



Clinical trial results:

A Phase 2, Randomized, Double-Blind, Placebo-Controlled Study of K0706 in Subjects With Early Parkinson's Disease

Summary

| | |
|--------------------------|----------------|
| EudraCT number | 2018-003337-15 |
| Trial protocol | HU SK ES |
| Global end of trial date | 06 June 2024 |

Results information

| | |
|--------------------------------|---------------|
| Result version number | v1 (current) |
| This version publication date | 20 April 2025 |
| First version publication date | 20 April 2025 |

Trial information

Trial identification

| | |
|-----------------------|-----------|
| Sponsor protocol code | CLR_18_06 |
|-----------------------|-----------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT03655236 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|--|
| Sponsor organisation name | Sun Pharma Advanced Research Company Limited (SPARC) |
| Sponsor organisation address | 17/B, Mahal Industrial Estate, Mahakali Caves Road, Mumbai, India, 400093 |
| Public contact | Orest Hurko, Sun Pharma Advanced Research Company Limited (SPARC), Orest.Hurko@sparcmail.com |
| Scientific contact | Orest Hurko, Sun Pharma Advanced Research Company Limited (SPARC), Orest.Hurko@sparcmail.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 | 06 June 2024 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 08 April 2024 |
| Global end of trial reached? | Yes |
| Global end of trial date | 06 June 2024 |
| Was the trial ended prematurely? | Yes |

Notes:

General information about the trial

Main objective of the trial:

To determine if K0706 reduces the rate of progression of early-stage Parkinson's disease (PD) versus placebo over 40 weeks, as assessed by the MDS-UPDRS (Movement Disorder Society – Unified Parkinson's Disease Rating Scale) Part III (motor examination) total score.

Protection of trial subjects:

The trial and site activities were monitored according to the ICH-GCP guidelines considering every aspect of the trial, ensuring that the rights, safety and well-being of patients are protected and consistent with the Declaration of Helsinki.

Background therapy: -

Evidence for comparator: -

| | |
|---|------------------|
| Actual start date of recruitment | 18 February 2019 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | No |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|--------------------|
| Country: Number of subjects enrolled | India: 89 |
| Country: Number of subjects enrolled | United States: 221 |
| Country: Number of subjects enrolled | Poland: 80 |
| Country: Number of subjects enrolled | Slovakia: 21 |
| Country: Number of subjects enrolled | Spain: 85 |
| Country: Number of subjects enrolled | Hungary: 17 |
| Worldwide total number of subjects | 513 |
| EEA total number of subjects | 203 |

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) | 241 |
| From 65 to 84 years | 266 |
| 85 years and over | 6 |

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Subjects aged ≥ 50 years in whom an initial diagnosis of PD had been made within three years of the Screening visit, who score on a modified Hoehn and Yahr stage ≤ 2 and who are not on any dopaminergic treatment other than MAO-B inhibitors will be eligible for screening.

Period 1

| | |
|------------------------------|--------------------------------------|
| Period 1 title | Subject Disposition in Part 1 Period |
| Is this the baseline period? | Yes |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Subject, Investigator, Assessor |

Arms

| | |
|------------------------------|-----------------|
| Are arms mutually exclusive? | Yes |
| Arm title | K0706, low dose |

Arm description:

Part 1; low dose K0706

| | |
|--|---|
| Arm type | Experimental |
| Investigational medicinal product name | K0706 |
| Investigational medicinal product code | |
| Other name | Vodobatinib |
| Pharmaceutical forms | Capsule, Powder for oral suspension in sachet |
| Routes of administration | Oral use |

Dosage and administration details:

The study drug will be administered in the form of a 96 mg capsule or 192 mg powder; subjects will be instructed to take the study drug orally once daily. They should not eat food two hours prior and at least one (but ideally two) hour after dosing. For the powder formulation, the entire contents of one sachet are to be added to a glass of water (at least 4 oz. [120 mL]), mixed uniformly using a spoon or other stirrer, and ingested promptly. Any residual powder remaining in the glass or on the stirrer should be mixed with additional water and consumed to ensure ingestion of the total dose.

| | |
|------------------|------------------|
| Arm title | K0706, high dose |
|------------------|------------------|

Arm description:

Part 1; high dose K0706

| | |
|--|---|
| Arm type | Experimental |
| Investigational medicinal product name | K0706 |
| Investigational medicinal product code | |
| Other name | Vodobatinib |
| Pharmaceutical forms | Capsule, Powder for oral suspension in sachet |
| Routes of administration | Oral use |

Dosage and administration details:

The study drug will be administered in the form of a 96 mg capsule or 192 mg powder; subjects will be instructed to take the study drug orally once daily. They should not eat food two hours prior and at least one (but ideally two) hour after dosing. For the powder formulation, the entire contents of one sachet are to be added to a glass of water (at least 4 oz. [120 mL]), mixed uniformly using a spoon or other stirrer, and ingested promptly. Any residual powder remaining in the glass or on the stirrer should be mixed with additional water and consumed to ensure ingestion of the total dose.

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

Arm description:

Part 1; placebo

| | |
|--|---|
| Arm type | Placebo |
| Investigational medicinal product name | Placebo |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Capsule, Powder for oral suspension in sachet |
| Routes of administration | Oral use |

Dosage and administration details:

The study drug will be administered in the form of a 96 mg capsule or 192 mg powder; subjects will be instructed to take the study drug orally once daily. They should not eat food two hours prior and at least one (but ideally two) hour after dosing. For the powder formulation, the entire contents of one sachet are to be added to a glass of water (at least 4 oz. [120 mL]), mixed uniformly using a spoon or other stirrer, and ingested promptly. Any residual powder remaining in the glass or on the stirrer should be mixed with additional water and consumed to ensure ingestion of the total dose.

The placebo formulation will contain the same excipients as that of the K0706 formulation and match the K0706 formulation in shape, size, and color.

| Number of subjects in period 1 | K0706, low dose | K0706, high dose | Placebo |
|---------------------------------------|-----------------|------------------|---------|
| Started | 171 | 174 | 168 |
| Completed | 114 | 66 | 120 |
| Not completed | 57 | 108 | 48 |
| Adverse event, serious fatal | 1 | - | - |
| Consent withdrawn by subject | 11 | 16 | 6 |
| Physician decision | - | 3 | 2 |
| Study terminated by Sponsor | 12 | 8 | 13 |
| Adverse event, non-fatal | 25 | 55 | 12 |
| Requires prohibited medication | 4 | 5 | 3 |
| Poor compliance | - | 2 | - |
| Not specified | - | 2 | 2 |
| Withdrawal by Subject | - | 5 | 3 |
| Lost to follow-up | 1 | 3 | 2 |
| Parkinson's disease progression | 2 | 8 | 5 |
| Protocol deviation | 1 | 1 | - |

Period 2

| | |
|------------------------------|--------------------------------------|
| Period 2 title | Subject Disposition in Part 2 Period |
| Is this the baseline period? | No |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Subject, Investigator, Assessor |

Arms

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

| | |
|--|---|
| Arm title | K0706, low dose |
| Arm description: Part 2; K0706 low dose | |
| Arm type | Experimental |
| Investigational medicinal product name | K0706 |
| Investigational medicinal product code | |
| Other name | Vodobatinib |
| Pharmaceutical forms | Capsule, Powder for oral suspension in sachet |
| Routes of administration | Oral use |

Dosage and administration details:

The study drug will be administered in the form of a 96 mg capsule or 192 mg powder; subjects will be instructed to take the study drug orally once daily. They should not eat food two hours prior and at least one (but ideally two) hour after dosing. For the powder formulation, the entire contents of one sachet are to be added to a glass of water (at least 4 oz. [120 mL]), mixed uniformly using a spoon or other stirrer, and ingested promptly. Any residual powder remaining in the glass or on the stirrer should be mixed with additional water and consumed to ensure ingestion of the total dose.

| | |
|---|---|
| Arm title | K0706, high dose |
| Arm description: Part 2, high dose; includes subjects from the prior Placebo arm, who were transitioned to K0706 High Dose | |
| Arm type | Experimental |
| Investigational medicinal product name | K0706 |
| Investigational medicinal product code | |
| Other name | Vodobatinib |
| Pharmaceutical forms | Capsule, Powder for oral suspension in sachet |
| Routes of administration | Oral use |

Dosage and administration details:

The study drug will be administered in the form of a 96 mg capsule or 192 mg powder; subjects will be instructed to take the study drug orally once daily. They should not eat food two hours prior and at least one (but ideally two) hour after dosing. For the powder formulation, the entire contents of one sachet are to be added to a glass of water (at least 4 oz. [120 mL]), mixed uniformly using a spoon or other stirrer, and ingested promptly. Any residual powder remaining in the glass or on the stirrer should be mixed with additional water and consumed to ensure ingestion of the total dose.

| | |
|--|---|
| Arm title | Placebo |
| Arm description: Part 2 placebo arm | |
| Arm type | Placebo |
| Investigational medicinal product name | Placebo |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Capsule, Powder for oral suspension in sachet |
| Routes of administration | Oral use |

Dosage and administration details:

The study drug will be administered in the form of a 96 mg capsule or 192 mg powder; subjects will be instructed to take the study drug orally once daily. They should not eat food two hours prior and at least one (but ideally two) hour after dosing. For the powder formulation, the entire contents of one sachet are to be added to a glass of water (at least 4 oz. [120 mL]), mixed uniformly using a spoon or other stirrer, and ingested promptly. Any residual powder remaining in the glass or on the stirrer should be mixed with additional water and consumed to ensure ingestion of the total dose. The placebo formulation will contain the same excipients as that of the K0706 formulation and match the K0706 formulation in shape, size, and color.

| Number of subjects in period 2 ^{[1][2]} | K0706, low dose | K0706, high dose | Placebo |
|---|-----------------|------------------|---------|
| Started | 72 | 21 | 77 |
| Completed | 36 | 29 | 27 |
| Not completed | 36 | 19 | 50 |
| Consent withdrawn by subject | 5 | 1 | 12 |
| Study terminated by Sponsor | 18 | 11 | 13 |
| Adverse event, non-fatal | 2 | 5 | 12 |
| Requires prohibited medication | 3 | 1 | 5 |
| Not specified | 1 | - | - |
| Withdrawal by Subject | 1 | 1 | 2 |
| Lost to follow-up | 1 | - | - |
| Parkinson's disease progression | 4 | - | 2 |
| Protocol deviation | 1 | - | 4 |
| Joined | 0 | 27 | 0 |
| Transferred in from other group/arm | - | 27 | - |

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: Subjects who had been randomized to placebo in Part 1 will be rolled over to a high dose K0706 at Week 40.

[2] - The number of subjects transferring in and out of the arms in the period are not the same. It is expected the net number of transfers in and out of the arms in a period, will be zero.

Justification: Subjects who had been randomized to placebo in Part 1 will be rolled over to a high dose K0706 at Week 40.

Baseline characteristics

Reporting groups

| | |
|-----------------------|--------------------------------------|
| Reporting group title | Subject Disposition in Part 1 Period |
|-----------------------|--------------------------------------|

Reporting group description: -

| Reporting group values | Subject Disposition in Part 1 Period | Total | |
|--|--------------------------------------|-------|--|
| Number of subjects | 513 | 513 | |
| Age categorical | | | |
| Units: Subjects | | | |
| In utero | 0 | 0 | |
| Preterm newborn infants (gestational age < 37 wks) | 0 | 0 | |
| Newborns (0-27 days) | 0 | 0 | |
| Infants and toddlers (28 days-23 months) | 0 | 0 | |
| Children (2-11 years) | 0 | 0 | |
| Adolescents (12-17 years) | 0 | 0 | |
| Adults (18-64 years) | 241 | 241 | |
| From 65-84 years | 266 | 266 | |
| 85 years and over | 6 | 6 | |
| Age continuous | | | |
| Units: years | | | |
| arithmetic mean | 65.0 | | |
| standard deviation | ± 8.05 | - | |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 179 | 179 | |
| Male | 334 | 334 | |

End points

End points reporting groups

| | |
|---|------------------|
| Reporting group title | K0706, low dose |
| Reporting group description: Part 1; low dose K0706 | |
| Reporting group title | K0706, high dose |
| Reporting group description: Part 1; high dose K0706 | |
| Reporting group title | Placebo |
| Reporting group description: Part 1; placebo | |
| Reporting group title | K0706, low dose |
| Reporting group description: Part 2; K0706 low dose | |
| Reporting group title | K0706, high dose |
| Reporting group description: Part 2, high dose; includes subjects from the prior Placebo arm, who were transitioned to K0706 High Dose | |
| Reporting group title | Placebo |
| Reporting group description: Part 2 placebo arm | |

Primary: Change From Baseline to Week 40 in the Movement Disorder Society - Unified Parkinson's Disease Rating Scale (MDS-UPDRS) Part III Total Score.

| | |
|-----------------|--|
| End point title | Change From Baseline to Week 40 in the Movement Disorder Society - Unified Parkinson's Disease Rating Scale (MDS-UPDRS) Part III Total Score. ^[1] |
|-----------------|--|

End point description:

| | |
|---------------------------------|---------|
| End point type | Primary |
| End point timeframe: Week 40 | |

Notes:

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

Justification: Calculated based on MDS-UPDRS.

| End point values | K0706, low dose | K0706, high dose | Placebo | |
|--------------------------------------|-----------------|------------------|-----------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 164 | 162 | 161 | |
| Units: Score on a scale | | | | |
| arithmetic mean (standard deviation) | 1.5 (± 8.77) | 1.0 (± 7.58) | -1.0 (± 8.13) | |

Statistical analyses

No statistical analyses for this end point

Primary: Incidence of Treatment-emergent Adverse Events

End point title Incidence of Treatment-emergent Adverse Events^[2]

End point description:

End point type Primary

End point timeframe:

Week 80

Notes:

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

Justification: Calculated based on the number of study participants.

| End point values | K0706, low dose | K0706, high dose | Placebo | K0706, low dose |
|-----------------------------|-----------------|------------------|-----------------|-----------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 171 | 173 | 167 | 72 |
| Units: Participants | 131 | 150 | 124 | 37 |

| End point values | K0706, high dose | Placebo | | |
|-----------------------------|------------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 40 | 77 | | |
| Units: Participants | 24 | 61 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Part 1: Change From Baseline to Week 40 in the Sum of the MDS-UPDRS Parts II and III Total Scores Part 2: Change From Week 40 to Week 76 in the Sum of the MDS-UPDRS Part III Scores

End point title Part 1: Change From Baseline to Week 40 in the Sum of the MDS-UPDRS Parts II and III Total Scores Part 2: Change From Week 40 to Week 76 in the Sum of the MDS-UPDRS Part III Scores

End point description:

End point type Secondary

End point timeframe:

Part 1: Week 40

| End point values | K0706, low dose | K0706, high dose | Placebo | |
|--------------------------------------|-----------------|------------------|-----------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 164 | 162 | 161 | |
| Units: Score on a scale | | | | |
| arithmetic mean (standard deviation) | 2.6 (± 10.83) | 2.7 (± 9.72) | -0.6 (± 9.53) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Time From First Dose in Part 1 to Initiation of Symptomatic PD Medications

| | |
|-----------------|--|
| End point title | Time From First Dose in Part 1 to Initiation of Symptomatic PD Medications |
|-----------------|--|

End point description:

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

End point timeframe:

Part 1: Week 40 and Part 2: Week 80

| End point values | K0706, low dose | K0706, high dose | Placebo | K0706, low dose |
|-----------------------------|--------------------|--------------------|--------------------|-------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 164 ^[3] | 162 ^[4] | 161 ^[5] | 70 ^[6] |
| Units: Participants | 149 | 129 | 144 | 60 |

Notes:

[3] - Part 1

[4] - Part 1

[5] - Part 1

[6] - Part 2

| End point values | K0706, high dose | Placebo | | |
|-----------------------------|-------------------|-------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 35 ^[7] | 71 ^[8] | | |
| Units: Participants | 33 | 57 | | |

Notes:

[7] - Part 2

[8] - Part 2

Statistical analyses

No statistical analyses for this end point

Secondary: Change in Health Related Quality of Life as Measured by the European Quality of Life Questionnaire 5 Level Version

| | |
|-----------------|--|
| End point title | Change in Health Related Quality of Life as Measured by the European Quality of Life Questionnaire 5 Level Version |
|-----------------|--|

End point description:

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

End point timeframe:

Week 40

| End point values | K0706, low dose | K0706, high dose | Placebo | |
|--------------------------------------|--------------------------|--------------------------|--------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 89 | 56 | 97 | |
| Units: Score on a scale | | | | |
| arithmetic mean (standard deviation) | -0.0419 (\pm 0.11060) | -0.0531 (\pm 0.16289) | -0.0140 (\pm 0.10787) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change in Clinician Global Impression Severity

| | |
|-----------------|--|
| End point title | Change in Clinician Global Impression Severity |
|-----------------|--|

End point description:

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

End point timeframe:

Week 40

| End point values | K0706, low dose | K0706, high dose | Placebo | |
|--------------------------------------|-------------------|-------------------|-------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 104 | 61 | 103 | |
| Units: Score on a scale | | | | |
| arithmetic mean (standard deviation) | 0.2 (\pm 0.68) | 0.0 (\pm 0.74) | 0.2 (\pm 0.91) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change in the Scales for Outcomes in Parkinson's Disease - Autonomic Questionnaire - Page

| | |
|-----------------|---|
| End point title | Change in the Scales for Outcomes in Parkinson's Disease - Autonomic Questionnaire - Page |
|-----------------|---|

| | |
|------------------------|-----------|
| End point description: | |
| Data Not Reported | |
| End point type | Secondary |
| End point timeframe: | |
| Week 40 | |

| End point values | K0706, low dose | K0706, high dose | Placebo | |
|-----------------------------|-----------------|------------------|-----------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 164 | 162 | 161 | |
| Units: NA | 105 | 64 | 103 | |

Statistical analyses

No statistical analyses for this end point

Secondary: Level of K0706

| | |
|------------------------|----------------|
| End point title | Level of K0706 |
| End point description: | |
| Data not captured | |
| End point type | Secondary |
| End point timeframe: | |
| Week 40 | |

| End point values | K0706, low dose | K0706, high dose | Placebo | K0706, low dose |
|-----------------------------|------------------|-------------------|-------------------|-------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 0 ^[9] | 0 ^[10] | 0 ^[11] | 0 ^[12] |
| Units: NA | | | | |

Notes:

[9] - Data not captured

[10] - Data not captured

[11] - Data not captured

[12] - Data not captured

| End point values | K0706, high dose | Placebo | | |
|-----------------------------|-------------------|-------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 0 ^[13] | 0 ^[14] | | |
| Units: NA | | | | |

Notes:

[13] - Data not captured

[14] - Data not captured

Statistical analyses

No statistical analyses for this end point

Secondary: Exploratory Outcome: Effect of K0706 on Dopamine Cell Health in Parkinson's Disease as Detected Via Dopamine Transporter Single Photon Emission Computed Tomography (DaT SPECT) Brain Imaging

| | |
|------------------------|---|
| End point title | Exploratory Outcome: Effect of K0706 on Dopamine Cell Health in Parkinson's Disease as Detected Via Dopamine Transporter Single Photon Emission Computed Tomography (DaT SPECT) Brain Imaging |
| End point description: | |
| Data not captured | |
| End point type | Secondary |
| End point timeframe: | |
| Week 40 | |

| End point values | K0706, low dose | K0706, high dose | Placebo | K0706, low dose |
|-----------------------------|-------------------|-------------------|-------------------|-------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 0 ^[15] | 0 ^[16] | 0 ^[17] | 0 ^[18] |
| Units: NA | | | | |

Notes:

[15] - Data not captured

[16] - Data not captured

[17] - Data not captured

[18] - Data not captured

| End point values | K0706, high dose | Placebo | | |
|-----------------------------|-------------------|-------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 0 ^[19] | 0 ^[20] | | |
| Units: NA | | | | |

Notes:

[19] - Data not captured

[20] - Data not captured

Statistical analyses

No statistical analyses for this end point

Secondary: CSF K0706 Levels Progression or Target Engagement of K0706.

| | |
|------------------------|---|
| End point title | CSF K0706 Levels Progression or Target Engagement of K0706. |
| End point description: | |
| Data not captured | |
| End point type | Secondary |
| End point timeframe: | |
| Week 40 | |

| End point values | K0706, low dose | K0706, high dose | Placebo | K0706, low dose |
|-----------------------------|-------------------|-------------------|-------------------|-------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 0 ^[21] | 0 ^[22] | 0 ^[23] | 0 ^[24] |
| Units: NA | | | | |

Notes:

[21] - Data not captured

[22] - Data not captured

[23] - Data not captured

[24] - Data not captured

| End point values | K0706, high dose | Placebo | | |
|-----------------------------|-------------------|-------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 0 ^[25] | 0 ^[26] | | |
| Units: NA | | | | |

Notes:

[25] - Data not captured

[26] - Data not captured

Statistical analyses

No statistical analyses for this end point

Secondary: Brain DaT SPECT - an Imaging Tool That is a Marker of Dopaminergic Cell Health.

| | |
|------------------------|---|
| End point title | Brain DaT SPECT - an Imaging Tool That is a Marker of Dopaminergic Cell Health. |
| End point description: | |
| Data not captured | |
| End point type | Secondary |
| End point timeframe: | |
| Week 40 | |

| End point values | K0706, low dose | K0706, high dose | Placebo | K0706, low dose |
|-----------------------------|-------------------|-------------------|-------------------|-------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 0 ^[27] | 0 ^[28] | 0 ^[29] | 0 ^[30] |
| Units: NA | | | | |

Notes:

[27] - Data not captured

[28] - Data not captured

[29] - Data not captured

[30] - Data not captured

| End point values | K0706, high dose | Placebo | | |
|------------------|------------------|---------|--|--|
|------------------|------------------|---------|--|--|

| | | | | |
|-----------------------------|-------------------|-------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 0 ^[31] | 0 ^[32] | | |
| Units: NA | | | | |

Notes:

[31] - Data not captured

[32] - Data not captured

Statistical analyses

No statistical analyses for this end point

Secondary: Blood K0706 Levels

| | |
|------------------------|--------------------|
| End point title | Blood K0706 Levels |
| End point description: | |
| Data not captured | |
| End point type | Secondary |
| End point timeframe: | |
| Week 40 | |

| End point values | K0706, low dose | K0706, high dose | Placebo | K0706, low dose |
|-----------------------------|-------------------|-------------------|-------------------|-------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 0 ^[33] | 0 ^[34] | 0 ^[35] | 0 ^[36] |
| Units: NA | | | | |

Notes:

[33] - Data not captured

[34] - Data not captured

[35] - Data not captured

[36] - Data not captured

| End point values | K0706, high dose | Placebo | | |
|-----------------------------|-------------------|-------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 0 ^[37] | 0 ^[38] | | |
| Units: NA | | | | |

Notes:

[37] - Data not captured

[38] - Data not captured

Statistical analyses

No statistical analyses for this end point

Secondary: Skin Punch Biopsy

| | |
|------------------------|-------------------|
| End point title | Skin Punch Biopsy |
| End point description: | |
| Data not captured | |
| End point type | Secondary |
| End point timeframe: | |
| Week 40 | |

| End point values | K0706, low dose | K0706, high dose | Placebo | K0706, low dose |
|-----------------------------|-------------------|-------------------|-------------------|-------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 0 ^[39] | 0 ^[40] | 0 ^[41] | 0 ^[42] |
| Units: NA | | | | |

Notes:

[39] - Data not captured

[40] - Data not captured

[41] - Data not captured

[42] - Data not captured

| End point values | K0706, high dose | Placebo | | |
|-----------------------------|-------------------|-------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 0 ^[43] | 0 ^[44] | | |
| Units: NA | | | | |

Notes:

[43] - Data not captured

[44] - Data not captured

Statistical analyses

No statistical analyses for this end point

Secondary: Part 1: Change From Baseline to Week 40 in the Sum of the MDS-UPDRS Parts II and III Total Scores Part 2: Change From Week 40 to Week 76 in the Sum of the MDS-UPDRS Part III Scores

| | |
|-----------------|--|
| End point title | Part 1: Change From Baseline to Week 40 in the Sum of the MDS-UPDRS Parts II and III Total Scores Part 2: Change From Week 40 to Week 76 in the Sum of the MDS-UPDRS Part III Scores |
|-----------------|--|

End point description:

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

End point timeframe:

Part 2: Week 76

| End point values | K0706, low dose | K0706, high dose | Placebo | |
|--------------------------------------|-----------------|------------------|-----------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 30 | 18 | 25 | |
| Units: Score on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Tremor Subscore | 0.4 (± 1.87) | -0.9 (± 2.54) | -0.4 (± 2.68) | |
| Bradykinesia Subscore | -0.7 (± 2.25) | -0.1 (± 0.83) | 0.0 (± 2.20) | |
| Rigidity Subscore | 1.7 (± 4.46) | 0.2 (± 3.81) | 0.8 (± 4.12) | |
| Axial Symptoms Subscore | 0.5 (± 1.22) | 0.4 (± 1.15) | 0.0 (± 1.37) | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Treatment-related TEAEs that occurred more than 30 days after the last dose date are included for reporting

Adverse event reporting additional description:

Multiple instances of occurrence of the same AE in the same patient will be considered as a single instance.

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

Dictionary used

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

| | |
|--------------------|----|
| Dictionary version | 23 |
|--------------------|----|

Reporting groups

| | |
|-----------------------|------------------------|
| Reporting group title | Part 1: K0706 low-dose |
|-----------------------|------------------------|

Reporting group description:

Multiple instances of occurrence of the same AE in the same patient will be considered as a single instance.

| | |
|-----------------------|-------------------------|
| Reporting group title | Part 1: K0706 high-dose |
|-----------------------|-------------------------|

Reporting group description:

Multiple instances of occurrence of the same AE in the same patient will be considered as a single instance.

| | |
|-----------------------|-----------------|
| Reporting group title | Part 1: Placebo |
|-----------------------|-----------------|

Reporting group description:

Part 1; Multiple instances of occurrence of the same AE in the same patient will be considered as a single instance.

| | |
|-----------------------|------------------------|
| Reporting group title | Part 2: K0706 low-dose |
|-----------------------|------------------------|

Reporting group description:

Part 2; Multiple instances of occurrence of the same AE in the same patient will be considered as a single instance.

| | |
|-----------------------|-------------------------|
| Reporting group title | Part 2: K0706 high-dose |
|-----------------------|-------------------------|

Reporting group description:

Multiple instances of occurrence of the same AE in the same patient will be considered as a single instance.

| | |
|-----------------------|-----------------|
| Reporting group title | Part 2: Placebo |
|-----------------------|-----------------|

Reporting group description:

Multiple instances of occurrence of the same AE in the same patient will be considered as a single instance; part 2: Prior Placebo transitioned to K0706 High Dose

| Serious adverse events | Part 1: K0706 low-dose | Part 1: K0706 high-dose | Part 1: Placebo |
|---|---|-------------------------|-----------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 2 / 171 (1.17%) | 7 / 173 (4.05%) | 5 / 167 (2.99%) |
| number of deaths (all causes) | 1 | 0 | 0 |
| number of deaths resulting from adverse events | 0 | 0 | 0 |
| Injury, poisoning and procedural complications | | | |
| Femur fracture | Additional description: For part 2: Prior Placebo transitioned to K0706 High Dose | | |

| | | | |
|---|---|-----------------|-----------------|
| subjects affected / exposed | 0 / 171 (0.00%) | 1 / 173 (0.58%) | 0 / 167 (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 |
| Cardiac disorders | | | |
| Coronary artery disease | Additional description: For part 2: Prior Placebo transitioned to K0706 High Dose | | |
| subjects affected / exposed | 0 / 171 (0.00%) | 0 / 173 (0.00%) | 0 / 167 (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 | | | |
| Parkinsonism | Additional description: For part 2: Prior Placebo transitioned to K0706 High Dose | | |
| subjects affected / exposed | 0 / 171 (0.00%) | 1 / 173 (0.58%) | 0 / 167 (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 |
| Encephalopathy | Additional description: For part 2: Prior Placebo transitioned to K0706 High Dose | | |
| subjects affected / exposed | 0 / 171 (0.00%) | 0 / 173 (0.00%) | 0 / 167 (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 |
| Idiopathic Intracranial Hypertension | Additional description: For part 2: Prior Placebo transitioned to K0706 High Dose | | |
| subjects affected / exposed | 0 / 171 (0.00%) | 0 / 173 (0.00%) | 0 / 167 (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 |
| Gastrointestinal disorders | | | |
| Gastrointestinal perforation | Additional description: For part 2: Prior Placebo transitioned to K0706 High Dose | | |
| subjects affected / exposed | 0 / 171 (0.00%) | 0 / 173 (0.00%) | 0 / 167 (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 | | | |
| Delirium | Additional description: For part 2: Prior Placebo transitioned to K0706 High Dose | | |
| subjects affected / exposed | 0 / 171 (0.00%) | 0 / 173 (0.00%) | 0 / 167 (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 |
| Psychotic disorder | Additional description: For part 2: Prior Placebo transitioned to K0706 High Dose | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 171 (0.00%) | 0 / 173 (0.00%) | 0 / 167 (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 | Part 2: K0706 low-dose | Part 2: K0706 high-dose | Part 2: Placebo |
|---|---|-------------------------|-----------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 3 / 72 (4.17%) | 2 / 67 (2.99%) | 4 / 77 (5.19%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | 0 | 0 | 0 |
| Injury, poisoning and procedural complications | | | |
| Femur fracture | Additional description: For part 2: Prior Placebo transitioned to K0706 High Dose | | |
| subjects affected / exposed | 0 / 72 (0.00%) | 0 / 67 (0.00%) | 0 / 77 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac disorders | | | |
| Coronary artery disease | Additional description: For part 2: Prior Placebo transitioned to K0706 High Dose | | |
| subjects affected / exposed | 1 / 72 (1.39%) | 0 / 67 (0.00%) | 0 / 77 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nervous system disorders | | | |
| Parkinsonism | Additional description: For part 2: Prior Placebo transitioned to K0706 High Dose | | |
| subjects affected / exposed | 0 / 72 (0.00%) | 0 / 67 (0.00%) | 0 / 77 (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 |
| Encephalopathy | Additional description: For part 2: Prior Placebo transitioned to K0706 High Dose | | |
| subjects affected / exposed | 0 / 72 (0.00%) | 1 / 67 (1.49%) | 0 / 77 (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 |
| Idiopathic Intracranial Hypertension | Additional description: For part 2: Prior Placebo transitioned to K0706 High Dose | | |
| subjects affected / exposed | 0 / 72 (0.00%) | 1 / 67 (1.49%) | 0 / 77 (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 |
| Gastrointestinal disorders | | | |
| Gastrointestinal perforation | Additional description: For part 2: Prior Placebo transitioned to K0706 High Dose | | |

| | | | |
|---|---|----------------|----------------|
| subjects affected / exposed | 0 / 72 (0.00%) | 1 / 67 (1.49%) | 0 / 77 (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 |
| Psychiatric disorders | | | |
| Delirium | Additional description: For part 2: Prior Placebo transitioned to K0706 High Dose | | |
| subjects affected / exposed | 0 / 72 (0.00%) | 1 / 67 (1.49%) | 0 / 77 (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 |
| Psychotic disorder | Additional description: For part 2: Prior Placebo transitioned to K0706 High Dose | | |
| subjects affected / exposed | 0 / 72 (0.00%) | 1 / 67 (1.49%) | 0 / 77 (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 |

Frequency threshold for reporting non-serious adverse events: 1 %

| Non-serious adverse events | Part 1: K0706 low-dose | Part 1: K0706 high-dose | Part 1: Placebo |
|---|------------------------|-------------------------|-------------------|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 80 / 171 (46.78%) | 114 / 173 (65.90%) | 48 / 167 (28.74%) |
| Vascular disorders | | | |
| Flushing | | | |
| subjects affected / exposed | 2 / 171 (1.17%) | 4 / 173 (2.31%) | 0 / 167 (0.00%) |
| occurrences (all) | 2 | 4 | 0 |
| Hypotension | | | |
| subjects affected / exposed | 1 / 171 (0.58%) | 1 / 173 (0.58%) | 0 / 167 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Raynaud's phenomenon | | | |
| subjects affected / exposed | 1 / 171 (0.58%) | 0 / 173 (0.00%) | 0 / 167 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Hypertension | | | |
| subjects affected / exposed | 0 / 171 (0.00%) | 0 / 173 (0.00%) | 0 / 167 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| General disorders and administration site conditions | | | |
| Peripheral swelling | | | |
| subjects affected / exposed | 2 / 171 (1.17%) | 1 / 173 (0.58%) | 1 / 167 (0.60%) |
| occurrences (all) | 3 | 1 | 1 |

| | | | |
|---------------------------------------|-----------------|-----------------|-----------------|
| Chest pain | | | |
| subjects affected / exposed | 0 / 171 (0.00%) | 0 / 173 (0.00%) | 1 / 167 (0.60%) |
| occurrences (all) | 0 | 0 | 1 |
| Early satiety | | | |
| subjects affected / exposed | 1 / 171 (0.58%) | 0 / 173 (0.00%) | 0 / 167 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Face oedema | | | |
| subjects affected / exposed | 1 / 171 (0.58%) | 0 / 173 (0.00%) | 0 / 167 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| General physical health deterioration | | | |
| subjects affected / exposed | 0 / 171 (0.00%) | 0 / 173 (0.00%) | 1 / 167 (0.60%) |
| occurrences (all) | 0 | 0 | 1 |
| Oedema peripheral | | | |
| subjects affected / exposed | 0 / 171 (0.00%) | 1 / 173 (0.58%) | 0 / 167 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Pain | | | |
| subjects affected / exposed | 0 / 171 (0.00%) | 4 / 173 (2.31%) | 2 / 167 (1.20%) |
| occurrences (all) | 0 | 5 | 2 |
| Chest discomfort | | | |
| subjects affected / exposed | 0 / 171 (0.00%) | 1 / 173 (0.58%) | 0 / 167 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Chills | | | |
| subjects affected / exposed | 0 / 171 (0.00%) | 2 / 173 (1.16%) | 0 / 167 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Facial pain | | | |
| subjects affected / exposed | 0 / 171 (0.00%) | 0 / 173 (0.00%) | 0 / 167 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Mucosal dryness | | | |
| subjects affected / exposed | 0 / 171 (0.00%) | 0 / 173 (0.00%) | 0 / 167 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Asthenia | | | |
| subjects affected / exposed | 1 / 171 (0.58%) | 5 / 173 (2.89%) | 0 / 167 (0.00%) |
| occurrences (all) | 1 | 5 | 0 |
| Immune system disorders | | | |
| Hypersensitivity | | | |

| | | | |
|--|----------------------|----------------------|----------------------|
| subjects affected / exposed occurrences (all) | 1 / 171 (0.58%) 2 | 0 / 173 (0.00%) 0 | 0 / 167 (0.00%) 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Nasal congestion | | | |
| subjects affected / exposed | 0 / 171 (0.00%) | 1 / 173 (0.58%) | 0 / 167 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Pleural effusion | | | |
| subjects affected / exposed | 1 / 171 (0.58%) | 0 / 173 (0.00%) | 0 / 167 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Pulmonary mass | | | |
| subjects affected / exposed | 1 / 171 (0.58%) | 0 / 173 (0.00%) | 0 / 167 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Cough | | | |
| subjects affected / exposed | 1 / 171 (0.58%) | 3 / 173 (1.73%) | 0 / 167 (0.00%) |
| occurrences (all) | 1 | 3 | 0 |
| Aphonia | | | |
| subjects affected / exposed | 0 / 171 (0.00%) | 0 / 173 (0.00%) | 0 / 167 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dyspnoea | | | |
| subjects affected / exposed | 0 / 171 (0.00%) | 1 / 173 (0.58%) | 0 / 167 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Throat irritation | | | |
| subjects affected / exposed | 0 / 171 (0.00%) | 0 / 173 (0.00%) | 0 / 167 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Rhinorrhoea | | | |
| subjects affected / exposed | 0 / 171 (0.00%) | 1 / 173 (0.58%) | 0 / 167 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Epistaxis | | | |
| subjects affected / exposed | 0 / 171 (0.00%) | 1 / 173 (0.58%) | 1 / 167 (0.60%) |
| occurrences (all) | 0 | 1 | 1 |
| Psychiatric disorders | | | |
| Depressed mood | | | |
| subjects affected / exposed | 0 / 171 (0.00%) | 0 / 173 (0.00%) | 1 / 167 (0.60%) |
| occurrences (all) | 0 | 0 | 1 |
| Affect lability | | | |

| | | | |
|--------------------------------|---|-----------------|-----------------|
| subjects affected / exposed | 0 / 171 (0.00%) | 0 / 173 (0.00%) | 1 / 167 (0.60%) |
| occurrences (all) | 0 | 0 | 1 |
| Irritability | | | |
| subjects affected / exposed | 0 / 171 (0.00%) | 0 / 173 (0.00%) | 0 / 167 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Mood altered | Additional description: Part 2: Prior Placebo transitioned to K0706 High Dose | | |
| subjects affected / exposed | 1 / 171 (0.58%) | 0 / 173 (0.00%) | 0 / 167 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Nightmare | | | |
| subjects affected / exposed | 1 / 171 (0.58%) | 0 / 173 (0.00%) | 0 / 167 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Anxiety | | | |
| subjects affected / exposed | 0 / 171 (0.00%) | 3 / 173 (1.73%) | 1 / 167 (0.60%) |
| occurrences (all) | 0 | 3 | 2 |
| Hallucination, visual | | | |
| subjects affected / exposed | 0 / 171 (0.00%) | 1 / 173 (0.58%) | 0 / 167 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Depression | | | |
| subjects affected / exposed | 0 / 171 (0.00%) | 1 / 173 (0.58%) | 1 / 167 (0.60%) |
| occurrences (all) | 0 | 1 | 1 |
| Agitation | | | |
| subjects affected / exposed | 0 / 171 (0.00%) | 0 / 173 (0.00%) | 0 / 167 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Impulse-control disorder | | | |
| subjects affected / exposed | 0 / 171 (0.00%) | 0 / 173 (0.00%) | 0 / 167 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Insomnia | | | |
| subjects affected / exposed | 2 / 171 (1.17%) | 2 / 173 (1.16%) | 0 / 167 (0.00%) |
| occurrences (all) | 2 | 2 | 0 |
| Abnormal dreams | | | |
| subjects affected / exposed | 0 / 171 (0.00%) | 1 / 173 (0.58%) | 0 / 167 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Affective disorder | | | |
| subjects affected / exposed | 0 / 171 (0.00%) | 1 / 173 (0.58%) | 0 / 167 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Persistent depressive disorder | | | |

| | | | |
|--|----------------------|----------------------|----------------------|
| subjects affected / exposed occurrences (all) | 0 / 171 (0.00%) 0 | 1 / 173 (0.58%) 1 | 0 / 167 (0.00%) 0 |
| Investigations | | | |
| Liver function test increased subjects affected / exposed occurrences (all) | 1 / 171 (0.58%) 1 | 0 / 173 (0.00%) 0 | 0 / 167 (0.00%) 0 |
| Mean platelet volume decreased subjects affected / exposed occurrences (all) | 1 / 171 (0.58%) 1 | 0 / 173 (0.00%) 0 | 0 / 167 (0.00%) 0 |
| Platelet count increased subjects affected / exposed occurrences (all) | 1 / 171 (0.58%) 1 | 0 / 173 (0.00%) 0 | 0 / 167 (0.00%) 0 |
| Protein total increased subjects affected / exposed occurrences (all) | 1 / 171 (0.58%) 1 | 0 / 173 (0.00%) 0 | 0 / 167 (0.00%) 0 |
| Prothrombin time prolonged subjects affected / exposed occurrences (all) | 1 / 171 (0.58%) 1 | 0 / 173 (0.00%) 0 | 0 / 167 (0.00%) 0 |
| Alanine aminotransferase increased subjects affected / exposed occurrences (all) | 1 / 171 (0.58%) 1 | 3 / 173 (1.73%) 3 | 1 / 167 (0.60%) 2 |
| Weight decreased subjects affected / exposed occurrences (all) | 2 / 171 (1.17%) 2 | 1 / 173 (0.58%) 1 | 0 / 167 (0.00%) 0 |
| Neutrophil count decreased subjects affected / exposed occurrences (all) | 0 / 171 (0.00%) 0 | 1 / 173 (0.58%) 1 | 0 / 167 (0.00%) 0 |
| Heart rate irregular subjects affected / exposed occurrences (all) | 0 / 171 (0.00%) 0 | 0 / 173 (0.00%) 0 | 0 / 167 (0.00%) 0 |
| Injury, poisoning and procedural complications | | | |
| Fall subjects affected / exposed occurrences (all) | 1 / 171 (0.58%) 1 | 0 / 173 (0.00%) 0 | 0 / 167 (0.00%) 0 |
| Cardiac disorders | | | |

| | | | |
|-----------------------------|---|-----------------|-----------------|
| Palpitations | | | |
| subjects affected / exposed | 1 / 171 (0.58%) | 0 / 173 (0.00%) | 0 / 167 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Atrial fibrillation | | | |
| subjects affected / exposed | 0 / 171 (0.00%) | 0 / 173 (0.00%) | 1 / 167 (0.60%) |
| occurrences (all) | 0 | 0 | 1 |
| Bradycardia | | | |
| subjects affected / exposed | 0 / 171 (0.00%) | 0 / 173 (0.00%) | 1 / 167 (0.60%) |
| occurrences (all) | 0 | 0 | 1 |
| Nervous system disorders | | | |
| Hypoaesthesia | | | |
| subjects affected / exposed | 0 / 171 (0.00%) | 1 / 173 (0.58%) | 0 / 167 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Lethargy | | | |
| subjects affected / exposed | 1 / 171 (0.58%) | 0 / 173 (0.00%) | 1 / 167 (0.60%) |
| occurrences (all) | 1 | 0 | 1 |
| Dysaesthesia | | | |
| subjects affected / exposed | 0 / 171 (0.00%) | 1 / 173 (0.58%) | 0 / 167 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Memory impairment | | | |
| subjects affected / exposed | 0 / 171 (0.00%) | 0 / 173 (0.00%) | 1 / 167 (0.60%) |
| occurrences (all) | 0 | 0 | 1 |
| Neurological symptom | | | |
| subjects affected / exposed | 0 / 171 (0.00%) | 0 / 173 (0.00%) | 2 / 167 (1.20%) |
| occurrences (all) | 0 | 0 | 2 |
| Headache | Additional description: Part 2: Prior Placebo transitioned to K0706 High Dose | | |
| subjects affected / exposed | 6 / 171 (3.51%) | 5 / 173 (2.89%) | 5 / 167 (2.99%) |
| occurrences (all) | 6 | 5 | 6 |
| Sciatica | | | |
| subjects affected / exposed | 1 / 171 (0.58%) | 0 / 173 (0.00%) | 0 / 167 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Paraesthesia | | | |
| subjects affected / exposed | 1 / 171 (0.58%) | 1 / 173 (0.58%) | 1 / 167 (0.60%) |
| occurrences (all) | 1 | 1 | 1 |
| Dysgeusia | | | |

| | | | |
|--------------------------------------|---|-----------------|-----------------|
| subjects affected / exposed | 2 / 171 (1.17%) | 1 / 173 (0.58%) | 3 / 167 (1.80%) |
| occurrences (all) | 2 | 1 | 4 |
| Migraine | | | |
| subjects affected / exposed | 0 / 171 (0.00%) | 0 / 173 (0.00%) | 0 / 167 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Somnolence | | | |
| subjects affected / exposed | 2 / 171 (1.17%) | 0 / 173 (0.00%) | 1 / 167 (0.60%) |
| occurrences (all) | 2 | 0 | 1 |
| Speech disorder | | | |
| subjects affected / exposed | 0 / 171 (0.00%) | 1 / 173 (0.58%) | 0 / 167 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Taste disorder | | | |
| subjects affected / exposed | 1 / 171 (0.58%) | 0 / 173 (0.00%) | 0 / 167 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Dizziness | Additional description: Part 2: Prior Placebo transitioned to K0706 High Dose | | |
| subjects affected / exposed | 2 / 171 (1.17%) | 8 / 173 (4.62%) | 4 / 167 (2.40%) |
| occurrences (all) | 2 | 9 | 6 |
| Tremor | Additional description: Part 2: Prior Placebo transitioned to K0706 High Dose | | |
| subjects affected / exposed | 2 / 171 (1.17%) | 8 / 173 (4.62%) | 1 / 167 (0.60%) |
| occurrences (all) | 2 | 8 | 1 |
| Burning sensation | | | |
| subjects affected / exposed | 1 / 171 (0.58%) | 0 / 173 (0.00%) | 0 / 167 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Cognitive disorder | | | |
| subjects affected / exposed | 0 / 171 (0.00%) | 1 / 173 (0.58%) | 0 / 167 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Syncope | | | |
| subjects affected / exposed | 0 / 171 (0.00%) | 0 / 173 (0.00%) | 1 / 167 (0.60%) |
| occurrences (all) | 0 | 0 | 1 |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 0 / 171 (0.00%) | 3 / 173 (1.73%) | 1 / 167 (0.60%) |
| occurrences (all) | 0 | 3 | 1 |
| Leukopenia | Additional description: Part 2: Prior Placebo transitioned to K0706 High Dose | | |
| subjects affected / exposed | 0 / 171 (0.00%) | 1 / 173 (0.58%) | 0 / 167 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |

| | | | |
|-----------------------------------|---|-----------------|-----------------|
| Neutropenia | | | |
| subjects affected / exposed | 0 / 171 (0.00%) | 1 / 173 (0.58%) | 0 / 167 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Thrombocytosis | | | |
| subjects affected / exposed | 0 / 171 (0.00%) | 1 / 173 (0.58%) | 0 / 167 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Ear and labyrinth disorders | | | |
| Vertigo | | | |
| subjects affected / exposed | 0 / 171 (0.00%) | 1 / 173 (0.58%) | 0 / 167 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Eye disorders | | | |
| Optic neuropathy | | | |
| subjects affected / exposed | 0 / 171 (0.00%) | 1 / 173 (0.58%) | 0 / 167 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Ocular hyperaemia | | | |
| subjects affected / exposed | 0 / 171 (0.00%) | 2 / 173 (1.16%) | 0 / 167 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Visual acuity reduced transiently | | | |
| subjects affected / exposed | 0 / 171 (0.00%) | 0 / 173 (0.00%) | 1 / 167 (0.60%) |
| occurrences (all) | 0 | 0 | 1 |
| Papilloedema | | | |
| subjects affected / exposed | 0 / 171 (0.00%) | 1 / 173 (0.58%) | 0 / 167 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Visual impairment | | | |
| subjects affected / exposed | 0 / 171 (0.00%) | 0 / 173 (0.00%) | 3 / 167 (1.80%) |
| occurrences (all) | 0 | 0 | 3 |
| Eye swelling | Additional description: Part 2: Prior Placebo transitioned to K0706 High Dose | | |
| subjects affected / exposed | 0 / 171 (0.00%) | 2 / 173 (1.16%) | 0 / 167 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Swelling of eyelid | | | |
| subjects affected / exposed | 0 / 171 (0.00%) | 2 / 173 (1.16%) | 0 / 167 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Xerophthalmia | | | |
| subjects affected / exposed | 0 / 171 (0.00%) | 1 / 173 (0.58%) | 0 / 167 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Gastrointestinal disorders | | | |

| | | | |
|-----------------------------|---|------------------|-----------------|
| Constipation | Additional description: For part 2: Prior Placebo transitioned to K0706 High Dose | | |
| subjects affected / exposed | 0 / 171 (0.00%) | 5 / 173 (2.89%) | 1 / 167 (0.60%) |
| occurrences (all) | 0 | 5 | 1 |
| Gastroesophageal reflux | | | |
| subjects affected / exposed | 1 / 171 (0.58%) | 0 / 173 (0.00%) | 1 / 167 (0.60%) |
| occurrences (all) | 2 | 0 | 1 |
| Haemorrhoids | | | |
| subjects affected / exposed | 0 / 171 (0.00%) | 0 / 173 (0.00%) | 0 / 167 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Anal incontinence | | | |
| subjects affected / exposed | 1 / 171 (0.58%) | 0 / 173 (0.00%) | 0 / 167 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Faeces soft | | | |
| subjects affected / exposed | 2 / 171 (1.17%) | 0 / 173 (0.00%) | 0 / 167 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Hiccups | | | |
| subjects affected / exposed | 1 / 171 (0.58%) | 0 / 173 (0.00%) | 0 / 167 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Lip oedema | | | |
| subjects affected / exposed | 1 / 171 (0.58%) | 0 / 173 (0.00%) | 0 / 167 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Oral dysaesthesia | | | |
| subjects affected / exposed | 0 / 171 (0.00%) | 1 / 173 (0.58%) | 0 / 167 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Tongue pruritus | | | |
| subjects affected / exposed | 0 / 171 (0.00%) | 0 / 173 (0.00%) | 1 / 167 (0.60%) |
| occurrences (all) | 0 | 0 | 1 |
| Ulcerative gastritis | | | |
| subjects affected / exposed | 1 / 171 (0.58%) | 0 / 173 (0.00%) | 0 / 167 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Diarrhoea | Additional description: For part 2: Prior Placebo transitioned to K0706 High Dose | | |
| subjects affected / exposed | 13 / 171 (7.60%) | 13 / 173 (7.51%) | 2 / 167 (1.20%) |
| occurrences (all) | 13 | 21 | 3 |
| Abdominal pain upper | Additional description: For part 2: Prior Placebo transitioned to K0706 High Dose | | |
| subjects affected / exposed | 2 / 171 (1.17%) | 5 / 173 (2.89%) | 1 / 167 (0.60%) |
| occurrences (all) | 3 | 6 | 2 |

| | | | |
|-----------------------------|---|------------------|-----------------|
| Dry mouth | | | |
| subjects affected / exposed | 1 / 171 (0.58%) | 1 / 173 (0.58%) | 2 / 167 (1.20%) |
| occurrences (all) | 1 | 1 | 2 |
| Nausea | | | |
| subjects affected / exposed | 13 / 171 (7.60%) | 14 / 173 (8.09%) | 6 / 167 (3.59%) |
| occurrences (all) | 14 | 17 | 6 |
| Gastrointestinal disorder | | | |
| subjects affected / exposed | 1 / 171 (0.58%) | 1 / 173 (0.58%) | 0 / 167 (0.00%) |
| occurrences (all) | 1 | 3 | 0 |
| Gastritis | | | |
| subjects affected / exposed | 0 / 171 (0.00%) | 1 / 173 (0.58%) | 0 / 167 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Abdominal distension | | | |
| subjects affected / exposed | 3 / 171 (1.75%) | 2 / 173 (1.16%) | 1 / 167 (0.60%) |
| occurrences (all) | 3 | 2 | 1 |
| Abdominal pain | Additional description: For part 2: Prior Placebo transitioned to K0706 High Dose | | |
| subjects affected / exposed | 4 / 171 (2.34%) | 5 / 173 (2.89%) | 1 / 167 (0.60%) |
| occurrences (all) | 4 | 7 | 1 |
| Dyspepsia | | | |
| subjects affected / exposed | 3 / 171 (1.75%) | 0 / 173 (0.00%) | 2 / 167 (1.20%) |
| occurrences (all) | 4 | 0 | 2 |
| Gastric disorder | | | |
| subjects affected / exposed | 0 / 171 (0.00%) | 1 / 173 (0.58%) | 0 / 167 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Gastritis erosive | | | |
| subjects affected / exposed | 0 / 171 (0.00%) | 0 / 173 (0.00%) | 0 / 167 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Glossitis | | | |
| subjects affected / exposed | 0 / 171 (0.00%) | 1 / 173 (0.58%) | 0 / 167 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Abdominal discomfort | | | |
| subjects affected / exposed | 0 / 171 (0.00%) | 5 / 173 (2.89%) | 1 / 167 (0.60%) |
| occurrences (all) | 0 | 6 | 1 |
| Vomiting | | | |
| subjects affected / exposed | 0 / 171 (0.00%) | 6 / 173 (3.47%) | 1 / 167 (0.60%) |
| occurrences (all) | 0 | 7 | 1 |

| | | | |
|--|---|-------------------|-----------------|
| Flatulence | | | |
| subjects affected / exposed | 3 / 171 (1.75%) | 2 / 173 (1.16%) | 0 / 167 (0.00%) |
| occurrences (all) | 3 | 2 | 0 |
| Eructation | | | |
| subjects affected / exposed | 0 / 171 (0.00%) | 1 / 173 (0.58%) | 0 / 167 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Lip swelling | | | |
| subjects affected / exposed | 0 / 171 (0.00%) | 1 / 173 (0.58%) | 0 / 167 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Rectal tenesmus | | | |
| subjects affected / exposed | 0 / 171 (0.00%) | 1 / 173 (0.58%) | 0 / 167 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Defaecation urgency | | | |
| subjects affected / exposed | 1 / 171 (0.58%) | 0 / 173 (0.00%) | 0 / 167 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Infrequent bowel movements | | | |
| subjects affected / exposed | 1 / 171 (0.58%) | 0 / 173 (0.00%) | 0 / 167 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Hepatobiliary disorders | | | |
| Hepatitis | | | |
| subjects affected / exposed | 0 / 171 (0.00%) | 2 / 173 (1.16%) | 0 / 167 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Skin and subcutaneous tissue disorders | | | |
| Butterfly rash | | | |
| subjects affected / exposed | 1 / 171 (0.58%) | 0 / 173 (0.00%) | 0 / 167 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Rash macular | | | |
| subjects affected / exposed | 1 / 171 (0.58%) | 0 / 173 (0.00%) | 0 / 167 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Rash | Additional description: For Part 2: Prior Placebo transitioned to K0706 High Dose | | |
| subjects affected / exposed | 18 / 171 (10.53%) | 27 / 173 (15.61%) | 3 / 167 (1.80%) |
| occurrences (all) | 23 | 30 | 3 |
| Pruritus | | | |
| subjects affected / exposed | 8 / 171 (4.68%) | 11 / 173 (6.36%) | 2 / 167 (1.20%) |
| occurrences (all) | 9 | 13 | 2 |
| Rash papular | | | |

| | | | |
|-----------------------------|---|------------------|-----------------|
| subjects affected / exposed | 1 / 171 (0.58%) | 1 / 173 (0.58%) | 0 / 167 (0.00%) |
| occurrences (all) | 1 | 3 | 0 |
| Mucocutaneous rash | | | |
| subjects affected / exposed | 0 / 171 (0.00%) | 0 / 173 (0.00%) | 0 / 167 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Urticaria | | | |
| subjects affected / exposed | 1 / 171 (0.58%) | 2 / 173 (1.16%) | 0 / 167 (0.00%) |
| occurrences (all) | 1 | 2 | 0 |
| Night sweats | | | |
| subjects affected / exposed | 1 / 171 (0.58%) | 1 / 173 (0.58%) | 0 / 167 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Erythema | Additional description: For Part 2: Prior Placebo transitioned to K0706 High Dose | | |
| subjects affected / exposed | 7 / 171 (4.09%) | 17 / 173 (9.83%) | 0 / 167 (0.00%) |
| occurrences (all) | 10 | 18 | 0 |
| Alopecia | | | |
| subjects affected / exposed | 4 / 171 (2.34%) | 2 / 173 (1.16%) | 0 / 167 (0.00%) |
| occurrences (all) | 4 | 3 | 0 |
| Dermatitis allergic | | | |
| subjects affected / exposed | 0 / 171 (0.00%) | 2 / 173 (1.16%) | 0 / 167 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Hyperhidrosis | | | |
| subjects affected / exposed | 0 / 171 (0.00%) | 1 / 173 (0.58%) | 0 / 167 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Madarosis | | | |
| subjects affected / exposed | 3 / 171 (1.75%) | 0 / 173 (0.00%) | 0 / 167 (0.00%) |
| occurrences (all) | 3 | 0 | 0 |
| Dermatitis acneiform | | | |
| subjects affected / exposed | 0 / 171 (0.00%) | 2 / 173 (1.16%) | 0 / 167 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Keratosis pilaris | | | |
| subjects affected / exposed | 1 / 171 (0.58%) | 1 / 173 (0.58%) | 0 / 167 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Photosensitivity reaction | | | |
| subjects affected / exposed | 1 / 171 (0.58%) | 1 / 173 (0.58%) | 0 / 167 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Rash pruritic | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 171 (0.00%) | 2 / 173 (1.16%) | 0 / 167 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Erythema multiforme | | | |
| subjects affected / exposed | 0 / 171 (0.00%) | 1 / 173 (0.58%) | 0 / 167 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Seborrhoeic dermatitis | | | |
| subjects affected / exposed | 0 / 171 (0.00%) | 1 / 173 (0.58%) | 0 / 167 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Skin depigmentation | | | |
| subjects affected / exposed | 1 / 171 (0.58%) | 0 / 173 (0.00%) | 0 / 167 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Skin exfoliation | | | |
| subjects affected / exposed | 0 / 171 (0.00%) | 1 / 173 (0.58%) | 0 / 167 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Skin reaction | | | |
| subjects affected / exposed | 0 / 171 (0.00%) | 1 / 173 (0.58%) | 0 / 167 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Sunburn | | | |
| subjects affected / exposed | 1 / 171 (0.58%) | 0 / 173 (0.00%) | 0 / 167 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Renal and urinary disorders | | | |
| Micturition urgency | | | |
| subjects affected / exposed | 0 / 171 (0.00%) | 0 / 173 (0.00%) | 0 / 167 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Calculus bladder | | | |
| subjects affected / exposed | 0 / 171 (0.00%) | 0 / 173 (0.00%) | 0 / 167 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Urinary hesitation | | | |
| subjects affected / exposed | 0 / 171 (0.00%) | 0 / 173 (0.00%) | 0 / 167 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pollakiuria | | | |
| subjects affected / exposed | 1 / 171 (0.58%) | 0 / 173 (0.00%) | 0 / 167 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Musculoskeletal and connective tissue disorders | | | |

| | | | |
|-----------------------------------|---|-----------------|-----------------|
| Arthralgia | | | |
| subjects affected / exposed | 0 / 171 (0.00%) | 0 / 173 (0.00%) | 1 / 167 (0.60%) |
| occurrences (all) | 0 | 0 | 1 |
| Flank pain | | | |
| subjects affected / exposed | 1 / 171 (0.58%) | 0 / 173 (0.00%) | 0 / 167 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Muscle spasms | | | |
| subjects affected / exposed | 0 / 171 (0.00%) | 6 / 173 (3.47%) | 0 / 167 (0.00%) |
| occurrences (all) | 0 | 6 | 0 |
| Myalgia | | | |
| subjects affected / exposed | 2 / 171 (1.17%) | 3 / 173 (1.73%) | 0 / 167 (0.00%) |
| occurrences (all) | 2 | 3 | 0 |
| Pain in extremity | | | |
| subjects affected / exposed | 0 / 171 (0.00%) | 2 / 173 (1.16%) | 1 / 167 (0.60%) |
| occurrences (all) | 0 | 2 | 1 |
| Musculoskeletal stiffness | | | |
| subjects affected / exposed | 0 / 171 (0.00%) | 1 / 173 (0.58%) | 0 / 167 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Muscle rigidity | | | |
| subjects affected / exposed | 0 / 171 (0.00%) | 1 / 173 (0.58%) | 0 / 167 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Back pain | | | |
| subjects affected / exposed | 2 / 171 (1.17%) | 2 / 173 (1.16%) | 0 / 167 (0.00%) |
| occurrences (all) | 3 | 2 | 0 |
| Infections and infestations | | | |
| Pharyngitis | | | |
| subjects affected / exposed | 1 / 171 (0.58%) | 0 / 173 (0.00%) | 0 / 167 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Urinary tract infection | Additional description: For part 2: Prior Placebo transitioned to K0706 High Dose | | |
| subjects affected / exposed | 3 / 171 (1.75%) | 4 / 173 (2.31%) | 5 / 167 (2.99%) |
| occurrences (all) | 4 | 4 | 7 |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 0 / 171 (0.00%) | 0 / 173 (0.00%) | 0 / 167 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Folliculitis | | | |

| | | | |
|--|---|----------------------|----------------------|
| subjects affected / exposed occurrences (all) | 0 / 171 (0.00%) 0 | 1 / 173 (0.58%) 1 | 0 / 167 (0.00%) 0 |
| Influenza | Additional description: Part 2: Prior Placebo transitioned to K0706 High Dose | | |
| subjects affected / exposed occurrences (all) | 2 / 171 (1.17%) 2 | 0 / 173 (0.00%) 0 | 0 / 167 (0.00%) 0 |
| Metabolism and nutrition disorders | | | |
| Increased appetite | | | |
| subjects affected / exposed occurrences (all) | 0 / 171 (0.00%) 0 | 0 / 173 (0.00%) 0 | 2 / 167 (1.20%) 2 |
| Vitamin D deficiency | | | |
| subjects affected / exposed occurrences (all) | 1 / 171 (0.58%) 1 | 0 / 173 (0.00%) 0 | 0 / 167 (0.00%) 0 |
| Decreased appetite | | | |
| subjects affected / exposed occurrences (all) | 0 / 171 (0.00%) 0 | 6 / 173 (3.47%) 6 | 0 / 167 (0.00%) 0 |
| Hyperglycaemia | | | |
| subjects affected / exposed occurrences (all) | 0 / 171 (0.00%) 0 | 0 / 173 (0.00%) 0 | 1 / 167 (0.60%) 1 |
| Metabolic acidosis | | | |
| subjects affected / exposed occurrences (all) | 0 / 171 (0.00%) 0 | 0 / 173 (0.00%) 0 | 0 / 167 (0.00%) 0 |

| Non-serious adverse events | Part 2: K0706 low-dose | Part 2: K0706 high-dose | Part 2: Placebo |
|---|------------------------|-------------------------|---------------------|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 8 / 72 (11.11%) | 46 / 67 (68.66%) | 0 / 77 (0.00%) |
| Vascular disorders | | | |
| Flushing | | | |
| subjects affected / exposed occurrences (all) | 0 / 72 (0.00%) 0 | 0 / 67 (0.00%) 0 | 0 / 77 (0.00%) 0 |
| Hypotension | | | |
| subjects affected / exposed occurrences (all) | 0 / 72 (0.00%) 0 | 0 / 67 (0.00%) 0 | 0 / 77 (0.00%) 0 |
| Raynaud's phenomenon | | | |
| subjects affected / exposed occurrences (all) | 0 / 72 (0.00%) 0 | 0 / 67 (0.00%) 0 | 0 / 77 (0.00%) 0 |
| Hypertension | | | |

| | | | |
|--|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 72 (0.00%) | 1 / 67 (1.49%) | 0 / 77 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| General disorders and administration site conditions | | | |
| Peripheral swelling | | | |
| subjects affected / exposed | 0 / 72 (0.00%) | 1 / 67 (1.49%) | 0 / 77 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Chest pain | | | |
| subjects affected / exposed | 0 / 72 (0.00%) | 0 / 67 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Early satiety | | | |
| subjects affected / exposed | 0 / 72 (0.00%) | 0 / 67 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Face oedema | | | |
| subjects affected / exposed | 0 / 72 (0.00%) | 0 / 67 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| General physical health deterioration | | | |
| subjects affected / exposed | 0 / 72 (0.00%) | 0 / 67 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Oedema peripheral | | | |
| subjects affected / exposed | 0 / 72 (0.00%) | 0 / 67 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pain | | | |
| subjects affected / exposed | 1 / 72 (1.39%) | 1 / 67 (1.49%) | 0 / 77 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Chest discomfort | | | |
| subjects affected / exposed | 0 / 72 (0.00%) | 1 / 67 (1.49%) | 0 / 77 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Chills | | | |
| subjects affected / exposed | 0 / 72 (0.00%) | 0 / 67 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Facial pain | | | |
| subjects affected / exposed | 0 / 72 (0.00%) | 1 / 67 (1.49%) | 0 / 77 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Mucosal dryness | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 72 (0.00%) | 1 / 67 (1.49%) | 0 / 77 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Asthenia | | | |
| subjects affected / exposed | 0 / 72 (0.00%) | 1 / 67 (1.49%) | 0 / 77 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Immune system disorders | | | |
| Hypersensitivity | | | |
| subjects affected / exposed | 0 / 72 (0.00%) | 0 / 67 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Nasal congestion | | | |
| subjects affected / exposed | 0 / 72 (0.00%) | 0 / 67 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pleural effusion | | | |
| subjects affected / exposed | 0 / 72 (0.00%) | 0 / 67 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pulmonary mass | | | |
| subjects affected / exposed | 0 / 72 (0.00%) | 0 / 67 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Cough | | | |
| subjects affected / exposed | 0 / 72 (0.00%) | 0 / 67 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Aphonia | | | |
| subjects affected / exposed | 0 / 72 (0.00%) | 1 / 67 (1.49%) | 0 / 77 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Dyspnoea | | | |
| subjects affected / exposed | 0 / 72 (0.00%) | 0 / 67 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Throat irritation | | | |
| subjects affected / exposed | 0 / 72 (0.00%) | 1 / 67 (1.49%) | 0 / 77 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Rhinorrhoea | | | |
| subjects affected / exposed | 0 / 72 (0.00%) | 0 / 67 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Epistaxis | | | |

| | | | |
|--|---|---------------------|---------------------|
| subjects affected / exposed occurrences (all) | 0 / 72 (0.00%) 0 | 0 / 67 (0.00%) 0 | 0 / 77 (0.00%) 0 |
| Psychiatric disorders | | | |
| Depressed mood | | | |
| subjects affected / exposed | 0 / 72 (0.00%) | 0 / 67 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Affect lability | | | |
| subjects affected / exposed | 0 / 72 (0.00%) | 0 / 67 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Irritability | | | |
| subjects affected / exposed | 0 / 72 (0.00%) | 1 / 67 (1.49%) | 0 / 77 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Mood altered | Additional description: Part 2: Prior Placebo transitioned to K0706 High Dose | | |
| subjects affected / exposed | 0 / 72 (0.00%) | 1 / 67 (1.49%) | 0 / 77 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Nightmare | | | |
| subjects affected / exposed | 0 / 72 (0.00%) | 0 / 67 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Anxiety | | | |
| subjects affected / exposed | 0 / 72 (0.00%) | 0 / 67 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hallucination, visual | | | |
| subjects affected / exposed | 0 / 72 (0.00%) | 0 / 67 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Depression | | | |
| subjects affected / exposed | 0 / 72 (0.00%) | 0 / 67 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Agitation | | | |
| subjects affected / exposed | 0 / 72 (0.00%) | 1 / 67 (1.49%) | 0 / 77 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Impulse-control disorder | | | |
| subjects affected / exposed | 0 / 72 (0.00%) | 1 / 67 (1.49%) | 0 / 77 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Insomnia | | | |
| subjects affected / exposed | 0 / 72 (0.00%) | 1 / 67 (1.49%) | 0 / 77 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |

| | | | |
|--|---------------------|---------------------|---------------------|
| Abnormal dreams subjects affected / exposed occurrences (all) | 0 / 72 (0.00%) 0 | 0 / 67 (0.00%) 0 | 0 / 77 (0.00%) 0 |
| Affective disorder subjects affected / exposed occurrences (all) | 0 / 72 (0.00%) 0 | 0 / 67 (0.00%) 0 | 0 / 77 (0.00%) 0 |
| Persistent depressive disorder subjects affected / exposed occurrences (all) | 0 / 72 (0.00%) 0 | 0 / 67 (0.00%) 0 | 0 / 77 (0.00%) 0 |
| Investigations | | | |
| Liver function test increased subjects affected / exposed occurrences (all) | 0 / 72 (0.00%) 0 | 1 / 67 (1.49%) 1 | 0 / 77 (0.00%) 0 |
| Mean platelet volume decreased subjects affected / exposed occurrences (all) | 0 / 72 (0.00%) 0 | 0 / 67 (0.00%) 0 | 0 / 77 (0.00%) 0 |
| Platelet count increased subjects affected / exposed occurrences (all) | 0 / 72 (0.00%) 0 | 0 / 67 (0.00%) 0 | 0 / 77 (0.00%) 0 |
| Protein total increased subjects affected / exposed occurrences (all) | 0 / 72 (0.00%) 0 | 0 / 67 (0.00%) 0 | 0 / 77 (0.00%) 0 |
| Prothrombin time prolonged subjects affected / exposed occurrences (all) | 0 / 72 (0.00%) 0 | 0 / 67 (0.00%) 0 | 0 / 77 (0.00%) 0 |
| Alanine aminotransferase increased subjects affected / exposed occurrences (all) | 1 / 72 (1.39%) 1 | 2 / 67 (2.99%) 2 | 0 / 77 (0.00%) 0 |
| Weight decreased subjects affected / exposed occurrences (all) | 0 / 72 (0.00%) 0 | 0 / 67 (0.00%) 0 | 0 / 77 (0.00%) 0 |
| Neutrophil count decreased subjects affected / exposed occurrences (all) | 0 / 72 (0.00%) 0 | 1 / 67 (1.49%) 1 | 0 / 77 (0.00%) 0 |
| Heart rate irregular | | | |

| | | | |
|--|---|---|---|
| subjects affected / exposed occurrences (all) | 0 / 72 (0.00%) 0 | 1 / 67 (1.49%) 1 | 0 / 77 (0.00%) 0 |
| Injury, poisoning and procedural complications Fall subjects affected / exposed occurrences (all) | 0 / 72 (0.00%) 0 | 0 / 67 (0.00%) 0 | 0 / 77 (0.00%) 0 |
| Cardiac disorders Palpitations subjects affected / exposed occurrences (all) Atrial fibrillation subjects affected / exposed occurrences (all) Bradycardia subjects affected / exposed occurrences (all) | 0 / 72 (0.00%) 0 0 / 72 (0.00%) 0 0 / 72 (0.00%) 0 | 0 / 67 (0.00%) 0 0 / 67 (0.00%) 0 0 / 67 (0.00%) 0 | 0 / 77 (0.00%) 0 0 / 77 (0.00%) 0 0 / 77 (0.00%) 0 |
| Nervous system disorders Hypoaesthesia subjects affected / exposed occurrences (all) Lethargy subjects affected / exposed occurrences (all) Dysaesthesia subjects affected / exposed occurrences (all) Memory impairment subjects affected / exposed occurrences (all) Neurological symptom subjects affected / exposed occurrences (all) | 0 / 72 (0.00%) 0 0 / 72 (0.00%) 0 0 / 72 (0.00%) 0 0 / 72 (0.00%) 0 0 / 72 (0.00%) 0 | 0 / 67 (0.00%) 0 0 / 67 (0.00%) 0 0 / 67 (0.00%) 0 0 / 67 (0.00%) 0 0 / 67 (0.00%) 0 | 0 / 77 (0.00%) 0 0 / 77 (0.00%) 0 0 / 77 (0.00%) 0 0 / 77 (0.00%) 0 0 / 77 (0.00%) 0 |
| Headache subjects affected / exposed occurrences (all) | Additional description: Part 2: Prior Placebo transitioned to K0706 High Dose | | |
| | 1 / 72 (1.39%) 1 | 3 / 67 (4.48%) 3 | 0 / 77 (0.00%) 0 |
| Sciatica | | | |

| | | | |
|--------------------------------------|---|----------------|----------------|
| subjects affected / exposed | 0 / 72 (0.00%) | 0 / 67 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Paraesthesia | | | |
| subjects affected / exposed | 0 / 72 (0.00%) | 0 / 67 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dysgeusia | | | |
| subjects affected / exposed | 0 / 72 (0.00%) | 0 / 67 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Migraine | | | |
| subjects affected / exposed | 0 / 72 (0.00%) | 1 / 67 (1.49%) | 0 / 77 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Somnolence | | | |
| subjects affected / exposed | 0 / 72 (0.00%) | 0 / 67 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Speech disorder | | | |
| subjects affected / exposed | 0 / 72 (0.00%) | 0 / 67 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Taste disorder | | | |
| subjects affected / exposed | 0 / 72 (0.00%) | 0 / 67 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dizziness | Additional description: Part 2: Prior Placebo transitioned to K0706 High Dose | | |
| subjects affected / exposed | 0 / 72 (0.00%) | 1 / 67 (1.49%) | 0 / 77 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Tremor | Additional description: Part 2: Prior Placebo transitioned to K0706 High Dose | | |
| subjects affected / exposed | 0 / 72 (0.00%) | 3 / 67 (4.48%) | 0 / 77 (0.00%) |
| occurrences (all) | 0 | 3 | 0 |
| Burning sensation | | | |
| subjects affected / exposed | 0 / 72 (0.00%) | 0 / 67 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Cognitive disorder | | | |
| subjects affected / exposed | 0 / 72 (0.00%) | 0 / 67 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Syncope | | | |
| subjects affected / exposed | 0 / 72 (0.00%) | 0 / 67 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Blood and lymphatic system disorders | | | |

| | | | |
|-----------------------------------|---|----------------|----------------|
| Anaemia | | | |
| subjects affected / exposed | 0 / 72 (0.00%) | 0 / 67 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Leukopenia | Additional description: Part 2: Prior Placebo transitioned to K0706 High Dose | | |
| subjects affected / exposed | 1 / 72 (1.39%) | 1 / 67 (1.49%) | 0 / 77 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Neutropenia | | | |
| subjects affected / exposed | 0 / 72 (0.00%) | 0 / 67 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Thrombocytosis | | | |
| subjects affected / exposed | 0 / 72 (0.00%) | 0 / 67 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Ear and labyrinth disorders | | | |
| Vertigo | | | |
| subjects affected / exposed | 0 / 72 (0.00%) | 0 / 67 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Eye disorders | | | |
| Optic neuropathy | | | |
| subjects affected / exposed | 0 / 72 (0.00%) | 0 / 67 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Ocular hyperaemia | | | |
| subjects affected / exposed | 0 / 72 (0.00%) | 0 / 67 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Visual acuity reduced transiently | | | |
| subjects affected / exposed | 0 / 72 (0.00%) | 0 / 67 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Papilloedema | | | |
| subjects affected / exposed | 0 / 72 (0.00%) | 0 / 67 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Visual impairment | | | |
| subjects affected / exposed | 1 / 72 (1.39%) | 1 / 67 (1.49%) | 0 / 77 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Eye swelling | Additional description: Part 2: Prior Placebo transitioned to K0706 High Dose | | |
| subjects affected / exposed | 0 / 72 (0.00%) | 1 / 67 (1.49%) | 0 / 77 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Swelling of eyelid | | | |

| | | | |
|-----------------------------|---|----------------|----------------|
| subjects affected / exposed | 0 / 72 (0.00%) | 0 / 67 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Xerophthalmia | | | |
| subjects affected / exposed | 0 / 72 (0.00%) | 0 / 67 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gastrointestinal disorders | | | |
| Constipation | Additional description: For part 2: Prior Placebo transitioned to K0706 High Dose | | |
| subjects affected / exposed | 0 / 72 (0.00%) | 2 / 67 (2.99%) | 0 / 77 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Gastroesophageal reflux | | | |
| subjects affected / exposed | 0 / 72 (0.00%) | 0 / 67 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Haemorrhoids | | | |
| subjects affected / exposed | 0 / 72 (0.00%) | 2 / 67 (2.99%) | 0 / 77 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Anal incontinence | | | |
| subjects affected / exposed | 0 / 72 (0.00%) | 0 / 67 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Faeces soft | | | |
| subjects affected / exposed | 0 / 72 (0.00%) | 0 / 67 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hiccups | | | |
| subjects affected / exposed | 0 / 72 (0.00%) | 0 / 67 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Lip oedema | | | |
| subjects affected / exposed | 0 / 72 (0.00%) | 0 / 67 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Oral dysaesthesia | | | |
| subjects affected / exposed | 0 / 72 (0.00%) | 0 / 67 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Tongue pruritus | | | |
| subjects affected / exposed | 0 / 72 (0.00%) | 0 / 67 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Ulcerative gastritis | | | |
| subjects affected / exposed | 0 / 72 (0.00%) | 0 / 67 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|-----------------------------|---|----------------|----------------|
| Diarrhoea | Additional description: For part 2: Prior Placebo transitioned to K0706 High Dose | | |
| subjects affected / exposed | 1 / 72 (1.39%) | 3 / 67 (4.48%) | 0 / 77 (0.00%) |
| occurrences (all) | 1 | 3 | 0 |
| Abdominal pain upper | Additional description: For part 2: Prior Placebo transitioned to K0706 High Dose | | |
| subjects affected / exposed | 0 / 72 (0.00%) | 4 / 67 (5.97%) | 0 / 77 (0.00%) |
| occurrences (all) | 0 | 4 | 0 |
| Dry mouth | | | |
| subjects affected / exposed | 0 / 72 (0.00%) | 0 / 67 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Nausea | | | |
| subjects affected / exposed | 2 / 72 (2.78%) | 3 / 67 (4.48%) | 0 / 77 (0.00%) |
| occurrences (all) | 2 | 3 | 0 |
| Gastrointestinal disorder | | | |
| subjects affected / exposed | 0 / 72 (0.00%) | 3 / 67 (4.48%) | 0 / 77 (0.00%) |
| occurrences (all) | 0 | 3 | 0 |
| Gastritis | | | |
| subjects affected / exposed | 0 / 72 (0.00%) | 0 / 67 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Abdominal distension | | | |
| subjects affected / exposed | 0 / 72 (0.00%) | 0 / 67 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Abdominal pain | Additional description: For part 2: Prior Placebo transitioned to K0706 High Dose | | |
| subjects affected / exposed | 0 / 72 (0.00%) | 1 / 67 (1.49%) | 0 / 77 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Dyspepsia | | | |
| subjects affected / exposed | 0 / 72 (0.00%) | 0 / 67 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gastric disorder | | | |
| subjects affected / exposed | 0 / 72 (0.00%) | 0 / 67 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gastritis erosive | | | |
| subjects affected / exposed | 0 / 72 (0.00%) | 1 / 67 (1.49%) | 0 / 77 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Glossitis | | | |
| subjects affected / exposed | 0 / 72 (0.00%) | 0 / 67 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|--|---|---------------------|---------------------|
| Abdominal discomfort subjects affected / exposed occurrences (all) | 0 / 72 (0.00%) 0 | 0 / 67 (0.00%) 0 | 0 / 77 (0.00%) 0 |
| Vomiting subjects affected / exposed occurrences (all) | 0 / 72 (0.00%) 0 | 0 / 67 (0.00%) 0 | 0 / 77 (0.00%) 0 |
| Flatulence subjects affected / exposed occurrences (all) | 0 / 72 (0.00%) 0 | 0 / 67 (0.00%) 0 | 0 / 77 (0.00%) 0 |
| Eructation subjects affected / exposed occurrences (all) | 0 / 72 (0.00%) 0 | 0 / 67 (0.00%) 0 | 0 / 77 (0.00%) 0 |
| Lip swelling subjects affected / exposed occurrences (all) | 0 / 72 (0.00%) 0 | 0 / 67 (0.00%) 0 | 0 / 77 (0.00%) 0 |
| Rectal tenesmus subjects affected / exposed occurrences (all) | 0 / 72 (0.00%) 0 | 0 / 67 (0.00%) 0 | 0 / 77 (0.00%) 0 |
| Defaecation urgency subjects affected / exposed occurrences (all) | 0 / 72 (0.00%) 0 | 0 / 67 (0.00%) 0 | 0 / 77 (0.00%) 0 |
| Infrequent bowel movements subjects affected / exposed occurrences (all) | 0 / 72 (0.00%) 0 | 0 / 67 (0.00%) 0 | 0 / 77 (0.00%) 0 |
| Hepatobiliary disorders Hepatitis subjects affected / exposed occurrences (all) | 0 / 72 (0.00%) 0 | 0 / 67 (0.00%) 0 | 0 / 77 (0.00%) 0 |
| Skin and subcutaneous tissue disorders Butterfly rash subjects affected / exposed occurrences (all) | 0 / 72 (0.00%) 0 | 0 / 67 (0.00%) 0 | 0 / 77 (0.00%) 0 |
| Rash macular subjects affected / exposed occurrences (all) | 0 / 72 (0.00%) 0 | 2 / 67 (2.99%) 2 | 0 / 77 (0.00%) 0 |
| Rash | Additional description: For Part 2: Prior Placebo transitioned to K0706 High Dose | | |

| | | | |
|-----------------------------|---|-----------------|----------------|
| subjects affected / exposed | 0 / 72 (0.00%) | 7 / 67 (10.45%) | 0 / 77 (0.00%) |
| occurrences (all) | 0 | 9 | 0 |
| Pruritus | | | |
| subjects affected / exposed | 0 / 72 (0.00%) | 2 / 67 (2.99%) | 0 / 77 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Rash papular | | | |
| subjects affected / exposed | 0 / 72 (0.00%) | 2 / 67 (2.99%) | 0 / 77 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Mucocutaneous rash | | | |
| subjects affected / exposed | 0 / 72 (0.00%) | 1 / 67 (1.49%) | 0 / 77 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Urticaria | | | |
| subjects affected / exposed | 0 / 72 (0.00%) | 0 / 67 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Night sweats | | | |
| subjects affected / exposed | 0 / 72 (0.00%) | 0 / 67 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Erythema | Additional description: For Part 2: Prior Placebo transitioned to K0706 High Dose | | |
| subjects affected / exposed | 0 / 72 (0.00%) | 7 / 67 (10.45%) | 0 / 77 (0.00%) |
| occurrences (all) | 0 | 8 | 0 |
| Alopecia | | | |
| subjects affected / exposed | 0 / 72 (0.00%) | 3 / 67 (4.48%) | 0 / 77 (0.00%) |
| occurrences (all) | 0 | 5 | 0 |
| Dermatitis allergic | | | |
| subjects affected / exposed | 0 / 72 (0.00%) | 0 / 67 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hyperhidrosis | | | |
| subjects affected / exposed | 0 / 72 (0.00%) | 1 / 67 (1.49%) | 0 / 77 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Madarosis | | | |
| subjects affected / exposed | 0 / 72 (0.00%) | 0 / 67 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dermatitis acneiform | | | |
| subjects affected / exposed | 0 / 72 (0.00%) | 0 / 67 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Keratosis pilaris | | | |

| | | | |
|-----------------------------|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 72 (0.00%) | 0 / 67 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Photosensitivity reaction | | | |
| subjects affected / exposed | 0 / 72 (0.00%) | 0 / 67 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Rash pruritic | | | |
| subjects affected / exposed | 0 / 72 (0.00%) | 0 / 67 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Erythema multiforme | | | |
| subjects affected / exposed | 0 / 72 (0.00%) | 0 / 67 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Seborrhoeic dermatitis | | | |
| subjects affected / exposed | 0 / 72 (0.00%) | 0 / 67 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Skin depigmentation | | | |
| subjects affected / exposed | 0 / 72 (0.00%) | 0 / 67 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Skin exfoliation | | | |
| subjects affected / exposed | 0 / 72 (0.00%) | 0 / 67 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Skin reaction | | | |
| subjects affected / exposed | 0 / 72 (0.00%) | 0 / 67 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Sunburn | | | |
| subjects affected / exposed | 0 / 72 (0.00%) | 0 / 67 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Renal and urinary disorders | | | |
| Micturition urgency | | | |
| subjects affected / exposed | 0 / 72 (0.00%) | 1 / 67 (1.49%) | 0 / 77 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Calculus bladder | | | |
| subjects affected / exposed | 0 / 72 (0.00%) | 1 / 67 (1.49%) | 0 / 77 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Urinary hesitation | | | |
| subjects affected / exposed | 0 / 72 (0.00%) | 1 / 67 (1.49%) | 0 / 77 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |

| | | | |
|---|---------------------|---------------------|---------------------|
| Pollakiuria subjects affected / exposed occurrences (all) | 0 / 72 (0.00%) 0 | 0 / 67 (0.00%) 0 | 0 / 77 (0.00%) 0 |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia subjects affected / exposed occurrences (all) | 0 / 72 (0.00%) 0 | 0 / 67 (0.00%) 0 | 0 / 77 (0.00%) 0 |
| Flank pain subjects affected / exposed occurrences (all) | 0 / 72 (0.00%) 0 | 0 / 67 (0.00%) 0 | 0 / 77 (0.00%) 0 |
| Muscle spasms subjects affected / exposed occurrences (all) | 0 / 72 (0.00%) 0 | 1 / 67 (1.49%) 1 | 0 / 77 (0.00%) 0 |
| Myalgia subjects affected / exposed occurrences (all) | 0 / 72 (0.00%) 0 | 1 / 67 (1.49%) 1 | 0 / 77 (0.00%) 0 |
| Pain in extremity subjects affected / exposed occurrences (all) | 0 / 72 (0.00%) 0 | 1 / 67 (1.49%) 1 | 0 / 77 (0.00%) 0 |
| Musculoskeletal stiffness subjects affected / exposed occurrences (all) | 0 / 72 (0.00%) 0 | 1 / 67 (1.49%) 1 | 0 / 77 (0.00%) 0 |
| Muscle rigidity subjects affected / exposed occurrences (all) | 0 / 72 (0.00%) 0 | 0 / 67 (0.00%) 0 | 0 / 77 (0.00%) 0 |
| Back pain subjects affected / exposed occurrences (all) | 0 / 72 (0.00%) 0 | 2 / 67 (2.99%) 2 | 0 / 77 (0.00%) 0 |
| Infections and infestations | | | |
| Pharyngitis subjects affected / exposed occurrences (all) | 0 / 72 (0.00%) 0 | 0 / 67 (0.00%) 0 | 0 / 77 (0.00%) 0 |
| Urinary tract infection subjects affected / exposed occurrences (all) | 0 / 72 (0.00%) 0 | 4 / 67 (5.97%) 4 | 0 / 77 (0.00%) 0 |
| Upper respiratory tract infection | | | |

Additional description: For part 2: Prior Placebo transitioned to K0706 High Dose

| | | | |
|------------------------------------|---|----------------|----------------|
| subjects affected / exposed | 0 / 72 (0.00%) | 1 / 67 (1.49%) | 0 / 77 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Folliculitis | | | |
| subjects affected / exposed | 0 / 72 (0.00%) | 0 / 67 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Influenza | Additional description: Part 2: Prior Placebo transitioned to K0706 High Dose | | |
| subjects affected / exposed | 0 / 72 (0.00%) | 0 / 67 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Metabolism and nutrition disorders | | | |
| Increased appetite | | | |
| subjects affected / exposed | 0 / 72 (0.00%) | 0 / 67 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Vitamin D deficiency | | | |
| subjects affected / exposed | 0 / 72 (0.00%) | 0 / 67 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Decreased appetite | | | |
| subjects affected / exposed | 0 / 72 (0.00%) | 0 / 67 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hyperglycaemia | | | |
| subjects affected / exposed | 0 / 72 (0.00%) | 0 / 67 (0.00%) | 0 / 77 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Metabolic acidosis | | | |
| subjects affected / exposed | 0 / 72 (0.00%) | 1 / 67 (1.49%) | 0 / 77 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|-------------------|---|
| 30 September 2019 | The protocol was amended due to the following reasons: (a.) Addition of new formulation: Powder for suspension (b.) Addition of new doses: 192 mg powder (low dose) and 384 mg powder (high dose) |
| 20 July 2021 | The study was amended because the study design was changed to add an optional long-term extension study. |
| 23 October 2023 | The protocol was amended because the primary endpoint was modified. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported