Clinical trial results:
A phase II, randomized, double-blind, placebo-controlled, parallel group study to evaluate the safety, efficacy, and pharmacodynamics of 52 weeks of treatment with basmisanil in participants aged 2 to 14 years old with Dup15q syndrome followed by a 2-year optional open-label extension

Summary

EudraCT number	2021-003791-13
Trial protocol	IT ES PT PL NL
Global end of trial date	04 March 2024

Results information

Result version number	v1 (current)
This version publication date	20 September 2024
First version publication date	20 September 2024

Trial information

Trial identification

Sponsor protocol code	BP42992

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT05307679
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	F. Hoffmann-La Roche AG
Sponsor organisation address	Grenzacherstrasse 124, Basel, Switzerland, 4058
Public contact	F. Hoffmann-La Roche AG, F. Hoffmann-La Roche AG, 41 616878333, global.trial_information@roche.com
Scientific contact	F. Hoffmann-La Roche AG, F. Hoffmann-La Roche AG, 41 616878333, global.trial_information@roche.com

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	30 May 2024
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	04 March 2024
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To evaluate the effects of 52 weeks of treatment with basmisanil on core symptom domains of Dup15q syndrome (language and social skills) and daily functioning

Protection of trial subjects:

All participants were required to sign an Informed Consent Form.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	27 May 2022
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Spain: 3
Country: Number of subjects enrolled	United Kingdom: 1
Country: Number of subjects enrolled	United States: 3
Worldwide total number of subjects	7
EEA total number of subjects	3

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)	7
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:

Aged 6-14 years with documented maternal duplication (3 copies) or triplication (4 copies) of the chromosome 15q11.2-q13.1 region including the Prader-Willi/Angelman critical region defined as [BP2-BP3] segment, and a Dup15q syndrome Clinician Global Impression of Severity scale (Dup15q CGI S)overall severity score >/= 4 (at least moderately ill).

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Part 1: Participants received oral placebo twice (BID) on the first day of treatment, then three times daily (TID) to Day 365.

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

Dosage and administration details:

Participants received oral placebo BID on Day 1, then TID on Days 2-365.

Arm title	Basmisanil

Arm description:

Part 1: Participants received oral basmisanil BID on the first day of treatment, then TID to Day 365.
Part 2: Participants who completed Part 1 were to receive oral basmisanil for approximately 2 years.

Arm type	Experimental
Investigational medicinal product name	Basmisanil
Investigational medicinal product code	
Other name	RO5186582
Pharmaceutical forms	Granules
Routes of administration	Oral use

Dosage and administration details:

Part 1: Participants received oral basmisanil BID on Day 1, then TID on Days 2-365. Part 2: Participants were to receive oral basmisanil for up to 2 years.

Number of subjects in period 1	Placebo	Basmisanil
Started	2	5
Completed	0	0
Not completed	2	5
Study terminated by sponsor or physician decision	2	5

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Part 1: Participants received oral placebo twice (BID) on the first day of treatment, then three times daily (TID) to Day 365.	
Reporting group title	Basmisanil
Reporting group description:	
Part 1: Participants received oral basmisanil BID on the first day of treatment, then TID to Day 365. Part 2: Participants who completed Part 1 were to receive oral basmisanil for approximately 2 years.	

Reporting group values	Placebo	Basmisanil	Total
Number of subjects	2	5	7
Age categorical Units: Subjects			
Children (2-11 years)	2	5	7
Age Continuous Units: Years			
arithmetic mean	8.0	8.8	
standard deviation	± 1.4	± 2.2	-
Sex: Female, Male			
The values for male and female participants are reported together due to an unacceptable risk of participant re-identification.			
Units: Participants			
Male and Female	2	5	7
Ethnicity (NIH/OMB)			
Participants were not consented on the collection of race and ethnicity data.			
Units: Subjects			
Unknown or Not Reported	2	5	7
Race (NIH/OMB)			
Participants were not consented on the collection of race and ethnicity data.			
Units: Subjects			
Unknown or Not Reported	2	5	7

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description:	
Part 1: Participants received oral placebo twice (BID) on the first day of treatment, then three times daily (TID) to Day 365.	
Reporting group title	Basmisanil
Reporting group description:	
Part 1: Participants received oral basmisanil BID on the first day of treatment, then TID to Day 365. Part 2: Participants who completed Part 1 were to receive oral basmisanil for approximately 2 years.	

Primary: Vineland-3 adaptive behavior composite scores

End point title	Vineland-3 adaptive behavior composite scores[1]
End point description:	
The Vineland-3 is an instrument that measures communication, daily living skills, socialization, and motor skills. Items are either scored as 2 = Usually, 1 = Sometimes, 0 = Never; or scored as 2 = Yes, 0 = No in the case of items that require a binary response. Lower scores indicate lower adaptive behavior abilities. Only baseline data have been reported. The low n for remaining timepoints (Day 183, Day 365) leads to an unacceptable risk of participant re-identification.	
End point type	Primary
End point timeframe:	
Baseline, Day 183, Day 365	

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 formal statistical analyses were performed due to the low number of trial participants.

End point values	Placebo	Basmisanil		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2	5		
Units: Units on a scale				
median (full range (min-max))				
Baseline	30.50 (30.0 to 31.0)	36.00 (27.0 to 52.0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Vineland-3 gross and fine motor subdomains scores

End point title	Vineland-3 gross and fine motor subdomains scores
End point description:	
The Vineland-3 is an instrument that measures communication, daily living skills, socialization, and motor skills. Items are either scored as 2 = Usually, 1 = Sometimes, 0 = Never; or scored as 2 = Yes, 0 = No in the case of items that require a binary response. Lower scores indicate lower adaptive behavior abilities.	

Only baseline data have been reported. The low n for remaining timepoints (Day 183, Day 365) leads to an unacceptable risk of participant re-identification.

End point type	Secondary

End point timeframe:

Baseline, Day 183, Day 365

End point values	Placebo	Basmisanil		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2	2[2]		
Units: Units on a scale				
median (full range (min-max))				
Gross Motor V-Scale Score - Baseline	1.00 (1.0 to 1.0)	4.50 (1.0 to 8.0)		
Fine Motor V-Scale Score - Baseline	1.00 (1.0 to 1.0)	3.00 (1.0 to 5.0)		

Notes:

[2] - Data not reported for participants older than 9 years; normative data only available for ages 0-9y

Statistical analyses

No statistical analyses for this end point

Secondary: Vineland 3 expressive and receptive communication subdomains

End point title	Vineland 3 expressive and receptive communication subdomains

End point description:

The Vineland-3 is an instrument that measures communication, daily living skills, socialization, and motor skills. Items are either scored as 2 = Usually,
1 = Sometimes, 0 = Never; or scored as 2 = Yes, 0 = No in the case of items that require a binary response. Lower scores indicate lower adaptive behavior abilities.

Only baseline data have been reported. The low n for remaining timepoints (Day 183, Day 365) leads to an unacceptable risk of participant re-identification.

End point type	Secondary

End point timeframe:

Baseline, Day 183, Day 365

End point values	Placebo	Basmisanil		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2	5		
Units: Units on a scale				
median (full range (min-max))				
Expressive Communication V-Scale Score - Baseline	1.00 (1.0 to 1.0)	1.00 (1.0 to 11.0)		
Receptive Communication V-Scale Score - Baseline	1.00 (1.0 to 1.0)	1.00 (1.0 to 6.0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Vineland-3 play and leisure time and interpersonal relationships subdomains

End point title	Vineland-3 play and leisure time and interpersonal relationships subdomains

End point description:

The Vineland-3 is an instrument that measures communication, daily living skills, socialization, and motor skills. Items are either scored as 2 = Usually,
1 = Sometimes, 0 = Never; or scored as 2 = Yes, 0 = No in the case of items that require a binary response. Lower scores indicate lower adaptive behavior abilities. V-scale scores are presented.

Only baseline data have been reported. The low n for remaining timepoints (Day 183, Day 365) leads to an unacceptable risk of participant re-identification.

End point type	Secondary

End point timeframe:

Baseline, Day 183, Day 365

End point values	Placebo	Basmisanil		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2	5		
Units: Units on a scale				
median (full range (min-max))				
Play and Leisure - Baseline	1.00 (1.0 to 1.0)	1.00 (1.0 to 9.0)		
Interpersonal Relationships - Baseline	1.50 (1.0 to 2.0)	1.00 (1.0 to 9.0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Mullen Scales of Early Learning (MSEL) gross and fine motor domains

End point title	Mullen Scales of Early Learning (MSEL) gross and fine motor domains

End point description:

The MSEL are designed for a certified rater to provide an assessment of cognitive ability and motor development of typically developing children from birth through age 68 months. It was administered to all participants in this study irrespective of their chronological age. The instrument consists of 124 items across five scales measuring Gross Motor, Visual Reception, Fine Motor, Expressive Language, and Receptive Language. The scoring for each item ranges from 0 to 5 points, with lower scores indicating lower developmental abilities.

Only baseline data have been reported. The low n for remaining timepoints leads to an unacceptable risk of participant re-identification.

End point type	Secondary

End point timeframe:

Baseline, Day 183, Day 365

End point values	Placebo	Basmisanil		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2	5		
Units: Units on a scale				
median (full range (min-max))				
Gross Motor - Baseline	20.50 (14.0 to 27.0)	19.00 (13.0 to 35.0)		
Fine Motor - Baseline	15.50 (13.0 to 18.0)	15.00 (6.0 to 30.0)		

Statistical analyses

No statistical analyses for this end point

Secondary: MSEL visual reception domain scores

End point title	MSEL visual reception domain scores

End point description:

The MSEL are designed for a certified rater to provide an assessment of cognitive ability and motor development of typically developing children from birth through age 68 months. It was administered to all participants in this study irrespective of their chronological age. The instrument consists of 124 items across five scales measuring Gross Motor, Visual Reception, Fine Motor, Expressive Language, and Receptive Language. The scoring for each item ranges from 0 to 5 points, with lower scores indicating lower developmental abilities.

Only baseline data have been reported. The low n for remaining timepoints leads to an unacceptable risk of participant re-identification.

End point type	Secondary

End point timeframe:

Baseline, Day 183, Day 365

End point values	Placebo	Basmisanil		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2	5		
Units: Units on a scale				
median (full range (min-max))				
Baseline	14.00 (11.0 to 17.0)	4.00 (2.0 to 42.0)		

Statistical analyses

No statistical analyses for this end point

Secondary: MSEL expressive and receptive language subdomains

End point title	MSEL expressive and receptive language subdomains

End point description:

The MSEL are designed for a certified rater to provide an assessment of cognitive ability and motor development of typically developing children from birth through age 68 months. It was administered to all participants in this study irrespective of their chronological age. The instrument consists of 124 items across five scales measuring Gross Motor, Visual Reception, Fine Motor, Expressive Language, and Receptive Language. The scoring for each item ranges from 0 to 5 points, with lower scores indicating lower developmental abilities.

Only baseline data have been reported. The low n for remaining timepoints leads to an unacceptable risk of participant re-identification.

End point type	Secondary

End point timeframe:

Baseline, Day 183, Day 365

End point values	Placebo	Basmisanil		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2	5		
Units: Units on a scale				
median (full range (min-max))				
Expressive Language - Baseline	12.50 (12.0 to 13.0)	17.00 (6.0 to 29.0)		
Receptive Language - Baseline	10.00 (7.0 to 13.0)	16.00 (9.0 to 28.0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Dup15q syndrome Clinician Global Impression of Severity (CGI-S) scale scores

End point title	Dup15q syndrome Clinician Global Impression of Severity (CGI-S) scale scores

End point description:

The Dup15q CGI-S is a 10-domain clinician-rated measure on a 6-point scale that measures global severity of illness at a given point in time. The ten domains are seizures, expressive communication difficulties, fine motor skills difficulties, gross motor skills difficulties, cognitive/intellectual impairment, impairment in activities of daily living/self-care, socialization, maladaptive behavior, sleep difficulties, and overall severity. Response options are:

1 = none
2 = very mild
3 = mild
4 = moderate
5 = severe
6 = very severe.

Only baseline and Day 28 data have been reported. The low n for remaining timepoints leads to an unacceptable risk of participant re-identification.

End point type	Secondary

End point timeframe:

Baseline - Day 365

End point values	Placebo	Basmisanil		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2	5		
Units: Units on a scale				
median (full range (min-max))				
Baseline	4.00 (4.0 to 4.0)	4.00 (4.0 to 6.0)		
Day 28	4.00 (4.0 to 4.0)	4.00 (3.0 to 6.0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Dup15q syndrome Clinician Global Impression of Change scale (CGI-C) scores

End point title	Dup15q syndrome Clinician Global Impression of Change scale (CGI-C) scores

End point description:

The Dup15q CGI-C is a 10-domain clinician-rated measure on a 7-point scale that assesses the clinician’s impression of change in illness compared with baseline. The ten domains are seizures, expressive communication difficulties, fine motor skills difficulties, gross motor skills difficulties, cognitive/intellectual impairment, impairment in activities of daily living/self-care, socialization, maladaptive behavior, sleep difficulties, and overall severity. Response options are:
1 = very much improved
2 = much improved
3 = minimally improved
4 = no change
5 = minimally worse
6 = much worse
7= very much worse

Only Day 28 data have been reported. The low n for remaining timepoints leads to an unacceptable risk of participant re-identification.

End point type	Secondary

End point timeframe:

Day 28 - Day 365

End point values	Placebo	Basmisanil		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2	4		
Units: Units on a scale				
median (full range (min-max))				
Day 28	3.50 (3.0 to 4.0)	3.00 (2.0 to 3.0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Aberrant Behavior Checklist - Second Edition - Community Version (ABC-2-C) domain scores - Irritability

End point title	Aberrant Behavior Checklist - Second Edition - Community Version (ABC-2-C) domain scores - Irritability

End point description:

The ABC-2 is an updated, empirically derived, validated 58-item caregiver-completed rating scale that measures the severity of a range of maladaptive behaviors commonly observed in children, adolescents, and adults with intellectual and developmental disabilities. The Community version of the scale (ABC-2-C) will be used. It is designed for use in individuals who are not residing in institutional settings. The checklist assesses symptoms across five domains: irritability,
social withdrawal, stereotypic behavior, hyperactive/noncompliance, and inappropriate speech. Items are scored on a 4-point scale from 0 (never) to 3 (severe problem). Subscale scores and a total score can be calculated with higher scores indicating greater severity.

Only baseline and Day 28 data have been reported. The low n for remaining timepoints leads to an unacceptable risk of participant re-identification.

End point type	Secondary

End point timeframe:

Baseline - Day 365

End point values	Placebo	Basmisanil		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2	5		
Units: Units on a scale				
median (full range (min-max))				
Baseline	11.00 (11.0 to 11.0)	15.00 (3.0 to 40.0)		
Day 28	10.00 (6.0 to 14.0)	15.00 (5.0 to 18.0)		

Statistical analyses

No statistical analyses for this end point

Secondary: ABC-2-C domain scores - Social Withdrawal

End point title	ABC-2-C domain scores - Social Withdrawal

End point description:

The ABC-2 is an updated, empirically derived, validated 58-item caregiver-completed rating scale that measures the severity of a range of maladaptive behaviors commonly observed in children, adolescents, and adults with intellectual and developmental disabilities. The Community version of the scale (ABC-2-C) will be used. It is designed for use in individuals who are not residing in institutional settings. The checklist assesses symptoms across five domains: irritability,
social withdrawal, stereotypic behavior, hyperactive/noncompliance, and inappropriate speech. Items are scored on a 4-point scale from 0 (never) to 3 (severe problem). Subscale scores and a total score can be calculated with higher scores indicating greater severity.

Only baseline and Day 28 data have been reported. The low n for remaining timepoints leads to an unacceptable risk of participant re-identification.

End point type	Secondary

End point timeframe:

Baseline - Day 365

End point values	Placebo	Basmisanil		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2	5		
Units: Units on a scale				
median (full range (min-max))				
Baseline	14.50 (11.0 to 18.0)	16.00 (2.0 to 25.0)		
Day 28	7.50 (6.0 to 9.0)	14.00 (7.0 to 17.0)		

Statistical analyses

No statistical analyses for this end point

Secondary: ABC-2-C domain scores - Stereotypic Behavior

End point title	ABC-2-C domain scores - Stereotypic Behavior

End point description:

The ABC-2 is an updated, empirically derived, validated 58-item caregiver-completed rating scale that measures the severity of a range of maladaptive behaviors commonly observed in children, adolescents, and adults with intellectual and developmental disabilities. The Community version of the scale (ABC-2-C) will be used. It is designed for use in individuals who are not residing in institutional settings. The checklist assesses symptoms across five domains: irritability,
social withdrawal, stereotypic behavior, hyperactive/noncompliance, and inappropriate speech. Items are scored on a 4-point scale from 0 (never) to 3 (severe problem). Subscale scores and a total score can be calculated with higher scores indicating greater severity.

Only baseline and Day 28 data have been reported. The low n for remaining timepoints leads to an unacceptable risk of participant re-identification.

End point type	Secondary

End point timeframe:

Baseline - Day 365

End point values	Placebo	Basmisanil		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2	5		
Units: Units on a scale				
median (full range (min-max))				
Baseline	8.00 (8.0 to 8.0)	6.00 (0.0 to 15.0)		
Day 28	5.50 (5.0 to 6.0)	13.00 (7.0 to 16.0)		

Statistical analyses

No statistical analyses for this end point

Secondary: ABC-2-C domain scores - Hyperactivity/Non-Compliance

End point title	ABC-2-C domain scores - Hyperactivity/Non-Compliance

End point description:

The ABC-2 is an updated, empirically derived, validated 58-item caregiver-completed rating scale that measures the severity of a range of maladaptive behaviors commonly observed in children, adolescents, and adults with intellectual and developmental disabilities. The Community version of the scale (ABC-2-C) will be used. It is designed for use in individuals who are not residing in institutional settings. The checklist assesses symptoms across five domains: irritability,
social withdrawal, stereotypic behavior, hyperactive/noncompliance, and inappropriate speech. Items are scored on a 4-point scale from 0 (never) to 3 (severe problem). Subscale scores and a total score can be calculated with higher scores indicating greater severity.

Only baseline and Day 28 data have been reported. The low n for remaining timepoints leads to an unacceptable risk of participant re-identification.

End point type	Secondary

End point timeframe:

Baseline - Day 365

End point values	Placebo	Basmisanil		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2	5		
Units: Units on a scale				
median (full range (min-max))				
Baseline	32.00 (23.0 to 41.0)	19.00 (13.0 to 38.0)		
Day 28	12.00 (6.0 to 18.0)	22.00 (15.0 to 33.0)		

Statistical analyses

No statistical analyses for this end point

Secondary: ABC-2-C domain scores - Inappropriate Speech

End point title	ABC-2-C domain scores - Inappropriate Speech

End point description:

The ABC-2 is an updated, empirically derived, validated 58-item caregiver-completed rating scale that measures the severity of a range of maladaptive behaviors commonly observed in children, adolescents, and adults with intellectual and developmental disabilities. The Community version of the scale (ABC-2-C) will be used. It is designed for use in individuals who are not residing in institutional settings. The checklist assesses symptoms across five domains: irritability,
social withdrawal, stereotypic behavior, hyperactive/noncompliance, and inappropriate speech. Items are scored on a 4-point scale from 0 (never) to 3 (severe problem). Subscale scores and a total score can be calculated with higher scores indicating greater severity.

Only baseline and Day 28 data have been reported. The low n for remaining timepoints leads to an unacceptable risk of participant re-identification.

End point type	Secondary

End point timeframe:

Baseline - Day 365

End point values	Placebo	Basmisanil		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2	5		
Units: Units on a scale				
median (full range (min-max))				
Baseline	5.00 (2.0 to 8.0)	2.00 (1.00 to 4.00)		
Day 28	1.50 (0.0 to 3.0)	0.00 (0.0 to 2.0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Plasma concentration of basmisanil

End point title	Plasma concentration of basmisanil[3]

End point description:

Data for certain timepoints (Day 1 Hour 7, Day 1 Hour 8, Day 14 Hour -1, Day 183 Hour 0) has been excluded due to an unacceptable risk of patient re-identification.

End point type	Secondary

End point timeframe:

Day 1 - Day 365

Notes:

[3] - 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 specific to the basmisanil arm as the placebo arm did not receive basmisanil.

End point values	Basmisanil			
Subject group type	Reporting group			
Number of subjects analysed	5			
Units: ng/mL				
arithmetic mean (standard deviation)				
Day 1 - Hour 1.5	2520 (± 965)			
Day 1 - Hour 3.5	2220 (± 955)			
Day 1 - Hour 5.5 (n=4)	1640 (± 756)			
Day 1 - Hour 7.5 (n=4)	1040 (± 392)			
Day 1 - Hour 9 (n=3)	791 (± 368)			
Day 2 - Hour 0	731 (± 535)			
Day 2 - Hour 1.5 (n=4)	2380 (± 576)			
Day 2 - Hour 3.5	2210 (± 864)			
Day 14 - Hour -1.5 (n=2)	1210 (± 1230)			
Day 14 - Hour 0 (n=4)	902 (± 973)			
Day 14 - Hour 1.5 (n=4)	2480 (± 355)			
Day 14 - Hour 3.5	2160 (± 698)			
Day 92 - Hour 0 (n=3)	896 (± 689)			

Statistical analyses

No statistical analyses for this end point

Secondary: Incidence of Adverse Events (AEs) and Serious Adverse Events (SAEs)

End point title	Incidence of Adverse Events (AEs) and Serious Adverse Events (SAEs)

End point description:

An adverse event is any untoward medical occurrence in a participant administered a pharmaceutical product and which does not necessarily have to have a causal relationship with the treatment. An adverse event can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding, for example), symptom, or disease temporally associated with the use of a pharmaceutical product, whether or not considered related to the pharmaceutical product. Preexisting conditions which worsen during a study are also considered as adverse events.

End point type	Secondary

End point timeframe:

Up to 52 weeks

End point values	Placebo	Basmisanil		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2	5		
Units: Count of participants				
AEs and SAEs	2	5		

Statistical analyses

No statistical analyses for this end point

Secondary: Plasma concentration of the basmisanil metabolite M1

End point title	Plasma concentration of the basmisanil metabolite M1[4]

End point description:

Data for certain timepoints (Day 1 Hour 7, Day 1 Hour 8, Day 14 Hour -1, Day 183 Hour 0) has been excluded due to an unacceptable risk of patient re-identification.

End point type	Secondary

End point timeframe:

Day 1 - Day 365

Notes:

[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 specific to the basmisanil arm as the placebo arm did not receive basmisanil.

End point values	Basmisanil			
Subject group type	Reporting group			
Number of subjects analysed	5			
Units: ng/mL				
arithmetic mean (standard deviation)				
Day 1 - Hour 1.5	1410 (± 585)			
Day 1 - Hour 3.5	1510 (± 417)			
Day 1 - Hour 5.5 (n=4)	985 (± 335)			
Day 1 - Hour 7.5 (n=4)	675 (± 221)			
Day 1 - Hour 9 (n=3)	535 (± 173)			
Day 2 - Hour 0	664 (± 568)			
Day 2 - Hour 1.5 (n=4)	1330 (± 358)			
Day 2 - Hour 3.5	1410 (± 506)			
Day 14 - Hour -1.5 (n=2)	1400 (± 1410)			
Day 14 - Hour 0 (n=4)	1060 (± 1470)			
Day 14 - 1.5 (n=4)	1510 (± 413)			
Day 14 - Hour 3.5	1250 (± 540)			
Day 92 - Hour 0 (n=3)	648 (± 522)			

Statistical analyses

No statistical analyses for this end point

Secondary: Quantitative EEG (qEEG) beta-band power

End point title	Quantitative EEG (qEEG) beta-band power

End point description:

End point type	Secondary

End point timeframe:

Baseline, Day 14

End point values	Placebo	Basmisanil		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2	5		
Units: µV2				
arithmetic mean (standard deviation)				
Baseline	9.47 (± 0.21)	11.39 (± 1.55)		
Day 14	9.44 (± 0.37)	9.74 (± 1.05)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information[1]

Timeframe for reporting adverse events:

Baseline - Day 365

Adverse event reporting additional description:

All subjects were affected by non-serious adverse events (NSAEs). One subject was affected by serious adverse events (SAEs). There were no deaths. The exact NSAEs and SAEs are not reported due to the risk of patient re-identification.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	27.0

Reporting groups

Reporting group title	Basmisanil

Reporting group description:

Part 1: Participants received oral basmisanil BID on the first day of treatment, then TID to Day 365.
Part 2: Participants who completed Part 1 were to receive oral basmisanil for approximately 2 years.

Reporting group title	Placebo

Reporting group description:

Part 1: Participants received oral placebo twice (BID) on the first day of treatment, then three times daily (TID) to Day 365.

Serious adverse events	Basmisanil	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	

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

Non-serious adverse events	Basmisanil	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.
Justification: All participants reported at least one AE. The exact nature of the AEs has not been disclosed due to the high risk of patient re-identification due to the low number of participants.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
25 January 2022	Changes to the schedule of activities, including additional assessments; updates to inclusion and exclusion criteria.
25 July 2023	Addition of optional open-label extension of two years; modification of age criteria; changes to study assessments.

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.

Data for certain timepoints with only 1 analyzed participant is not reported due to an unacceptable risk of participant re-identification.

Notes: