



## Clinical trial results:

### A Phase III, Multicenter, Double-Blind, Randomized Trial to Evaluate the Safety and Efficacy of MK-3102 Compared With Glimepiride in Subjects With Type 2 Diabetes Mellitus For Whom Metformin is Inappropriate due to Intolerance or Contraindication

#### Summary

|                          |                               |
|--------------------------|-------------------------------|
| EudraCT number           | 2013-000301-23                |
| Trial protocol           | HU IT AT BE SK ES DE EE BG PL |
| Global end of trial date | 03 April 2014                 |

#### Results information

|                                |                  |
|--------------------------------|------------------|
| Result version number          | v1 (current)     |
| This version publication date  | 16 February 2016 |
| First version publication date | 05 July 2015     |

#### Trial information

##### Trial identification

|                       |          |
|-----------------------|----------|
| Sponsor protocol code | 3102-027 |
|-----------------------|----------|

##### Additional study identifiers

|                                    |                                    |
|------------------------------------|------------------------------------|
| ISRCTN number                      | -                                  |
| ClinicalTrials.gov id (NCT number) | NCT01863667                        |
| WHO universal trial number (UTN)   | -                                  |
| Other trial identifiers            | Merck Protocol Number: MK-3102-027 |

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.,<br>ClinicalTrialsDisclosure@merck.com |
| Scientific contact           | Clinical Trials Disclosure, Merck Sharp & Dohme Corp.,<br>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:

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**Results analysis stage**

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|  |               |
|--|---------------|
| Analysis stage                                       | Final         |
| Date of interim/final analysis                       | 03 April 2014 |
| Is this the analysis of the primary completion data? | Yes           |
| Primary completion date                              | 03 April 2014 |
| Global end of trial reached?                         | Yes           |
| Global end of trial date                             | 03 April 2014 |
| Was the trial ended prematurely?                     | Yes           |

Notes:

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**General information about the trial**

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Main objective of the trial:

This trial will assess the safety and efficacy of omarigliptin (MK-3102) compared with the sulfonylurea, glimepiride, in type 2 diabetes mellitus participants who are metformin intolerant or who have a contraindication to the use of metformin. The primary hypothesis is that after 54 weeks, the mean change from baseline in hemoglobin A1c (A1C) in participants treated with omarigliptin is noninferior compared with that in participants treated with glimepiride.

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: -

Evidence for comparator: -

|   |              |
|---|--------------|
| Actual start date of recruitment                          | 08 July 2013 |
| Long term follow-up planned                               | No           |
| Independent data monitoring committee (IDMC) involvement? | Yes          |

Notes:

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**Population of trial subjects**

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**Subjects enrolled per country**

|                                      |                       |
|--------------------------------------|-----------------------|
| Country: Number of subjects enrolled | Bulgaria: 3           |
| Country: Number of subjects enrolled | Germany: 1            |
| Country: Number of subjects enrolled | Hungary: 13           |
| Country: Number of subjects enrolled | Russian Federation: 1 |
| Country: Number of subjects enrolled | Slovakia: 4           |
| Country: Number of subjects enrolled | Spain: 6              |
| Country: Number of subjects enrolled | United States: 37     |
| Worldwide total number of subjects   | 65                    |
| EEA total number of subjects         | 27                    |

Notes:

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**Subjects enrolled per age group**

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|   |   |
|---|---|
| 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)                     | 45 |
| From 65 to 84 years                      | 20 |
| 85 years and over                        | 0  |

## Subject disposition

### Recruitment

Recruitment details:

The study included participants who were diagnosed with type 2 diabetes mellitus and had intolerance to metformin  $\geq 1000$  mg/day or had a contraindication to the use of metformin.

### Pre-assignment

Screening details:

The study had a 1-week Screening Period; an oral antihyperglycemic agent (AHA) "wash-off" period of 8 weeks for participants on oral AHAs; a 2-week single-blind placebo run-in period; and a 54-week double-blind treatment period.

### 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          |
| <b>Arm title</b>             | Omarigliptin |

Arm description:

Participants receive an omarigliptin (MK-3102) 25 mg capsule once weekly and glimepiride placebo tablet(s) once daily, for 54 weeks.

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

Dosage and administration details:

Omarigliptin (MK-3102) 25 mg capsule administered orally once weekly.

|  |                     |
|--|---------------------|
| Investigational medicinal product name | Glimepiride placebo |
| Investigational medicinal product code |                     |
| Other name                             |                     |
| Pharmaceutical forms                   | Tablet              |
| Routes of administration               | Oral use            |

Dosage and administration details:

Matching placebo to glimepiride tablet administered orally once daily with breakfast or the first main meal.

|                  |             |
|------------------|-------------|
| <b>Arm title</b> | Glimepiride |
|------------------|-------------|

Arm description:

Participants receive glimepiride 1 mg and/or 2 mg tablet(s) (maximum dose 6 mg/day) once daily and an omarigliptin placebo capsule once weekly, for 54 weeks.

|  |                   |
|--|-------------------|
| Arm type                               | Active comparator |
| Investigational medicinal product name | Glimepiride       |
| Investigational medicinal product code |                   |
| Other name                             |                   |
| Pharmaceutical forms                   | Tablet            |
| Routes of administration               | Oral use          |

Dosage and administration details:

Glimepiride tablet 1 mg and/or 2 mg (up-titrated to a maximum dose 6 mg/day) administered orally once daily with breakfast or the first main meal.

|  |                      |
|--|----------------------|
| Investigational medicinal product name | Omarigliptin placebo |
| 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 weekly.

| <b>Number of subjects in period 1</b> | Omarigliptin | Glimepiride |
|---------------------------------------|--------------|-------------|
| Started                               | 33           | 32          |
| Completed                             | 0            | 0           |
| Not completed                         | 33           | 32          |
| Consent withdrawn by subject          | 2            | 2           |
| Study terminated by Sponsor           | 30           | 30          |
| Adverse event, non-fatal              | 1            | -           |

## Baseline characteristics

### Reporting groups

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

Reporting group description:

Participants receive an omarigliptin (MK-3102) 25 mg capsule once weekly and glimepiride placebo tablet(s) once daily, for 54 weeks.

|                       |             |
|-----------------------|-------------|
| Reporting group title | Glimepiride |
|-----------------------|-------------|

Reporting group description:

Participants receive glimepiride 1 mg and/or 2 mg tablet(s) (maximum dose 6 mg/day) once daily and an omarigliptin placebo capsule once weekly, for 54 weeks.

| Reporting group values             | Omarigliptin | Glimepiride | Total |
|------------------------------------|--------------|-------------|-------|
| Number of subjects                 | 33           | 32          | 65    |
| Age categorical<br>Units: Subjects |              |             |       |

|   |              |               |    |
|---|--------------|---------------|----|
| Age Continuous<br>Units: Years<br>arithmetic mean<br>standard deviation | 58<br>± 14.1 | 56.8<br>± 9.9 | -  |
| Gender, Male/Female<br>Units: Participants                              |              |               |    |
| Female  | 19           | 16            | 35 |
| Male  | 14           | 16            | 30 |

## End points

### End points reporting groups

|   |              |
|---|--------------|
| Reporting group title   | Omarigliptin |
| Reporting group description:<br>Participants receive an omarigliptin (MK-3102) 25 mg capsule once weekly and glimepiride placebo tablet(s) once daily, for 54 weeks.                          |              |
| Reporting group title   | Glimepiride  |
| Reporting group description:<br>Participants receive glimepiride 1 mg and/or 2 mg tablet(s) (maximum dose 6 mg/day) once daily and an omarigliptin placebo capsule once weekly, for 54 weeks. |              |

### Primary: Percentage of Participants Who Experienced at Least One Adverse Event

|  |  |
|--|--|
| End point title  | Percentage of Participants Who Experienced at Least One Adverse Event <sup>[1]</sup> |
| End point description:<br>An adverse event is any untoward medical occurrence in a participant administered study drug which does not necessarily have a causal relationship with the treatment. Adverse events may include the onset of new illness and the exacerbation of pre-existing conditions. All participants as treated defined as all randomized participants who received at least one dose of study drug and were included in the treatment group corresponding to the study drug they actually received. |  |
| End point type   | Primary  |
| End point timeframe:<br>Up to 57 weeks (including 3 weeks following the last dose of study drug)   |  |

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: No statistical analysis was planned or performed for this end point.

| End point values                  | Omarigliptin    | Glimepiride     |  |  |
|-----------------------------------|-----------------|-----------------|--|--|
| Subject group type                | Reporting group | Reporting group |  |  |
| Number of subjects analysed       | 33              | 32              |  |  |
| Units: Percentage of participants |                 |                 |  |  |
| number (not applicable)           | 9.1             | 15.6            |  |  |

### Statistical analyses

No statistical analyses for this end point

### Primary: Change from Baseline in Hemoglobin A1C (A1C) at Week 54

|   |  |
|---|--|
| End point title   | Change from Baseline in Hemoglobin A1C (A1C) at Week 54 <sup>[2]</sup> |
| End point description:<br>A1C is measured as a percent. Thus, this change from baseline reflects the Week 54 A1C percent minus the Week 0 A1C percent. Full Analysis Set defined as all participants who received at least one dose of study drug and had a baseline measurement or a post-randomization measurement. Due to the early termination of the study, no participants completed Week 54. |  |
| End point type  | Primary  |
| End point timeframe:<br>Baseline and Week 54  |  |

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: Due to the early termination of the study, no statistical analysis was performed for this end point.

| End point values                             | Omarigliptin     | Glimepiride      |  |  |
|--|------------------|------------------|--|--|
| Subject group type                           | Reporting group  | Reporting group  |  |  |
| Number of subjects analysed                  | 0 <sup>[3]</sup> | 0 <sup>[4]</sup> |  |  |
| Units: Percent                               |                  |                  |  |  |
| least squares mean (confidence interval 95%) | ( to )           | ( to )           |  |  |

Notes:

[3] - Due to the early termination of the study, no participants completed Week 54.

[4] - Due to the early termination of the study, no participants completed Week 54.

## Statistical analyses

No statistical analyses for this end point

## Primary: Percentage of Participants Who Discontinued Study Drug Due to an Adverse Event

|                 |   |
|-----------------|---|
| End point title | Percentage of Participants Who Discontinued Study Drug Due to an Adverse Event <sup>[5]</sup> |
|-----------------|---|

End point description:

An adverse event is any untoward medical occurrence in a participant administered study drug which does not necessarily have a causal relationship with the treatment. Adverse events may include the onset of new illness and the exacerbation of pre-existing conditions. All participants as treated defined as all randomized participants who received at least one dose of study drug and were included in the treatment group corresponding to the study drug they actually received.

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

End point timeframe:

Up to 54 weeks

Notes:

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

Justification: No statistical analysis was planned or performed for this end point.

| End point values                  | Omarigliptin    | Glimepiride     |  |  |
|-----------------------------------|-----------------|-----------------|--|--|
| Subject group type                | Reporting group | Reporting group |  |  |
| Number of subjects analysed       | 33              | 32              |  |  |
| Units: Percentage of participants |                 |                 |  |  |
| number (not applicable)           | 3               | 0               |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change from Baseline in Fasting Plasma Glucose (FPG) at Week 54

|                 |   |
|-----------------|---|
| End point title | Change from Baseline in Fasting Plasma Glucose (FPG) at Week 54 |
|-----------------|---|



End point description:

This change from baseline reflects the FPG level at Week 54 minus the FPG level at Week 0. Full Analysis Set defined as all participants who received at least one dose of study drug and had a baseline measurement or a post-randomization measurement. Due to the early termination of the study, no participants completed Week 54.

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

End point timeframe:

Baseline and Week 54

| End point values                             | Omarigliptin     | Glimepiride      |  |  |
|--|------------------|------------------|--|--|
| Subject group type                           | Reporting group  | Reporting group  |  |  |
| Number of subjects analysed                  | 0 <sup>[6]</sup> | 0 <sup>[7]</sup> |  |  |
| Units: mg/dL                                 |                  |                  |  |  |
| least squares mean (confidence interval 95%) | ( to )           | ( to )           |  |  |

Notes:

[6] - Due to the early termination of the study, no participants completed Week 54.

[7] - Due to the early termination of the study, no participants completed Week 54.

## Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of Participants Achieving an A1C Goal <7.0% or <6.5% After 54 Weeks of Treatment

|                 |   |
|-----------------|---|
| End point title | Percentage of Participants Achieving an A1C Goal <7.0% or <6.5% After 54 Weeks of Treatment |
|-----------------|---|

End point description:

Percentage of participants achieving glycemic goal (A1C <7% or <6.5%) after 54 weeks of treatment. Full Analysis Set defined as all participants who received at least one dose of study drug and had a baseline measurement or a post-randomization measurement. Due to the early termination of the study, no participants completed Week 54.

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

End point timeframe:

54 weeks

| End point values                  | Omarigliptin     | Glimepiride      |  |  |
|-----------------------------------|------------------|------------------|--|--|
| Subject group type                | Reporting group  | Reporting group  |  |  |
| Number of subjects analysed       | 0 <sup>[8]</sup> | 0 <sup>[9]</sup> |  |  |
| Units: Percentage of participants |                  |                  |  |  |
| number (not applicable)           |                  |                  |  |  |

Notes:

[8] - Due to the early termination of the study, no participants completed Week 54.

[9] - Due to the early termination of the study, no participants completed Week 54.

## Statistical analyses

No statistical analyses for this end point

**Secondary: Percentage of Participants Meeting the Composite Endpoint of an A1C Decrease >0.5%, No Symptomatic Hypoglycemia, and No Body Weight Gain After 54 Weeks of Treatment**

|                 |  |
|-----------------|--|
| End point title | Percentage of Participants Meeting the Composite Endpoint of an A1C Decrease >0.5%, No Symptomatic Hypoglycemia, and No Body Weight Gain After 54 Weeks of Treatment |
|-----------------|--|

## End point description:

Percentage of Participants who had an A1C decrease >0.5%, no symptomatic hypoglycemia, and no body weight gain after 54 weeks of treatment. Full Analysis Set defined as all participants who received at least one dose of study drug and had a baseline measurement or a post-randomization measurement. Due to the early termination of the study, no participants completed Week 54.

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

## End point timeframe:

54 weeks

| End point values                  | Omarigliptin      | Glimepiride       |  |  |
|-----------------------------------|-------------------|-------------------|--|--|
| Subject group type                | Reporting group   | Reporting group   |  |  |
| Number of subjects analysed       | 0 <sup>[10]</sup> | 0 <sup>[11]</sup> |  |  |
| Units: Percentage of participants |                   |                   |  |  |
| number (not applicable)           |                   |                   |  |  |

## Notes:

[10] - Due to the early termination of the study, no participants completed Week 54.

[11] - Due to the early termination of the study, no participants completed Week 54.

**Statistical analyses**

No statistical analyses for this end point

**Secondary: Percentage of Participants with an Adverse Event of Symptomatic Hypoglycemia**

|                 |  |
|-----------------|--|
| End point title | Percentage of Participants with an Adverse Event of Symptomatic Hypoglycemia |
|-----------------|--|

## End point description:

An adverse event is any untoward medical occurrence in a participant administered study drug which does not necessarily have a causal relationship with the treatment. Adverse events may include the onset of new illness and the exacerbation of pre-existing conditions. All participants as treated defined as all randomized participants who received at least one dose of study drug and were included in the treatment group corresponding to the study drug they actually received.

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

## End point timeframe:

Up to 54 weeks

| End point values                  | Omarigliptin      | Glimepiride       |  |  |
|-----------------------------------|-------------------|-------------------|--|--|
| Subject group type                | Reporting group   | Reporting group   |  |  |
| Number of subjects analysed       | 0 <sup>[12]</sup> | 0 <sup>[13]</sup> |  |  |
| Units: Percentage of participants |                   |                   |  |  |
| number (not applicable)           |                   |                   |  |  |

Notes:

[12] - Due to the early termination of the study, this endpoint was not analyzed.

[13] - Due to the early termination of the study, this endpoint was not analyzed.

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change from Baseline in Body Weight at Week 54

|                 |  |
|-----------------|--|
| End point title | Change from Baseline in Body Weight at Week 54 |
|-----------------|--|

End point description:

Body weight was to be measured (in duplicate) using a calibrated digital scale. All participants as treated defined as all randomized participants who received at least one dose of study drug and were included in the treatment group corresponding to the study drug they actually received. Due to the early termination of the study, no participants completed Week 54.

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

End point timeframe:

Baseline and Week 54

| End point values                     | Omarigliptin      | Glimepiride       |  |  |
|--------------------------------------|-------------------|-------------------|--|--|
| Subject group type                   | Reporting group   | Reporting group   |  |  |
| Number of subjects analysed          | 0 <sup>[14]</sup> | 0 <sup>[15]</sup> |  |  |
| Units: Kilograms                     |                   |                   |  |  |
| arithmetic mean (standard deviation) | ()                | ()                |  |  |

Notes:

[14] - Due to the early termination of the study, no participants completed Week 54.

[15] - Due to the early termination of the study, no participants completed Week 54.

## Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information<sup>[1]</sup>

Timeframe for reporting adverse events:

Up to 57 weeks (including 3 weeks following last dose of study drug)

Adverse event reporting additional description:

All participants as treated defined as all randomized participants who received at least one dose of study drug and were included in the treatment group corresponding to the study drug they actually received.

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

### Dictionary used

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

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

### Reporting groups

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

Reporting group description:

Participants receive an omarigliptin (MK-3102) 25 mg capsule once weekly and glimepiride placebo tablet(s) once daily, for 54 weeks.

|                       |             |
|-----------------------|-------------|
| Reporting group title | Glimepiride |
|-----------------------|-------------|

Reporting group description:

Participants receive glimepiride 1 mg and/or 2 mg tablet(s) (maximum dose 6 mg/day) once daily and an omarigliptin placebo capsule once weekly, for 54 weeks.

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.

Justification: No non-serious adverse events exceeded the 5% threshold for any treatment group.

| Serious adverse events                            | Omarigliptin   | Glimepiride    |  |
|---|----------------|----------------|--|
| Total subjects affected by serious adverse events |                |                |  |
| subjects affected / exposed                       | 1 / 33 (3.03%) | 0 / 32 (0.00%) |  |
| number of deaths (all causes)                     | 0              | 0              |  |
| number of deaths resulting from adverse events    |                |                |  |
| Nervous system disorders                          |                |                |  |
| Epilepsy  |                |                |  |
| subjects affected / exposed                       | 1 / 33 (3.03%) | 0 / 32 (0.00%) |  |
| occurrences causally related to treatment / all   | 0 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all        | 0 / 0          | 0 / 0          |  |

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

| Non-serious adverse events                            | Omarigliptin   | Glimepiride    |  |
|---|----------------|----------------|--|
| Total subjects affected by non-serious adverse events |                |                |  |
| subjects affected / exposed                           | 0 / 33 (0.00%) | 0 / 32 (0.00%) |  |



## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

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### Interruptions (globally)

Were there any global interruptions to the trial? Yes

| Date          | Interruption  | Restart date |
|---------------|---|--------------|
| 03 April 2014 | The study was terminated based on business decisions only, and not due to any unexpected safety or efficacy concerns. | -            |

Notes:

### Limitations and caveats

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

|   |
|---|
| The study was terminated based on business decisions only, and not due to any unexpected safety or efficacy concerns. |
|---|

Notes: