



Clinical trial results: PHARMACODYNAMIC EFFECTS OF NICOTINE MOUTH SPRAY AND CYTISINE TABLET. A STUDY IN HEALTHY SMOKERS

Summary

| | |
|--------------------------|-----------------|
| EudraCT number | 2016-001267-36 |
| Trial protocol | SE |
| Global end of trial date | 07 October 2016 |

Results information

| | |
|--------------------------------|--------------|
| Result version number | v1 (current) |
| This version publication date | 26 July 2017 |
| First version publication date | 26 July 2017 |

Trial information

Trial identification

| | |
|-----------------------|----------------------|
| Sponsor protocol code | CO-160310091324-SCCT |
|-----------------------|----------------------|

Additional study identifiers

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

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | McNeil AB |
| Sponsor organisation address | 251 09, Helsingborg, Sweden, Box 941 |
| Public contact | Global Regulatory Affairs OTC Hsbg, McNeil AB, 46 42288734, GRAREGH@its.jnj.com |
| Scientific contact | Global Regulatory Affairs OTC Hsbg, McNeil AB, 46 42288734, GRAREGH@its.jnj.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 | 07 October 2016 |
| Is this the analysis of the primary completion data? | No |

| | |
|----------------------------------|-----------------|
| Global end of trial reached? | Yes |
| Global end of trial date | 07 October 2016 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study was to compare oromucosal nicotine spray (ONS), two sprays of 1 milligram (mg) nicotine, and one Tabex tablet of 1.5 mg cytisine after 12 hours of overnight abstinence with respect to reduction of urges to smoke during the first 5 minutes after start of treatment and to compare the two treatments with respect to the urges-to-smoke scores at 30, 45, and 60 seconds, 3 and 5 minutes versus baseline.

Protection of trial subjects:

Safety was evaluated by monitoring of adverse events (AEs) throughout study and, vital signs measurements, physical and other observational examinations was evaluated during screening phase.

Background therapy: -

Evidence for comparator: -

| | |
|---|--------------|
| Actual start date of recruitment | 08 June 2016 |
| 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 | Sweden: 61 |
| Worldwide total number of subjects | 61 |
| EEA total number of subjects | 61 |

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) | 61 |
| From 65 to 84 years | 0 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

This study was conducted from 27 June 2016 to 07 October 2016 in Sweden.

Pre-assignment

Screening details:

A total of 61 subjects were enrolled in study out of which 28 were males and 33 were females.

Period 1

| | |
|------------------------------|-------------------------|
| Period 1 title | Treatment Period 1 |
| Is this the baseline period? | Yes |
| Allocation method | Randomised - controlled |
| Blinding used | Not blinded |

Arms

| | |
|------------------------------|---|
| Are arms mutually exclusive? | Yes |
| Arm title | Sequence 1: Nicorette Oromucosal Nicotine Spray (ONS), Tabex |

Arm description:

Subjects received nicorette peppermint oromucosal spray 2 milligram (mg) as two consecutive sprays of unit dose of 1 mg at two separate visits as treatment A followed by tabex tablet 1.5 mg orally with 150 milliliter (mL) of ambient temperature water as treatment B. Each treatment was separated by wash-out periods of at least 36 hours.

| | |
|--|--------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Tabex |
| Investigational medicinal product code | SUB31171 |
| Other name | |
| Pharmaceutical forms | Film-coated tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Subjects received tabex tablet 1.5 mg orally with 150 milliliter (mL) of ambient temperature water as treatment B.

| | |
|--|---------------------------------|
| Investigational medicinal product name | Nicorette Peppermint 1 mg/spray |
| Investigational medicinal product code | SUB14645MIG |
| Other name | |
| Pharmaceutical forms | Oromucosal spray, solution |
| Routes of administration | Oromucosal use |

Dosage and administration details:

Subjects received nicorette peppermint oromucosal spray 2 mg as two consecutive sprays of unit dose of 1 mg at two separate visits as treatment A.

| | |
|------------------|----------------------------------|
| Arm title | Sequence 2: Tabex, Nicorette ONS |
|------------------|----------------------------------|

Arm description:

Subjects received tabex tablet 1.5 mg orally with 150 milliliter (mL) of ambient temperature water as treatment B followed by nicorette peppermint oromucosal spray 2 milligram (mg) as two consecutive sprays of unit dose of 1 mg at two separate visits as treatment A. Each treatment was separated by wash-out periods of at least 36 hours.

| | |
|--|--------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Tabex |
| Investigational medicinal product code | SUB31171 |
| Other name | |
| Pharmaceutical forms | Film-coated tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Subjects received tabex tablet 1.5 mg orally with 150 milliliter (mL) of ambient temperature water as treatment B.

| | |
|--|---------------------------------|
| Investigational medicinal product name | Nicorette Peppermint 1 mg/spray |
| Investigational medicinal product code | SUB14645MIG |
| Other name | |
| Pharmaceutical forms | Oromucosal spray, solution |
| Routes of administration | Oromucosal use |

Dosage and administration details:

Subjects received nicorette peppermint oromucosal spray 2 mg as two consecutive sprays of unit dose of 1 mg at two separate visits as treatment A.

| Number of subjects in period 1 | Sequence 1: Nicorette Oromucosal Nicotine Spray (ONS), Tabex | Sequence 2: Tabex, Nicorette ONS |
|--------------------------------|---|-------------------------------------|
| | | |
| Started | 31 | 30 |
| Completed | 31 | 30 |

Period 2

| | |
|------------------------------|-------------------------|
| Period 2 title | Treatment Period 2 |
| Is this the baseline period? | No |
| Allocation method | Randomised - controlled |
| Blinding used | Not blinded |

Arms

| | |
|------------------------------|----------------------------------|
| Are arms mutually exclusive? | Yes |
| Arm title | Sequence 1: Nicorette ONS, Tabex |

Arm description:

Subjects received nicorette peppermint oromucosal spray 2 mg as two consecutive sprays of unit dose of 1 mg at two separate visits as treatment A followed by tabex tablet 1.5 mg orally with 150 mL of ambient temperature water as treatment B. Each treatment was separated by wash-out periods of at least 36 hours.

| | |
|--|--------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Tabex |
| Investigational medicinal product code | SUB31171 |
| Other name | |
| Pharmaceutical forms | Film-coated tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Subjects received tabex tablet 1.5 mg orally with 150 milliliter (mL) of ambient temperature water as treatment B.

| | |
|--|---------------------------------|
| Investigational medicinal product name | Nicorette Peppermint 1 mg/spray |
| Investigational medicinal product code | SUB14645MIG |
| Other name | |
| Pharmaceutical forms | Oromucosal spray, solution |

| | |
|--------------------------|----------------|
| Routes of administration | Oromucosal use |
|--------------------------|----------------|

Dosage and administration details:

Subjects received nicorette peppermint oromucosal spray 2 mg as two consecutive sprays of unit dose of 1 mg at two separate visits as treatment A.

| | |
|------------------|----------------------------------|
| Arm title | Sequence 2: Tabex, Nicorette ONS |
|------------------|----------------------------------|

Arm description:

Subjects received tabex tablet 1.5 mg orally with 150 milliliter (mL) of ambient temperature water as treatment B followed by nicorette peppermint oromucosal spray 2 milligram (mg) as two consecutive sprays of unit dose of 1 mg at two separate visits as treatment A. Each treatment was separated by wash-out periods of at least 36 hours.

| | |
|--|---------------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Nicorette Peppermint 1 mg/spray |
| Investigational medicinal product code | SUB14645MIG |
| Other name | |
| Pharmaceutical forms | Oromucosal spray, solution |
| Routes of administration | Oromucosal use |

Dosage and administration details:

Subjects received nicorette peppermint oromucosal spray 2 mg as two consecutive sprays of unit dose of 1 mg at two separate visits as treatment A.

| | |
|--|--------------------|
| Investigational medicinal product name | Tabex |
| Investigational medicinal product code | SUB31171 |
| Other name | |
| Pharmaceutical forms | Film-coated tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Subjects received tabex tablet 1.5 mg orally with 150 milliliter (mL) of ambient temperature water as treatment B.

| Number of subjects in period 2 | Sequence 1: Nicorette ONS, Tabex | Sequence 2: Tabex, Nicorette ONS |
|---------------------------------------|--|-------------------------------------|
| Started | 31 | 30 |
| Completed | 26 | 28 |
| Not completed | 5 | 2 |
| Consent withdrawn by subject | - | 1 |
| Other | 2 | - |
| Lost to follow-up | 3 | 1 |

Baseline characteristics

Reporting groups

| | |
|-----------------------|--|
| Reporting group title | Sequence 1: Nicorette Oromucosal Nicotine Spray (ONS), Tabex |
|-----------------------|--|

Reporting group description:

Subjects received nicorette peppermint oromucosal spray 2 milligram (mg) as two consecutive sprays of unit dose of 1 mg at two separate visits as treatment A followed by tabex tablet 1.5 mg orally with 150 milliliter (mL) of ambient temperature water as treatment B. Each treatment was separated by wash-out periods of at least 36 hours.

| | |
|-----------------------|----------------------------------|
| Reporting group title | Sequence 2: Tabex, Nicorette ONS |
|-----------------------|----------------------------------|

Reporting group description:

Subjects received tabex tablet 1.5 mg orally with 150 milliliter (mL) of ambient temperature water as treatment B followed by nicorette peppermint oromucosal spray 2 milligram (mg) as two consecutive sprays of unit dose of 1 mg at two separate visits as treatment A. Each treatment was separated by wash-out periods of at least 36 hours.

| Reporting group values | Sequence 1: Nicorette Oromucosal Nicotine Spray (ONS), Tabex | Sequence 2: Tabex, Nicorette ONS | Total |
|---|---|-------------------------------------|-------|
| Number of subjects | 31 | 30 | 61 |
| Title for AgeCategorical Units: subjects | | | |
| Children (2-11 years) | 0 | 0 | 0 |
| Adolescents (12-17 years) | 0 | 0 | 0 |
| Adults (18-64 years) | 31 | 30 | 61 |
| From 65 to 84 years | 0 | 0 | 0 |
| 85 years and over | 0 | 0 | 0 |
| Title for AgeContinuous Units: years | | | |
| arithmetic mean | 33 | 31.6 | |
| standard deviation | ± 10.97 | ± 10.85 | - |
| Title for Gender Units: subjects | | | |
| Female | 15 | 18 | 33 |
| Male | 16 | 12 | 28 |

End points

End points reporting groups

| | |
|-----------------------|--|
| Reporting group title | Sequence 1: Nicorette Oromucosal Nicotine Spray (ONS), Tabex |
|-----------------------|--|

Reporting group description:

Subjects received nicorette peppermint oromucosal spray 2 milligram (mg) as two consecutive sprays of unit dose of 1 mg at two separate visits as treatment A followed by tabex tablet 1.5 mg orally with 150 milliliter (mL) of ambient temperature water as treatment B. Each treatment was separated by wash-out periods of at least 36 hours.

| | |
|-----------------------|----------------------------------|
| Reporting group title | Sequence 2: Tabex, Nicorette ONS |
|-----------------------|----------------------------------|

Reporting group description:

Subjects received tabex tablet 1.5 mg orally with 150 milliliter (mL) of ambient temperature water as treatment B followed by nicorette peppermint oromucosal spray 2 milligram (mg) as two consecutive sprays of unit dose of 1 mg at two separate visits as treatment A. Each treatment was separated by wash-out periods of at least 36 hours.

| | |
|-----------------------|----------------------------------|
| Reporting group title | Sequence 1: Nicorette ONS, Tabex |
|-----------------------|----------------------------------|

Reporting group description:

Subjects received nicorette peppermint oromucosal spray 2 mg as two consecutive sprays of unit dose of 1 mg at two separate visits as treatment A followed by tabex tablet 1.5 mg orally with 150 mL of ambient temperature water as treatment B. Each treatment was separated by wash-out periods of at least 36 hours.

| | |
|-----------------------|----------------------------------|
| Reporting group title | Sequence 2: Tabex, Nicorette ONS |
|-----------------------|----------------------------------|

Reporting group description:

Subjects received tabex tablet 1.5 mg orally with 150 milliliter (mL) of ambient temperature water as treatment B followed by nicorette peppermint oromucosal spray 2 milligram (mg) as two consecutive sprays of unit dose of 1 mg at two separate visits as treatment A. Each treatment was separated by wash-out periods of at least 36 hours.

| | |
|----------------------------|-----------------------------|
| Subject analysis set title | Nicorette ONS (Treatment A) |
|----------------------------|-----------------------------|

| | |
|---------------------------|---------------|
| Subject analysis set type | Full analysis |
|---------------------------|---------------|

Subject analysis set description:

All randomized subjects with any efficacy assessments and received nicorette peppermint oromucosal spray 2 milligram (mg) as two consecutive sprays of unit dose of 1 mg at two separate visits.

| | |
|----------------------------|---------------------|
| Subject analysis set title | Tabex (Treatment B) |
|----------------------------|---------------------|

| | |
|---------------------------|---------------|
| Subject analysis set type | Full analysis |
|---------------------------|---------------|

Subject analysis set description:

All randomized subjects with any efficacy assessments and received tabex tablet 1.5 mg orally with 150 milliliter (mL) of ambient temperature water.

| | |
|----------------------------|------------------------|
| Subject analysis set title | ONS Versus (vs.) Tabex |
|----------------------------|------------------------|

| | |
|---------------------------|---------------|
| Subject analysis set type | Full analysis |
|---------------------------|---------------|

Subject analysis set description:

All randomized subjects with any efficacy assessments and involved in comparisons of ONS vs. Tabex with respect to time to reduce craving score.

Primary: Average Change in Visual Analog Scale (VAS) Craving Score Compared to Baseline

| | |
|-----------------|--|
| End point title | Average Change in Visual Analog Scale (VAS) Craving Score Compared to Baseline |
|-----------------|--|

End point description:

Urges to smoke was scored on a 100 millimeter (mm) VAS before treatment and then repeatedly during 2 hours. Baseline urges to smoke was also rated using a 4- grade scale. On the scale, 0 corresponds to "no urge to smoke" and 100 mm corresponds to "extreme urge to smoke". Full analysis set population included all randomized subjects with any efficacy assessments.

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

End point timeframe:

Baseline, 30 seconds (sec), 45 sec, 1 minute (min), 3 min and 5 min

| End point values | Nicorette ONS (Treatment A) | Tabex (Treatment B) | | |
|--------------------------------------|--------------------------------|------------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 58 | 56 | | |
| Units: millimeter | | | | |
| arithmetic mean (standard deviation) | | | | |
| 30 seconds (sec) | -8 (± 9.8) | -0.8 (± 4.9) | | |
| 45 sec | -11.8 (± 14.1) | -1 (± 6.1) | | |
| 1 minute (min) | -14.7 (± 16.5) | -1.3 (± 6) | | |
| 3 min | -23 (± 21) | -3.8 (± 9.7) | | |
| 5 min | -26.3 (± 22) | -5.8 (± 12) | | |

Statistical analyses

| Statistical analysis title | Statistical analysis 1 |
|--|---|
| Statistical analysis description: | |
| Analysis was done for average change in VAS craving score compared to baseline up to 30 seconds. Treatment comparison was based on a mixed linear model including sequence, treatment and period as fixed effects and subject, nested within sequence, as random effect. Additionally, the baseline urges-to-smoke score at time zero, was calculated as an average of the three pretreatment urge assessments, was included as a co-varying fixed effect. | |
| Comparison groups | Tabex (Treatment B) v Nicorette ONS (Treatment A) |
| Number of subjects included in analysis | 114 |
| Analysis specification | Pre-specified |
| Analysis type | superiority ^[1] |
| P-value | < 0.001 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -7 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -9.8 |
| upper limit | -4.2 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 1.4 |

Notes:

[1] - 58 subjects from treatment A and 56 subjects from treatment B were involved in the analysis (Cross over design with random model). In total 61 unique subjects were included in the analysis.

| Statistical analysis title | Statistical analysis 2 |
|--|---|
| Statistical analysis description: | |
| Analysis was done for average change in VAS craving score compared to baseline up to 45 seconds. Treatment comparison was based on a mixed linear model including sequence, treatment and period as fixed effects and subject, nested within sequence, as random effect. Additionally, the baseline urges-to-smoke score at time zero, was calculated as an average of the three pretreatment urge assessments, was included as a co-varying fixed effect. | |
| Comparison groups | Nicorette ONS (Treatment A) v Tabex (Treatment B) |

| | |
|---|--------------------------------|
| Number of subjects included in analysis | 114 |
| Analysis specification | Pre-specified |
| Analysis type | superiority ^[2] |
| P-value | < 0.001 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -10.5 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -14.5 |
| upper limit | -6.5 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 2 |

Notes:

[2] - 58 subjects from treatment A and 56 subjects from treatment B were involved in the analysis (Cross over design with random model). In total 61 unique subjects were included in the analysis.

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

Statistical analysis description:

Analysis was done for average change in VAS craving score compared to baseline up to 1 minute. Treatment comparison was based on a mixed linear model including sequence, treatment and period as fixed effects and subject, nested within sequence, as random effect. Additionally, the baseline urges-to-smoke score at time zero, was calculated as an average of the three pretreatment urge assessments, was included as a co-varying fixed effect.

| | |
|---|---|
| Comparison groups | Tabex (Treatment B) v Nicorette ONS (Treatment A) |
| Number of subjects included in analysis | 114 |
| Analysis specification | Pre-specified |
| Analysis type | superiority ^[3] |
| P-value | < 0.001 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -13.1 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -17.6 |
| upper limit | -8.6 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 2.2 |

Notes:

[3] - 58 subjects from treatment A and 56 subjects from treatment B were involved in the analysis (Cross over design with random model). In total 61 unique subjects were included in the analysis.

| | |
|-----------------------------------|------------------------|
| Statistical analysis title | Statistical analysis 4 |
|-----------------------------------|------------------------|

Statistical analysis description:

Analysis was done for average change in VAS craving score compared to baseline up to 3 minutes. Treatment comparison was based on a mixed linear model including sequence, treatment and period as fixed effects and subject, nested within sequence, as random effect. Additionally, the baseline urges-to-smoke score at time zero, was calculated as an average of the three pretreatment urge assessments, was included as a co-varying fixed effect.

| | |
|-------------------|---|
| Comparison groups | Nicorette ONS (Treatment A) v Tabex (Treatment B) |
|-------------------|---|

| | |
|---|--------------------------------|
| Number of subjects included in analysis | 114 |
| Analysis specification | Pre-specified |
| Analysis type | superiority ^[4] |
| P-value | < 0.001 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -18.6 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -24 |
| upper limit | -13.2 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 2.7 |

Notes:

[4] - 58 subjects from treatment A and 56 subjects from treatment B were involved in the analysis (Cross over design with random model). In total 61 unique subjects were included in the analysis.

| | |
|-----------------------------------|------------------------|
| Statistical analysis title | Statistical analysis 5 |
|-----------------------------------|------------------------|

Statistical analysis description:

Analysis was done for average change in VAS craving score compared to baseline up to 5 minutes. Treatment comparison was based on a mixed linear model including sequence, treatment and period as fixed effects and subject, nested within sequence, as random effect. Additionally, the baseline urges-to-smoke score at time zero, was calculated as an average of the three pretreatment urge assessments, was included as a co-varying fixed effect.

| | |
|---|---|
| Comparison groups | Nicorette ONS (Treatment A) v Tabex (Treatment B) |
| Number of subjects included in analysis | 114 |
| Analysis specification | Pre-specified |
| Analysis type | superiority ^[5] |
| P-value | < 0.001 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -19.8 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -25.3 |
| upper limit | -14.3 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 2.7 |

Notes:

[5] - 58 subjects from treatment A and 56 subjects from treatment B were involved in the analysis (Cross over design with random model). In total 61 unique subjects were included in the analysis.

Primary: Change in VAS Craving Score Compared to Baseline

| | |
|-----------------|--|
| End point title | Change in VAS Craving Score Compared to Baseline |
|-----------------|--|

End point description:

Urges to smoke was scored on a 100 millimeter (mm) VAS before treatment and then repeatedly during 2 hours. Baseline urges to smoke was also rated using a 4- grade scale. On the scale, 0 corresponds to "no urge to smoke" and 100 mm corresponds to "extreme urge to smoke". Full analysis set population included all randomized subjects with any efficacy assessments.

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

End point timeframe:

Baseline, 30 seconds (sec), 45 sec, 1 minute (min), 3 min and 5 min

| End point values | Nicorette ONS (Treatment A) | Tabex (Treatment B) | | |
|--------------------------------------|--------------------------------|------------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 58 | 56 | | |
| Units: millimeter | | | | |
| arithmetic mean (standard deviation) | | | | |
| 30 sec | -15.9 (± 19.5) | -1.5 (± 9.7) | | |
| 45 sec | -21.9 (± 23.9) | -1.6 (± 8.2) | | |
| 1 min | -24.5 (± 24.2) | -2.8 (± 10.6) | | |
| 3 min | -30.3 (± 25.9) | -6.8 (± 14.6) | | |
| 5 min | -34.3 (± 26) | -10.7 (± 18) | | |

Statistical analyses

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

Statistical analysis description:

Analysis was done for change in VAS craving score compared to baseline at 30 seconds. Treatment comparison was based on a mixed linear model including sequence, treatment and period as fixed effects and subject, nested within sequence, as random effect. Additionally, the baseline urges-to-smoke score at time zero, was calculated as an average of the three pretreatment urge assessments, was included as a co-varying fixed effect.

| | |
|---|---|
| Comparison groups | Nicorette ONS (Treatment A) v Tabex (Treatment B) |
| Number of subjects included in analysis | 114 |
| Analysis specification | Pre-specified |
| Analysis type | superiority ^[6] |
| P-value | < 0.001 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -14 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -19.7 |
| upper limit | -8.3 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 2.8 |

Notes:

[6] - 58 subjects from treatment A and 56 subjects from treatment B were involved in the analysis (Cross over design with random model). In total 61 unique subjects were included in the analysis.

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

Statistical analysis description:

Analysis was done for change in VAS craving score compared to baseline at 45 seconds. Treatment comparison was based on a mixed linear model including sequence, treatment and period as fixed effects and subject, nested within sequence, as random effect. Additionally, the baseline urges-to-smoke score at time zero, was calculated as an average of the three pretreatment urge assessments, was included as a co-varying fixed effect.

| | |
|-------------------|---|
| Comparison groups | Nicorette ONS (Treatment A) v Tabex (Treatment B) |
|-------------------|---|

| | |
|---|--------------------------------|
| Number of subjects included in analysis | 114 |
| Analysis specification | Pre-specified |
| Analysis type | superiority ^[7] |
| P-value | < 0.001 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -20 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -26.4 |
| upper limit | -13.5 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 3.2 |

Notes:

[7] - 58 subjects from treatment A and 56 subjects from treatment B were involved in the analysis (Cross over design with random model). In total 61 unique subjects were included in the analysis.

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

Statistical analysis description:

Analysis was done for change in VAS craving score compared to baseline at 1 minute. Treatment comparison was based on a mixed linear model including sequence, treatment and period as fixed effects and subject, nested within sequence, as random effect. Additionally, the baseline urges-to-smoke score at time zero, was calculated as an average of the three pretreatment urge assessments, was included as a co-varying fixed effect.

| | |
|---|---|
| Comparison groups | Nicorette ONS (Treatment A) v Tabex (Treatment B) |
| Number of subjects included in analysis | 114 |
| Analysis specification | Pre-specified |
| Analysis type | superiority ^[8] |
| P-value | < 0.001 |
| Method | ANCOVA |
| Parameter estimate | Median difference (final values) |
| Point estimate | -21.2 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -27.7 |
| upper limit | -14.7 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 3.2 |

Notes:

[8] - 58 subjects from treatment A and 56 subjects from treatment B were involved in the analysis (Cross over design with random model). In total 61 unique subjects were included in the analysis.

| | |
|-----------------------------------|------------------------|
| Statistical analysis title | Statistical analysis 4 |
|-----------------------------------|------------------------|

Statistical analysis description:

Analysis was done for change in VAS craving score compared to baseline at 3 minutes. Treatment comparison was based on a mixed linear model including sequence, treatment and period as fixed effects and subject, nested within sequence, as random effect. Additionally, the baseline urges-to-smoke score at time zero, was calculated as an average of the three pretreatment urge assessments, was included as a co-varying fixed effect.

| | |
|-------------------|---|
| Comparison groups | Nicorette ONS (Treatment A) v Tabex (Treatment B) |
|-------------------|---|

| | |
|---|--------------------------------|
| Number of subjects included in analysis | 114 |
| Analysis specification | Pre-specified |
| Analysis type | superiority ^[9] |
| P-value | < 0.001 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -22.4 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -28.7 |
| upper limit | -16.2 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 3.1 |

Notes:

[9] - 58 subjects from treatment A and 56 subjects from treatment B were involved in the analysis (Cross over design with random model). In total 61 unique subjects were included in the analysis.

| | |
|-----------------------------------|------------------------|
| Statistical analysis title | Statistical analysis 5 |
|-----------------------------------|------------------------|

Statistical analysis description:

Analysis was done for change in VAS craving score compared to baseline at 5 minutes. Treatment comparison was based on a mixed linear model including sequence, treatment and period as fixed effects and subject, nested within sequence, as random effect. Additionally, the baseline urges-to-smoke score at time zero, was calculated as an average of the three pretreatment urge assessments, was included as a co-varying fixed effect.

| | |
|---|---|
| Comparison groups | Nicorette ONS (Treatment A) v Tabex (Treatment B) |
| Number of subjects included in analysis | 114 |
| Analysis specification | Pre-specified |
| Analysis type | superiority ^[10] |
| P-value | < 0.001 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -22.3 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -28.4 |
| upper limit | -16.1 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 3.1 |

Notes:

[10] - 58 subjects from treatment A and 56 subjects from treatment B were involved in the analysis (Cross over design with random model). In total 61 unique subjects were included in the analysis.

Secondary: Time to a 25 Percent (%) Reduction From Baseline Intensity of Urges to Smoke Score

| | |
|-----------------|--|
| End point title | Time to a 25 Percent (%) Reduction From Baseline Intensity of Urges to Smoke Score |
|-----------------|--|

End point description:

Kaplan-Meier survival estimates method was used for the time to 25% reduction in urges to smoke. Full analysis set population included all randomized subjects with any efficacy assessments. Here '99999' represents that no estimate was available for median and confidence interval for this specific outcome result.

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

End point timeframe:

up to 2 hours

| End point values | Nicorette ONS (Treatment A) | Tabex (Treatment B) | | |
|----------------------------------|--------------------------------|---------------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 58 | 56 | | |
| Units: Minutes | | | | |
| median (confidence interval 95%) | | | | |
| 25 % quartiles | 0.245 (0.195 to 0.356) | 3.085 (1.274 to 7.871) | | |
| 50 % quartiles | 0.707 (0.378 to 2.142) | 16.51 (7.871 to 44.46) | | |
| 75 % quartiles | 3.183 (2.142 to 12.97) | 99999 (69.37 to 99999) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Rating of Withdrawal Symptoms

| | |
|-----------------|-------------------------------|
| End point title | Rating of Withdrawal Symptoms |
|-----------------|-------------------------------|

End point description:

The four negative affect related items of the Minnesota Nicotine Withdrawal Scale (MNWS) were used. These include depressed mood, irritability, anxiety, and difficulty concentrating. Each was rated on a 5-grade scale; 0 – not present, 1 – slight, 2 – mild, 3 – moderate, 4 – severe within 10 minutes before treatment and at 5 and 30 minutes, as well as 1 and 2 hours after treatment. Full analysis set population included all randomized subjects with any efficacy assessments.

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

End point timeframe:

Baseline, 5 min, 30 min, 1 hour and 2 hour

| End point values | Nicorette ONS (Treatment A) | Tabex (Treatment B) | | |
|--------------------------------------|--------------------------------|------------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 59 | 56 | | |
| Units: Unit on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Depressed Mood: Baseline | 1.6 (± 1.1) | 1.6 (± 1) | | |
| Depressed Mood: 5 min | 1.1 (± 1) | 1.1 (± 0.9) | | |
| Depressed Mood: 30 min | 1 (± 1) | 0.9 (± 1) | | |
| Depressed Mood: 1 hour | 0.9 (± 1) | 0.8 (± 0.9) | | |
| Depressed Mood: 2 hour | 0.9 (± 0.9) | 0.9 (± 1) | | |
| Irritability: Baseline | 1.8 (± 1.2) | 1.7 (± 1.2) | | |
| Irritability: 5 min | 1.3 (± 1.1) | 1.3 (± 1.1) | | |
| Irritability: 30 min | 1 (± 1) | 1.1 (± 1.1) | | |

| | | | | |
|------------------------------------|-------------|-------------|--|--|
| Irritability: 1 hour | 0.9 (± 1) | 1.1 (± 1.1) | | |
| Irritability: 2 hour | 1.1 (± 1) | 1 (± 1) | | |
| Anxiety: Baseline | 1.4 (± 1.1) | 1.2 (± 1.1) | | |
| Anxiety: 5 min | 0.9 (± 0.9) | 0.8 (± 0.9) | | |
| Anxiety: 30 min | 0.8 (± 0.9) | 0.8 (± 0.8) | | |
| Anxiety: 1 hour | 0.8 (± 0.9) | 0.9 (± 1) | | |
| Anxiety: 2 hour | 0.9 (± 1) | 0.9 (± 1) | | |
| Difficulty Concentrating: Baseline | 1.8 (± 1.2) | 1.6 (± 1.2) | | |
| Difficulty Concentrating: 5 min | 1.2 (± 1.1) | 1.3 (± 1.1) | | |
| Difficulty Concentrating: 30 min | 1.2 (± 1) | 1.2 (± 1) | | |
| Difficulty Concentrating: 1 hour | 1.1 (± 1) | 1.2 (± 1.1) | | |
| Difficulty Concentrating: 2 hour | 1.3 (± 1.1) | 1.2 (± 1.1) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects in Preference of Treatment With Respect to Craving Relief

| | |
|-----------------|--|
| End point title | Percentage of Subjects in Preference of Treatment With Respect to Craving Relief |
|-----------------|--|

End point description:

Product preference was decided by asking the question at the end of the last treatment visit that which of the two treatments do you prefer with regards to relief of urges to smoke?. Full analysis set population included all randomized subjects with any efficacy assessments.

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

End point timeframe:

End of visit 2

| End point values | Nicorette ONS (Treatment A) | Tabex (Treatment B) | | |
|-------------------------------|--------------------------------|------------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 59 | 56 | | |
| Units: percentage of subjects | | | | |
| number (not applicable) | 64.8 | 35.2 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Treatment Emergent Adverse Events

| | |
|-----------------|---|
| End point title | Number of Subjects With Treatment Emergent Adverse Events |
|-----------------|---|

End point description:

An adverse event (AE) was any untoward medical occurrence in a subject who received study drug without regard to possibility of causal relationship. Treatment-emergent were events between administration of study drug and up to end of visit 2 that were absent before treatment or that

worsened relative to pretreatment state. All subjects who received at least one dose of treatment were included in the safety analysis set.

| | |
|----------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| End of Visit 2 | |

| End point values | Nicorette ONS (Treatment A) | Tabex (Treatment B) | | |
|-----------------------------|--------------------------------|------------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 59 | 56 | | |
| Units: Subjects | 52 | 13 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Time to a 50 Percent (%) Reduction From Baseline Intensity of Urges to Smoke Score

| | |
|-----------------|--|
| End point title | Time to a 50 Percent (%) Reduction From Baseline Intensity of Urges to Smoke Score |
|-----------------|--|

End point description:

Kaplan-Meier survival estimates method was used for the time to 50% reduction in urges to smoke. Full analysis set population included all randomized subjects with any efficacy assessments. Here '99999' represents that no estimate was available for median and confidence interval for this specific outcome result.

| | |
|----------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| up to 2 hours | |

| End point values | Nicorette ONS (Treatment A) | Tabex (Treatment B) | | |
|----------------------------------|--------------------------------|------------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 58 | 56 | | |
| Units: Minutes | | | | |
| median (confidence interval 95%) | | | | |
| 25% quartiles | 0.491 (0.39 to 0.794) | 11.69 (5.2 to 19.48) | | |
| 50% quartiles | 4.364 (0.806 to 8.361) | 54.01 (19.48 to 99999) | | |
| 75% quartiles | 68.19 (8.361 to 99999) | 99999 (99999 to 99999) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Time to a 75 Percent (%) Reduction From Baseline Intensity of Urges to Smoke Score

| | |
|-----------------|--|
| End point title | Time to a 75 Percent (%) Reduction From Baseline Intensity of Urges to Smoke Score |
|-----------------|--|

End point description:

Kaplan-Meier survival estimates method was used for the time to 25% reduction in urges to smoke. Full analysis set population included all randomized subjects with any efficacy assessments. Here '99999' represents that no estimate was available for median and confidence interval for this specific outcome result.

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

End point timeframe:

up to 2 hours

| End point values | Nicorette ONS (Treatment A) | Tabex (Treatment B) | | |
|----------------------------------|--------------------------------|---------------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 58 | 56 | | |
| Units: Minutes | | | | |
| median (confidence interval 95%) | | | | |
| 25% quartiles | 0.876 (0.585 to 2.885) | 75.52 (23.12 to 99999) | | |
| 50% quartiles | 33.17 (9.868 to 99999) | 99999 (99999 to 99999) | | |
| 75% quartiles | 99999 (99999 to 99999) | 99999 (99999 to 99999) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Time to a 90 Percent (%) Reduction From Baseline Intensity of Urges to Smoke Score

| | |
|-----------------|--|
| End point title | Time to a 90 Percent (%) Reduction From Baseline Intensity of Urges to Smoke Score |
|-----------------|--|

End point description:

Kaplan-Meier survival estimates method was used for the time to 90% reduction in urges to smoke. Full analysis set population included all randomized subjects with any efficacy assessments. Here '99999' represents that no estimate was available for median and confidence interval for this specific outcome result.

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

End point timeframe:

up to 2 hours

| End point values | Nicorette ONS (Treatment A) | Tabex (Treatment B) | | |
|----------------------------------|--------------------------------|---------------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 58 | 56 | | |
| Units: Minutes | | | | |
| median (confidence interval 95%) | | | | |
| 25% quartiles | 3.218 (0.785 to 99999) | 99999 (74.53 to 99999) | | |
| 50% quartiles | 99999 (99999 to 99999) | 99999 (99999 to 99999) | | |
| 75% quartiles | 99999 (99999 to 99999) | 99999 (99999 to 99999) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Attaining 25%, 50%, 75%, and 90% Reduced Craving Score Compared to Baseline

| | |
|------------------------|--|
| End point title | Percentage of Subjects Attaining 25%, 50%, 75%, and 90% Reduced Craving Score Compared to Baseline |
| End point description: | Full analysis set population included all randomized subjects with any efficacy assessments. |
| End point type | Secondary |
| End point timeframe: | upto 2 hours |

| End point values | Nicorette ONS (Treatment A) | Tabex (Treatment B) | | |
|-------------------------------|--------------------------------|------------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 58 | 56 | | |
| Units: Percentage of subjects | | | | |
| number (not applicable) | | | | |
| 25% Reduction (30 sec) | 43.1 | 5.4 | | |
| 25% Reduction (45 sec) | 53.4 | 8.9 | | |
| 25% Reduction (1 min) | 58.6 | 10.7 | | |
| 25% Reduction (3 min) | 72.9 | 23.2 | | |
| 25% Reduction (5 min) | 81.4 | 32.1 | | |
| 25% Reduction (10 min) | 83.1 | 39.3 | | |
| 50% Reduction (30 sec) | 27.6 | 1.8 | | |
| 50% Reduction (45 sec) | 32.8 | 1.8 | | |
| 50% Reduction (1 min) | 41.4 | 3.6 | | |
| 50% Reduction (3 min) | 47.5 | 5.4 | | |
| 50% Reduction (5 min) | 54.2 | 12.5 | | |
| 50% Reduction (10 min) | 64.4 | 19.6 | | |
| 75% Reduction (30 sec) | 6.9 | 1.8 | | |
| 75% Reduction (45 sec) | 24.1 | 1.8 | | |
| 75% Reduction (1 min) | 25.9 | 1.8 | | |

| | | | | |
|------------------------|------|-----|--|--|
| 75% Reduction (3 min) | 37.3 | 3.6 | | |
| 75% Reduction (5 min) | 37.3 | 3.6 | | |
| 75% Reduction (10 min) | 39 | 5.4 | | |
| 90% Reduction (30 sec) | 0 | 1.8 | | |
| 90% Reduction (45 sec) | 12.1 | 1.8 | | |
| 90% Reduction (1 min) | 15.5 | 1.8 | | |
| 90% Reduction (3 min) | 22 | 1.8 | | |
| 90% Reduction (5 min) | 30.5 | 1.8 | | |
| 90% Reduction (10 min) | 30.5 | 3.6 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Attaining 25% Reduced Craving Score Compared to Baseline in Comparisons of ONS vs. Tabex

| | |
|-----------------|---|
| End point title | Percentage of Subjects Attaining 25% Reduced Craving Score Compared to Baseline in Comparisons of ONS vs. Tabex |
|-----------------|---|

End point description:

For the outcome classification in terms of Success or Failure in a given time frame the first outcome was the outcome during treatment with ONS 2 mg whereas the second outcome refers to treatment with Tabex

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

End point timeframe:

upto 2 hours

| End point values | ONS Versus (vs.) Tabex | | | |
|-------------------------------|------------------------|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 54 | | | |
| Units: Percentage of subjects | | | | |
| number (not applicable) | | | | |
| 0-30 sec (Fail, Fail) | 29 | | | |
| 0-30 sec (Success, Fail) | 21 | | | |
| 0-30 sec (Success, Success) | 3 | | | |
| 0-45 sec (Fail, Fail) | 24 | | | |
| 0-45 sec (Success, Fail) | 24 | | | |
| 0-45 sec (Success, Success) | 5 | | | |
| 0-1 min (Fail, Fail) | 22 | | | |
| 0-1 min (Success, Fail) | 25 | | | |
| 0-1 min (Success, Success) | 6 | | | |
| 0-3 min (Fail, Fail) | 15 | | | |
| 0-3 min (Success, Fail) | 27 | | | |
| 0-3 min (Success, Success) | 12 | | | |
| 0-5 min (Fail, Fail) | 10 | | | |
| 0-5 min (Fail, Success) | 1 | | | |
| 0-5 min (Success, Fail) | 27 | | | |
| 0-5 min (Success, Success) | 16 | | | |

| | | | | |
|-----------------------------|----|--|--|--|
| 0-10 min (Fail, Fail) | 9 | | | |
| 0-10 min (Fail, Success) | 1 | | | |
| 0-10 min (Success, Fail) | 24 | | | |
| 0-10 min (Success, Success) | 20 | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Attaining 50% Reduced Craving Score Compared to Baseline in Comparisons of ONS vs. Tabex

| | |
|-----------------|---|
| End point title | Percentage of Subjects Attaining 50% Reduced Craving Score Compared to Baseline in Comparisons of ONS vs. Tabex |
|-----------------|---|

End point description:

For the outcome classification in terms of Success or Failure in a given time frame the first outcome was the outcome during treatment with ONS 2 mg whereas the second outcome refers to treatment with Tabex. Full analysis set population included all randomized subjects with any efficacy assessments.

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

End point timeframe:

up to 2 hours

| End point values | ONS Versus (vs.) Tabex | | | |
|-------------------------------|------------------------|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 54 | | | |
| Units: percentage of subjects | | | | |
| number (not applicable) | | | | |
| 0-30 sec (Fail, Fail) | 38 | | | |
| 0-30 sec (Success, Fail) | 14 | | | |
| 0-30 sec (Success, Success) | 1 | | | |
| 0-45 sec (Fail, Fail) | 35 | | | |
| 0-45 sec (Success, Fail) | 17 | | | |
| 0-45 sec (Success, Success) | 1 | | | |
| 0-1 min (Fail, Fail) | 31 | | | |
| 0-1 min (Success, Fail) | 20 | | | |
| 0-1 min (Success, Success) | 2 | | | |
| 0-3 min (Fail, Fail) | 28 | | | |
| 0-3 min (Success, Fail) | 23 | | | |
| 0-3 min (Success, Success) | 3 | | | |
| 0-5 min (Fail, Fail) | 23 | | | |
| 0-5 min (Fail, Success) | 1 | | | |
| 0-5 min (Success, Fail) | 24 | | | |
| 0-5 min (Success, Success) | 6 | | | |
| 0-10 min (Fail, Fail) | 18 | | | |
| 0-10 min (Fail, Success) | 1 | | | |
| 0-10 min (Success, Fail) | 26 | | | |
| 0-10 min (Success, Success) | 9 | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Attaining 75% Reduced Craving Score Compared to Baseline in Comparisons of ONS vs. Tabex

| | |
|-----------------|---|
| End point title | Percentage of Subjects Attaining 75% Reduced Craving Score Compared to Baseline in Comparisons of ONS vs. Tabex |
|-----------------|---|

End point description:

For the outcome classification in terms of Success or Failure in a given time frame the first outcome was the outcome during treatment with ONS 2 mg whereas the second outcome refers to treatment with Tabex. Full analysis set population included all randomized subjects with any efficacy assessments.

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

End point timeframe:

up to 2 hours

| End point values | ONS Versus (vs.) Tabex | | | |
|-------------------------------|------------------------|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 54 | | | |
| Units: percentage of subjects | | | | |
| number (not applicable) | | | | |
| 0-30 sec (Fail, Fail) | 48 | | | |
| 0-30 sec (Success, Fail) | 1 | | | |
| 0-30 sec (Success, Success) | 4 | | | |
| 0-45 sec (Fail, Fail) | 40 | | | |
| 0-45 sec (Success, Fail) | 12 | | | |
| 0-45 sec (Success, Success) | 1 | | | |
| 0-1 min (Fail, Fail) | 39 | | | |
| 0-1 min (Success, Fail) | 13 | | | |
| 0-1 min (Success, Success) | 1 | | | |
| 0-3 min (Fail, Fail) | 34 | | | |
| 0-3 min (Success, Fail) | 18 | | | |
| 0-3 min (Success, Success) | 2 | | | |
| 0-5 min (Fail, Fail) | 34 | | | |
| 0-5 min (Success, Fail) | 18 | | | |
| 0-5 min (Success, Success) | 2 | | | |
| 0-10 min (Fail, Fail) | 32 | | | |
| 0-10 min (Fail, Success) | 1 | | | |
| 0-10 min (Success, Fail) | 19 | | | |
| 0-10 min (Success, Success) | 2 | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Attaining 90% Reduced Craving Score Compared to Baseline in Comparisons of ONS vs. Tabex

| | |
|-----------------|---|
| End point title | Percentage of Subjects Attaining 90% Reduced Craving Score Compared to Baseline in Comparisons of ONS vs. Tabex |
|-----------------|---|

End point description:

For the outcome classification in terms of Success or Failure in a given time frame the first outcome was the outcome during treatment with ONS 2 mg whereas the second outcome refers to treatment with Tabex.

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

End point timeframe:

upto 2 hours

| End point values | ONS Versus (vs.) Tabex | | | |
|-------------------------------|------------------------|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 54 | | | |
| Units: Percentage of subjects | | | | |
| number (not applicable) | | | | |
| 0-30 sec (Fail, Fail) | 52 | | | |
| 0-30 sec (Fail, Success) | 1 | | | |
| 0-45 sec (Fail, Fail) | 46 | | | |
| 0-45 sec (Success, Fail) | 6 | | | |
| 0-45 sec (Success, Success) | 1 | | | |
| 0-1 min (Fail, Fail) | 45 | | | |
| 0-1 min (Success, Fail) | 7 | | | |
| 0-1 min (Success, Success) | 1 | | | |
| 0-3 min (Fail, Fail) | 42 | | | |
| 0-3 min (Success, Fail) | 11 | | | |
| 0-3 min (Success, Success) | 1 | | | |
| 0-5 min (Fail, Fail) | 37 | | | |
| 0-5 min (Success, Fail) | 16 | | | |
| 0-5 min (Success, Success) | 1 | | | |
| 0-10 min (Fail, Fail) | 36 | | | |
| 0-10 min (Fail, Success) | 1 | | | |
| 0-10 min (Success, Fail) | 16 | | | |
| 0-10 min (Success, Success) | 1 | | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Screening up to end of treatment visit 2

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

Dictionary used

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

| | |
|--------------------|------|
| Dictionary version | 19.0 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|-----------------------------|
| Reporting group title | Nicorette ONS (Treatment A) |
|-----------------------|-----------------------------|

Reporting group description:

All randomized subjects with any efficacy assessments and received nicorette peppermint oromucosal spray 2 milligram (mg) as two consecutive sprays of unit dose of 1 mg at two separate visits.

| | |
|-----------------------|---------------------|
| Reporting group title | Tabex (Treatment B) |
|-----------------------|---------------------|

Reporting group description:

All randomized subjects with any efficacy assessments and received tabex tablet 1.5 mg orally with 150 milliliter (mL) of ambient temperature water.

| Serious adverse events | Nicorette ONS (Treatment A) | Tabex (Treatment B) | |
|---|--------------------------------|---------------------|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 0 / 56 (0.00%) | |
| number of deaths (all causes) | 0 | 0 | |
| number of deaths resulting from adverse events | | | |

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

| Non-serious adverse events | Nicorette ONS (Treatment A) | Tabex (Treatment B) | |
|---|--------------------------------|---------------------|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 52 / 59 (88.14%) | 9 / 56 (16.07%) | |
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 2 / 59 (3.39%) | 4 / 56 (7.14%) | |
| occurrences (all) | 2 | 5 | |
| Eye disorders | | | |
| Lacrimation Increased | | | |
| subjects affected / exposed | 12 / 59 (20.34%) | 0 / 56 (0.00%) | |
| occurrences (all) | 12 | 0 | |
| Gastrointestinal disorders | | | |

| | | | |
|---|------------------|----------------|--|
| Dysphagia | | | |
| subjects affected / exposed | 4 / 59 (6.78%) | 0 / 56 (0.00%) | |
| occurrences (all) | 4 | 0 | |
| Nausea | | | |
| subjects affected / exposed | 13 / 59 (22.03%) | 2 / 56 (3.57%) | |
| occurrences (all) | 14 | 2 | |
| Oral Discomfort | | | |
| subjects affected / exposed | 10 / 59 (16.95%) | 0 / 56 (0.00%) | |
| occurrences (all) | 10 | 0 | |
| Salivary Hypersecretion | | | |
| subjects affected / exposed | 11 / 59 (18.64%) | 0 / 56 (0.00%) | |
| occurrences (all) | 11 | 0 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Cough | | | |
| subjects affected / exposed | 8 / 59 (13.56%) | 0 / 56 (0.00%) | |
| occurrences (all) | 8 | 0 | |
| Hiccups | | | |
| subjects affected / exposed | 16 / 59 (27.12%) | 0 / 56 (0.00%) | |
| occurrences (all) | 16 | 0 | |
| Throat Irritation | | | |
| subjects affected / exposed | 19 / 59 (32.20%) | 1 / 56 (1.79%) | |
| occurrences (all) | 19 | 1 | |
| Throat Tightness | | | |
| subjects affected / exposed | 5 / 59 (8.47%) | 1 / 56 (1.79%) | |
| occurrences (all) | 5 | 1 | |
| Skin and subcutaneous tissue disorders | | | |
| Hyperhidrosis | | | |
| subjects affected / exposed | 3 / 59 (5.08%) | 0 / 56 (0.00%) | |
| occurrences (all) | 3 | 0 | |
| Pruritus | | | |
| subjects affected / exposed | 0 / 59 (0.00%) | 3 / 56 (5.36%) | |
| occurrences (all) | 0 | 3 | |
| Psychiatric disorders | | | |
| Hypervigilance | | | |
| subjects affected / exposed | 3 / 59 (5.08%) | 1 / 56 (1.79%) | |
| occurrences (all) | 3 | 1 | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|-------------|---|
| 19 May 2016 | Amendment included the changes/addition of procedure and texts in following sections; Independent ethics committee, Ethical conduct of the study; Regulatory authority, Risk benefit evaluation, Rationale, Previous and concomitant medications, Determination of sample size, Analysis of primary efficacy endpoints, Study monitoring, Case report forms / Electronic data capture and list of references. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported