



## Clinical trial results:

### The effect of mirtazapine (REMERGON®) on gastric motility and satiation in healthy subjects

#### Summary

|                          |                  |
|--------------------------|------------------|
| EudraCT number           | 2014-004862-89   |
| Trial protocol           | BE               |
| Global end of trial date | 23 February 2016 |

#### Results information

|                                |                  |
|--------------------------------|------------------|
| Result version number          | v1 (current)     |
| This version publication date  | 14 February 2021 |
| First version publication date | 14 February 2021 |

#### Trial information

##### Trial identification

|                       |              |
|-----------------------|--------------|
| Sponsor protocol code | mirtazapine1 |
|-----------------------|--------------|

##### Additional study identifiers

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

Notes:

##### Sponsors

|                              |                                                                                                   |
|------------------------------|---------------------------------------------------------------------------------------------------|
| Sponsor organisation name    | UZLeuven / KULeuven / TARGID                                                                      |
| Sponsor organisation address | Herestraat 49, Leuven, Belgium, 3000                                                              |
| Public contact               | Jan Tack, UZLeuven / KULeuven / TARGID, 0032 16344225, jan.tack@kuleuven.be                       |
| Scientific contact           | Florencia Carbone, UZLeuven / KULeuven / TARGID, 0032 16377535, florencia.carbone@med.kuleuven.be |

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**

|                                                      |                  |
|------------------------------------------------------|------------------|
| Analysis stage                                       | Final            |
| Date of interim/final analysis                       | 22 November 2016 |
| Is this the analysis of the primary completion data? | No               |
| Global end of trial reached?                         | Yes              |
| Global end of trial date                             | 23 February 2016 |
| Was the trial ended prematurely?                     | No               |

Notes:

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**General information about the trial**

Main objective of the trial:

The aim of the study is to investigate the mechanism of work of mitrazipine (Remergon) in gastric motility and sensivity, and satiation in healthy volunteers.

Protection of trial subjects:

not applicable

Background therapy: -

Evidence for comparator: -

|                                                           |                  |
|-----------------------------------------------------------|------------------|
| Actual start date of recruitment                          | 12 February 2015 |
| Long term follow-up planned                               | No               |
| Independent data monitoring committee (IDMC) involvement? | No               |

Notes:

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**Population of trial subjects**

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**Subjects enrolled per country**

|                                      |             |
|--------------------------------------|-------------|
| Country: Number of subjects enrolled | Belgium: 31 |
| Worldwide total number of subjects   | 31          |
| EEA total number of subjects         | 31          |

Notes:

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**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)                      | 31 |
| From 65 to 84 years                       | 0  |
| 85 years and over                         | 0  |

## Subject disposition

### Recruitment

Recruitment details:

Healthy volunteers had to be devoid of GI symptoms and of the use of medications known to influence gastrointestinal sensorimotor function.

### Pre-assignment

Screening details:

Healthy volunteers, recruited by public advertisement

### Period 1

|                              |                                       |
|------------------------------|---------------------------------------|
| Period 1 title               | overall study period (overall period) |
| Is this the baseline period? | Yes                                   |
| Allocation method            | Randomised - controlled               |
| Blinding used                | Single blind                          |
| Roles blinded                | Subject                               |

### Arms

|                              |             |
|------------------------------|-------------|
| Are arms mutually exclusive? | Yes         |
| <b>Arm title</b>             | mirtazapine |

Arm description: -

|                                        |                       |
|----------------------------------------|-----------------------|
| Arm type                               | Experimental          |
| Investigational medicinal product name | mirtazapine           |
| Investigational medicinal product code |                       |
| Other name                             |                       |
| Pharmaceutical forms                   | Orodispersible tablet |
| Routes of administration               | Oral use              |

Dosage and administration details:

Treatment consisted of a 3-week dosing of mirtazapine (15 mg) every night before sleeping for 3 weeks

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

Arm description: -

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

Dosage and administration details:

Treatment consisted of a 3-week dosing of 1 placebo tablet every night before sleeping for 3 weeks

| Number of subjects in period 1 | mirtazapine | placebo |
|--------------------------------|-------------|---------|
| Started                        | 16          | 15      |
| Completed                      | 14          | 14      |
| Not completed                  | 2           | 1       |
| Adverse event, non-fatal       | 1           | -       |

|                                   |   |   |
|-----------------------------------|---|---|
| intolerance of barostat procedure | 1 | 1 |
|-----------------------------------|---|---|

## Baseline characteristics

### Reporting groups

|                                |             |
|--------------------------------|-------------|
| Reporting group title          | mirtazapine |
| Reporting group description: - |             |
| Reporting group title          | placebo     |
| Reporting group description: - |             |

| Reporting group values                                | mirtazapine | placebo | Total |
|-------------------------------------------------------|-------------|---------|-------|
| Number of subjects                                    | 16          | 15      | 31    |
| Age categorical<br>Units: Subjects                    |             |         |       |
| In utero                                              | 0           | 0       | 0     |
| Preterm newborn infants<br>(gestational age < 37 wks) | 0           | 0       | 0     |
| Newborns (0-27 days)                                  | 0           | 0       | 0     |
| Infants and toddlers (28 days-23<br>months)           | 0           | 0       | 0     |
| Children (2-11 years)                                 | 0           | 0       | 0     |
| Adolescents (12-17 years)                             | 0           | 0       | 0     |
| Adults (18-64 years)                                  | 16          | 15      | 31    |
| From 65-84 years                                      | 0           | 0       | 0     |
| 85 years and over                                     | 0           | 0       | 0     |
| Age continuous<br>Units: years                        |             |         |       |
| arithmetic mean                                       | 23.9        | 24.9    |       |
| standard deviation                                    | ± 1.3       | ± 1.0   | -     |
| Gender categorical<br>Units: Subjects                 |             |         |       |
| Female                                                | 9           | 9       | 18    |
| Male                                                  | 7           | 6       | 13    |

## End points

### End points reporting groups

|                                |             |
|--------------------------------|-------------|
| Reporting group title          | mirtazapine |
| Reporting group description: - |             |
| Reporting group title          | placebo     |
| Reporting group description: - |             |

### Primary: The effect of mirtazapine on intragastric volume after a meal

|                                                                                                                                                                       |                                                               |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------|
| End point title                                                                                                                                                       | The effect of mirtazapine on intragastric volume after a meal |
| End point description:                                                                                                                                                |                                                               |
| End point type                                                                                                                                                        | Primary                                                       |
| End point timeframe:                                                                                                                                                  |                                                               |
| the effect of mirtazapine/placebo on gastric accommodation was measured with gastric barostat measurement at the end of a 3 week treatment with mirtazapine / placebo |                                                               |

| End point values                     | mirtazapine           | placebo               |  |  |
|--------------------------------------|-----------------------|-----------------------|--|--|
| Subject group type                   | Reporting group       | Reporting group       |  |  |
| Number of subjects analysed          | 14                    | 14                    |  |  |
| Units: ml                            |                       |                       |  |  |
| arithmetic mean (standard deviation) | 216.23 ( $\pm$ 29.25) | 297.17 ( $\pm$ 40.65) |  |  |

### Statistical analyses

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |                                              |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------|
| Statistical analysis title                                                                                                                                                                                                                                                                                                                                                                                                                                         | gastric accommodation after 3 week treatment |
| Statistical analysis description:                                                                                                                                                                                                                                                                                                                                                                                                                                  |                                              |
| At baseline, the meal-induced increase in intragastric balloon volume (accommodation) was similar in both treatment groups (placebo: 271.49 $\pm$ 42.67 mL and mirtazapine: 206.08 $\pm$ 50.5 mL, P=.24). No differences were observed after 3 weeks of treatment with placebo (297.17 $\pm$ 40.65 mL; P=.69). After 3 weeks of treatment with mirtazapine, the intragastric barostat balloon volume was not significantly altered (216.23 $\pm$ 29.25 mL; P=.85). |                                              |
| Comparison groups                                                                                                                                                                                                                                                                                                                                                                                                                                                  | mirtazapine v placebo                        |
| Number of subjects included in analysis                                                                                                                                                                                                                                                                                                                                                                                                                            | 28                                           |
| Analysis specification                                                                                                                                                                                                                                                                                                                                                                                                                                             | Pre-specified                                |
| Analysis type                                                                                                                                                                                                                                                                                                                                                                                                                                                      | superiority                                  |
| P-value                                                                                                                                                                                                                                                                                                                                                                                                                                                            | < 0.05 <sup>[1]</sup>                        |
| Method                                                                                                                                                                                                                                                                                                                                                                                                                                                             | t-test, 2-sided                              |

Notes:

[1] - In all analyses, P < .05 was considered statistically significant. No significant differences were found in the gastric accommodation.

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

For each individual, corresponds to timeframe of study participation (from signing of informed consent until last visit).

|                 |                |
|-----------------|----------------|
| Assessment type | Non-systematic |
|-----------------|----------------|

### Dictionary used

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

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

### Reporting groups

|                       |                 |
|-----------------------|-----------------|
| Reporting group title | mirtazapine arm |
|-----------------------|-----------------|

Reporting group description: -

|                       |               |
|-----------------------|---------------|
| Reporting group title | placebo group |
|-----------------------|---------------|

Reporting group description: -

| Serious adverse events                            | mirtazapine arm | placebo group  |  |
|---------------------------------------------------|-----------------|----------------|--|
| Total subjects affected by serious adverse events |                 |                |  |
| subjects affected / exposed                       | 0 / 16 (0.00%)  | 0 / 15 (0.00%) |  |
| number of deaths (all causes)                     | 0               | 0              |  |
| number of deaths resulting from adverse events    | 0               | 0              |  |

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

| Non-serious adverse events                            | mirtazapine arm  | placebo group   |  |
|-------------------------------------------------------|------------------|-----------------|--|
| Total subjects affected by non-serious adverse events |                  |                 |  |
| subjects affected / exposed                           | 10 / 16 (62.50%) | 6 / 15 (40.00%) |  |
| Nervous system disorders                              |                  |                 |  |
| Headache                                              |                  |                 |  |
| subjects affected / exposed                           | 4 / 16 (25.00%)  | 3 / 15 (20.00%) |  |
| occurrences (all)                                     | 4                | 3               |  |
| General disorders and administration site conditions  |                  |                 |  |
| Fatigue                                               |                  |                 |  |
| subjects affected / exposed                           | 8 / 16 (50.00%)  | 2 / 15 (13.33%) |  |
| occurrences (all)                                     | 8                | 2               |  |
| Dizziness                                             |                  |                 |  |
| subjects affected / exposed                           | 1 / 16 (6.25%)   | 0 / 15 (0.00%)  |  |
| occurrences (all)                                     | 1                | 0               |  |

|                                        |                                         |                 |  |
|----------------------------------------|-----------------------------------------|-----------------|--|
| Gastrointestinal disorders             |                                         |                 |  |
| Gastroenteritis                        |                                         |                 |  |
| subjects affected / exposed            | 2 / 16 (12.50%)                         | 2 / 15 (13.33%) |  |
| occurrences (all)                      | 2                                       | 2               |  |
| Skin and subcutaneous tissue disorders |                                         |                 |  |
| Skin reaction                          | Additional description: urticarial rash |                 |  |
| subjects affected / exposed            | 1 / 16 (6.25%)                          | 0 / 15 (0.00%)  |  |
| occurrences (all)                      | 1                                       | 0               |  |

## 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? No

### Limitations and caveats

None reported

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### Online references

<http://www.ncbi.nlm.nih.gov/pubmed/28695632>