



## Clinical trial results:

**Randomized double blind parallel design study comparing risk of nocturnal hypoglycemia and critical arrhythmias with sitagliptin versus glimepiride in patients with type 2 diabetes insufficiently controlled with metformin monotherapy**

### Summary

|                          |                 |
|--------------------------|-----------------|
| EudraCT number           | 2014-003792-34  |
| Trial protocol           | DE              |
| Global end of trial date | 24 January 2017 |

### Results information

|                                |              |
|--------------------------------|--------------|
| Result version number          | v1 (current) |
| This version publication date  | 06 June 2024 |
| First version publication date | 06 June 2024 |

### Trial information

#### Trial identification

|                       |                |
|-----------------------|----------------|
| Sponsor protocol code | DIA-2-REDESIGN |
|-----------------------|----------------|

#### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT02373865 |
| WHO universal trial number (UTN)   | -           |

Notes:

### Sponsors

|                              |                                                                               |
|------------------------------|-------------------------------------------------------------------------------|
| Sponsor organisation name    | GWT-TUD GmbH                                                                  |
| Sponsor organisation address | Freiberger Str. 33, Dresden, Germany, 01067                                   |
| Public contact               | Katja Reichardt, GWT-TUD GmbH, 0049 35125933188, katja.reichardt@gwtonline.de |
| Scientific contact           | Katja Reichardt, GWT-TUD GmbH, 0049 35125933188, katja.reichardt@gwtonline.de |

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                       | 20 June 2017    |
| Is this the analysis of the primary completion data? | Yes             |
| Primary completion date                              | 24 January 2017 |
| Global end of trial reached?                         | Yes             |
| Global end of trial date                             | 24 January 2017 |
| Was the trial ended prematurely?                     | Yes             |

Notes:

## General information about the trial

Main objective of the trial:

Hypoglycemic episodes (HE) and time spent below critical values are the primary objectives of this study. We will calculate overall episodes/time (5 days) and nocturnal episodes.

Protection of trial subjects:

The conduct of this trial was in compliance with the Good Clinical Practice Guidelines and under the guiding principles detailed in the Declaration of Helsinki. The study was also carried out in keeping with applicable local law(s) and regulation(s).

Both IMPs were used in the authorized therapeutic indication.

Background therapy: -

Evidence for comparator: -

|                                                           |                 |
|-----------------------------------------------------------|-----------------|
| Actual start date of recruitment                          | 15 October 2015 |
| 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 | Germany: 4 |
| Worldwide total number of subjects   | 4          |
| EEA total number of subjects         | 4          |

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)                      | 2 |

|                     |   |
|---------------------|---|
| From 65 to 84 years | 2 |
| 85 years and over   | 0 |

## Subject disposition

### Recruitment

Recruitment details:

The trial was conducted at one study site in Germany. Of originally planned 68 patients only 4 patients could be included into the trial.

### Pre-assignment

Screening details:

The inclusion and exclusion criteria were yielding to an impeded recruitment of patients. Thus, in the time period between the start of the clinical trial in March 2015 (Approval of BfArM) and the premature termination at Jan 24, 2017 (09/2015 – 12/2015) only 4 patients could be recruited and medicated.

### Period 1

|                              |                                   |
|------------------------------|-----------------------------------|
| Period 1 title               | Treatment period (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>             | Treatment group |

Arm description:

Patients received Sitagliptin 100 mg (qd) + Glimepiride Placebo (qd) (titrated up to 6 mg) for the duration of 12 weeks.

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

Dosage and administration details:

Sitagliptin was continuously administered at a dose of 100 mg once daily (each 24 h)

|                                        |                        |
|----------------------------------------|------------------------|
| Investigational medicinal product name | Glimepiride-Placebo    |
| Investigational medicinal product code |                        |
| Other name                             |                        |
| Pharmaceutical forms                   | Capsule, hard + tablet |
| Routes of administration               | Oral use               |

Dosage and administration details:

The starting dose is 1 mg glimepiride-placebo per day titrated up to 6 mg per day.

Oral administration, shortly before or during a meal  
tablets encapsulated in capsules for blinding

|                  |               |
|------------------|---------------|
| <b>Arm title</b> | Control group |
|------------------|---------------|

Arm description:

Patients will receive Glimepiride 1 mg (qd) (titrated up to 6 mg) + Sitagliptin Placebo 100 mg (qd) for the duration of 12 weeks.

|                                        |                        |
|----------------------------------------|------------------------|
| Arm type                               | Active comparator      |
| Investigational medicinal product name | Glimepiride            |
| Investigational medicinal product code |                        |
| Other name                             |                        |
| Pharmaceutical forms                   | Capsule, hard + tablet |
| Routes of administration               | Oral use               |

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Dosage and administration details:

The starting dose is 1 mg glimepiride per day titrated up to 6 mg glimepiride per day.  
Oral administration, shortly before or during a meal  
tablets encapsulated in capsules for blinding

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

Dosage and administration details:

Sitagliptin-placebo was continuously administered at a dose of 100 mg once daily (each 24 h)

| <b>Number of subjects in period 1</b> | Treatment group | Control group |
|---------------------------------------|-----------------|---------------|
| Started                               | 2               | 2             |
| Completed                             | 2               | 2             |

## Baseline characteristics

### Reporting groups

|                       |                  |
|-----------------------|------------------|
| Reporting group title | Treatment period |
|-----------------------|------------------|

Reporting group description: -

| Reporting group values                                | Treatment period | Total |  |
|-------------------------------------------------------|------------------|-------|--|
| Number of subjects                                    | 4                | 4     |  |
| Age categorical                                       |                  |       |  |
| Units: Subjects                                       |                  |       |  |
| In utero                                              | 0                | 0     |  |
| Preterm newborn infants<br>(gestational age < 37 wks) | 0                | 0     |  |
| Newborns (0-27 days)                                  | 0                | 0     |  |
| Infants and toddlers (28 days-23<br>months)           | 0                | 0     |  |
| Children (2-11 years)                                 | 0                | 0     |  |
| Adolescents (12-17 years)                             | 0                | 0     |  |
| Adults (18-64 years)                                  | 2                | 2     |  |
| From 65-84 years                                      | 2                | 2     |  |
| 85 years and over                                     | 0                | 0     |  |
| Gender categorical                                    |                  |       |  |
| Units: Subjects                                       |                  |       |  |
| Female                                                | 0                | 0     |  |
| Male                                                  | 4                | 4     |  |

## End points

### End points reporting groups

|                                                                                                                                                                   |                 |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------|
| Reporting group title                                                                                                                                             | Treatment group |
| Reporting group description:<br>Patients received Sitagliptin 100 mg (qd) + Glimepiride Placebo (qd) (titrated up to 6 mg) for the duration of 12 weeks.          |                 |
| Reporting group title                                                                                                                                             | Control group   |
| Reporting group description:<br>Patients will receive Glimepiride 1 mg (qd) (titrated up to 6 mg) + Sitagliptin Placebo 100 mg (qd) for the duration of 12 weeks. |                 |

### Primary: Hypoglycemic episodes

|                                                                                                                                                                                                                                                                                                                                                                                                                                            |                                      |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------|
| End point title                                                                                                                                                                                                                                                                                                                                                                                                                            | Hypoglycemic episodes <sup>[1]</sup> |
| End point description:<br>Primary command variables of the trial were the number hypoglycemic episodes per patient and the overall duration of hypoglycemia (time of interstitial glucose below 3,1 mmol/l, according to CGMS iPro <sup>®</sup> Continuous Glucose Reporter, measured over 5 days).<br>Total duration of hypoglycemic episodes were calculated (5 days) including nocturnal episodes. Night was defined as: 10 pm - 06 am. |                                      |
| End point type                                                                                                                                                                                                                                                                                                                                                                                                                             | Primary                              |
| End point timeframe:<br>5 days                                                                                                                                                                                                                                                                                                                                                                                                             |                                      |

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: Given the low number of only 4 patients at this time point, a reliable conclusion cannot be drawn. All included patients showed an improvement of HbA1C during the trial, which was leading at the end of the treatment to an HbA1C of 1,25 % average.

| End point values            | Treatment group | Control group   |  |  |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type          | Reporting group | Reporting group |  |  |
| Number of subjects analysed | 2               | 2               |  |  |
| Units: percent              |                 |                 |  |  |
| number (not applicable)     | 1.5             | 1.0             |  |  |

### Statistical analyses

No statistical analyses for this end point

## Adverse events

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

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Timeframe for reporting adverse events:

12 weeks

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

### Dictionary used

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

|                    |      |
|--------------------|------|
| Dictionary version | 20.0 |
|--------------------|------|

Frequency threshold for reporting non-serious adverse events: 0 %

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#### 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: During the analyzed period of time no serious adverse events could be occurring. 1 patient showed once symptoms of a hypoglycemia with a blood sugar value of 4,2 mmol/l in combination with a slight tachycardia. Again the low number of patients and the shortened period of examination do not allow any reliable evaluation of issues relevant for safety. Additional risk factor could not be identified upon the given results and informations.

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date          | Amendment                                                                                                                                                                                                                                                                                                                                                                                                      |
|---------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 25 March 2015 | Specification of inclusion criteria; Specification of visit schedule and addition of ECG evaluation as well as patient diary; Specification of screening failure definition; Specification of treatment description; Specification of CGM recordings and blood glucose measurement as well as test meal description; Specification of glimepiride titration (dose adaption); Addition of unblinding procedures |

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

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

|                                                                                                                                                                                                               |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Early termination on 16.01.2017 due to immense delay in patient recruitment (difficult inclusion and exclusion profile); increase in the study costs due to conditions imposed on the investigational product |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|

Notes: