



Clinical trial results:

A Phase III, Multicenter, Randomized, Double-Blind, Placebo-Controlled Clinical Trial to Study the Safety and Efficacy of the Addition of MK-3102 to Subjects With Type 2 Diabetes Mellitus Who Have Inadequate Glycemic Control on Combination Therapy with Glimepiride and Metformin

Due to the EudraCT – Results system being out of service between 31 July 2015 and 12 January 2016, these results have been published in compliance with revised timelines.

Summary

| | |
|--------------------------|------------------|
| EudraCT number | 2012-002612-10 |
| Trial protocol | PL |
| Global end of trial date | 23 December 2014 |

Results information

| | |
|--------------------------------|------------------|
| Result version number | v1 (current) |
| This version publication date | 23 December 2016 |
| First version publication date | 23 December 2016 |

Trial information

Trial identification

| | |
|-----------------------|----------|
| Sponsor protocol code | 3102-022 |
|-----------------------|----------|

Additional study identifiers

| | |
|------------------------------------|------------------------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT01704261 |
| WHO universal trial number (UTN) | - |
| Other trial identifiers | Protocol number: MK-3102-022 |

Notes:

Sponsors

| | |
|------------------------------|--|
| Sponsor organisation name | Merck Sharp & Dohme Corp. |
| Sponsor organisation address | 2000 Galloping Hill Road, Kenilworth, NJ, United States, 07033 |
| Public contact | Clinical Trials Disclosure, Merck Sharp & Dohme Corp., ClinicalTrialsDisclosure@merck.com |
| Scientific contact | Clinical Trials Disclosure, Merck Sharp & Dohme Corp., ClinicalTrialsDisclosure@merck.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 | 23 December 2014 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 23 December 2014 |
| Global end of trial reached? | Yes |
| Global end of trial date | 23 December 2014 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

After 24 weeks, to assess the effect of the addition of treatment with omarigliptin (MK-3102) compared with the addition of placebo on hemoglobin A1C.

Protection of trial subjects:

This study was conducted in conformance with Good Clinical Practice standards and applicable country and/or local statutes and regulations regarding ethical committee review, informed consent, and the protection of human subjects participating in biomedical research.

Background therapy:

Participants should remain on a stable dose of metformin (≥ 1500 mg/day) throughout the trial.

Participants should remain on a stable dose of glimepiride (≥ 4 mg/day) throughout the trial. In the event of hypoglycemia, the glimepiride dose can be down-titrated to a minimum dose of 1 mg/day.

Evidence for comparator: -

| | |
|---|-----------------|
| Actual start date of recruitment | 19 October 2012 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|--|
| Country: Number of subjects enrolled | Poland: 20 |
| Country: Number of subjects enrolled | Romania: 130 |
| Country: Number of subjects enrolled | Russian Federation: 13 |
| Country: Number of subjects enrolled | South Africa: 40 |
| Country: Number of subjects enrolled | Korea, Democratic People's Republic of: 35 |
| Country: Number of subjects enrolled | United States: 69 |
| Worldwide total number of subjects | 307 |
| EEA total number of subjects | 150 |

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) | 238 |
| From 65 to 84 years | 69 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

Fifty-one sites received IEC/IRB approval and were shipped clinical supplies.

Pre-assignment

Screening details:

In total, 583 participants were screened and 276 participants were excluded during screening. The most common reason for participants not being randomized was screen failure. The most common reasons for screen failure were not meeting the metformin and glimepiride dose requirements inclusion criterion or meeting exclusionary laboratory values.

Period 1

| | |
|------------------------------|--------------------------------|
| Period 1 title | Overall Study (overall period) |
| Is this the baseline period? | Yes |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Subject, Investigator |

Arms

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

Arm description:

Omarigliptin 25 mg capsule administered orally once a week for 24 weeks. Participants continue pre-study concomitant therapy of open-label glimepiride tablet(s) orally once daily (total daily dose ≥ 4 mg per day) and metformin tablet(s) orally once or twice daily (total daily dose ≥ 1500 mg per day).

| | |
|--|--------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Omarigliptin 25 mg |
| Investigational medicinal product code | |
| Other name | MK-3102 |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |

Dosage and administration details:

Omarigliptin 25 mg capsule administered orally once a week for 24 weeks. Participants continue pre-study concomitant therapy of open-label glimepiride tablet(s) orally once daily (total daily dose ≥ 4 mg per day) and metformin tablet(s) orally once or twice daily (total daily dose ≥ 1500 mg per day).

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

Arm description:

Matching placebo to omarigliptin capsule administered orally once a week for 24 weeks. Participants continue pre-study concomitant therapy of open-label glimepiride tablet(s) orally once daily (total daily dose ≥ 4 mg per day) and metformin tablet(s) orally once or twice daily (total daily dose ≥ 1500 mg per day).

| | |
|--|-------------------------|
| Arm type | Placebo |
| Investigational medicinal product name | Placebo to Omarigliptin |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |

Dosage and administration details:

Matching placebo to omarigliptin capsule administered orally once a week for 24 weeks. Participants continue pre-study concomitant therapy of open-label glimepiride tablet(s) orally once daily (total daily dose ≥ 4 mg per day) and metformin tablet(s) orally once or twice daily (total daily dose ≥ 1500 mg per day).

| Number of subjects in period 1 | Omarigliptin | Placebo |
|---------------------------------------|--------------|---------|
| Started | 154 | 153 |
| Completed | 141 | 138 |
| Not completed | 13 | 15 |
| Consent withdrawn by subject | 12 | 15 |
| Lost to follow-up | 1 | - |

Baseline characteristics

Reporting groups

| | |
|-----------------------|--------------|
| Reporting group title | Omarigliptin |
|-----------------------|--------------|

Reporting group description:

Omarigliptin 25 mg capsule administered orally once a week for 24 weeks. Participants continue pre-study concomitant therapy of open-label glimepiride tablet(s) orally once daily (total daily dose ≥ 4 mg per day) and metformin tablet(s) orally once or twice daily (total daily dose ≥ 1500 mg per day).

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

Reporting group description:

Matching placebo to omarigliptin capsule administered orally once a week for 24 weeks. Participants continue pre-study concomitant therapy of open-label glimepiride tablet(s) orally once daily (total daily dose ≥ 4 mg per day) and metformin tablet(s) orally once or twice daily (total daily dose ≥ 1500 mg per day).

| Reporting group values | Omarigliptin | Placebo | Total |
|---|--------------|-----------|-------|
| Number of subjects | 154 | 153 | 307 |
| Age categorical Units: Subjects | | | |
| In utero | 0 | 0 | 0 |
| Preterm newborn infants (gestational age < 37 wks) | 0 | 0 | 0 |
| Newborns (0-27 days) | 0 | 0 | 0 |
| Infants and toddlers (28 days-23 months) | 0 | 0 | 0 |
| Children (2-11 years) | 0 | 0 | 0 |
| Adolescents (12-17 years) | 0 | 0 | 0 |
| Adults (18-64 years) | 126 | 112 | 238 |
| From 65-84 years | 28 | 41 | 69 |
| 85 years and over | 0 | 0 | 0 |
| Age Continuous Units: Years | | | |
| arithmetic mean | 57.2 | 58.4 | |
| standard deviation | ± 8.4 | ± 9.4 | - |
| Gender, Male/Female Units: Participants | | | |
| Female | 81 | 79 | 160 |
| Male | 73 | 74 | 147 |

End points

End points reporting groups

| | |
|---|--------------|
| Reporting group title | Omarigliptin |
| Reporting group description: Omarigliptin 25 mg capsule administered orally once a week for 24 weeks. Participants continue pre-study concomitant therapy of open-label glimepiride tablet(s) orally once daily (total daily dose ≥ 4 mg per day) and metformin tablet(s) orally once or twice daily (total daily dose ≥ 1500 mg per day). | |
| Reporting group title | Placebo |
| Reporting group description: Matching placebo to omarigliptin capsule administered orally once a week for 24 weeks. Participants continue pre-study concomitant therapy of open-label glimepiride tablet(s) orally once daily (total daily dose ≥ 4 mg per day) and metformin tablet(s) orally once or twice daily (total daily dose ≥ 1500 mg per day). | |

Primary: Change from baseline in hemoglobin A1c (A1C) at Week 24

| | |
|--|---|
| End point title | Change from baseline in hemoglobin A1c (A1C) at Week 24 |
| End point description: A1C is blood marker used to report average blood glucose levels over a prolonged periods of time and is reported as a percentage (%). Thus, this change from baseline reflects the Week 24 A1C minus the Week 0 A1C. The Full Analysis Set (FAS) population consisted of all randomized participants who received at least 1 dose of study medication and had a baseline measurement or a measurement for the analysis endpoint after receiving study medication. One participant was in 2 clinical trials in parallel and was excluded from all efficacy and safety analysis. | |
| End point type | Primary |
| End point timeframe: Baseline and Week 24 | |

| End point values | Omarigliptin | Placebo | | |
|--|-----------------------|-----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 153 | 153 | | |
| Units: %A1C | | | | |
| least squares mean (confidence interval 95%) | -0.67 (-0.84 to -0.5) | -0.06 (-0.23 to 0.12) | | |

Statistical analyses

| | |
|--|---------------------------------------|
| Statistical analysis title | Difference in the least squares means |
| Statistical analysis description: Based on a constrained longitudinal data analysis (cLDA) method with a restriction of the same baseline mean across treatment groups. | |
| Comparison groups | Omarigliptin v Placebo |

| | |
|---|---------------------------------------|
| Number of subjects included in analysis | 306 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | < 0.001 |
| Method | Difference in the least squares means |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -0.61 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.85 |
| upper limit | -0.38 |

Primary: Percentage of Participants Who Experienced at Least One Adverse Event (AE)

| | |
|-----------------|--|
| End point title | Percentage of Participants Who Experienced at Least One Adverse Event (AE) |
|-----------------|--|

End point description:

An AE is defined as any unfavorable and unintended sign including an abnormal laboratory finding, symptom or disease associated with the use of a medical treatment or procedure, regardless of whether it is considered related to the medical treatment or procedure. All Subjects as Treated (ASaT) population, defined as all randomized participants who received at least 1 dose of study medication. Participants were included in the treatment group corresponding to the study treatment they actually received. One participant was in 2 clinical trials and was excluded from all efficacy and safety analysis.

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

End point timeframe:

Up to Week 27

| End point values | Omarigliptin | Placebo | | |
|-----------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 153 | 153 | | |
| Units: Percentage of participants | | | | |
| number (not applicable) | 57.5 | 47.7 | | |

Statistical analyses

| | |
|---|---|
| Statistical analysis title | Difference in % Omarigliptin vs Placebo |
| Comparison groups | Omarigliptin v Placebo |
| Number of subjects included in analysis | 306 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Parameter estimate | Difference in % Omarigliptin vs Placebo |
| Point estimate | 9.8 |

| | |
|---------------------|---------|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.4 |
| upper limit | 20.8 |

Primary: Percentage of Participants Who Discontinued from the Study Due to an AE

| | |
|-----------------|---|
| End point title | Percentage of Participants Who Discontinued from the Study Due to an AE |
|-----------------|---|

End point description:

An AE is defined as any unfavorable and unintended sign including an abnormal laboratory finding, symptom or disease associated with the use of a medical treatment or procedure, regardless of whether it is considered related to the medical treatment or procedure. The ASaT Population was defined as all randomized participants who received at least 1 dose of study medication. Participants were included in the treatment group corresponding to the study treatment they actually received. One participant was in 2 clinical trials and was excluded from all efficacy and safety analysis.

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

End point timeframe:

Up to Week 24

| End point values | Omarigliptin | Placebo | | |
|-----------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 153 | 153 | | |
| Units: Percentage of participants | | | | |
| number (not applicable) | 2.6 | 2.6 | | |

Statistical analyses

| | |
|---|---|
| Statistical analysis title | Difference in % Omarigliptin vs Placebo |
| Comparison groups | Omarigliptin v Placebo |
| Number of subjects included in analysis | 306 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Parameter estimate | Difference in % Omarigliptin vs Placebo |
| Point estimate | 0 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -4.3 |
| upper limit | 4.3 |

Secondary: Change from baseline in fasting plasma glucose (FPG) at Week 24

| | |
|-----------------|--|
| End point title | Change from baseline in fasting plasma glucose (FPG) at Week |
|-----------------|--|

End point description:

Blood glucose was measured on a fasting basis. FPG is expressed as mg/dL. Blood was drawn at predose on Day 1 and after 24 weeks of treatment to determine change in plasma glucose levels (i.e., FPG at Week 24 minus FPG at baseline). The FAS population consisted of all randomized participants who received at least 1 dose of study medication and had a baseline measurement or a measurement for the analysis endpoint after receiving study medication. One participant was in 2 clinical trials in parallel and was excluded from all efficacy and safety analysis.

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

End point timeframe:

Baseline and Week 24

| End point values | Omarigliptin | Placebo | | |
|--|------------------------|-------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 153 | 153 | | |
| Units: mg/dL | | | | |
| least squares mean (confidence interval 95%) | -19.6 (-26.7 to -12.5) | -3 (-10.2 to 4.1) | | |

Statistical analyses

| | |
|----------------------------|---------------------------------------|
| Statistical analysis title | Difference in the least squares means |
|----------------------------|---------------------------------------|

Statistical analysis description:

Based on a constrained longitudinal data analysis (cLDA) method with a restriction of the same baseline mean across treatment groups.

| | |
|---|---------------------------------------|
| Comparison groups | Omarigliptin v Placebo |
| Number of subjects included in analysis | 306 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | < 0.001 |
| Method | Difference in the least squares means |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -16.6 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -25.5 |
| upper limit | -7.8 |

Secondary: Percentage of participants attaining A1C glycemic goals of <7% and <6.5% at Week 24

| | |
|-----------------|---|
| End point title | Percentage of participants attaining A1C glycemic goals of <7% and <6.5% at Week 24 |
|-----------------|---|

End point description:

The percentage of participants who achieved A1C values <6.5% (48 mmol/mol) or <7.0% (53 mmol/mol) in the FAS population at Week 24. The FAS Population consisted of all randomized participants who received at least 1 dose of study medication and had a baseline measurement or a

measurement for the analysis endpoint after receiving study medication. One participant was in 2 clinical trials in parallel and was excluded from all efficacy and safety analysis.

| | |
|----------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| 24 weeks | |

| End point values | Omarigliptin | Placebo | | |
|-----------------------------------|---------------------|------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 153 | 153 | | |
| Units: Percentage of participants | | | | |
| number (confidence interval 95%) | | | | |
| <7.0% | 23.8 (17.5 to 31.5) | 4.4 (2.1 to 9.3) | | |
| <6.5% | 10.1 (6.1 to 16.4) | 2.1 (0.7 to 6) | | |

Statistical analyses

| | |
|---|---|
| Statistical analysis title | Between-group Rate Difference |
| Statistical analysis description: | |
| | Between-group confidence intervals and p-value (%) A1C <7.0%; estimated using standard multiple imputation techniques. Miettinen & Nurminen method. |
| Comparison groups | Omarigliptin v Placebo |
| Number of subjects included in analysis | 306 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.005 |
| Method | Miettinen & Nurminen method |
| Parameter estimate | Between-group Rate Difference (%) |
| Point estimate | 8 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 2.7 |
| upper limit | 14.5 |

| | |
|-----------------------------------|---|
| Statistical analysis title | Between-group Rate Difference |
| Statistical analysis description: | |
| | Between-group confidence intervals and p-value (%) A1C <7.0%; estimated using standard multiple imputation techniques. Miettinen & Nurminen method. |
| Comparison groups | Omarigliptin v Placebo |

| | |
|---|-----------------------------------|
| Number of subjects included in analysis | 306 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | < 0.001 |
| Method | Miettinen & Nurminen method |
| Parameter estimate | Between-group Rate Difference (%) |
| Point estimate | 19.3 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 11.7 |
| upper limit | 27.6 |

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to Week 27

Adverse event reporting additional description:

The ASaT Population was all randomized participants who received at least one study drug. Participants were included in the treatment group corresponding to the study treatment they actually received. One participant was in 2 clinical trials and was excluded from all efficacy and safety analysis.

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

Dictionary used

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

| | |
|--------------------|------|
| Dictionary version | 17.1 |
|--------------------|------|

Reporting groups

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

Reporting group description:

Matching placebo to omarigliptin capsule administered orally once a week for 24 weeks. Participants continue pre-study concomitant therapy of open-label glimepiride tablet(s) orally once daily (total daily dose ≥ 4 mg per day) and metformin tablet(s) orally once or twice daily (total daily dose ≥ 1500 mg per day).

| | |
|-----------------------|--------------|
| Reporting group title | Omarigliptin |
|-----------------------|--------------|

Reporting group description:

Omarigliptin 25 mg capsule administered orally once a week for 24 weeks. Participants continue pre-study concomitant therapy of open-label glimepiride tablet(s) orally once daily (total daily dose ≥ 4 mg per day) and metformin tablet(s) orally once or twice daily (total daily dose ≥ 1500 mg per day).

| Serious adverse events | Placebo | Omarigliptin | |
|---|-----------------|-----------------|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 5 / 153 (3.27%) | 3 / 153 (1.96%) | |
| number of deaths (all causes) | 0 | 0 | |
| number of deaths resulting from adverse events | 0 | 0 | |
| Injury, poisoning and procedural complications | | | |
| Road traffic accident | | | |
| subjects affected / exposed | 1 / 153 (0.65%) | 0 / 153 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nervous system disorders | | | |
| Cerebrovascular accident | | | |
| subjects affected / exposed | 1 / 153 (0.65%) | 0 / 153 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cerebrovascular disorder | | | |

| | | | |
|--|-----------------|-----------------|--|
| subjects affected / exposed | 0 / 153 (0.00%) | 1 / 153 (0.65%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| General disorders and administration site conditions | | | |
| Non-cardiac chest pain | | | |
| subjects affected / exposed | 0 / 153 (0.00%) | 1 / 153 (0.65%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ear and labyrinth disorders | | | |
| Vertigo | | | |
| subjects affected / exposed | 0 / 153 (0.00%) | 1 / 153 (0.65%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal disorders | | | |
| Duodenal ulcer haemorrhage | | | |
| subjects affected / exposed | 1 / 153 (0.65%) | 0 / 153 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Oesophagitis | | | |
| subjects affected / exposed | 1 / 153 (0.65%) | 0 / 153 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pancreatitis | | | |
| subjects affected / exposed | 1 / 153 (0.65%) | 0 / 153 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatobiliary disorders | | | |
| Cholecystitis | | | |
| subjects affected / exposed | 0 / 153 (0.00%) | 1 / 153 (0.65%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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

| Non-serious adverse events | Placebo | Omarigliptin | |
|---|-------------------|-------------------|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 23 / 153 (15.03%) | 29 / 153 (18.95%) | |
| Infections and infestations | | | |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 9 / 153 (5.88%) | 4 / 153 (2.61%) | |
| occurrences (all) | 11 | 4 | |
| Urinary tract infection | | | |
| subjects affected / exposed | 3 / 153 (1.96%) | 9 / 153 (5.88%) | |
| occurrences (all) | 4 | 9 | |
| Metabolism and nutrition disorders | | | |
| Hypoglycaemia | | | |
| subjects affected / exposed | 13 / 153 (8.50%) | 18 / 153 (11.76%) | |
| occurrences (all) | 44 | 65 | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|-----------------|--|
| 18 January 2013 | AM1 - Modification of inclusion criteria regarding contraception |
| 26 April 2013 | AM4 - Addition of amylase and lipase to the chemistry panel |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported