: Change from baseline in Left Ventricular Ejection Fraction (LVEF).[16][17]

End point description:

Mean change from baseline in Left Ventricular Ejection Fraction.

LVEF is defined as the percentage of blood volume ejected from the left ventricle during systole (contraction phase) relative to the total volume of blood present in the ventricle at the end of diastole (relaxation phase).

No statistical analysis was planned for this primary outcome.

End point type	Primary

End point timeframe:

Baseline, day 84

Notes:

[16] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analysis was planned for this primary outcome.

[17] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was planned to be applicable only to cohort 5

End point values	BLZ945 800mg - Cohort 5 Arm #1 (Part 2)	BLZ945 800mg - Cohort 5 Arm #2 (Part 2)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2	2		
Units: Change from baseline				
arithmetic mean (standard deviation)	1.533 (± 2.9713)	5.021 (± 2.0796)		

Statistical analyses

No statistical analyses for this end point

Secondary: Cohorts 1-5: Plasma Pharmacokinetics (PK) of BLZ945 - Cmax

End point title	Cohorts 1-5: Plasma Pharmacokinetics (PK) of BLZ945 - Cmax

End point description:

Measured by Cmax - The maximum plasma concentration of BLZ945

End point type	Secondary

End point timeframe:

Cohort 1-4: Pre-dose, 0.5, 1, 2, 4, 6, 8, 12 and 24 hours after BLZ945 dosing on Day 1 and Day 4.
Cohort 5: pre-dose, 1, 2 and 4 hours after BLZ945 dosing on Day 1 (Arm#2 only) and Day 4 (Arm#1 only)

End point values	BLZ945 300mg - Cohort 1 (Part 1)	BLZ945 600mg - Cohort 2 (Part 1)	BLZ945 800mg - Cohort 4 (Part 1)	BLZ945 1200mg - Cohort 3 (Part 1)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	4	4	3
Units: ng/mL of BLZ945				
arithmetic mean (standard deviation)				
Day 1	6850 (± 780)	16000 (± 2510)	21100 (± 5630)	25900 (± 2630)
Day 4	12100 (± 2300)	25900 (± 3440)	30700 (± 7800)	37600 (± 4270)

End point values	BLZ945 800mg - Cohort 5 Arm #1 (Part 2)	BLZ945 800mg - Cohort 5 Arm #2 (Part 2)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4[18]	6[19]		
Units: ng/mL of BLZ945				
arithmetic mean (standard deviation)				
Day 1	999 (± 999)	19900 (± 5990)		
Day 4	22400 (± 3120)	999 (± 999)		

Notes:

[18] - 0 participants analyzed at day 1

[19] - 0 participants analyzed at day 4

Statistical analyses

No statistical analyses for this end point

Secondary: Cohorts 1-5: Plasma Pharmacokinetics (PK) of BLZ945 - Tmax

End point title	Cohorts 1-5: Plasma Pharmacokinetics (PK) of BLZ945 - Tmax

End point description:

Measured by Tmax - Time to Reach the Maximum Concentration After Drug Administration of BLZ945.

Actual recorded sampling times were taken into consideration for the calculation of PK parameters.

End point type	Secondary

End point timeframe:

Cohort 1-4: Pre-dose, 0.5, 1, 2, 4, 6, 8, 12 and 24 hours after BLZ945 dosing on Day 1 and Day 4.
Cohort 5: pre-dose, 1, 2 and 4 hours after BLZ945 dosing on Day 1 (Arm#2 only) and Day 4 (Arm#1 only)

End point values	BLZ945 300mg - Cohort 1 (Part 1)	BLZ945 600mg - Cohort 2 (Part 1)	BLZ945 800mg - Cohort 4 (Part 1)	BLZ945 1200mg - Cohort 3 (Part 1)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	4	4	3
Units: hours				
median (full range (min-max))				
Day 1	1.02 (1.00 to 1.07)	2.01 (1.00 to 2.08)	2.01 (1.00 to 7.00)	1.00 (1.00 to 1.00)
Day 4	1.01 (0.500 to 1.03)	1.50 (1.00 to 4.00)	3.00 (1.00 to 6.08)	2.02 (1.00 to 4.00)

End point values	BLZ945 800mg - Cohort 5 Arm #1 (Part 2)	BLZ945 800mg - Cohort 5 Arm #2 (Part 2)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4[20]	6[21]		
Units: hours				
median (full range (min-max))				
Day 1	999 (999 to 999)	2.00 (1.00 to 4.17)		
Day 4	1.49 (0.817 to 2.00)	999 (999 to 999)		

Notes:

[20] - 0 participants analyzed at day 1

[21] - 0 participants analyzed at day 4

Statistical analyses

No statistical analyses for this end point

Secondary: Cohorts 1-5: Plasma Pharmacokinetics (PK) of BLZ945 - AUC

End point title	Cohorts 1-5: Plasma Pharmacokinetics (PK) of BLZ945 - AUC

End point description:

Measured by AUC - Area under the curve of BLZ945

AUC0-24h is the AUC calculated from time zero to 24 hours after dosing (end of a dosing interval).

AUClast is the AUC from time zero to the last measurable concentration sampling time.

End point type	Secondary

End point timeframe:

Day 1; Day 4

End point values	BLZ945 300mg - Cohort 1 (Part 1)	BLZ945 600mg - Cohort 2 (Part 1)	BLZ945 800mg - Cohort 4 (Part 1)	BLZ945 1200mg - Cohort 3 (Part 1)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	4	4	3
Units: hour * ng/mL				
arithmetic mean (standard deviation)				
AUC 0-24h - Day 1	93000 (± 2510)	204000 (± 28000)	278000 (± 49600)	391000 (± 10600)
AUC 0-24h - Day 4	175000 (± 14100)	401000 (± 88700)	535000 (± 157000)	680000 (± 48300)
AUClast - Day 1	92600 (± 2750)	203000 (± 26800)	277000 (± 99500)	34100 (± 91100)
AUClast - Day 4	170000 (± 20300)	399000 (± 87800)	533000 (± 158000)	671000 (± 43400)

End point values	BLZ945 800mg - Cohort 5 Arm #1 (Part 2)	BLZ945 800mg - Cohort 5 Arm #2 (Part 2)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4[22]	6[23]		
Units: hour * ng/mL				
arithmetic mean (standard deviation)				
AUC 0-24h - Day 1	999 (± 999)	999 (± 999)		
AUC 0-24h - Day 4	999 (± 999)	999 (± 999)		
AUClast - Day 1	999 (± 999)	56900 (± 21400)		
AUClast - Day 4	73400 (± 7710)	999 (± 999)		

Notes:

[22] - 0 participants analyzed at day 1

[23] - 0 participants analyzed at day 4

Statistical analyses

No statistical analyses for this end point

Secondary: Cohorts 1-4: Plasma Pharmacokinetics (PK) of BLZ945 - T1/2

End point title	Cohorts 1-4: Plasma Pharmacokinetics (PK) of BLZ945 -

End point description:

Measured by T1/2 - The elimination half-life of BLZ945

End point type	Secondary

End point timeframe:

Cohort 1-4: Pre-dose, 0.5, 1, 2, 4, 6, 8, 12 and 24 hours after BLZ945 dosing on Day 1 and Day 4.

Notes:

[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: This endpoint was planned to be applicable only to cohorts 1-4

End point values	BLZ945 300mg - Cohort 1 (Part 1)	BLZ945 600mg - Cohort 2 (Part 1)	BLZ945 800mg - Cohort 4 (Part 1)	BLZ945 1200mg - Cohort 3 (Part 1)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	4	3	4
Units: Hours				
arithmetic mean (standard deviation)				
Day 1	999 (± 999)	999 (± 999)	999 (± 999)	999 (± 999)
Day 4	999 (± 999)	999 (± 999)	999 (± 999)	999 (± 999)

Statistical analyses

No statistical analyses for this end point

Secondary: Cohorts 1-5: Number of patients with adverse events (AEs) and serious adverse events (SAEs)

End point title	Cohorts 1-5: Number of patients with adverse events (AEs) and serious adverse events (SAEs)

End point description:

Incidence and severity of AEs and SAEs by treatment group.

AE grades to characterize the severity of the AEs were based on the Common Terminology Criteria for Adverse Events (CTCAE) version 5. For CTCAE, Grade 1 = mild; Grade 2 = moderate; Grade 3 = severe; Grade 4 = life-threatening; Grade 5 = death related to AE

End point type	Secondary

End point timeframe:

From first dose of study treatment up to 32 days after last dose (Day 36) for Cohorts 1-4 and up to 4 weeks after last dose (Day 330) for Cohort 5. *Maxim duration of exposure in Cohort 5 was 302 days. 302 + 28 days of FU=330 days

End point values	BLZ945 300mg - Cohort 1 (Part 1)	BLZ945 600mg - Cohort 2 (Part 1)	BLZ945 800mg - Cohort 4 (Part 1)	BLZ945 1200mg - Cohort 3 (Part 1)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	4	4	4
Units: Participants				
Total AEs	2	2	4	4
AE of grade 1	2	2	4	4
AE of grade 2	2	1	3	2
AE of grade 3	0	0	2	0
AE of grade 4	0	0	0	0
AE of grade 5	0	0	0	0
Study drug-related AEs	2	2	3	2
Serious AEs	0	0	1	0

AEs leading to discontinuation of study treatment	0	0	0	0
BLZ945 related AEs causing drug discontinuation	0	0	0	0

End point values	BLZ945 800mg - Cohort 5 Arm #1 (Part 2)	BLZ945 800mg - Cohort 5 Arm #2 (Part 2)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	6		
Units: Participants				
Total AEs	6	6		
AE of grade 1	5	6		
AE of grade 2	5	5		
AE of grade 3	1	5		
AE of grade 4	0	1		
AE of grade 5	0	2		
Study drug-related AEs	5	5		
Serious AEs	0	4		
AEs leading to discontinuation of study treatment	0	4		
BLZ945 related AEs causing drug discontinuation	0	3		

Statistical analyses

No statistical analyses for this end point

Secondary: Cohorts 1-4: Renal Clearance (CLR) of BLZ945

End point title	Cohorts 1-4: Renal Clearance (CLR) of BLZ945[25]

End point description:

Urine renal clearance (CLR) of BLZ945

End point type	Secondary

End point timeframe:

pre-dose, 0-4, 4-8, 8-12 and 12-24 hours after BLZ945 dosing on Day 1 and Day 4

Notes:

[25] - 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: This endpoint was planned to be applicable only to cohorts 1-4

End point values	BLZ945 300mg - Cohort 1 (Part 1)	BLZ945 600mg - Cohort 2 (Part 1)	BLZ945 800mg - Cohort 4 (Part 1)	BLZ945 1200mg - Cohort 3 (Part 1)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	4	4	3
Units: liter/hour (L/hr)				
arithmetic mean (standard deviation)				

Day 1	0.00597 (± 0.00184)	0.00844 (± 0.00675)	0.00466 (± 0.00312)	0.0213 (± 0.0258)
Day 4	0.00667 (± 0.00127)	0.00410 (± 0.00205)	0.00362 (± 0.00262)	0.00550 (± 0.00129)

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: From first dose of study treatment up to 32 days after last dose (Day 36) for Cohorts 1-4 and up to 4 weeks after last dose (Day 330) for Cohort 5. *Maxim duration of exposure in Cohort 5 was 302 days. 302 + 28 days of FU=330 days	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	27.0

Reporting groups	
Reporting group title	BLZ945 300mg
Reporting group description: BLZ945 300mg	
Reporting group title	BLZ945 600mg
Reporting group description: BLZ945 600mg	
Reporting group title	BLZ945 800mg
Reporting group description: BLZ945 800mg	
Reporting group title	BLZ945 1200mg
Reporting group description: BLZ945 1200mg	
Reporting group title	Arm 1 (4/10)
Reporting group description: Arm 1 (4/10)	
Reporting group title	Arm 2 (4/10) QW
Reporting group description: Arm 2 (4/10) QW	
Reporting group title	Total
Reporting group description: Total	

Serious adverse events	BLZ945 300mg	BLZ945 600mg	BLZ945 800mg
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Investigations			
Transaminases increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 4 (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 / 4 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Pneumonia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia aspiration			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Hyponatraemia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 4 (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	BLZ945 1200mg	Arm 1 (4/10)	Arm 2 (4/10) QW
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 4 (25.00%)	0 / 6 (0.00%)	4 / 6 (66.67%)
number of deaths (all causes)	0	0	2
number of deaths resulting from adverse events	0	0	0
Investigations			
Transaminases increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
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 / 4 (0.00%)	0 / 6 (0.00%)	2 / 6 (33.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 2

Infections and infestations			
Pneumonia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Pneumonia aspiration			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	2 / 6 (33.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Hyponatraemia			
subjects affected / exposed	1 / 4 (25.00%)	0 / 6 (0.00%)	0 / 6 (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

Serious adverse events	Total		
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 28 (17.86%)		
number of deaths (all causes)	2		
number of deaths resulting from adverse events	0		
Investigations			
Transaminases increased			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Respiratory failure			
subjects affected / exposed	2 / 28 (7.14%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 2		
Infections and infestations			
Pneumonia			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Pneumonia aspiration			

subjects affected / exposed	2 / 28 (7.14%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Hyponatraemia			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	BLZ945 300mg	BLZ945 600mg	BLZ945 800mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	2 / 4 (50.00%)	2 / 4 (50.00%)	4 / 4 (100.00%)
Vascular disorders			
Haematoma			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Flushing			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Hypertension			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Swelling face			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Peripheral swelling			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Pain			

subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Fatigue			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Seasonal allergy			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Atelectasis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Dyspnoea			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Pleurisy			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Pulmonary oedema			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Stridor			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Panic attack			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Anxiety			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Product issues			

Device dislocation			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Blood bilirubin increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Blood urine present			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Electrocardiogram T wave inversion			
subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Faecal volume decreased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Hepatic enzyme increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Transaminases increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Weight decreased			

subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Troponin increased			
subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Contusion			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Epicondylitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Rib fracture			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Wound			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Tachycardia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Brain fog			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Amyotrophic lateral sclerosis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Paraesthesia			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Muscle contractions involuntary			

subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Migraine			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	2	0	0
Hypogeusia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Headache			
subjects affected / exposed	2 / 4 (50.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	2	0	0
Dizziness			
subjects affected / exposed	2 / 4 (50.00%)	0 / 4 (0.00%)	2 / 4 (50.00%)
occurrences (all)	2	0	2
Somnolence			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Tremor			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Syncope			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Ear and labyrinth disorders			
Vertigo positional			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Vertigo			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Eye swelling			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Eye pain			

subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Eye irritation			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Periorbital oedema			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Abdominal pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Vomiting			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	1 / 4 (25.00%)
occurrences (all)	1	0	1
Salivary hypersecretion			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	1 / 4 (25.00%)
occurrences (all)	1	0	2
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Diarrhoea			
subjects affected / exposed	1 / 4 (25.00%)	1 / 4 (25.00%)	1 / 4 (25.00%)
occurrences (all)	1	1	1
Constipation			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Hepatobiliary disorders			
Ocular icterus			

subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Rash maculo-papular			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Rash			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Pruritus			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Renal and urinary disorders			
Chromaturia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Urine abnormality			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	2
Musculoskeletal and connective tissue disorders			
Groin pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Arthralgia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Muscle fatigue			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Muscle spasms			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Muscular weakness			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Myokymia			

subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Infections and infestations			
Mucosal infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Sinusitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Wound infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Urinary tract infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Tooth infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Hyponatraemia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Decreased appetite			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	BLZ945 1200mg	Arm 1 (4/10)	Arm 2 (4/10) QW
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 4 (100.00%)	6 / 6 (100.00%)	6 / 6 (100.00%)
Vascular disorders			
Haematoma			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Flushing			

subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Hypertension			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	4	0
Swelling face			
subjects affected / exposed	1 / 4 (25.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Peripheral swelling			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Fatigue			
subjects affected / exposed	2 / 4 (50.00%)	3 / 6 (50.00%)	2 / 6 (33.33%)
occurrences (all)	2	4	2
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Seasonal allergy			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Respiratory, thoracic and mediastinal disorders			
Atelectasis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Dyspnoea			
subjects affected / exposed	0 / 4 (0.00%)	2 / 6 (33.33%)	0 / 6 (0.00%)
occurrences (all)	0	2	0
Pleurisy			

subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Pulmonary oedema			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Stridor			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Psychiatric disorders			
Panic attack			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Anxiety			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Product issues			
Device dislocation			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	2 / 6 (33.33%)
occurrences (all)	0	0	2
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	2 / 6 (33.33%)
occurrences (all)	0	1	2
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Blood bilirubin increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Blood creatine phosphokinase increased			
subjects affected / exposed	2 / 4 (50.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
Blood urine present			

subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Electrocardiogram T wave inversion			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Faecal volume decreased			
subjects affected / exposed	1 / 4 (25.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Hepatic enzyme increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Transaminases increased			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Weight decreased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Troponin increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	1 / 4 (25.00%)	2 / 6 (33.33%)	2 / 6 (33.33%)
occurrences (all)	1	2	3
Contusion			
subjects affected / exposed	1 / 4 (25.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	1	0	2
Epicondylitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Rib fracture			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Wound			

subjects affected / exposed	1 / 4 (25.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Cardiac disorders			
Tachycardia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Nervous system disorders			
Brain fog			
subjects affected / exposed	1 / 4 (25.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	1	0	1
Amyotrophic lateral sclerosis			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Paraesthesia			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Muscle contractions involuntary			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	1 / 6 (16.67%)
occurrences (all)	0	2	1
Migraine			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Hypogeusia			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Headache			
subjects affected / exposed	3 / 4 (75.00%)	3 / 6 (50.00%)	2 / 6 (33.33%)
occurrences (all)	3	4	2
Dizziness			
subjects affected / exposed	1 / 4 (25.00%)	1 / 6 (16.67%)	1 / 6 (16.67%)
occurrences (all)	1	6	4
Somnolence			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Tremor			

subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Syncope			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Ear and labyrinth disorders			
Vertigo positional			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Vertigo			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	2
Eye disorders			
Eye swelling			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	1 / 6 (16.67%)
occurrences (all)	0	1	2
Eye pain			
subjects affected / exposed	1 / 4 (25.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Eye irritation			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Periorbital oedema			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	2	0
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Abdominal pain			
subjects affected / exposed	1 / 4 (25.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	1	2	0
Vomiting			
subjects affected / exposed	1 / 4 (25.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Salivary hypersecretion			

subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Nausea			
subjects affected / exposed	3 / 4 (75.00%)	3 / 6 (50.00%)	1 / 6 (16.67%)
occurrences (all)	3	5	1
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	1 / 6 (16.67%)
occurrences (all)	0	1	1
Diarrhoea			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Constipation			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Hepatobiliary disorders			
Ocular icterus			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Skin and subcutaneous tissue disorders			
Rash maculo-papular			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Rash			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Pruritus			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Renal and urinary disorders			
Chromaturia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Urine abnormality			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			

Groin pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Arthralgia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Muscle fatigue			
subjects affected / exposed	1 / 4 (25.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Muscle spasms			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	1 / 6 (16.67%)
occurrences (all)	0	2	1
Muscular weakness			
subjects affected / exposed	1 / 4 (25.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Myokymia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Mucosal infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Nasopharyngitis			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Sinusitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Wound infection			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Urinary tract infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Tooth infection			

subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Metabolism and nutrition disorders			
Hyponatraemia			
subjects affected / exposed	1 / 4 (25.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Decreased appetite			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	2	0

Non-serious adverse events	Total		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	24 / 28 (85.71%)		
Vascular disorders			
Haematoma			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Flushing			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Hypertension			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	4		
Swelling face			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Peripheral swelling			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Pain			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Fatigue			

subjects affected / exposed	8 / 28 (28.57%)		
occurrences (all)	9		
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Seasonal allergy			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Respiratory, thoracic and mediastinal disorders			
Atelectasis			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Dyspnoea			
subjects affected / exposed	2 / 28 (7.14%)		
occurrences (all)	2		
Pleurisy			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Pulmonary oedema			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Stridor			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Psychiatric disorders			
Panic attack			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Anxiety			
subjects affected / exposed	2 / 28 (7.14%)		
occurrences (all)	2		
Product issues			
Device dislocation			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		

Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	2 / 28 (7.14%)		
occurrences (all)	2		
Aspartate aminotransferase increased			
subjects affected / exposed	4 / 28 (14.29%)		
occurrences (all)	4		
Blood alkaline phosphatase increased			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Blood bilirubin increased			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Blood creatine phosphokinase increased			
subjects affected / exposed	2 / 28 (7.14%)		
occurrences (all)	2		
Blood urine present			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Electrocardiogram T wave inversion			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Faecal volume decreased			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Hepatic enzyme increased			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Transaminases increased			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Weight decreased			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Troponin increased			

subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	5 / 28 (17.86%)		
occurrences (all)	6		
Contusion			
subjects affected / exposed	2 / 28 (7.14%)		
occurrences (all)	3		
Epicondylitis			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Rib fracture			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Wound			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Cardiac disorders			
Tachycardia			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Nervous system disorders			
Brain fog			
subjects affected / exposed	2 / 28 (7.14%)		
occurrences (all)	2		
Amyotrophic lateral sclerosis			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Paraesthesia			
subjects affected / exposed	2 / 28 (7.14%)		
occurrences (all)	2		
Muscle contractions involuntary			
subjects affected / exposed	2 / 28 (7.14%)		
occurrences (all)	3		
Migraine			

subjects affected / exposed	2 / 28 (7.14%)		
occurrences (all)	3		
Hypogeusia			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Headache			
subjects affected / exposed	10 / 28 (35.71%)		
occurrences (all)	11		
Dizziness			
subjects affected / exposed	7 / 28 (25.00%)		
occurrences (all)	15		
Somnolence			
subjects affected / exposed	2 / 28 (7.14%)		
occurrences (all)	2		
Tremor			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Syncope			
subjects affected / exposed	2 / 28 (7.14%)		
occurrences (all)	2		
Ear and labyrinth disorders			
Vertigo positional			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Vertigo			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	2		
Eye disorders			
Eye swelling			
subjects affected / exposed	2 / 28 (7.14%)		
occurrences (all)	3		
Eye pain			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Eye irritation			

subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Periorbital oedema			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	2		
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Abdominal pain			
subjects affected / exposed	2 / 28 (7.14%)		
occurrences (all)	3		
Vomiting			
subjects affected / exposed	3 / 28 (10.71%)		
occurrences (all)	3		
Salivary hypersecretion			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Nausea			
subjects affected / exposed	9 / 28 (32.14%)		
occurrences (all)	12		
Gastrooesophageal reflux disease			
subjects affected / exposed	2 / 28 (7.14%)		
occurrences (all)	2		
Diarrhoea			
subjects affected / exposed	4 / 28 (14.29%)		
occurrences (all)	4		
Constipation			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Hepatobiliary disorders			
Ocular icterus			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Skin and subcutaneous tissue disorders			

Rash maculo-papular subjects affected / exposed occurrences (all) Rash subjects affected / exposed occurrences (all) Pruritus subjects affected / exposed occurrences (all)	 1 / 28 (3.57%) 1 1 / 28 (3.57%) 1 2 / 28 (7.14%) 2		
Renal and urinary disorders Chromaturia subjects affected / exposed occurrences (all) Urine abnormality subjects affected / exposed occurrences (all)	 1 / 28 (3.57%) 1 1 / 28 (3.57%) 2		
Musculoskeletal and connective tissue disorders Groin pain subjects affected / exposed occurrences (all) Arthralgia subjects affected / exposed occurrences (all) Muscle fatigue subjects affected / exposed occurrences (all) Muscle spasms subjects affected / exposed occurrences (all) Muscular weakness subjects affected / exposed occurrences (all) Myokymia subjects affected / exposed occurrences (all)	 1 / 28 (3.57%) 1 1 / 28 (3.57%) 1 1 / 28 (3.57%) 1 2 / 28 (7.14%) 3 2 / 28 (7.14%) 2 1 / 28 (3.57%) 1		
Infections and infestations			

Mucosal infection subjects affected / exposed occurrences (all) Nasopharyngitis subjects affected / exposed occurrences (all) Sinusitis subjects affected / exposed occurrences (all) Wound infection subjects affected / exposed occurrences (all) Urinary tract infection subjects affected / exposed occurrences (all) Tooth infection subjects affected / exposed occurrences (all)	1 / 28 (3.57%) 1 2 / 28 (7.14%) 2 1 / 28 (3.57%) 1 1 / 28 (3.57%) 1 1 / 28 (3.57%) 1 1 / 28 (3.57%) 1		
Metabolism and nutrition disorders Hyponatraemia subjects affected / exposed occurrences (all) Decreased appetite subjects affected / exposed occurrences (all)	1 / 28 (3.57%) 1 1 / 28 (3.57%) 2		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
09 July 2019	The original version of the protocol was amended before submission to competent authorities/Ethics committee to incorporate input from investigators on the use of alternatives types of pet scanning.
19 September 2019	The trial protocol was amended to address comments from health authorities by adding discontinuation rules related to QT prolongation, aligning stopping rules with dole limiting toxicities, adding ALS diagnostic criteria and including IUD, IUS, and hormonal contraception methods.
03 September 2020	Protocol was amended to remove age limitations, incorporate home nursing as an option for study procedures and add flexibility around PET and MRI imaging
04 May 2021	The primary purpose of this amendment was to address the potential for additional pharmacokinetic drug-drug interactions.
13 July 2022	The protocol was amended to evaluate the safety and preliminary efficacy of repeated cycles of BLZ945 using two dosing regimens in Cohort 5. Additional safety monitoring assessments, as well as new clinical and pharmacodynamic outcome measures were added in Cohort 5. Amendment 5 introduced a new study structure and an extension of the recruitment numbers
20 January 2023	The main purpose of this amendment was to ensure a continuation of treatment in participants already enrolled in the study, to continue to assess long term safety, tolerability, and pharmacokinetic and pharmacodynamic data beyond 12 weeks of treatment.
05 October 2023	The main purpose of this amendment was to update the BLZ945 dose in both treatment arms of Cohort 5

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

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

Due to EudraCT system limitations, which EMA is aware of, data using 999 as data points in this record are not an accurate representation of the clinical trial results. Please use https://www.novctrd.com/#/

Notes: