



## Clinical trial results: Specific immunotherapy of birch pollen-related food allergy Summary

|                          |                |
|--------------------------|----------------|
| EudraCT number           | 2011-001221-24 |
| Trial protocol           | AT             |
| Global end of trial date | 02 July 2020   |

### Results information

|                                   |                       |
|-----------------------------------|-----------------------|
| Result version number             | v1 (current)          |
| This version publication date     | 10 April 2021         |
| First version publication date    | 10 April 2021         |
| Summary attachment (see zip file) | summary (Summary.pdf) |

### Trial information

#### Trial identification

|                       |           |
|-----------------------|-----------|
| Sponsor protocol code | 01/2011tk |
|-----------------------|-----------|

#### Additional study identifiers

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

Notes:

#### Sponsors

|                              |  |
|------------------------------|--|
| Sponsor organisation name    | Medical University of Vienna   |
| Sponsor organisation address | Währinger Gürtel 18-20, Vienn, Austria, 1090   |
| Public contact               | Barbara Bohle, Medical University of Vienna, +43 01404005114, barbara.bohle@meduniwien.ac.at |
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Notes:

#### Paediatric regulatory details

|  |    |
|--|----|
| Is trial part of an agreed paediatric investigation plan (PIP)       | No |
| Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial? | No |
| Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial? | No |

Notes:

## Results analysis stage

|  |                  |
|--|------------------|
| Analysis stage                                       | Final            |
| Date of interim/final analysis                       | 07 February 2020 |
| Is this the analysis of the primary completion data? | Yes              |
| Primary completion date                              | 07 February 2020 |
| Global end of trial reached?                         | Yes              |
| Global end of trial date                             | 02 July 2020     |
| Was the trial ended prematurely?                     | No               |

Notes:

## General information about the trial

Main objective of the trial:

Treatment of apple allergy in birch pollen allergic patients

Protection of trial subjects:

Allergies are observed

Background therapy: -

Evidence for comparator: -

|   |              |
|---|--------------|
| Actual start date of recruitment                          | 04 June 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 | Austria: 60 |
| Worldwide total number of subjects   | 60          |
| EEA total number of subjects         | 60          |

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)                      | 60 |
| From 65 to 84 years                       | 0  |
| 85 years and over                         | 0  |

## Subject disposition

### Recruitment

Recruitment details:

preselection of patients June to December 2012

### Pre-assignment

Screening details:

in a 6 months recruitment period, we screened 72 patients for the study. 60/72 patients were selected and randomly assigned to daily sublingual application of placebo or 25 µg Mal d 1 or 25 µg Bet v 1 (n 20 in each group)

### Period 1

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

Blinding implementation details:

60 patients were randomized by Randomizer(R) in 3 treatment arms each 20 patients

### Arms

|                              |                        |
|------------------------------|------------------------|
| Are arms mutually exclusive? | Yes                    |
| <b>Arm title</b>             | rMal d 1 Treatment arm |

Arm description:

20 patients were treated with 25µg rMal d 1 liquid per day sublingually over a period of 4 months

|  |                 |
|--|-----------------|
| Arm type                               | Experimental    |
| Investigational medicinal product name | rMal d 1 liquid |
| Investigational medicinal product code |                 |
| Other name                             |                 |
| Pharmaceutical forms                   | Oral liquid     |
| Routes of administration               | Submucosal use  |

Dosage and administration details:

25µg id rMal d 1 liquid per day sublingually

|                  |                       |
|------------------|-----------------------|
| <b>Arm title</b> | rBet v1 treatment arm |
|------------------|-----------------------|

Arm description:

20 patients were treated with 25µg rBet v1 liquid per day sublingually over a period of 4 months

|  |                   |
|--|-------------------|
| Arm type                               | Active comparator |
| Investigational medicinal product name | rBet v1           |
| Investigational medicinal product code |                   |
| Other name                             |                   |
| Pharmaceutical forms                   | Oral liquid       |
| Routes of administration               | Sublingual use    |

Dosage and administration details:

25µg rBet v1 liquid per day sublingually administered over a period of 4 months

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

Arm description:

20 patients were treated with 25µg of solvent liquid per day sublingually over a period of 4 months

|          |         |
|----------|---------|
| Arm type | Placebo |
|----------|---------|

|  |                |
|--|----------------|
| Investigational medicinal product name | Placebo        |
| Investigational medicinal product code |                |
| Other name                             |                |
| Pharmaceutical forms                   | Oral liquid    |
| Routes of administration               | Sublingual use |

Dosage and administration details:

25µg solvent liquid per day sublingually over a period of 4 months

| <b>Number of subjects in period 1</b> | rMal d 1 Treatment arm | rBet v1 treatment arm | placebo |
|---------------------------------------|------------------------|-----------------------|---------|
| Started                               | 20                     | 20                    | 20      |
| Completed                             | 20                     | 17                    | 19      |
| Not completed                         | 0                      | 3                     | 1       |
| Consent withdrawn by subject          | -                      | 1                     | -       |
| moved                                 | -                      | 1                     | -       |
| Lost to follow-up                     | -                      | 1                     | 1       |

## Baseline characteristics

### Reporting groups

|                       |                               |
|-----------------------|-------------------------------|
| Reporting group title | Study period (overall period) |
|-----------------------|-------------------------------|

Reporting group description: -

| Reporting group values                             | Study period (overall period) | Total |  |
|--|-------------------------------|-------|--|
| Number of subjects                                 | 60                            | 60    |  |
| Age categorical<br>Units: Subjects                 |                               |       |  |
| In utero   | 0                             | 0     |  |
| Preterm newborn infants (gestational age < 37 wks) | 0                             | 0     |  |
| Newborns (0-27 days)                               | 0                             | 0     |  |
| Infants and toddlers (28 days-23 months)           | 0                             | 0     |  |
| Children (2-11 years)                              | 0                             | 0     |  |
| Adolescents (12-17 years)                          | 0                             | 0     |  |
| Adults (18-64 years)                               | 60                            | 60    |  |
| From 65-84 years                                   | 0                             | 0     |  |
| 85 years and over                                  | 0                             | 0     |  |
| Gender categorical<br>Units: Subjects              |                               |       |  |
| Female   | 31                            | 31    |  |
| Male   | 29                            | 29    |  |

## End points

### End points reporting groups

|                              |   |
|------------------------------|---|
| Reporting group title        | rMal d 1 Treatment arm  |
| Reporting group description: | 20 patients were treated with 25µg rMal d 1 liquid per day sublingually over a period of 4 months   |
| Reporting group title        | rBet v1 treatment arm   |
| Reporting group description: | 20 patients were treated with 25µg rBet v1 liquid per day sublingually over a period of 4 months    |
| Reporting group title        | placebo   |
| Reporting group description: | 20 patients were treated with 25µg of solvent liquid per day sublingually over a period of 4 months |

### Primary: DBPC sublingual challenge with increasing dosages of r Mal d1 and fresh apple

|                        |  |
|------------------------|--|
| End point title        | DBPC sublingual challenge with increasing dosages of r Mal d1 and fresh apple  |
| End point description: |  |
| End point type         | Primary  |
| End point timeframe:   | Comparison of DBPC sublingual challenge with increasing dosages of r Mal d1 and fresh apple before and after the treatment with r Mal d1 |

| End point values            | rMal d 1 Treatment arm | rBet v1 treatment arm | placebo         |  |
|-----------------------------|------------------------|-----------------------|-----------------|--|
| Subject group type          | Reporting group        | Reporting group       | Reporting group |  |
| Number of subjects analysed | 20                     | 20                    | 20              |  |
| Units: µg                   |                        |                       |                 |  |
| number (not applicable)     | 15                     | 6                     | 0               |  |

### Statistical analyses

|   |  |
|---|--|
| Statistical analysis title              | DBPC sublingual challenge with increasing dosages        |
| Comparison groups                       | rMal d 1 Treatment arm v rBet v1 treatment arm v placebo |
| Number of subjects included in analysis | 60   |
| Analysis specification                  | Pre-specified  |
| Analysis type                           | equivalence  |
| P-value                                 | ≥ 0.001  |
| Method                                  | Sign test  |

## Adverse events

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

Timeframe for reporting adverse events:

From August 2013 to End of November 2013 during the treatment period of 4 months

Adverse event reporting additional description:

in all three groups, all patients reported at first application slight tingling in the lining of the mouth, itching in the mouth and ear that disappeared without any treatment within 15 minutes.  
in the course of the treatment, this symptoms decreased in both verum groups while in the placebo group no significant symptom decrease was seen.

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

### Dictionary used

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

|                    |   |
|--------------------|---|
| Dictionary version | 1 |
|--------------------|---|

### Reporting groups

|                       |                           |
|-----------------------|---------------------------|
| Reporting group title | r Mal d 1 treatment group |
|-----------------------|---------------------------|

Reporting group description:

20 patients with birch pollen associated apple allergy who were treated with daily sublingually applied 25µg r Mal d 1 over 4 months

|                       |                           |
|-----------------------|---------------------------|
| Reporting group title | r Bet v 1 treatment group |
|-----------------------|---------------------------|

Reporting group description:

20 patients with birch pollen associated apple allergy who were treated with daily sublingually applied 25µg r Bet v 1 over 4 months

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

Reporting group description:

20 patients with birch pollen associated apple allergy who were treated with daily sublingually applied 25µg of the solvent of the verum preparations over 4 months

| <b>Serious adverse events</b>                     | r Mal d 1 treatment group | r Bet v 1 treatment group | placebo group  |
|---|---------------------------|---------------------------|----------------|
| Total subjects affected by serious adverse events |                           |                           |                |
| subjects affected / exposed                       | 0 / 20 (0.00%)            | 0 / 20 (0.00%)            | 0 / 20 (0.00%) |
| number of deaths (all causes)                     | 0                         | 0                         | 0              |
| number of deaths resulting from adverse events    | 0                         | 0                         | 0              |

Frequency threshold for reporting non-serious adverse events: 1 %

| <b>Non-serious adverse events</b>                     | r Mal d 1 treatment group | r Bet v 1 treatment group | placebo group  |
|---|---------------------------|---------------------------|----------------|
| Total subjects affected by non-serious adverse events |                           |                           |                |
| subjects affected / exposed                           | 0 / 20 (0.00%)            | 0 / 20 (0.00%)            | 0 / 20 (0.00%) |

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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: no serious adverse events have occurred

## **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