



Clinical trial results:

A Multicenter, Randomized, Double-Blind, Placebo-Controlled, Parallel-Group Study to Evaluate the Efficacy and Safety of Padsevonil as Adjunctive Treatment of Focal-Onset Seizures in Adult Subjects With Drug-Resistant Epilepsy

Summary

| | |
|--------------------------|--|
| EudraCT number | 2018-002303-33 |
| Trial protocol | EE DE BE GB HU NL DK SE AT GR BG FI ES CZ HR FR PT SK IT |
| Global end of trial date | 28 September 2020 |

Results information

| | |
|--------------------------------|-----------------|
| Result version number | v1 (current) |
| This version publication date | 10 October 2021 |
| First version publication date | 10 October 2021 |

Trial information

Trial identification

| | |
|-----------------------|--------|
| Sponsor protocol code | EP0092 |
|-----------------------|--------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT03739840 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | UCB Biopharma SRL |
| Sponsor organisation address | Allée de la Recherche 60, Brussels, Belgium, 1070 |
| Public contact | Clin Trial Reg & Results Disclosure, UCB BIOSCIENCES GmbH, clinicaltrials@ucb.com |
| Scientific contact | Clin Trial Reg & Results Disclosure, UCB BIOSCIENCES GmbH, clinicaltrials@ucb.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 | 16 November 2020 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 28 September 2020 |
| Was the trial ended prematurely? | Yes |

Notes:

General information about the trial

Main objective of the trial:

The primary objective was to evaluate the efficacy of the 3 selected dose regimens of padsevonil (PSL) administered concomitantly with up to 3 anti-epileptic drugs (AEDs) compared with placebo for treatment of observable focal-onset seizures in subjects with drug-resistant epilepsy.

Protection of trial subjects:

During the conduct of the study all participants were closely monitored.

Background therapy:

Background therapy as permitted in the protocol.

Evidence for comparator: -

| | |
|---|---------------|
| Actual start date of recruitment | 06 March 2019 |
| Long term follow-up planned | Yes |
| Long term follow-up rationale | Safety |
| Long term follow-up duration | 7 Months |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|----------------------------|
| Country: Number of subjects enrolled | Japan: 23 |
| Country: Number of subjects enrolled | Australia: 5 |
| Country: Number of subjects enrolled | Bosnia and Herzegovina: 10 |
| Country: Number of subjects enrolled | Bulgaria: 26 |
| Country: Number of subjects enrolled | Croatia: 8 |
| Country: Number of subjects enrolled | Czechia: 7 |
| Country: Number of subjects enrolled | Denmark: 14 |
| Country: Number of subjects enrolled | Estonia: 8 |
| Country: Number of subjects enrolled | Finland: 3 |
| Country: Number of subjects enrolled | France: 2 |
| Country: Number of subjects enrolled | Germany: 9 |
| Country: Number of subjects enrolled | Greece: 5 |
| Country: Number of subjects enrolled | Hungary: 2 |
| Country: Number of subjects enrolled | Ireland: 4 |
| Country: Number of subjects enrolled | Italy: 2 |
| Country: Number of subjects enrolled | Norway: 1 |
| Country: Number of subjects enrolled | Poland: 19 |
| Country: Number of subjects enrolled | Portugal: 1 |

| | |
|--------------------------------------|-------------------|
| Country: Number of subjects enrolled | Romania: 5 |
| Country: Number of subjects enrolled | Serbia: 4 |
| Country: Number of subjects enrolled | Spain: 16 |
| Country: Number of subjects enrolled | Sweden: 4 |
| Country: Number of subjects enrolled | Turkey: 17 |
| Country: Number of subjects enrolled | United Kingdom: 5 |
| Country: Number of subjects enrolled | United States: 29 |
| Country: Number of subjects enrolled | Belgium: 3 |
| Worldwide total number of subjects | 232 |
| EEA total number of subjects | 139 |

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) | 218 |
| From 65 to 84 years | 14 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

The study started to enroll participants in March 2019 and concluded in September 2020.

Pre-assignment

Screening details:

The study included: a 4-week Baseline Period, a 16-week Treatment Period, a 4-week Taper Period (for participants who discontinued or choose not to enroll in the open-label extension study) and a Safety Follow-up Period. Participants continuing to the OLE study had a 3-week Conversion Period. The Participant Flow refers to the Randomized Set.

Period 1

| | |
|------------------------------|--|
| Period 1 title | Treatment Period: Wk0-16 |
| Is this the baseline period? | Yes |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Subject, Investigator, Carer, Assessor |

Arms

| | |
|------------------------------|---------|
| Are arms mutually exclusive? | Yes |
| Arm title | Placebo |

Arm description:

Participants randomized to the placebo group received 5-6 placebo tablets to maintain the blinding, twice daily (bid) up to Week 19.

| | |
|--|--------------------|
| Arm type | Placebo |
| Investigational medicinal product name | Placebo |
| Investigational medicinal product code | PBO |
| Other name | |
| Pharmaceutical forms | Film-coated tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Placebo was provided as tablets of matching size and aspect to padsevonil tablets allowing a double-blind packaging. All study participants were instructed to take 5 or 6 tablets containing either PSL or placebo bid, approximately 12 hours apart. The IMP was to be dosed within 30 minutes after food when practically feasible.

| | |
|------------------|-----------------------|
| Arm title | Padsevonil 100 mg BID |
|------------------|-----------------------|

Arm description:

Participants were randomized to receive a combination of tablets of padsevonil 100 mg and placebo (as appropriate) to maintain the blinding, bid up to Week 19.

| | |
|--|--------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Padsevonil |
| Investigational medicinal product code | PSL |
| Other name | |
| Pharmaceutical forms | Film-coated tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Padsevonil was administered as film-coated tablets of different doses, sizes, and appearance. All study participants were instructed to take 5 or 6 tablets containing either PSL or placebo bid, approximately 12 hours apart. The IMP was to be dosed within 30 minutes after food when practically feasible.

| | |
|------------------|-----------------------|
| Arm title | Padsevonil 200 mg BID |
|------------------|-----------------------|

Arm description:

Participants were randomized to receive a combination of tablets of padsevonil 200 mg and placebo (as

appropriate) to maintain the blinding, bid up to Week 19.

| | |
|--|--------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Padsevonil |
| Investigational medicinal product code | PSL |
| Other name | |
| Pharmaceutical forms | Film-coated tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Padsevonil was administered as film-coated tablets of different doses, sizes, and appearance. All study participants were instructed to take 5 or 6 tablets containing either PSL or placebo bid, approximately 12 hours apart. The IMP was to be dosed within 30 minutes after food when practically feasible.

| | |
|------------------|-----------------------|
| Arm title | Padsevonil 400 mg BID |
|------------------|-----------------------|

Arm description:

Participants were randomized to receive a combination of tablets of padsevonil 400 mg and placebo (as appropriate) to maintain the blinding, bid up to Week 19

| | |
|--|--------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Padsevonil |
| Investigational medicinal product code | PSL |
| Other name | |
| Pharmaceutical forms | Film-coated tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Padsevonil was administered as film-coated tablets of different doses, sizes, and appearance. All study participants were instructed to take 5 or 6 tablets containing either PSL or placebo bid, approximately 12 hours apart. The IMP was to be dosed within 30 minutes after food when practically feasible.

| Number of subjects in period 1 | Placebo | Padsevonil 100 mg BID | Padsevonil 200 mg BID |
|---|---------|--------------------------|--------------------------|
| Started | 56 | 60 | 57 |
| Completed Titration and Stabilization | 54 | 58 | 51 |
| Completed Maintenance Period | 46 | 44 | 44 |
| Completed | 46 | 44 | 44 |
| Not completed | 10 | 16 | 13 |
| Study Early Closure | - | - | 1 |
| Due To Sponsor Instruction | - | - | - |
| Trial Closed By Sponsor | - | 1 | - |
| Study Has Been Cancelled By The Sponsor | - | - | - |
| Program Termination | 3 | - | 1 |
| Consent Withdrawn | 1 | 3 | 1 |
| Promotor Decision | - | 1 | - |
| Premature Closure Of The Study | - | - | 1 |
| Sponsor Closed Study- Subject Was Discontinued | 1 | - | - |
| Trial Was Closed By Sponsor | - | - | - |
| Adverse event, non-fatal | 2 | 6 | 6 |
| Premature Program Termination | - | 1 | - |

| | | | |
|--|---|---|---|
| Premature Study Termination By Sponsor | - | - | 1 |
| Per Sponsor Study Closed | - | 1 | - |
| Sponsors Decision | 3 | 2 | 1 |
| Lack of efficacy | - | 1 | - |
| Protocol deviation | - | - | 1 |

| Number of subjects in period 1 | Padsevonil 400 mg BID |
|--|-----------------------|
| Started | 59 |
| Completed Titration and Stabilization | 54 |
| Completed Maintenance Period | 36 |
| Completed | 36 |
| Not completed | 23 |
| Study Early Closure | - |
| Due To Sponsor Instruction | 1 |
| Trial Closed By Sponsor | - |
| Study Has Been Cancelled By The Sponsor | 1 |
| Program Termination | 1 |
| Consent Withdrawn | 1 |
| Promotor Decision | - |
| Premature Closure Of The Study | - |
| Sponsor Closed Study- Subject Was Discontinued | - |
| Trial Was Closed By Sponsor | 1 |
| Adverse event, non-fatal | 12 |
| Premature Program Termination | - |
| Premature Study Termination By Sponsor | - |
| Per Sponsor Study Closed | - |
| Sponsors Decision | 3 |
| Lack of efficacy | 3 |
| Protocol deviation | - |

Period 2

| | |
|------------------------------|--|
| Period 2 title | Post-Treatment Period: Wk16-23 |
| Is this the baseline period? | No |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Subject, Investigator, Carer, Assessor |

Arms

| | |
|------------------------------|-----|
| Are arms mutually exclusive? | Yes |
|------------------------------|-----|

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

Arm description:

Participants randomized to the placebo group received 5-6 placebo tablets to maintain the blinding, bid up to Week 19.

| | |
|--|--------------------|
| Arm type | Placebo |
| Investigational medicinal product name | Placebo |
| Investigational medicinal product code | PBO |
| Other name | |
| Pharmaceutical forms | Film-coated tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Placebo was provided as tablets of matching size and aspect to padsevonil tablets allowing a double-blind packaging. All study participants were instructed to take 5 or 6 tablets containing either PSL or placebo bid, approximately 12 hours apart. The IMP was to be dosed within 30 minutes after food when practically feasible.

| | |
|------------------|-----------------------|
| Arm title | Padsevonil 100 mg BID |
|------------------|-----------------------|

Arm description:

Participants were randomized to receive a combination of tablets of padsevonil 100 mg and placebo (as appropriate) to maintain the blinding, bid up to Week 19.

| | |
|--|--------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Padsevonil |
| Investigational medicinal product code | PSL |
| Other name | |
| Pharmaceutical forms | Film-coated tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Padsevonil was administered as film-coated tablets of different doses, sizes, and appearance. All study participants were instructed to take 5 or 6 tablets containing either PSL or placebo bid, approximately 12 hours apart. The IMP was to be dosed within 30 minutes after food when practically feasible.

| | |
|------------------|-----------------------|
| Arm title | Padsevonil 200 mg BID |
|------------------|-----------------------|

Arm description:

Participants were randomized to receive a combination of tablets of padsevonil 200 mg and placebo (as appropriate) to maintain the blinding, bid up to Week 19.

| | |
|--|--------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Padsevonil |
| Investigational medicinal product code | PSL |
| Other name | |
| Pharmaceutical forms | Film-coated tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Padsevonil was administered as film-coated tablets of different doses, sizes, and appearance. All study participants were instructed to take 5 or 6 tablets containing either PSL or placebo bid, approximately 12 hours apart. The IMP was to be dosed within 30 minutes after food when practically feasible.

| | |
|------------------|-----------------------|
| Arm title | Padsevonil 400 mg BID |
|------------------|-----------------------|

Arm description:

Participants were randomized to receive a combination of tablets of padsevonil 400 mg and placebo (as appropriate) to maintain the blinding, bid up to Week 19

| | |
|----------|--------------|
| Arm type | Experimental |
|----------|--------------|

| | |
|--|--------------------|
| Investigational medicinal product name | Padsevonil |
| Investigational medicinal product code | PSL |
| Other name | |
| Pharmaceutical forms | Film-coated tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Padsevonil was administered as film-coated tablets of different doses, sizes, and appearance. All study participants were instructed to take 5 or 6 tablets containing either PSL or placebo bid, approximately 12 hours apart. The IMP was to be dosed within 30 minutes after food when practically feasible.

| Number of subjects in period 2 | Placebo | Padsevonil 100 mg BID | Padsevonil 200 mg BID |
|--|--------------------|--------------------------|--------------------------|
| Started | 46 | 44 | 44 |
| Started Conversion Period | 33 ^[1] | 31 ^[2] | 29 ^[3] |
| Completed Conversion Period | 33 ^[4] | 31 ^[5] | 29 ^[6] |
| Started Taper and Safety Follow-up | 19 ^[7] | 18 ^[8] | 21 ^[9] |
| Completed Taper and Safety Follow-up | 15 ^[10] | 16 ^[11] | 18 ^[12] |
| Enrolled in EP0093 | 27 ^[13] | 26 ^[14] | 23 ^[15] |
| Completed | 42 | 42 | 41 |
| Not completed | 4 | 2 | 3 |
| Sponsor's Decision | - | 1 | - |
| Sponsor Closed Study- Subject Was Discontinued | - | 1 | - |
| Trial Closed By Sponsor Decision | - | - | 1 |
| Adverse event, non-fatal | 3 | - | - |
| Sponsor Decision + Subject Refusal | - | - | 1 |
| Early Study Closure | - | - | 1 |
| Sponsor Decision To Terminate The Study | 1 | - | - |
| Consent Withdrawn | - | - | - |

| Number of subjects in period 2 | Padsevonil 400 mg BID |
|--|--------------------------|
| Started | 36 |
| Started Conversion Period | 28 ^[16] |
| Completed Conversion Period | 28 ^[17] |
| Started Taper and Safety Follow-up | 13 ^[18] |
| Completed Taper and Safety Follow-up | 12 ^[19] |
| Enrolled in EP0093 | 23 ^[20] |
| Completed | 35 |
| Not completed | 1 |
| Sponsor's Decision | - |
| Sponsor Closed Study- Subject Was Discontinued | - |
| Trial Closed By Sponsor Decision | - |

| | |
|---|---|
| Adverse event, non-fatal | - |
| Sponsor Decision + Subject Refusal | - |
| Early Study Closure | - |
| Sponsor Decision To Terminate The Study | - |
| Consent Withdrawn | 1 |

Notes:

[1] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: Number of participants at this milestone reflect those who were randomized to Placebo and entered to conversion period, completed conversion period, had taper and safety follow-up or enrolled in EP0093. Participants could enter taper and safety follow-up after period 1.

[2] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: Number of participants at this milestone reflect those who were randomized to Padsevonil 100 mg BID and entered to conversion period, completed conversion period, had taper and safety follow-up or enrolled in EP0093. Participants could enter taper and safety follow-up after period 1.

[3] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: Number of participants at this milestone reflect those who were randomized to Padsevonil 200 mg BID and entered to conversion period, completed conversion period, had taper and safety follow-up or enrolled in EP0093. Participants could enter taper and safety follow-up after period 1.

[4] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: Number of participants at this milestone reflect those who were randomized to Placebo and entered to conversion period, completed conversion period, had taper and safety follow-up or enrolled in EP0093. Participants could enter taper and safety follow-up after period 1.

[5] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: Number of participants at this milestone reflect those who were randomized to Padsevonil 100 mg BID and entered to conversion period, completed conversion period, had taper and safety follow-up or enrolled in EP0093. Participants could enter taper and safety follow-up after period 1.

[6] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: Number of participants at this milestone reflect those who were randomized to Padsevonil 200 mg BID and entered to conversion period, completed conversion period, had taper and safety follow-up or enrolled in EP0093. Participants could enter taper and safety follow-up after period 1.

[7] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: Number of participants at this milestone reflect those who were randomized to Placebo and entered to conversion period, completed conversion period, had taper and safety follow-up or enrolled in EP0093. Participants could enter taper and safety follow-up after period 1.

[8] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: Number of participants at this milestone reflect those who were randomized to Padsevonil 100 mg BID and entered to conversion period, completed conversion period, had taper and safety follow-up or enrolled in EP0093. Participants could enter taper and safety follow-up after period 1.

[9] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: Number of participants at this milestone reflect those who were randomized to Padsevonil 200 mg BID and entered to conversion period, completed conversion period, had taper and safety follow-up or enrolled in EP0093. Participants could enter taper and safety follow-up after period 1.

Baseline characteristics

Reporting groups

| | |
|---|-----------------------|
| Reporting group title | Placebo |
| Reporting group description: Participants randomized to the placebo group received 5-6 placebo tablets to maintain the blinding, twice daily (bid) up to Week 19. | |
| Reporting group title | Padsevonil 100 mg BID |
| Reporting group description: Participants were randomized to receive a combination of tablets of padsevonil 100 mg and placebo (as appropriate) to maintain the blinding, bid up to Week 19. | |
| Reporting group title | Padsevonil 200 mg BID |
| Reporting group description: Participants were randomized to receive a combination of tablets of padsevonil 200 mg and placebo (as appropriate) to maintain the blinding, bid up to Week 19. | |
| Reporting group title | Padsevonil 400 mg BID |
| Reporting group description: Participants were randomized to receive a combination of tablets of padsevonil 400 mg and placebo (as appropriate) to maintain the blinding, bid up to Week 19 | |

| Reporting group values | Placebo | Padsevonil 100 mg BID | Padsevonil 200 mg BID |
|---|--------------------------|--------------------------|--------------------------|
| Number of subjects | 56 | 60 | 57 |
| Age Categorical Units: Participants | | | |
| <=18 years | 1 | 0 | 4 |
| Between 18 and 65 years | 52 | 57 | 48 |
| >=65 years | 3 | 3 | 5 |
| Age Continuous Units: years | | | |
| arithmetic mean | 41.9 | 40.7 | 39.5 |
| standard deviation | ± 13.6 | ± 13.0 | ± 14.3 |
| Sex: Female, Male Units: Participants | | | |
| Female | 34 | 34 | 29 |
| Male | 22 | 26 | 28 |
| Race/Ethnicity, Customized Units: Subjects | | | |
| American Indian or Alaska Native | 1 | 0 | 0 |
| Asian | 5 | 5 | 7 |
| Black | 0 | 1 | 1 |
| Native Hawaiian or Other Pacific Islander | 0 | 2 | 0 |
| White | 49 | 50 | 49 |
| Other/mixed | 1 | 2 | 0 |
| Reporting group values | Padsevonil 400 mg BID | Total | |
| Number of subjects | 59 | 232 | |

| | | | |
|---|--------|-----|--|
| Age Categorical Units: Participants | | | |
| <=18 years | 0 | 5 | |
| Between 18 and 65 years | 56 | 213 | |
| >=65 years | 3 | 14 | |
| Age Continuous Units: years | | | |
| arithmetic mean | 39.7 | | |
| standard deviation | ± 13.6 | - | |
| Sex: Female, Male Units: Participants | | | |
| Female | 34 | 131 | |
| Male | 25 | 101 | |
| Race/Ethnicity, Customized Units: Subjects | | | |
| American Indian or Alaska Native | 0 | 1 | |
| Asian | 7 | 24 | |
| Black | 1 | 3 | |
| Native Hawaiian or Other Pacific Islander | 0 | 2 | |
| White | 51 | 199 | |
| Other/mixed | 0 | 3 | |

End points

End points reporting groups

| | |
|---|-----------------------------|
| Reporting group title | Placebo |
| Reporting group description: Participants randomized to the placebo group received 5-6 placebo tablets to maintain the blinding, twice daily (bid) up to Week 19. | |
| Reporting group title | Padsevonil 100 mg BID |
| Reporting group description: Participants were randomized to receive a combination of tablets of padsevonil 100 mg and placebo (as appropriate) to maintain the blinding, bid up to Week 19. | |
| Reporting group title | Padsevonil 200 mg BID |
| Reporting group description: Participants were randomized to receive a combination of tablets of padsevonil 200 mg and placebo (as appropriate) to maintain the blinding, bid up to Week 19. | |
| Reporting group title | Padsevonil 400 mg BID |
| Reporting group description: Participants were randomized to receive a combination of tablets of padsevonil 400 mg and placebo (as appropriate) to maintain the blinding, bid up to Week 19 | |
| Reporting group title | Placebo |
| Reporting group description: Participants randomized to the placebo group received 5-6 placebo tablets to maintain the blinding, bid up to Week 19. | |
| Reporting group title | Padsevonil 100 mg BID |
| Reporting group description: Participants were randomized to receive a combination of tablets of padsevonil 100 mg and placebo (as appropriate) to maintain the blinding, bid up to Week 19. | |
| Reporting group title | Padsevonil 200 mg BID |
| Reporting group description: Participants were randomized to receive a combination of tablets of padsevonil 200 mg and placebo (as appropriate) to maintain the blinding, bid up to Week 19. | |
| Reporting group title | Padsevonil 400 mg BID |
| Reporting group description: Participants were randomized to receive a combination of tablets of padsevonil 400 mg and placebo (as appropriate) to maintain the blinding, bid up to Week 19 | |
| Subject analysis set title | Placebo (FAS) |
| Subject analysis set type | Full analysis |
| Subject analysis set description: Participants randomized to the placebo group received 5-6 placebo tablets to maintain the blinding, bid up to Week 19. Participants formed the Full Analysis Set (FAS). | |
| Subject analysis set title | Padsevonil 100 mg BID (FAS) |
| Subject analysis set type | Full analysis |
| Subject analysis set description: Participants were randomized to receive a combination of tablets of padsevonil 100 mg and placebo (as appropriate) to maintain the blinding, bid up to Week 19. Participants formed the FAS. | |
| Subject analysis set title | Padsevonil 200 mg BID (FAS) |
| Subject analysis set type | Full analysis |
| Subject analysis set description: Participants were randomized to receive a combination of tablets of padsevonil 200 mg and placebo (as appropriate) to maintain the blinding, bid up to Week 19. Participants formed the FAS. | |
| Subject analysis set title | Padsevonil 400 mg BID (FAS) |
| Subject analysis set type | Full analysis |
| Subject analysis set description: Participants were randomized to receive a combination of tablets of padsevonil 400 mg and placebo (as | |

appropriate) to maintain the blinding, bid up to Week 19. Participants formed the FAS.

| | |
|----------------------------|-----------------|
| Subject analysis set title | Placebo (SS) |
| Subject analysis set type | Safety analysis |

Subject analysis set description:

Participants randomized to the placebo group received 5-6 placebo tablets to maintain the blinding, bid up to Week 19. Participants formed the Safety Set (SS).

| | |
|----------------------------|----------------------------|
| Subject analysis set title | Padsevonil 100 mg BID (SS) |
| Subject analysis set type | Safety analysis |

Subject analysis set description:

Participants were randomized to receive a combination of tablets of padsevonil 100 mg and placebo (as appropriate) to maintain the blinding, bid up to Week 19. Participants formed the SS.

| | |
|----------------------------|----------------------------|
| Subject analysis set title | Padsevonil 200 mg BID (SS) |
| Subject analysis set type | Safety analysis |

Subject analysis set description:

Participants were randomized to receive a combination of tablets of padsevonil 200 mg and placebo (as appropriate) to maintain the blinding, bid up to Week 19. Participants formed the SS.

| | |
|----------------------------|----------------------------|
| Subject analysis set title | Padsevonil 400 mg BID (SS) |
| Subject analysis set type | Safety analysis |

Subject analysis set description:

Participants were randomized to receive a combination of tablets of padsevonil 400 mg and placebo (as appropriate) to maintain the blinding, bid up to Week 19. Participants formed the SS.

| | |
|----------------------------|-------------------------------|
| Subject analysis set title | Placebo Treatment Period (SS) |
| Subject analysis set type | Safety analysis |

Subject analysis set description:

Participants randomized to the placebo group received 5-6 placebo tablets to maintain the blinding, bid up to Week 19. Participants formed the Safety Set (SS).

| | |
|----------------------------|---|
| Subject analysis set title | Padsevonil 100 mg BID Treatment Period (SS) |
| Subject analysis set type | Safety analysis |

Subject analysis set description:

Participants were randomized to receive a combination of tablets of padsevonil 100 mg and placebo (as appropriate) to maintain the blinding, bid up to Week 19. Participants formed the SS.

| | |
|----------------------------|---|
| Subject analysis set title | Padsevonil 200 mg BID Treatment Period (SS) |
| Subject analysis set type | Safety analysis |

Subject analysis set description:

Participants were randomized to receive a combination of tablets of padsevonil 200 mg and placebo (as appropriate) to maintain the blinding, bid up to Week 19. Participants formed the SS.

| | |
|----------------------------|---|
| Subject analysis set title | Padsevonil 400 mg BID Treatment Period (SS) |
| Subject analysis set type | Safety analysis |

Subject analysis set description:

Participants were randomized to receive a combination of tablets of padsevonil 400 mg and placebo (as appropriate) to maintain the blinding, bid up to Week 19. Participants formed the SS.

| | |
|----------------------------|--------------------------------|
| Subject analysis set title | Placebo Conversion Period (SS) |
| Subject analysis set type | Safety analysis |

Subject analysis set description:

A 3-Week Conversion Period was required for study participants who chose to enroll in the open-label extension (OLE) study at the end of the 12-Week Maintenance Period. Participants initially randomized to placebo progressively received padsevonil in a blinded way to reach the entry dose of 400 mg/day for the OLE. Participants formed the Safety Set (SS).

| | |
|----------------------------|--|
| Subject analysis set title | Padsevonil 100 mg BID Conversion Period (SS) |
| Subject analysis set type | Safety analysis |

Subject analysis set description:

A 3-Week Conversion Period was required for study participants who chose to enroll in the OLE study at the end of the 12-Week Maintenance Period. The dose for participants initially randomized to padsevonil 100 mg bid was gradually adapted (increased or decreased) in a blinded way to reach the entry dose of 400 mg/day for the OLE. Participants formed the SS.

| | |
|----------------------------|--|
| Subject analysis set title | Padsevonil 200 mg BID Conversion Period (SS) |
|----------------------------|--|

| | |
|---------------------------|-----------------|
| Subject analysis set type | Safety analysis |
|---------------------------|-----------------|

Subject analysis set description:

A 3-Week Conversion Period was required for study participants who chose to enroll in the OLE study at the end of the 12-Week Maintenance Period. The dose for participants initially randomized to padsevonil 200 mg bid was gradually adapted (increased or decreased) in a blinded way to reach the entry dose of 400 mg/day for the OLE. Participants formed the SS.

| | |
|----------------------------|--|
| Subject analysis set title | Padsevonil 400 mg BID Conversion Period (SS) |
|----------------------------|--|

| | |
|---------------------------|-----------------|
| Subject analysis set type | Safety analysis |
|---------------------------|-----------------|

Subject analysis set description:

A 3-Week Conversion Period was required for study participants who chose to enroll in the OLE study at the end of the 12-Week Maintenance Period. The dose for participants initially randomized to padsevonil 400 mg bid was gradually adapted (increased or decreased) in a blinded way to reach the entry dose of 400 mg/day for the OLE. Participants formed the SS.

| | |
|----------------------------|-----------------------------------|
| Subject analysis set title | Placebo Taper and SFU Period (SS) |
|----------------------------|-----------------------------------|

| | |
|---------------------------|-----------------|
| Subject analysis set type | Safety analysis |
|---------------------------|-----------------|

Subject analysis set description:

A 4-Week Taper Period was required for participants who chose not to enroll in the OLE study or discontinued before the end of the 12-Week Maintenance Period. Participants initially randomized to the placebo group received 5-6 placebo tablets to maintain the blinding and have been gradually tapered off the IMP over a 3-Week period followed by 1-week drug-free period. Afterward, participants had a Safety Follow-Up visit 30 days after the last IMP intake. Participants formed the Safety Set (SS).

| | |
|----------------------------|--|
| Subject analysis set title | Padsevonil 100mg BID Taper and SFU Period (SS) |
|----------------------------|--|

| | |
|---------------------------|-----------------|
| Subject analysis set type | Safety analysis |
|---------------------------|-----------------|

Subject analysis set description:

A 4-Week Taper Period was required for participants who chose not to enroll in the OLE study or discontinued before the end of the 12-Week Maintenance Period. Participants initially randomized to padsevonil 100 mg bid have been gradually tapered off the IMP over a 3-Week period followed by 1-week drug-free period. Afterward, participants had a Safety Follow-Up visit 30 days after the last IMP intake. Participants formed the SS.

| | |
|----------------------------|--|
| Subject analysis set title | Padsevonil 200mg BID Taper and SFU Period (SS) |
|----------------------------|--|

| | |
|---------------------------|-----------------|
| Subject analysis set type | Safety analysis |
|---------------------------|-----------------|

Subject analysis set description:

A 4-Week Taper Period was required for participants who chose not to enroll in the OLE study or discontinued before the end of the 12-Week Maintenance Period. Participants initially randomized to padsevonil 200 mg bid have been gradually tapered off the IMP over a 3-Week period followed by 1-week drug-free period. Afterward, participants had a Safety Follow-Up visit 30 days after the last IMP intake. Participants formed the SS.

| | |
|----------------------------|--|
| Subject analysis set title | Padsevonil 400mg BID Taper and SFU Period (SS) |
|----------------------------|--|

| | |
|---------------------------|-----------------|
| Subject analysis set type | Safety analysis |
|---------------------------|-----------------|

Subject analysis set description:

A 4-Week Taper Period was required for participants who chose not to enroll in the OLE study or discontinued before the end of the 12-Week Maintenance Period. Participants initially randomized to padsevonil 200 mg bid have been gradually tapered off the IMP over a 3-Week period followed by 1-week drug-free period. Afterward, participants had a Safety Follow-Up visit 30 days after the last IMP intake. Participants formed the SS.

Primary: 75% responder rate from Baseline over the 12-week Maintenance Period

| | |
|-----------------|--|
| End point title | 75% responder rate from Baseline over the 12-week Maintenance Period |
|-----------------|--|

End point description:

The 75 % responder rate, where a responder was a participant experiencing a ≥ 75 % reduction in observable focal-onset seizure frequency from Baseline, over the 12-Week Maintenance Period. The Full Analysis Set (FAS) consisted of all study participants in the RS who were administered at least 1 dose or a partial dose of IMP and had Baseline and at least 1 post-Baseline seizure frequency data during the 16-week Treatment Period. Here, number of participants were included who were evaluable for the assessment.

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

End point timeframe:

From Baseline over the 12 Week Maintenance Period (up to Week 16)

| End point values | Placebo (FAS) | Padsevonil 100 mg BID (FAS) | Padsevonil 200 mg BID (FAS) | Padsevonil 400 mg BID (FAS) |
|-----------------------------------|----------------------|-----------------------------|-----------------------------|-----------------------------|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 54 | 59 | 56 | 56 |
| Units: percentage of participants | | | | |
| number (not applicable) | 13.0 | 15.3 | 12.5 | 14.3 |

Statistical analyses

| Statistical analysis title | Statistical analysis 1 |
|--|---|
| Statistical analysis description: | |
| PSL dose/Placebo calculated using logistic regression with categorical factors for treatment group (each PSL dose group referenced to the placebo group), Region (Europe, non-Europe), Baseline SV2A use (Yes, No) and log-transformed Baseline seizure frequency as a continuous covariate. | |
| Comparison groups | Placebo (FAS) v Padsevonil 100 mg BID (FAS) |
| Number of subjects included in analysis | 113 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.803 ^[1] |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 1.15 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.39 |
| upper limit | 3.38 |

Notes:

[1] - Nominal p-values were not adjusted for multiplicity.

| Statistical analysis title | Statistical analysis 2 |
|--|---|
| Statistical analysis description: | |
| PSL dose/Placebo calculated using logistic regression with categorical factors for treatment group (each PSL dose group referenced to the placebo group), Region (Europe, non-Europe), Baseline SV2A use (Yes, No) and log-transformed Baseline seizure frequency as a continuous covariate. | |
| Comparison groups | Placebo (FAS) v Padsevonil 200 mg BID (FAS) |
| Number of subjects included in analysis | 110 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.772 ^[2] |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 0.84 |

| | |
|---------------------|---------|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.27 |
| upper limit | 2.65 |

Notes:

[2] - Nominal p-values were not adjusted for multiplicity.

| | |
|-----------------------------------|------------------------|
| Statistical analysis title | Statistical analysis 3 |
|-----------------------------------|------------------------|

Statistical analysis description:

PSL dose/Placebo calculated using logistic regression with categorical factors for treatment group (each PSL dose group referenced to the placebo group), Region (Europe, non-Europe), Baseline SV2A use (Yes, No) and log-transformed Baseline seizure frequency as a continuous covariate.

| | |
|---|---|
| Comparison groups | Placebo (FAS) v Padsevonil 400 mg BID (FAS) |
| Number of subjects included in analysis | 110 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.989 ^[3] |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 1.01 |

Confidence interval

| | |
|-------------|---------|
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.33 |
| upper limit | 3.08 |

Notes:

[3] - Nominal p-values were not adjusted for multiplicity.

Primary: Percentage of Participants With Treatment-Emergent Adverse Events (TEAEs)

| | |
|-----------------|--|
| End point title | Percentage of Participants With Treatment-Emergent Adverse Events (TEAEs) ^[4] |
|-----------------|--|

End point description:

An Adverse Event is any untoward medical occurrence in a patient or clinical investigation subject administered a pharmaceutical product that does not necessarily have a causal relationship with this treatment. A TEAE was defined as any event not present before the initiation of the first dose of study treatment or any unresolved event already present before initiation of the first dose that worsened in intensity following exposure to the treatment. The Safety Set consisted of all study participants who were administered at least 1 dose or a partial dose of IMP.

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

End point timeframe:

From Baseline until Safety Follow-Up (up to Week 23)

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: No formal statistical hypothesis testing was planned for this endpoint. Results were summarized as descriptive statistics only.

| End point values | Placebo (SS) | Padsevonil 100 mg BID (SS) | Padsevonil 200 mg BID (SS) | Padsevonil 400 mg BID (SS) |
|-----------------------------------|----------------------|----------------------------|----------------------------|----------------------------|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 55 | 60 | 57 | 59 |
| Units: percentage of participants | | | | |
| number (not applicable) | 69.1 | 83.3 | 78.9 | 84.7 |

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Participants With Treatment-Emergent Adverse Events (TEAEs) leading to study withdrawal

| | |
|-----------------|--|
| End point title | Percentage of Participants With Treatment-Emergent Adverse Events (TEAEs) leading to study withdrawal ^[5] |
|-----------------|--|

End point description:

An Adverse Event is any untoward medical occurrence in a patient or clinical investigation subject administered a pharmaceutical product that does not necessarily have a causal relationship with this treatment. A TEAE was defined as any event not present before the initiation of the first dose of study treatment or any unresolved event already present before initiation of the first dose that worsened in intensity following exposure to the treatment. The Safety Set consisted of all study participants who were administered at least 1 dose or a partial dose of IMP.

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

End point timeframe:

From Baseline until Safety Follow-Up (up to Week 23)

Notes:

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

Justification: No formal statistical hypothesis testing was planned for this endpoint. Results were summarized as descriptive statistics only.

| End point values | Placebo (SS) | Padsevonil 100 mg BID (SS) | Padsevonil 200 mg BID (SS) | Padsevonil 400 mg BID (SS) |
|-----------------------------------|----------------------|----------------------------|----------------------------|----------------------------|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 55 | 60 | 57 | 59 |
| Units: percentage of participants | | | | |
| number (not applicable) | 7.3 | 10.0 | 10.5 | 20.3 |

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Participants With Treatment-Emergent Serious Adverse Events (SAEs)

| | |
|-----------------|---|
| End point title | Percentage of Participants With Treatment-Emergent Serious Adverse Events (SAEs) ^[6] |
|-----------------|---|

End point description:

A Serious Adverse Event (SAE) is any untoward medical occurrence that at any dose: Results in death, is life-threatening, requires inpatient hospitalization or prolongation of existing hospitalization, is a congenital anomaly or birth defect, is an infection that requires treatment parenteral antibiotics, other important medical events which based on medical or scientific judgement may jeopardize the patients, or may require medical or surgical intervention to prevent any of the above. A TEAE was defined as any

event not present before the initiation of the first dose of study treatment or any unresolved event already present before initiation of the first dose that worsened in intensity following exposure to the treatment. The Safety Set consisted of all study participants who were administered at least 1 dose or a partial dose of IMP.

| | |
|--|---------|
| End point type | Primary |
| End point timeframe: | |
| From Baseline until Safety Follow-Up (up to Week 23) | |

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 formal statistical hypothesis testing was planned for this endpoint. Results were summarized as descriptive statistics only.

| End point values | Placebo (SS) | Padsevonil 100 mg BID (SS) | Padsevonil 200 mg BID (SS) | Padsevonil 400 mg BID (SS) |
|-----------------------------------|----------------------|----------------------------|----------------------------|----------------------------|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 55 | 60 | 57 | 59 |
| Units: percentage of participants | | | | |
| number (not applicable) | 9.1 | 3.3 | 1.8 | 10.2 |

Statistical analyses

No statistical analyses for this end point

Secondary: Change in log-transformed observable focal-onset seizure frequency from Baseline over the 12-week Maintenance Period

| | |
|-----------------|--|
| End point title | Change in log-transformed observable focal-onset seizure frequency from Baseline over the 12-week Maintenance Period |
|-----------------|--|

End point description:

During the study, participants kept diaries to record daily seizure activity. Seizure frequency refers to 28-day adjusted frequency. Seizure frequency was based on investigator assessment of participants' reports of daily seizure type and frequency. Observable focal-onset seizures refer to Type IA1, IB, and IC (ILAE Classification of Epileptic Seizures, 1981). Based on ANCOVA on change in log-transformed seizure frequency from Baseline, with treatment group as the main factor, Baseline log-transformed seizure frequency as a continuous covariate, Baseline SV2A use (Yes or No) and Region (Europe, non-Europe) as categorical factors. The Full Analysis Set (FAS) consisted of all study participants in the RS who were administered at least 1 dose or a partial dose of IMP and had Baseline and at least 1 post-Baseline seizure frequency data during the 16-week Treatment Period. Here, number of participants were included who were evaluable for the assessment.

| | |
|---|-----------|
| End point type | Secondary |
| End point timeframe: | |
| From Baseline over the 12 Week Maintenance Period (up to Week 16) | |

| End point values | Placebo (FAS) | Padsevonil 100 mg BID (FAS) | Padsevonil 200 mg BID (FAS) | Padsevonil 400 mg BID (FAS) |
|--|----------------------------|------------------------------|------------------------------|------------------------------|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 54 | 59 | 56 | 56 |
| Units: log e seizures per 28 days | | | | |
| least squares mean (confidence interval 95%) | -0.41 (-0.6133 to -0.2025) | -0.35 (-0.54906 to -0.15705) | -0.47 (-0.67559 to -0.27382) | -0.47 (-0.67267 to -0.27361) |

Statistical analyses

| Statistical analysis title | Statistical analysis 1 |
|---|---|
| Statistical analysis description: Percent reduction over placebo was calculated as $100 \times (1 - \exp(\text{diff}))$, where diff was the model estimate of the log ratio between each PSL group and placebo group. | |
| Comparison groups | Placebo (FAS) v Padsevonil 100 mg BID (FAS) |
| Number of subjects included in analysis | 113 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.687 ^[7] |
| Method | ANCOVA |
| Parameter estimate | Percent reduction |
| Point estimate | -5.6 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -38.1 |
| upper limit | 19.2 |

Notes:

[7] - Adjusted p-values are from the Hochberg step-up procedure within SAS® Proc Multtest to control Type I error.

| Statistical analysis title | Statistical analysis 3 |
|---|---|
| Statistical analysis description: Percent reduction over placebo was calculated as $100 \times (1 - \exp(\text{diff}))$, where diff was the model estimate of the log ratio between each PSL group and placebo group. | |
| Comparison groups | Placebo (FAS) v Padsevonil 400 mg BID (FAS) |
| Number of subjects included in analysis | 110 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.687 ^[8] |
| Method | ANCOVA |
| Parameter estimate | Percent reduction |
| Point estimate | 6.3 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -22.9 |
| upper limit | 28.6 |

Notes:

[8] - Adjusted p-values were from the Hochberg step-up procedure within SAS® Proc Multtest to control Type I error.

| Statistical analysis title | Statistical analysis 2 |
|----------------------------|------------------------|
|----------------------------|------------------------|

Statistical analysis description:

Percent reduction over placebo was calculated as $100 \times (1 - \exp(\text{diff}))$, where diff was the model estimate

of the log ratio between each PSL group and placebo group.

| | |
|---|---|
| Comparison groups | Placebo (FAS) v Padsevonil 200 mg BID (FAS) |
| Number of subjects included in analysis | 110 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.687 ^[9] |
| Method | ANCOVA |
| Parameter estimate | Percent reduction |
| Point estimate | 6.5 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -22.7 |
| upper limit | 28.7 |

Notes:

[9] - Adjusted p-values were from the Hochberg step-up procedure within SAS® Proc Multtest to control Type I error.

Secondary: Percent change in observable focal-onset seizure frequency from Baseline over the 12-week Maintenance Period

| | |
|-----------------|--|
| End point title | Percent change in observable focal-onset seizure frequency from Baseline over the 12-week Maintenance Period |
|-----------------|--|

End point description:

During the study, participants kept diaries to record daily seizure activity. The percentage of participants who experienced a 50 % or greater reduction in seizure frequency per 28 days relative to Baseline (responders) were assessed. The Full Analysis Set (FAS) consisted of all study participants in the RS who were administered at least 1 dose or a partial dose of IMP and had Baseline and at least 1 post-Baseline seizure frequency data during the 16-week Treatment Period. Here, number of participants were included who were evaluable for the assessment.

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

End point timeframe:

From Baseline over the 12 Week Maintenance Period (up to Week 16)

| End point values | Placebo (FAS) | Padsevonil 100 mg BID (FAS) | Padsevonil 200 mg BID (FAS) | Padsevonil 400 mg BID (FAS) |
|--------------------------------------|----------------------|-----------------------------|-----------------------------|-----------------------------|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 54 | 59 | 56 | 56 |
| Units: percent change | | | | |
| arithmetic mean (standard deviation) | 22.34 (± 44.56) | 11.72 (± 81.52) | 30.29 (± 39.58) | 22.41 (± 62.80) |

Statistical analyses

| | |
|----------------------------|------------------------|
| Statistical analysis title | Statistical analysis 1 |
|----------------------------|------------------------|

Statistical analysis description:

Dose group comparisons to Placebo p-value are based on the Wilcoxon-Mann-Whitney test. Hodges Lehmann nonparametric effect estimates and corresponding two-sided 95% asymptotic confidence intervals are provided for the effect difference between each PSL dose and placebo.

| | |
|-------------------|---|
| Comparison groups | Placebo (FAS) v Padsevonil 100 mg BID (FAS) |
|-------------------|---|

| | |
|---|----------------------------------|
| Number of subjects included in analysis | 113 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.737 ^[10] |
| Method | Wilcoxon (Mann-Whitney) |
| Parameter estimate | Median difference (final values) |
| Point estimate | 3.25 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -17.08 |
| upper limit | 20.36 |

Notes:

[10] - Nominal p-values were not adjusted for multiplicity.

| | |
|-----------------------------------|------------------------|
| Statistical analysis title | Statistical analysis 3 |
|-----------------------------------|------------------------|

Statistical analysis description:

Dose group comparisons to Placebo p-value are based on the Wilcoxon-Mann-Whitney test. Hodges Lehmann nonparametric effect estimates and corresponding two-sided 95% asymptotic confidence intervals are provided for the effect difference between each PSL dose and placebo.

| | |
|---|---|
| Comparison groups | Placebo (FAS) v Padsevonil 400 mg BID (FAS) |
| Number of subjects included in analysis | 110 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.341 ^[11] |
| Method | Wilcoxon (Mann-Whitney) |
| Parameter estimate | Median difference (net) |
| Point estimate | 9.31 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -10.92 |
| upper limit | 28.21 |

Notes:

[11] - Nominal p-values were not adjusted for multiplicity.

| | |
|-----------------------------------|------------------------|
| Statistical analysis title | Statistical analysis 2 |
|-----------------------------------|------------------------|

Statistical analysis description:

Dose group comparisons to Placebo p-value are based on the Wilcoxon-Mann-Whitney test. Hodges Lehmann nonparametric effect estimates and corresponding two-sided 95% asymptotic confidence intervals are provided for the effect difference between each PSL dose and placebo.

| | |
|---|---|
| Comparison groups | Placebo (FAS) v Padsevonil 200 mg BID (FAS) |
| Number of subjects included in analysis | 110 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.458 ^[12] |
| Method | Wilcoxon (Mann-Whitney) |
| Parameter estimate | Median difference (net) |
| Point estimate | 6.17 |

| | |
|---------------------|---------|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -10 |
| upper limit | 21.91 |

Notes:

[12] - Nominal p-values were not adjusted for multiplicity.

Secondary: 50% responder rate from Baseline over the 12-week Maintenance Period

| | |
|-----------------|--|
| End point title | 50% responder rate from Baseline over the 12-week Maintenance Period |
|-----------------|--|

End point description:

The 50% responder rate, where a responder was a participant experiencing a $\geq 50\%$ reduction in observable focal-onset seizure frequency from Baseline, over the 12-week Maintenance Period. The Full Analysis Set (FAS) consisted of all study participants in the RS who were administered at least 1 dose or a partial dose of IMP and had Baseline and at least 1 post-Baseline seizure frequency data during the 16-week Treatment Period. Here, number of participants were included who were evaluable for the assessment.

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

End point timeframe:

From Baseline over the 12 Week Maintenance Period (up to Week 16)

| End point values | Placebo (FAS) | Padsevonil 100 mg BID (FAS) | Padsevonil 200 mg BID (FAS) | Padsevonil 400 mg BID (FAS) |
|-----------------------------------|----------------------|-----------------------------|-----------------------------|-----------------------------|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 54 | 59 | 56 | 56 |
| Units: percentage of participants | | | | |
| number (not applicable) | 27.8 | 35.6 | 33.9 | 42.9 |

Statistical analyses

| | |
|----------------------------|------------------------|
| Statistical analysis title | Statistical analysis 1 |
|----------------------------|------------------------|

Statistical analysis description:

PSL dose/Placebo calculated using logistic regression with categorical factors for treatment group (each PSL dose group referenced to the placebo group), Region (Europe, non-Europe), Baseline SV2A use (Yes, No) and log-transformed Baseline seizure frequency as a continuous covariate.

| | |
|---|---|
| Comparison groups | Placebo (FAS) v Padsevonil 100 mg BID (FAS) |
| Number of subjects included in analysis | 113 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.425 ^[13] |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 1.4 |

| | |
|---------------------|---------|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.61 |
| upper limit | 3.18 |

Notes:

[13] - Nominal p-values were not adjusted for multiplicity.

| | |
|-----------------------------------|------------------------|
| Statistical analysis title | Statistical analysis 2 |
|-----------------------------------|------------------------|

Statistical analysis description:

PSL dose/Placebo calculated using logistic regression with categorical factors for treatment group (each PSL dose group referenced to the placebo group), Region (Europe, non-Europe), Baseline SV2A use (Yes, No) and log-transformed Baseline seizure frequency as a continuous covariate

| | |
|---|---|
| Comparison groups | Placebo (FAS) v Padsevonil 200 mg BID (FAS) |
| Number of subjects included in analysis | 110 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.625 ^[14] |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 1.23 |

Confidence interval

| | |
|-------------|---------|
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.53 |
| upper limit | 2.85 |

Notes:

[14] - Nominal p-values were not adjusted for multiplicity.

| | |
|-----------------------------------|------------------------|
| Statistical analysis title | Statistical analysis 3 |
|-----------------------------------|------------------------|

Statistical analysis description:

PSL dose/Placebo calculated using logistic regression with categorical factors for treatment group (each PSL dose group referenced to the placebo group), Region (Europe, non-Europe), Baseline SV2A use (Yes, No) and log-transformed Baseline seizure frequency as a continuous covariate

| | |
|---|---|
| Comparison groups | Placebo (FAS) v Padsevonil 400 mg BID (FAS) |
| Number of subjects included in analysis | 110 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.125 ^[15] |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 1.9 |

Confidence interval

| | |
|-------------|---------|
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.84 |
| upper limit | 4.34 |

Notes:

[15] - Nominal p-values were not adjusted for multiplicity.

Adverse events

Adverse events information

Timeframe for reporting adverse events:

TEAEs were collected from Baseline until Safety Follow-Up (up to Week 23)

Adverse event reporting additional description:

TEAEs counts are for the number of study participants who entered the respective study period regardless of whether or not they completed the previous period. This is the reason for the difference in number of participants in Taper and SFU period in adverse events section and participant flow.

| | |
|-----------------|----------------|
| Assessment type | Non-systematic |
|-----------------|----------------|

Dictionary used

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

| | |
|--------------------|------|
| Dictionary version | 22.1 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|---|
| Reporting group title | Padsevonil 100 mg BID Treatment Period (SS) |
|-----------------------|---|

Reporting group description:

Participants were randomized to receive a combination of tablets of padsevonil 100 mg and placebo (as appropriate) to maintain the blinding, bid up to Week 19. Participants formed the SS.

| | |
|-----------------------|-------------------------------|
| Reporting group title | Placebo Treatment Period (SS) |
|-----------------------|-------------------------------|

Reporting group description:

Participants randomized to the placebo group received 5-6 placebo tablets to maintain the blinding, bid up to Week 19. Participants formed the Safety Set (SS).

| | |
|-----------------------|---|
| Reporting group title | Padsevonil 200 mg BID Treatment Period (SS) |
|-----------------------|---|

Reporting group description:

Participants were randomized to receive a combination of tablets of padsevonil 200 mg and placebo (as appropriate) to maintain the blinding, bid up to Week 19. Participants formed the SS.

| | |
|-----------------------|--------------------------------|
| Reporting group title | Placebo Conversion Period (SS) |
|-----------------------|--------------------------------|

Reporting group description:

A 3-Week Conversion Period was required for study participants who chose to enroll in the open-label extension (OLE) study at the end of the 12-Week Maintenance Period. Participants initially randomized to placebo progressively received padsevonil in a blinded way to reach the entry dose of 400 mg/day for the OLE. Participants formed the Safety Set (SS).

| | |
|-----------------------|---|
| Reporting group title | Padsevonil 400 mg BID Treatment Period (SS) |
|-----------------------|---|

Reporting group description:

Participants were randomized to receive a combination of tablets of padsevonil 400 mg and placebo (as appropriate) to maintain the blinding, bid up to Week 19. Participants formed the SS.

| | |
|-----------------------|--|
| Reporting group title | Padsevonil 100 mg BID Conversion Period (SS) |
|-----------------------|--|

Reporting group description:

A 3-Week Conversion Period was required for study participants who chose to enroll in the OLE study at the end of the 12-Week Maintenance Period. The dose for participants initially randomized to padsevonil 100 mg bid was gradually adapted (increased or decreased) in a blinded way to reach the entry dose of 400 mg/day for the OLE. Participants formed the SS.

| | |
|-----------------------|--|
| Reporting group title | Padsevonil 200 mg BID Conversion Period (SS) |
|-----------------------|--|

Reporting group description:

A 3-Week Conversion Period was required for study participants who chose to enroll in the OLE study at the end of the 12-Week Maintenance Period. The dose for participants initially randomized to padsevonil 200 mg bid was gradually adapted (increased or decreased) in a blinded way to reach the entry dose of 400 mg/day for the OLE. Participants formed the SS.

| | |
|-----------------------|--|
| Reporting group title | Padsevonil 400 mg BID Conversion Period (SS) |
|-----------------------|--|

Reporting group description:

A 3-Week Conversion Period was required for study participants who chose to enroll in the OLE study at the end of the 12-Week Maintenance Period. The dose for participants initially randomized to padsevonil 400 mg bid was gradually adapted (increased or decreased) in a blinded way to reach the entry dose of 400 mg/day for the OLE. Participants formed the SS.

| | |
|-----------------------|-----------------------------------|
| Reporting group title | Placebo Taper and SFU Period (SS) |
|-----------------------|-----------------------------------|

Reporting group description:

A 4-Week Taper Period was required for participants who chose not to enroll in the OLE study or who discontinued prior to the end of the 12-Week Maintenance Period. Participants initially randomized to placebo group received 5-6 placebo tablets to maintain the blinding and have been gradually tapered off the IMP over a 3-week period followed by 1-week drug-free period. Afterwards, participants had a Safety Follow-Up visit 30 days after the last IMP intake. Participants formed the Safety Set (SS).

| | |
|-----------------------|---|
| Reporting group title | Padsevonil 100 mg BID Taper and SFU Period (SS) |
|-----------------------|---|

Reporting group description:

A 4-Week Taper Period was required for participants who chose not to enroll in the OLE study or who discontinued prior to the end of the 12-Week Maintenance Period. Participants initially randomized to padsevonil 100 mg bid have been gradually tapered off the IMP over a 3-week period followed by 1-week drug-free period. Afterwards, participants had a Safety Follow-Up visit 30 days after the last IMP intake. Participants formed the SS.

| | |
|-----------------------|---|
| Reporting group title | Padsevonil 200 mg BID Taper and SFU Period (SS) |
|-----------------------|---|

Reporting group description:

A 4-Week Taper Period was required for participants who chose not to enroll in the OLE study or who discontinued prior to the end of the 12-Week Maintenance Period. Participants initially randomized to padsevonil 200 mg bid have been gradually tapered off the IMP over a 3-week period followed by 1-week drug-free period. Afterwards, participants had a Safety Follow-Up visit 30 days after the last IMP intake. Participants formed the SS.

| | |
|-----------------------|---|
| Reporting group title | Padsevonil 400 mg BID Taper and SFU Period (SS) |
|-----------------------|---|

Reporting group description:

A 4-Week Taper Period was required for participants who chose not to enroll in the OLE study or who discontinued prior to the end of the 12-Week Maintenance Period. Participants initially randomized to padsevonil 400 mg bid have been gradually tapered off the IMP over a 3-week period followed by 1-week drug-free period. Afterwards, participants had a Safety Follow-Up visit 30 days after the last IMP intake. Participants formed the SS.

| Serious adverse events | Padsevonil 100 mg BID Treatment Period (SS) | Placebo Treatment Period (SS) | Padsevonil 200 mg BID Treatment Period (SS) |
|---|---|-------------------------------|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | 3 / 55 (5.45%) | 1 / 57 (1.75%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | | | |
| Injury, poisoning and procedural complications | | | |
| Radius fracture | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | 0 / 55 (0.00%) | 0 / 57 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Skin laceration | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | 1 / 55 (1.82%) | 0 / 57 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Subdural haematoma | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 60 (0.00%) | 1 / 55 (1.82%) | 0 / 57 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Wrist fracture | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | 0 / 55 (0.00%) | 0 / 57 (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 |
| Contusion | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | 0 / 55 (0.00%) | 0 / 57 (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 |
| Humerus fracture | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | 0 / 55 (0.00%) | 0 / 57 (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 |
| Rib fracture | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | 0 / 55 (0.00%) | 0 / 57 (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 |
| Surgical and medical procedures | | | |
| Abortion induced | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | 1 / 55 (1.82%) | 0 / 57 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nervous system disorders | | | |
| Epilepsy | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | 0 / 55 (0.00%) | 1 / 57 (1.75%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Focal dyscognitive seizures | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | 1 / 55 (1.82%) | 0 / 57 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Seizure | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 60 (0.00%) | 0 / 55 (0.00%) | 0 / 57 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Status epilepticus | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | 0 / 55 (0.00%) | 0 / 57 (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 | | | |
| Pneumothorax | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | 0 / 55 (0.00%) | 0 / 57 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Psychiatric disorders | | | |
| Aggression | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | 0 / 55 (0.00%) | 0 / 57 (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 |
| Emotional disorder | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | 0 / 55 (0.00%) | 0 / 57 (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 |
| Suicidal ideation | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | 0 / 55 (0.00%) | 0 / 57 (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 |
| Musculoskeletal and connective tissue disorders | | | |
| Muscular weakness | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | 0 / 55 (0.00%) | 0 / 57 (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 / 60 (0.00%) | 0 / 55 (0.00%) | 0 / 57 (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 | Placebo Conversion Period (SS) | Padsevonil 400 mg BID Treatment Period (SS) | Padsevonil 100 mg BID Conversion Period (SS) |
|---|--------------------------------|---|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 1 / 33 (3.03%) | 5 / 59 (8.47%) | 0 / 31 (0.00%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | | | |
| Injury, poisoning and procedural complications | | | |
| Radius fracture | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 1 / 59 (1.69%) | 0 / 31 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Skin laceration | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 59 (0.00%) | 0 / 31 (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 |
| Subdural haematoma | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 59 (0.00%) | 0 / 31 (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 |
| Wrist fracture | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 1 / 59 (1.69%) | 0 / 31 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Contusion | | | |
| subjects affected / exposed | 1 / 33 (3.03%) | 0 / 59 (0.00%) | 0 / 31 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Humerus fracture | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 1 / 33 (3.03%) | 0 / 59 (0.00%) | 0 / 31 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Rib fracture | | | |
| subjects affected / exposed | 1 / 33 (3.03%) | 0 / 59 (0.00%) | 0 / 31 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Surgical and medical procedures | | | |
| Abortion induced | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 59 (0.00%) | 0 / 31 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nervous system disorders | | | |
| Epilepsy | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 1 / 59 (1.69%) | 0 / 31 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Focal dyscognitive seizures | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 59 (0.00%) | 0 / 31 (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 |
| Seizure | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 59 (0.00%) | 0 / 31 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Status epilepticus | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 59 (0.00%) | 0 / 31 (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 | | | |
| Pneumothorax | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 59 (0.00%) | 0 / 31 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|----------------|----------------|----------------|
| Psychiatric disorders | | | |
| Aggression | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 1 / 59 (1.69%) | 0 / 31 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Emotional disorder | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 59 (0.00%) | 0 / 31 (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 |
| Suicidal ideation | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 59 (0.00%) | 0 / 31 (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 |
| Musculoskeletal and connective tissue disorders | | | |
| Muscular weakness | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 1 / 59 (1.69%) | 0 / 31 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Metabolism and nutrition disorders | | | |
| Hyponatraemia | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 1 / 59 (1.69%) | 0 / 31 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| Serious adverse events | Padsevonil 200 mg BID Conversion Period (SS) | Padsevonil 400 mg BID Conversion Period (SS) | Placebo Taper and SFU Period (SS) |
|---|--|--|--------------------------------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 28 (0.00%) | 1 / 27 (3.70%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | | | |
| Injury, poisoning and procedural complications | | | |
| Radius fracture | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 28 (0.00%) | 0 / 27 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|----------------|----------------|----------------|
| Skin laceration | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 28 (0.00%) | 0 / 27 (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 |
| Subdural haematoma | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 28 (0.00%) | 0 / 27 (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 |
| Wrist fracture | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 28 (0.00%) | 0 / 27 (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 |
| Contusion | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 28 (0.00%) | 0 / 27 (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 |
| Humerus fracture | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 28 (0.00%) | 0 / 27 (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 |
| Rib fracture | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 28 (0.00%) | 0 / 27 (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 |
| Surgical and medical procedures | | | |
| Abortion induced | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 28 (0.00%) | 0 / 27 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nervous system disorders | | | |
| Epilepsy | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 28 (0.00%) | 0 / 27 (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 |

| | | | |
|---|----------------|----------------|----------------|
| Focal dyscognitive seizures | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 28 (0.00%) | 0 / 27 (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 |
| Seizure | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 28 (0.00%) | 0 / 27 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Status epilepticus | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 28 (0.00%) | 0 / 27 (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 | | | |
| Pneumothorax | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 28 (0.00%) | 0 / 27 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Psychiatric disorders | | | |
| Aggression | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 28 (0.00%) | 0 / 27 (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 |
| Emotional disorder | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 28 (0.00%) | 1 / 27 (3.70%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Suicidal ideation | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 28 (0.00%) | 1 / 27 (3.70%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Musculoskeletal and connective tissue disorders | | | |
| Muscular weakness | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 28 (0.00%) | 0 / 27 (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 / 29 (0.00%) | 0 / 28 (0.00%) | 0 / 27 (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 | Padsevonil 100 mg BID Taper and SFU Period (SS) | Padsevonil 200 mg BID Taper and SFU Period (SS) | Padsevonil 400 mg BID Taper and SFU Period (SS) |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 2 / 30 (6.67%) | 0 / 31 (0.00%) | 1 / 32 (3.13%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | | | |
| Injury, poisoning and procedural complications | | | |
| Radius fracture | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 0 / 31 (0.00%) | 0 / 32 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Skin laceration | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 0 / 31 (0.00%) | 0 / 32 (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 |
| Subdural haematoma | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 0 / 31 (0.00%) | 0 / 32 (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 |
| Wrist fracture | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 0 / 31 (0.00%) | 0 / 32 (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 |
| Contusion | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 30 (0.00%) | 0 / 31 (0.00%) | 0 / 32 (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 |
| Humerus fracture | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 0 / 31 (0.00%) | 0 / 32 (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 |
| Rib fracture | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 0 / 31 (0.00%) | 0 / 32 (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 |
| Surgical and medical procedures | | | |
| Abortion induced | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 0 / 31 (0.00%) | 0 / 32 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nervous system disorders | | | |
| Epilepsy | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 0 / 31 (0.00%) | 0 / 32 (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 |
| Focal dyscognitive seizures | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 0 / 31 (0.00%) | 0 / 32 (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 |
| Seizure | | | |
| subjects affected / exposed | 1 / 30 (3.33%) | 0 / 31 (0.00%) | 0 / 32 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Status epilepticus | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 0 / 31 (0.00%) | 1 / 32 (3.13%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory, thoracic and mediastinal | | | |

| | | | |
|---|----------------|----------------|----------------|
| disorders | | | |
| Pneumothorax | | | |
| subjects affected / exposed | 1 / 30 (3.33%) | 0 / 31 (0.00%) | 0 / 32 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Psychiatric disorders | | | |
| Aggression | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 0 / 31 (0.00%) | 0 / 32 (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 |
| Emotional disorder | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 0 / 31 (0.00%) | 0 / 32 (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 |
| Suicidal ideation | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 0 / 31 (0.00%) | 0 / 32 (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 |
| Musculoskeletal and connective tissue disorders | | | |
| Muscular weakness | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 0 / 31 (0.00%) | 0 / 32 (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 / 30 (0.00%) | 0 / 31 (0.00%) | 0 / 32 (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 |

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

| Non-serious adverse events | Padsevonil 100 mg BID Treatment Period (SS) | Placebo Treatment Period (SS) | Padsevonil 200 mg BID Treatment Period (SS) |
|---|---|----------------------------------|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 37 / 60 (61.67%) | 25 / 55 (45.45%) | 40 / 57 (70.18%) |

| | | | |
|--|------------------|-----------------|------------------|
| Injury, poisoning and procedural complications | | | |
| Fall | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | 0 / 55 (0.00%) | 3 / 57 (5.26%) |
| occurrences (all) | 0 | 0 | 4 |
| Contusion | | | |
| subjects affected / exposed | 1 / 60 (1.67%) | 3 / 55 (5.45%) | 2 / 57 (3.51%) |
| occurrences (all) | 1 | 4 | 2 |
| Vascular disorders | | | |
| Hypotension | | | |
| subjects affected / exposed | 1 / 60 (1.67%) | 0 / 55 (0.00%) | 0 / 57 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Nervous system disorders | | | |
| Somnolence | | | |
| subjects affected / exposed | 10 / 60 (16.67%) | 2 / 55 (3.64%) | 19 / 57 (33.33%) |
| occurrences (all) | 11 | 2 | 22 |
| Dizziness | | | |
| subjects affected / exposed | 14 / 60 (23.33%) | 4 / 55 (7.27%) | 10 / 57 (17.54%) |
| occurrences (all) | 14 | 5 | 13 |
| Headache | | | |
| subjects affected / exposed | 10 / 60 (16.67%) | 8 / 55 (14.55%) | 9 / 57 (15.79%) |
| occurrences (all) | 22 | 13 | 16 |
| Memory impairment | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | 1 / 55 (1.82%) | 3 / 57 (5.26%) |
| occurrences (all) | 0 | 1 | 3 |
| Tremor | | | |
| subjects affected / exposed | 3 / 60 (5.00%) | 1 / 55 (1.82%) | 0 / 57 (0.00%) |
| occurrences (all) | 5 | 1 | 0 |
| Disturbance in attention | | | |
| subjects affected / exposed | 1 / 60 (1.67%) | 1 / 55 (1.82%) | 5 / 57 (8.77%) |
| occurrences (all) | 1 | 1 | 5 |
| Balance disorder | | | |
| subjects affected / exposed | 1 / 60 (1.67%) | 0 / 55 (0.00%) | 3 / 57 (5.26%) |
| occurrences (all) | 1 | 0 | 3 |
| Dysarthria | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | 1 / 55 (1.82%) | 0 / 57 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |

| | | | |
|--|----------------------|---------------------|----------------------|
| Seizure subjects affected / exposed occurrences (all) | 0 / 60 (0.00%) 0 | 1 / 55 (1.82%) 1 | 4 / 57 (7.02%) 5 |
| General disorders and administration site conditions | | | |
| Fatigue subjects affected / exposed occurrences (all) | 5 / 60 (8.33%) 5 | 4 / 55 (7.27%) 4 | 7 / 57 (12.28%) 7 |
| Asthenia subjects affected / exposed occurrences (all) | 6 / 60 (10.00%) 6 | 2 / 55 (3.64%) 2 | 3 / 57 (5.26%) 4 |
| Gait disturbance subjects affected / exposed occurrences (all) | 2 / 60 (3.33%) 2 | 0 / 55 (0.00%) 0 | 2 / 57 (3.51%) 3 |
| Gastrointestinal disorders | | | |
| Nausea subjects affected / exposed occurrences (all) | 1 / 60 (1.67%) 1 | 3 / 55 (5.45%) 5 | 3 / 57 (5.26%) 4 |
| Diarrhoea subjects affected / exposed occurrences (all) | 1 / 60 (1.67%) 1 | 3 / 55 (5.45%) 4 | 0 / 57 (0.00%) 0 |
| Psychiatric disorders | | | |
| Insomnia subjects affected / exposed occurrences (all) | 1 / 60 (1.67%) 1 | 0 / 55 (0.00%) 0 | 5 / 57 (8.77%) 6 |
| Irritability subjects affected / exposed occurrences (all) | 4 / 60 (6.67%) 4 | 3 / 55 (5.45%) 3 | 3 / 57 (5.26%) 3 |
| Anxiety subjects affected / exposed occurrences (all) | 0 / 60 (0.00%) 0 | 1 / 55 (1.82%) 1 | 1 / 57 (1.75%) 2 |
| Infections and infestations | | | |
| Nasopharyngitis subjects affected / exposed occurrences (all) | 1 / 60 (1.67%) 1 | 4 / 55 (7.27%) 4 | 4 / 57 (7.02%) 4 |
| Metabolism and nutrition disorders | | | |

| | | | |
|--|---------------------|---------------------|---------------------|
| Decreased appetite subjects affected / exposed occurrences (all) | 0 / 60 (0.00%) 0 | 1 / 55 (1.82%) 1 | 3 / 57 (5.26%) 3 |
|--|---------------------|---------------------|---------------------|

| Non-serious adverse events | Placebo Conversion Period (SS) | Padsevonil 400 mg BID Treatment Period (SS) | Padsevonil 100 mg BID Conversion Period (SS) |
|---|-----------------------------------|---|--|
| Total subjects affected by non-serious adverse events subjects affected / exposed | 7 / 33 (21.21%) | 41 / 59 (69.49%) | 0 / 31 (0.00%) |
| Injury, poisoning and procedural complications Fall subjects affected / exposed occurrences (all) | 0 / 33 (0.00%) 0 | 2 / 59 (3.39%) 2 | 0 / 31 (0.00%) 0 |
| Contusion subjects affected / exposed occurrences (all) | 1 / 33 (3.03%) 1 | 1 / 59 (1.69%) 1 | 0 / 31 (0.00%) 0 |
| Vascular disorders Hypotension subjects affected / exposed occurrences (all) | 2 / 33 (6.06%) 2 | 0 / 59 (0.00%) 0 | 0 / 31 (0.00%) 0 |
| Nervous system disorders Somnolence subjects affected / exposed occurrences (all) | 1 / 33 (3.03%) 1 | 20 / 59 (33.90%) 23 | 0 / 31 (0.00%) 0 |
| Dizziness subjects affected / exposed occurrences (all) | 0 / 33 (0.00%) 0 | 18 / 59 (30.51%) 19 | 0 / 31 (0.00%) 0 |
| Headache subjects affected / exposed occurrences (all) | 0 / 33 (0.00%) 0 | 5 / 59 (8.47%) 8 | 0 / 31 (0.00%) 0 |
| Memory impairment subjects affected / exposed occurrences (all) | 0 / 33 (0.00%) 0 | 6 / 59 (10.17%) 6 | 0 / 31 (0.00%) 0 |
| Tremor subjects affected / exposed occurrences (all) | 0 / 33 (0.00%) 0 | 4 / 59 (6.78%) 4 | 0 / 31 (0.00%) 0 |
| Disturbance in attention | | | |

| | | | |
|--|---------------------|------------------------|---------------------|
| subjects affected / exposed occurrences (all) | 0 / 33 (0.00%) 0 | 2 / 59 (3.39%) 2 | 0 / 31 (0.00%) 0 |
| Balance disorder subjects affected / exposed occurrences (all) | 0 / 33 (0.00%) 0 | 2 / 59 (3.39%) 2 | 0 / 31 (0.00%) 0 |
| Dysarthria subjects affected / exposed occurrences (all) | 0 / 33 (0.00%) 0 | 5 / 59 (8.47%) 5 | 0 / 31 (0.00%) 0 |
| Seizure subjects affected / exposed occurrences (all) | 0 / 33 (0.00%) 0 | 0 / 59 (0.00%) 0 | 0 / 31 (0.00%) 0 |
| General disorders and administration site conditions Fatigue subjects affected / exposed occurrences (all) | 1 / 33 (3.03%) 1 | 14 / 59 (23.73%) 15 | 0 / 31 (0.00%) 0 |
| Asthenia subjects affected / exposed occurrences (all) | 0 / 33 (0.00%) 0 | 2 / 59 (3.39%) 2 | 0 / 31 (0.00%) 0 |
| Gait disturbance subjects affected / exposed occurrences (all) | 0 / 33 (0.00%) 0 | 4 / 59 (6.78%) 4 | 0 / 31 (0.00%) 0 |
| Gastrointestinal disorders Nausea subjects affected / exposed occurrences (all) | 0 / 33 (0.00%) 0 | 1 / 59 (1.69%) 1 | 0 / 31 (0.00%) 0 |
| Diarrhoea subjects affected / exposed occurrences (all) | 0 / 33 (0.00%) 0 | 2 / 59 (3.39%) 2 | 0 / 31 (0.00%) 0 |
| Psychiatric disorders Insomnia subjects affected / exposed occurrences (all) | 0 / 33 (0.00%) 0 | 4 / 59 (6.78%) 4 | 0 / 31 (0.00%) 0 |
| Irritability subjects affected / exposed occurrences (all) | 1 / 33 (3.03%) 1 | 3 / 59 (5.08%) 3 | 0 / 31 (0.00%) 0 |
| Anxiety | | | |

| | | | |
|--|---------------------|---------------------|---------------------|
| subjects affected / exposed occurrences (all) | 0 / 33 (0.00%) 0 | 3 / 59 (5.08%) 3 | 0 / 31 (0.00%) 0 |
| Infections and infestations Nasopharyngitis subjects affected / exposed occurrences (all) | 1 / 33 (3.03%) 1 | 1 / 59 (1.69%) 1 | 0 / 31 (0.00%) 0 |
| Metabolism and nutrition disorders Decreased appetite subjects affected / exposed occurrences (all) | 0 / 33 (0.00%) 0 | 1 / 59 (1.69%) 1 | 0 / 31 (0.00%) 0 |

| Non-serious adverse events | Padsevonil 200 mg BID Conversion Period (SS) | Padsevonil 400 mg BID Conversion Period (SS) | Placebo Taper and SFU Period (SS) |
|---|--|--|--------------------------------------|
| Total subjects affected by non-serious adverse events subjects affected / exposed | 1 / 29 (3.45%) | 1 / 28 (3.57%) | 2 / 27 (7.41%) |
| Injury, poisoning and procedural complications Fall subjects affected / exposed occurrences (all) | 1 / 29 (3.45%) 1 | 0 / 28 (0.00%) 0 | 1 / 27 (3.70%) 1 |
| Contusion subjects affected / exposed occurrences (all) | 1 / 29 (3.45%) 1 | 0 / 28 (0.00%) 0 | 0 / 27 (0.00%) 0 |
| Vascular disorders Hypotension subjects affected / exposed occurrences (all) | 0 / 29 (0.00%) 0 | 0 / 28 (0.00%) 0 | 0 / 27 (0.00%) 0 |
| Nervous system disorders Somnolence subjects affected / exposed occurrences (all) | 0 / 29 (0.00%) 0 | 0 / 28 (0.00%) 0 | 0 / 27 (0.00%) 0 |
| Dizziness subjects affected / exposed occurrences (all) | 0 / 29 (0.00%) 0 | 0 / 28 (0.00%) 0 | 1 / 27 (3.70%) 1 |
| Headache subjects affected / exposed occurrences (all) | 0 / 29 (0.00%) 0 | 0 / 28 (0.00%) 0 | 0 / 27 (0.00%) 0 |
| Memory impairment | | | |

| | | | |
|---|---------------------|---------------------|---------------------|
| subjects affected / exposed occurrences (all) | 0 / 29 (0.00%) 0 | 0 / 28 (0.00%) 0 | 0 / 27 (0.00%) 0 |
| Tremor | | | |
| subjects affected / exposed occurrences (all) | 0 / 29 (0.00%) 0 | 1 / 28 (3.57%) 1 | 0 / 27 (0.00%) 0 |
| Disturbance in attention | | | |
| subjects affected / exposed occurrences (all) | 0 / 29 (0.00%) 0 | 0 / 28 (0.00%) 0 | 0 / 27 (0.00%) 0 |
| Balance disorder | | | |
| subjects affected / exposed occurrences (all) | 0 / 29 (0.00%) 0 | 0 / 28 (0.00%) 0 | 0 / 27 (0.00%) 0 |
| Dysarthria | | | |
| subjects affected / exposed occurrences (all) | 0 / 29 (0.00%) 0 | 0 / 28 (0.00%) 0 | 0 / 27 (0.00%) 0 |
| Seizure | | | |
| subjects affected / exposed occurrences (all) | 0 / 29 (0.00%) 0 | 0 / 28 (0.00%) 0 | 0 / 27 (0.00%) 0 |
| General disorders and administration site conditions | | | |
| Fatigue | | | |
| subjects affected / exposed occurrences (all) | 0 / 29 (0.00%) 0 | 0 / 28 (0.00%) 0 | 0 / 27 (0.00%) 0 |
| Asthenia | | | |
| subjects affected / exposed occurrences (all) | 0 / 29 (0.00%) 0 | 0 / 28 (0.00%) 0 | 0 / 27 (0.00%) 0 |
| Gait disturbance | | | |
| subjects affected / exposed occurrences (all) | 0 / 29 (0.00%) 0 | 0 / 28 (0.00%) 0 | 0 / 27 (0.00%) 0 |
| Gastrointestinal disorders | | | |
| Nausea | | | |
| subjects affected / exposed occurrences (all) | 0 / 29 (0.00%) 0 | 0 / 28 (0.00%) 0 | 0 / 27 (0.00%) 0 |
| Diarrhoea | | | |
| subjects affected / exposed occurrences (all) | 0 / 29 (0.00%) 0 | 0 / 28 (0.00%) 0 | 0 / 27 (0.00%) 0 |
| Psychiatric disorders | | | |

| | | | |
|------------------------------------|----------------|----------------|----------------|
| Insomnia | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 28 (0.00%) | 0 / 27 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Irritability | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 28 (0.00%) | 0 / 27 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Anxiety | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 28 (0.00%) | 0 / 27 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Infections and infestations | | | |
| Nasopharyngitis | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 28 (0.00%) | 0 / 27 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Metabolism and nutrition disorders | | | |
| Decreased appetite | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 28 (0.00%) | 0 / 27 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| Non-serious adverse events | Padsevonil 100 mg BID Taper and SFU Period (SS) | Padsevonil 200 mg BID Taper and SFU Period (SS) | Padsevonil 400 mg BID Taper and SFU Period (SS) |
|--|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 6 / 30 (20.00%) | 4 / 31 (12.90%) | 2 / 32 (6.25%) |
| Injury, poisoning and procedural complications | | | |
| Fall | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 1 / 31 (3.23%) | 1 / 32 (3.13%) |
| occurrences (all) | 0 | 1 | 1 |
| Contusion | | | |
| subjects affected / exposed | 1 / 30 (3.33%) | 0 / 31 (0.00%) | 0 / 32 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Vascular disorders | | | |
| Hypotension | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 0 / 31 (0.00%) | 0 / 32 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Nervous system disorders | | | |
| Somnolence | | | |
| subjects affected / exposed | 1 / 30 (3.33%) | 0 / 31 (0.00%) | 0 / 32 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Dizziness | | | |

| | | | |
|--|-----------------|----------------|----------------|
| subjects affected / exposed | 0 / 30 (0.00%) | 0 / 31 (0.00%) | 0 / 32 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Headache | | | |
| subjects affected / exposed | 4 / 30 (13.33%) | 2 / 31 (6.45%) | 1 / 32 (3.13%) |
| occurrences (all) | 12 | 2 | 1 |
| Memory impairment | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 0 / 31 (0.00%) | 0 / 32 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Tremor | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 0 / 31 (0.00%) | 0 / 32 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Disturbance in attention | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 0 / 31 (0.00%) | 0 / 32 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Balance disorder | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 1 / 31 (3.23%) | 0 / 32 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Dysarthria | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 0 / 31 (0.00%) | 0 / 32 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Seizure | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 0 / 31 (0.00%) | 0 / 32 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| General disorders and administration site conditions | | | |
| Fatigue | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 0 / 31 (0.00%) | 0 / 32 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Asthenia | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 1 / 31 (3.23%) | 0 / 32 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Gait disturbance | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 0 / 31 (0.00%) | 0 / 32 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gastrointestinal disorders | | | |

| | | | |
|--|---------------------|---------------------|---------------------|
| Nausea subjects affected / exposed occurrences (all) | 0 / 30 (0.00%) 0 | 0 / 31 (0.00%) 0 | 0 / 32 (0.00%) 0 |
| Diarrhoea subjects affected / exposed occurrences (all) | 0 / 30 (0.00%) 0 | 0 / 31 (0.00%) 0 | 0 / 32 (0.00%) 0 |
| Psychiatric disorders Insomnia subjects affected / exposed occurrences (all) | 0 / 30 (0.00%) 0 | 0 / 31 (0.00%) 0 | 0 / 32 (0.00%) 0 |
| Irritability subjects affected / exposed occurrences (all) | 0 / 30 (0.00%) 0 | 0 / 31 (0.00%) 0 | 0 / 32 (0.00%) 0 |
| Anxiety subjects affected / exposed occurrences (all) | 0 / 30 (0.00%) 0 | 0 / 31 (0.00%) 0 | 0 / 32 (0.00%) 0 |
| Infections and infestations Nasopharyngitis subjects affected / exposed occurrences (all) | 0 / 30 (0.00%) 0 | 0 / 31 (0.00%) 0 | 0 / 32 (0.00%) 0 |
| Metabolism and nutrition disorders Decreased appetite subjects affected / exposed occurrences (all) | 0 / 30 (0.00%) 0 | 0 / 31 (0.00%) 0 | 0 / 32 (0.00%) 0 |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|-----------------|---|
| 21 January 2020 | <p>Protocol Amendment 1 was dated 21 Jan 2020; at the time, 143 study participants had received IMP.</p> <p>The primary rationale for the global amendment was to update the name of the legal form of the Sponsor, UCB Biopharma. At the time, Belgium had adopted a new Code of Companies and Associations, resulting in a mandatory change of the name of the legal form of the entity "société privée à responsabilité limitée", abbreviated "SPRL", to "société à responsabilité limitée", abbreviated "SRL".</p> <p>In addition, the following changes were introduced:</p> <ul style="list-style-type: none">• A summary of the known and expected risks and benefits of PSL was included.• The changes introduced by the local Protocol Amendment 0.1 for China were incorporated:<ul style="list-style-type: none">- The percentage of Chinese study participants planned to be randomized in the study increased from 10% to 20% in response to a request by the Chinese Center for Drug Evaluation.- It was specified that the exploratory PK analysis would not be done in Chinese study participants.- The blood volumes required for hematology and chemistry were revised to meet the requirements of the central laboratory.• The changes introduced by the local Protocol Amendment 0.2 for Switzerland were incorporated:<ul style="list-style-type: none">- The following language regarding expedited reporting of SAEs was added to meet a request by Swissmedic: "Expedited reporting to regulatory authorities will be in line with local laws". |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported