



Clinical trial results:

A Randomized, Double-Blind, Placebo-Controlled, Parallel Group, Safety, Efficacy and Pharmacodynamic Study of Basmisaniil (RO5186582) in Adults with Severe Motor Impairment Following an Ischemic Stroke

Summary

| | |
|--------------------------|------------------|
| EudraCT number | 2015-003227-66 |
| Trial protocol | ES |
| Global end of trial date | 03 November 2017 |

Results information

| | |
|--------------------------------|------------------|
| Result version number | v1 (current) |
| This version publication date | 08 November 2018 |
| First version publication date | 08 November 2018 |

Trial information

Trial identification

| | |
|-----------------------|---------|
| Sponsor protocol code | BP29937 |
|-----------------------|---------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT02928393 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|-----------------------------------------------------------------------------------------------------|
| Sponsor organisation name | F. Hoffmann-La Roche AG |
| Sponsor organisation address | Grenzacherstrasse 124, Basel, Switzerland, CH-4070 |
| 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? | No |

Notes:

Results analysis stage

| | |
|------------------------------------------------------|------------------|
| Analysis stage | Final |
| Date of interim/final analysis | 25 January 2018 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 03 November 2017 |
| Global end of trial reached? | Yes |
| Global end of trial date | 03 November 2017 |
| Was the trial ended prematurely? | Yes |

Notes:

General information about the trial

Main objective of the trial:

The main objective of this Phase IIa, randomized, double-blind, placebo-controlled, parallel group study was to evaluate the safety, efficacy and pharmacodynamics of basmisanil in adult participants with severe motor impairment following an ischemic stroke.

Protection of trial subjects:

All study subjects were required to read and sign an Informed Consent form.

Background therapy: -

Evidence for comparator: -

| | |
|-----------------------------------------------------------|------------------|
| Actual start date of recruitment | 20 February 2017 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|----------|
| Country: Number of subjects enrolled | Spain: 5 |
| Worldwide total number of subjects | 5 |
| EEA total number of subjects | 5 |

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) | 3 |
| From 65 to 84 years | 2 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

The study population consisted of male and female subjects aged 40-85 years with severe motor impairment following an acute middle cerebral artery (MCA) ischemic stroke and was conducted across three sites in Spain.

Pre-assignment

Screening details:

Male and female subjects between 40-85 years old that had an acute middle cerebral artery (MCA) ischemic stroke within 3-4 days of study enrollment were eligible for the study.

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 | Basmisanil |

Arm description:

Subjects received 240 milligrams (mg) of basmisanil (RO5186582) as granules packaged in stick packs, taken orally twice daily for 90 days.

| | |
|----------------------------------------|--------------|
| 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:

Subjects received 240 mg of basmisanil, taken orally, twice-daily (morning and evening), within 30 minutes of a meal for 90 days.

| | |
|------------------|---------|
| Arm title | Placebo |
|------------------|---------|

Arm description:

Subjects received the placebo equivalent to basmisanil (RO5186582) as granules packaged in stick packs, taken orally twice daily for 90 days.

| | |
|----------------------------------------|----------|
| 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:

Subjects received two stick packs of placebo, taken orally, twice daily (morning and evening), within 30 minutes of a meal for 90 days.

| Number of subjects in period 1 | Basmisanil | Placebo |
|---------------------------------------|------------|---------|
| Started | 3 | 2 |
| Completed | 3 | 2 |

Baseline characteristics

Reporting groups

| | |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------|
| Reporting group title | Basmisanil |
| Reporting group description: Subjects received 240 milligrams (mg) of basmisanil (RO5186582) as granules packaged in stick packs, taken orally twice daily for 90 days. | |
| Reporting group title | Placebo |
| Reporting group description: Subjects received the placebo equivalent to basmisanil (RO5186582) as granules packaged in stick packs, taken orally twice daily for 90 days. | |

| Reporting group values | Basmisanil | Placebo | Total |
|-------------------------------------------------------------------------|----------------|---------------|-------|
| Number of subjects | 3 | 2 | 5 |
| Age Categorical Units: Subjects | | | |
| Age Continuous Units: years arithmetic mean standard deviation | 59.3 ± 11.8 | 66.0 ± 5.7 | - |
| Gender Categorical Units: Subjects | | | |
| Male | 3 | 2 | 5 |
| Female | 0 | 0 | 0 |
| Race (NIH/OMB) Units: Subjects | | | |
| White | 2 | 2 | 4 |
| Unknown | 1 | 0 | 1 |
| Ethnicity (NIH/OMB) Units: Subjects | | | |
| Hispanic or Latino | 2 | 0 | 2 |
| Not Hispanic or Latino | 1 | 0 | 1 |
| Not Stated | 0 | 2 | 2 |

Subject analysis sets

| | |
|------------------------------------------------------------------------------------------------------------|--------------------|
| Subject analysis set title | Basmisanil A |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: All study subjects were included in the safety and efficacy analyses. | |
| Subject analysis set title | Basmisanil B |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: All study subjects were included in the safety and efficacy analyses. | |
| Subject analysis set title | Basmisanil C |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: All study subjects were included in the safety and efficacy analyses. | |

| | |
|------------------------------------------------------------------------------------------------------------|--------------------|
| Subject analysis set title | Placebo A |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: All study subjects were included in the safety and efficacy analyses. | |
| Subject analysis set title | Placebo B |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: All study subjects were included in the safety and efficacy analyses. | |

| Reporting group values | Basmisanil A | Basmisanil B | Basmisanil C |
|------------------------------------|--------------|--------------|--------------|
| Number of subjects | 1 | 1 | 1 |
| Age Categorical Units: Subjects | | | |

| | | | |
|-------------------------------------------------------------------------|---|---|---|
| Age Continuous Units: years arithmetic mean standard deviation | | | |
| | ± | ± | ± |
| Gender Categorical Units: Subjects | | | |
| Male | 1 | 1 | 1 |
| Female | 0 | 0 | 0 |
| Race (NIH/OMB) Units: Subjects | | | |
| White | 1 | 0 | 1 |
| Unknown | 0 | 1 | 0 |
| Ethnicity (NIH/OMB) Units: Subjects | | | |
| Hispanic or Latino | 1 | 0 | 1 |
| Not Hispanic or Latino | 0 | 1 | 0 |
| Not Stated | 0 | 0 | 0 |

| Reporting group values | Placebo A | Placebo B | |
|------------------------------------|-----------|-----------|--|
| Number of subjects | 1 | 1 | |
| Age Categorical Units: Subjects | | | |

| | | | |
|-------------------------------------------------------------------------|---|---|--|
| Age Continuous Units: years arithmetic mean standard deviation | | | |
| | ± | ± | |
| Gender Categorical Units: Subjects | | | |
| Male | 1 | 1 | |
| Female | 0 | 0 | |
| Race (NIH/OMB) Units: Subjects | | | |
| White | 1 | 1 | |
| Unknown | 0 | 0 | |
| Ethnicity (NIH/OMB) Units: Subjects | | | |

| | | | |
|------------------------|---|---|--|
| Hispanic or Latino | 0 | 0 | |
| Not Hispanic or Latino | 0 | 0 | |
| Not Stated | 1 | 1 | |

End points

End points reporting groups

| | |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------|
| Reporting group title | Basmisanil |
| Reporting group description: Subjects received 240 milligrams (mg) of basmisanil (RO5186582) as granules packaged in stick packs, taken orally twice daily for 90 days. | |
| Reporting group title | Placebo |
| Reporting group description: Subjects received the placebo equivalent to basmisanil (RO5186582) as granules packaged in stick packs, taken orally twice daily for 90 days. | |
| Subject analysis set title | Basmisanil A |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: All study subjects were included in the safety and efficacy analyses. | |
| Subject analysis set title | Basmisanil B |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: All study subjects were included in the safety and efficacy analyses. | |
| Subject analysis set title | Basmisanil C |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: All study subjects were included in the safety and efficacy analyses. | |
| Subject analysis set title | Placebo A |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: All study subjects were included in the safety and efficacy analyses. | |
| Subject analysis set title | Placebo B |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: All study subjects were included in the safety and efficacy analyses. | |

Primary: Change from Baseline in Fugl-Meyer Motor Scale (FMMS) Total Score at Day 90

| | |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------|
| End point title | Change from Baseline in Fugl-Meyer Motor Scale (FMMS) Total Score at Day 90 ^[1] |
| End point description: The FMMS is a subscale of the Fugl-Meyer Assessment (FMA) scale used to evaluate and measure recovery of motor function in post-stroke participants. The subscale contains 33 items to assess upper extremity function, and 17 items to assess lower extremity function. Each item is scored on a 3-point scale, where 0 means an item cannot be performed, 1 means an item can be partially performed, and 2 means an item may be fully performed. The maximum score is 66 for upper limbs and 34 for lower limbs. | |
| End point type | Primary |
| End point timeframe: Baseline (Day 1), Day 90 | |
| Notes: [1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point. Justification: Statistical analyses were not performed due to low enrollment and early study termination. | |

| End point values | Basmisanil | Placebo | | |
|--------------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 3 | 2 | | |
| Units: None | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline (Day 1) | 29.33 (± 5.69) | 30.50 (± 3.54) | | |
| Day 90 | 56.33 (± 14.19) | 60.00 (± 2.83) | | |

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects with Adverse Events

| | |
|-----------------|-------------------------------------------------------|
| End point title | Number of Subjects with Adverse Events ^[2] |
|-----------------|-------------------------------------------------------|

End point description:

An adverse event is any untoward medical occurrence in a subject 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 to be adverse

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Baseline (Day 1) up to 28 days after last dose of study drug

Notes:

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

Justification: Statistical analyses were not performed due to low enrollment and early study termination.

| End point values | Basmisanil | Placebo | | |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 3 | 2 | | |
| Units: Subjects | 1 | 1 | | |

Statistical analyses

No statistical analyses for this end point

Primary: Change from Baseline in National Institute of Health Stroke Scale (NIHSS) Score

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|-----------------|------------------------------------------------------------------------------------------------|
| End point title | Change from Baseline in National Institute of Health Stroke Scale (NIHSS) Score ^[3] |
|-----------------|------------------------------------------------------------------------------------------------|

End point description:

NIHSS: The NIHSS is an 11-item scale administered to all study subjects developed to assess function and degree of impairment in acute post-stroke subjects. The scale contains 11 elements rating the ability to respond to questions and to obey simple commands, eye gaze, vision, facial palsy, motor function, ataxia, sensation, language, articulation, and attention. Each element is scored between 0 and 4, with 0 indicating normal function and 4 indicating complete impairment. The highest score possible is 42.

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|---------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------|----------------------|----------------------|----------------------|
| End point type | Primary | | | |
| End point timeframe: | | | | |
| Baseline (Day 1), Days 3, 10, 30, 90, and at follow-up | | | | |
| 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: Statistical analyses were not performed due to low enrollment and early study termination. | | | | |
| End point values | Basmisanil A | Basmisanil B | Basmisanil C | Placebo A |
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 1 | 1 | 1 | 1 |
| Units: None | | | | |
| number (not applicable) | | | | |
| Baseline (Day 1) | 9 | 10 | 9 | 14 |
| Change from Baseline at Day 3 | -1 | -2 | -3 | -3 |
| Change from Baseline at Day 10 | -1 | -4 | -4 | -6 |
| Change from Baseline at Day 30 | -3 | -5 | -5 | -9 |
| Change from Baseline at Day 90 | -4 | -8 | -6 | -9 |
| Change from Baseline at Follow-Up | -1 | -8 | -6 | -11 |

| | | | | |
|-----------------------------------|----------------------|--|--|--|
| End point values | Placebo B | | | |
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 1 | | | |
| Units: None | | | | |
| number (not applicable) | | | | |
| Baseline (Day 1) | 7 | | | |
| Change from Baseline at Day 3 | -1 | | | |
| Change from Baseline at Day 10 | -3 | | | |
| Change from Baseline at Day 30 | -3 | | | |
| Change from Baseline at Day 90 | -6 | | | |
| Change from Baseline at Follow-Up | -6 | | | |

Statistical analyses

No statistical analyses for this end point

Primary: Change from Baseline in Montreal Cognitive Assessment (MoCA) Score

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|-----------------|-----------------------------------------------------------------------------------|
| End point title | Change from Baseline in Montreal Cognitive Assessment (MoCA) Score ^[4] |
|-----------------|-----------------------------------------------------------------------------------|

End point description:

The MoCA is a screening tool used to detect mild cognitive impairment in patients with dementia or stroke. Points are given for tasks completed in the following domains: visuospatial, naming, memory, attention, language, abstraction, delayed recall, and orientation. The maximum score is 30, with higher scores indicating higher ability to complete the administered tasks. Subjects unable to complete the written portion of the tool due to hemiplegia are scored on a modified scale. 99999 = N/A

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Baseline (Day 1), Days 30 and 90

Notes:

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

Justification: Statistical analyses were not performed due to low enrollment and early study termination.

| End point values | Basmisanil A | Basmisanil B | Basmisanil C | Placebo A |
|-----------------------------|----------------------|----------------------|----------------------|----------------------|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 1 ^[5] | 1 | 1 | 1 |
| Units: None | | | | |
| number (not applicable) | | | | |
| Score at Baseline (Day 1) | 99999 | 27 | 26 | 5 |
| Score at Day 30 | 11 | 28 | 28 | 8 |
| Score at Day 90 | 99999 | 27 | 28 | 8 |

Notes:

[5] - A baseline (day 1) score was not reported.

| End point values | Placebo B | | | |
|-----------------------------|----------------------|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 1 | | | |
| Units: None | | | | |
| number (not applicable) | | | | |
| Score at Baseline (Day 1) | 15 | | | |
| Score at Day 30 | 25 | | | |
| Score at Day 90 | 26 | | | |

Statistical analyses

No statistical analyses for this end point

Primary: Change from Baseline in Columbia-Suicide Severity Rating Scale (C-SSRS) Scores

| | |
|-----------------|-----------------------------------------------------------------------------------------------|
| End point title | Change from Baseline in Columbia-Suicide Severity Rating Scale (C-SSRS) Scores ^[6] |
|-----------------|-----------------------------------------------------------------------------------------------|

End point description:

The C-SSRS is used to assess the lifetime suicidality of a subject (taken at baseline), and new instances of suicidal ideation that may occur during the study (measured for each time period since the last study visit). Subjects are rated on a scale ranging from a "wish to die" to "active suicidal thought with plan and intent."

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Baseline (Day 1), Days 3, 30, 60, 90, and 28 days after the last dose of study drug

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: Statistical analyses were not performed due to low enrollment and early study termination.

| End point values | Basmisanil A | Basmisanil B | Basmisanil C | Placebo A |
|-----------------------------------|----------------------|----------------------|----------------------|----------------------|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 1 | 1 | 1 | 1 |
| Units: Subjects | | | | |
| number (not applicable) | | | | |
| Suicidal Ideation | 0 | 0 | 0 | 0 |
| Suicidal Ideation - Lifetime | 0 | 0 | 0 | 0 |
| Suicidal Ideation - Past 6 Months | 0 | 0 | 0 | 0 |
| Suicidal Behavior | 0 | 0 | 0 | 0 |
| Suicidal Behavior - Lifetime | 0 | 0 | 0 | 0 |

| End point values | Placebo B | | | |
|-----------------------------------|----------------------|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 1 | | | |
| Units: Subjects | | | | |
| number (not applicable) | | | | |
| Suicidal Ideation | 0 | | | |
| Suicidal Ideation - Lifetime | 0 | | | |
| Suicidal Ideation - Past 6 Months | 0 | | | |
| Suicidal Behavior | 0 | | | |
| Suicidal Behavior - Lifetime | 0 | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Fugl-Meyer Assessment (FMA) Total Score at Day 90

| | |
|-----------------|---------------------------------------------------------------------------|
| End point title | Change from Baseline in Fugl-Meyer Assessment (FMA) Total Score at Day 90 |
|-----------------|---------------------------------------------------------------------------|

End point description:

The FMA is a scale used to evaluate and measure recovery in post-stroke participants across five domains - motor function, sensory function, balance, range of motion, and joint pain. Items are scored on a 3-point scale, where 0 means an item cannot be performed, 1 means an item can be partially performed, and 2 means an item may be fully performed.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline (Day 1), Day 90

| End point values | Basmisanil A | Basmisanil B | Basmisanil C | Placebo A |
|--------------------------------|----------------------|----------------------|----------------------|----------------------|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 1 | 1 | 1 | 1 |
| Units: None | | | | |
| Baseline (Day 1) | 129 | 135 | 145 | 139 |
| Change from Baseline at Day 90 | 69 | 49 | 80 | 76 |

| End point values | Placebo B | | | |
|--------------------------------|----------------------|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 1 | | | |
| Units: None | | | | |
| Baseline (Day 1) | 142 | | | |
| Change from Baseline at Day 90 | 69 | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in FMA Subscale Score at Day 90

End point title Change from Baseline in FMA Subscale Score at Day 90

End point description:

The FMA is a scale used to evaluate and measure recovery in post-stroke participants across five domains - motor function, sensory function, balance, range of motion, and joint pain. Items are scored on a 3-point scale, where 0 means an item cannot be performed, 1 means an item can be partially performed, and 2 means an item may be fully performed.

End point type Secondary

End point timeframe:

Baseline (Day 1), Day 90

| End point values | Basmisanil A | Basmisanil B | Basmisanil C | Placebo A |
|-------------------------------------------------|----------------------|----------------------|----------------------|----------------------|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 1 | 1 | 1 | 1 |
| Units: None | | | | |
| number (not applicable) | | | | |
| Baseline (Day 1) FM Balance Scale Score | 4 | 0 | 2 | 4 |
| Change in FM Balance Score, Day 90 | 6 | 11 | 11 | 10 |
| Baseline (Day 1) FM Sensation Scale Score | 3 | 24 | 24 | 18 |
| Change in FM Sensation Score, Day 90 | 7 | 0 | 0 | 2 |
| Baseline (Day 1) FM Pain Assessment Scale Score | 44 | 44 | 44 | 44 |
| Change in FM Pain Assessment Score, Day 90 | -3 | 0 | 0 | 0 |

| | | | | |
|-------------------------------------------------|----|----|----|----|
| Baseline (Day 1) FM Range of Motion Scale Score | 44 | 44 | 44 | 40 |
| Change in FM Range of Motion Score, Day 90 | 0 | -3 | 0 | 2 |

| End point values | Placebo B | | | |
|-------------------------------------------------|----------------------|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 1 | | | |
| Units: None | | | | |
| number (not applicable) | | | | |
| Baseline (Day 1) FM Balance Scale Score | 2 | | | |
| Change in FM Balance Score, Day 90 | 11 | | | |
| Baseline (Day 1) FM Sensation Scale Score | 24 | | | |
| Change in FM Sensation Score, Day 90 | 0 | | | |
| Baseline (Day 1) FM Pain Assessment Scale Score | 44 | | | |
| Change in FM Pain Assessment Score, Day 90 | 0 | | | |
| Baseline (Day 1) FM Range of Motion Scale Score | 44 | | | |
| Change in FM Range of Motion Score, Day 90 | 0 | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Modified Rankin Scale (mRS) Score at Day 90

| | |
|-----------------|---------------------------------------------------------------------|
| End point title | Change from Baseline in Modified Rankin Scale (mRS) Score at Day 90 |
|-----------------|---------------------------------------------------------------------|

End point description:

The mRS is a single-item scale used to measure the degree of functional independence and is commonly used with stroke patients. Subjects were rated on a scale of 1-5, as follows: 1 = No significant disability; 2 = Slight disability; 3= Moderate disability; 4 = Moderately severe disability; 5 = Severe disability.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline (Day 1), Day 90

| End point values | Basmisaniil A | Basmisaniil B | Basmisaniil C | Placebo A |
|-----------------------------|----------------------|----------------------|----------------------|----------------------|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 1 | 1 | 1 | 1 |
| Units: None | | | | |
| number (not applicable) | | | | |
| Baseline (Day 1) | 4 | 4 | 5 | 4 |
| Day 90/Early Termination | 3 | 3 | 2 | 3 |

| | | | | |
|--------------------------------|----|----|----|----|
| Change from Baseline at Day 90 | -1 | -1 | -3 | -1 |
|--------------------------------|----|----|----|----|

| End point values | Placebo B | | | |
|--------------------------------|----------------------|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 1 | | | |
| Units: None | | | | |
| number (not applicable) | | | | |
| Baseline (Day 1) | 4 | | | |
| Day 90/Early Termination | 1 | | | |
| Change from Baseline at Day 90 | -3 | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Plasma Concentration of Basmisanil (RO5185682)

| | |
|------------------------|----------------------------------------------------------------------------------------------|
| End point title | Plasma Concentration of Basmisanil (RO5185682) |
| End point description: | Pharmacokinetic (PK) sampling was done for all subjects that received basmisanil (RO518562). |
| End point type | Secondary |
| End point timeframe: | Days 1, 3, 10, 30, and 90 |

| End point values | Basmisanil A | Basmisanil B | Basmisanil C | |
|-----------------------------|----------------------|----------------------|----------------------|--|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | |
| Number of subjects analysed | 1 ^[7] | 1 | 1 ^[8] | |
| Units: ng/mL | | | | |
| number (not applicable) | | | | |
| Day 1, Hour 4 | 1280 | 2690 | 1020 | |
| Day 1, Hour 8 | 776 | 1820 | 2490 | |
| Day 3, Pre-Dose | 2170 | 2460 | 3870 | |
| Day 3, Hour 4 | 3480 | 3290 | 3210 | |
| Day 10, Pre-Dose | 2810 | 3440 | 2050 | |
| Day 30, Pre-Dose | 3660 | 4100 | 3290 | |
| Day 90 | 3700 | 9630 | 3480 | |

Notes:

[7] - 99999 = No value reported for time point

[8] - 99999 = No value reported for time point

Statistical analyses

No statistical analyses for this end point

Secondary: Change in Infarct Lesion Volume as Determined by Magnetic Resonance Imaging (MRI)

| | |
|-----------------|-----------------------------------------------------------------------------------|
| End point title | Change in Infarct Lesion Volume as Determined by Magnetic Resonance Imaging (MRI) |
|-----------------|-----------------------------------------------------------------------------------|

End point description:

Infarct lesion volume was monitored using MRI. Baseline lesion measurements occurred approximately 5-7 after the stroke event.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline (Day 1), Days 3 and 90

| End point values | Basmisanil A | Basmisanil B | Basmisanil C | Placebo A |
|--------------------------------------------------|----------------------|----------------------|----------------------|----------------------|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 1 | 1 | 1 | 1 |
| Units: Cubic millimeters (mm ³) | | | | |
| number (not applicable) | | | | |
| Baseline Infarct Volume | 1492.19 | 23678.26 | 3225.33 | 90212.7 |
| Change from Baseline in Infarct Volume at Day 3 | 320.62 | -3036.44 | -743.77 | -7833.17 |
| Change from Baseline in Infarct Volume at Day 90 | 1179.37 | -1867.85 | 634.3 | 10402.38 |

| End point values | Placebo B | | | |
|--------------------------------------------------|----------------------|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 1 | | | |
| Units: Cubic millimeters (mm ³) | | | | |
| number (not applicable) | | | | |
| Baseline Infarct Volume | 31456.58 | | | |
| Change from Baseline in Infarct Volume at Day 3 | -1805.62 | | | |
| Change from Baseline in Infarct Volume at Day 90 | -14827.85 | | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From Baseline (Day 1) up to 28 days after last dose of study drug.

| | |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

Dictionary used

| | |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

| | |
|--------------------|------|
| Dictionary version | 20.1 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|---------|
| Reporting group title | Placebo |
|-----------------------|---------|

Reporting group description:

Subjects received the placebo equivalent to basmisanil (RO5186582) as granules packaged in stick packs, taken orally twice daily for 90 days.

| | |
|-----------------------|------------|
| Reporting group title | Basmisanil |
|-----------------------|------------|

Reporting group description:

Subjects received 240 mg of basmisanil (RO5186582) as granules packaged in stick packs, taken orally twice daily for 90 days.

| Serious adverse events | Placebo | Basmisanil | |
|---------------------------------------------------|---------------|---------------|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 3 (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 | Placebo | Basmisanil | |
|-------------------------------------------------------|----------------|----------------|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 1 / 2 (50.00%) | 1 / 3 (33.33%) | |
| Eye disorders | | | |
| Dacryocystitis | | | |
| subjects affected / exposed | 1 / 2 (50.00%) | 0 / 3 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Renal and urinary disorders | | | |
| Urinary tract infection | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | 1 / 3 (33.33%) | |
| occurrences (all) | 0 | 1 | |
| Musculoskeletal and connective tissue disorders | | | |

| | | | |
|-------------------------------------------------------------------|---------------------|--------------------|--|
| Metatarsalgia subjects affected / exposed occurrences (all) | 1 / 2 (50.00%) 1 | 0 / 3 (0.00%) 0 | |
|-------------------------------------------------------------------|---------------------|--------------------|--|

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 20 December 2016 | Removed references to health authorities outside the area of study conduct; replaced Joint Monitoring Committee (JMC) with independent data monitoring committee (iDMC); clarified methods permitted to record body temperature; made Day 1 PK sample collection optional. |
| 24 July 2017 | Expanded subject population; clarified discontinuation criteria; modified interim analysis; modified caregiver eligibility requirement; clarified assessment schedule. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

| Date | Interruption | Restart date |
|------------------|----------------------------------------------------------------------------|--------------|
| 03 November 2017 | The study was prematurely terminated by the sponsor due to low enrollment. | - |

Notes:

Limitations and caveats

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

| |
|--------------------------------------------------------------------------------------------------------------|
| The low number of subjects enrolled in the study limits conclusions that may be derived from the study data. |
|--------------------------------------------------------------------------------------------------------------|

Notes: