



## Clinical trial results:

### Die antidementive Therapie mit Acetylcholinesteraseinhibitoren: Untersuchung von Plasmakonzentrationen, Arzneimittelinteraktionen und Therapieeffekt in Abhängigkeit von genetischen Polymorphismen Summary

|                          |                  |
|--------------------------|------------------|
| EudraCT number           | 2008-005472-27   |
| Trial protocol           | AT               |
| Global end of trial date | 30 November 2011 |

#### Results information

|                                |                 |
|--------------------------------|-----------------|
| Result version number          | v1 (current)    |
| This version publication date  | 20 October 2022 |
| First version publication date | 20 October 2022 |

#### Trial information

##### Trial identification

|                       |       |
|-----------------------|-------|
| Sponsor protocol code | 70639 |
|-----------------------|-------|

##### Additional study identifiers

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

Notes:

#### Sponsors

|                              |                                                                                                                                                                                                          |
|------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Sponsor organisation name    | Medical University Innsbruck                                                                                                                                                                             |
| Sponsor organisation address | Christoph-Probst-Platz 1, Innrain 52, Innsbruck, Austria, 6020                                                                                                                                           |
| Public contact               | Ao. Univ.Prof. Eberhard Deisenhammer, Medical University Innsbruck,<br>University Hospital for Psychiatry I<br>Anichstrasse 35, 6020 IBK, +43 (0)50504-23669,<br>eberhard.deisenhammer@tirol-kliniken.at |
| Scientific contact           | Ao. Univ.Prof. Eberhard Deisenhammer, Medical University Innsbruck,<br>University Hospital for Psychiatry I<br>Anichstrasse 35, 6020 IBK, +43 (0)50504-23669,<br>eberhard.deisenhammer@tirol-kliniken.at |

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                       | 30 November 2011 |
| Is this the analysis of the primary completion data? | Yes              |
| Primary completion date                              | 30 November 2011 |
| Global end of trial reached?                         | Yes              |
| Global end of trial date                             | 30 November 2011 |
| Was the trial ended prematurely?                     | No               |

Notes:

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**General information about the trial**

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Main objective of the trial:

Das primäre Ziel der Studie ist, den Einfluss genetischer Polymorphismen im CYP2D6-Gen auf die Wirkstoffkonzentration im Plasma der Acetylcholinesterase-inhibitoren Donezepil und Rivastigmin zu untersuchen.

Protection of trial subjects:

Es ist einmalig ein Mundhöhlenabstrich für die genetische Untersuchung notwendig.

Background therapy:

-

Evidence for comparator:

-

|                                                           |               |
|-----------------------------------------------------------|---------------|
| Actual start date of recruitment                          | 31 March 2009 |
| 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**

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|                                      |              |
|--------------------------------------|--------------|
| Country: Number of subjects enrolled | Austria: 126 |
| Worldwide total number of subjects   | 126          |
| EEA total number of subjects         | 126          |

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)                      | 5  |
| From 65 to 84 years                       | 90 |
| 85 years and over                         | 31 |

## Subject disposition

### Recruitment

Recruitment details:

Die Rekrutierung der Demenzpatienten erfolgt über die Universitätsklinik für Psychiatrie Innsbruck, (zum Hauptanteil über die Gedächtnissprechstunde), die bereits über ein großes und gut untersuchtes Patientenkollektiv verfügt.

### Pre-assignment

Screening details:

Inkludiert werden geschäftsfähige Patienten mit der Diagnose einer Demenz vom Alzheimer Typ oder gemischt vaskulärem Typ. Vor Studieneinschluss erfolgt ein ausführliches Informationsgespräch bzw. eine genetische Aufklärung.

### Period 1

|                              |                             |
|------------------------------|-----------------------------|
| Period 1 title               | Behandlung (overall period) |
| Is this the baseline period? | Yes                         |
| Allocation method            | Not applicable              |
| Blinding used                | Not blinded                 |

### Arms

|                                        |                           |
|----------------------------------------|---------------------------|
| <b>Arm title</b>                       | Behandlung                |
| Arm description: -                     |                           |
| Arm type                               | Experimental              |
| Investigational medicinal product name | Aricept 5mg-Filmtabletten |
| Investigational medicinal product code |                           |
| Other name                             | Donepezil Hydrochloride   |
| Pharmaceutical forms                   | Tablet                    |
| Routes of administration               | Oral use                  |

Dosage and administration details:

Nach einer klinischen Beurteilung der Behandlung mit 5 mg/Tag nach einem Monat kann die Aricept-Dosis bei Bedarf auf 10 mg/Tag (einmal tägliche Gabe) erhöht werden. Die empfohlene Maximaldosis beträgt 10 mg/Tag.

|                                        |                            |
|----------------------------------------|----------------------------|
| Investigational medicinal product name | Aricept 10mg-Filmtabletten |
| Investigational medicinal product code |                            |
| Other name                             | Donepezil Hydrochloride    |
| Pharmaceutical forms                   | Tablet                     |
| Routes of administration               | Oral use                   |

Dosage and administration details:

Nach einer klinischen Beurteilung der Behandlung mit 5 mg/Tag nach einem Monat kann die Aricept-Dosis bei Bedarf auf 10 mg/Tag (einmal tägliche Gabe) erhöht werden. Die empfohlene Maximaldosis beträgt 10 mg/Tag.

|                                        |                           |
|----------------------------------------|---------------------------|
| Investigational medicinal product name | Reminyl 4mg-Filmtabletten |
| Investigational medicinal product code |                           |
| Other name                             | Galantamine Hydrobromide  |
| Pharmaceutical forms                   | Tablet                    |
| Routes of administration               | Oral use                  |

Dosage and administration details:

Initialdosis: 4 mg 2mal / Tag, über 4 Wochen

anfängliche Erhaltungsdosis : 8 mg 2mal / Tag; über mind. 4 Wochen

gesteigerte Erhaltungsdosis: 12 mg 2mal / Tag; individuell nach sorgfältiger Beurteilung der Behandlung im Hinblick auf therapeutischen Nutzen und Verträglichkeit

reduzierte Erhaltungsdosis: 16 mg / Tag; bei einzelnen Patienten, die bei Gabe von 24 mg / Tag keine erhöhte Ansprechrage zeigen oder die diese Dosis nicht vertragen

|                                        |                            |
|----------------------------------------|----------------------------|
| Investigational medicinal product name | Reminyl 8 mg-Filmdabletten |
| Investigational medicinal product code |                            |
| Other name                             | Galantamine Hydrobromide   |
| Pharmaceutical forms                   | Tablet                     |
| Routes of administration               | Oral use                   |

Dosage and administration details:

Die Behandlung wird mit der 8-mg-Hartkapsel, die einmal täglich eingenommen wird, begonnen. Nach 4 Behandlungswochen wird die Dosis erhöht. Dann wird die 16-mg-Hartkapsel einmal täglich eingenommen. Frühestens nach weiteren 4 Behandlungswochen kann die Dosis auf 24-mg einmal täglich erhöht werden.

|                                        |                                                 |
|----------------------------------------|-------------------------------------------------|
| Investigational medicinal product name | Exelon 4,6 mg/24 Stunden transdermales Pflaster |
| Investigational medicinal product code |                                                 |
| Other name                             | Rivastigmine                                    |
| Pharmaceutical forms                   | Transdermal patch                               |
| Routes of administration               | Transdermal use                                 |

Dosage and administration details:

Normalerweise beginnt die Behandlung mit Exelon 4,6 mg/24 Stunden.

Die empfohlene übliche Tagesdosis ist Exelon 9,5 mg/24 Stunden. Wird sie gut vertragen, kann der behandelnde Arzt eine Erhöhung der Dosis auf 13,3 mg/24 Stunden in Betracht ziehen.

Ein Pflaster wird pro Tag angewendet.

|                                        |                                                 |
|----------------------------------------|-------------------------------------------------|
| Investigational medicinal product name | Exelon 9,5 mg/24 Stunden transdermales Pflaster |
| Investigational medicinal product code |                                                 |
| Other name                             | Rivastigmine                                    |
| Pharmaceutical forms                   | Transdermal patch                               |
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Ein Pflaster wird pro Tag angewendet.

| Number of subjects in period 1 | Behandlung |
|--------------------------------|------------|
| Started                        | 126        |
| Completed                      | 126        |

## Baseline characteristics

### Reporting groups

Reporting group title

Behandlung

Reporting group description: -

| Reporting group values                                | Behandlung | Total |  |
|-------------------------------------------------------|------------|-------|--|
| Number of subjects                                    | 126        | 126   |  |
| 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)                                  | 5          | 5     |  |
| From 65-84 years                                      | 90         | 90    |  |
| 85 years and over                                     | 31         | 31    |  |
| Age continuous                                        |            |       |  |
| Units: years                                          |            |       |  |
| arithmetic mean                                       | 78.4       |       |  |
| full range (min-max)                                  | 58 to 93   | -     |  |
| Gender categorical                                    |            |       |  |
| Units: Subjects                                       |            |       |  |
| Female                                                | 86         | 86    |  |
| Male                                                  | 40         | 40    |  |

## End points

### End points reporting groups

|                                |            |
|--------------------------------|------------|
| Reporting group title          | Behandlung |
| Reporting group description: - |            |

### Primary: CYP2D6

|                        |                       |
|------------------------|-----------------------|
| End point title        | CYP2D6 <sup>[1]</sup> |
| End point description: |                       |

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

End point timeframe:

Tag 0

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: Für eine statistische Auswertung hätten 300 Patienten eingeschlossen werden müssen (100 Patienten je Medikament)

| End point values            | Behandlung      |  |  |  |
|-----------------------------|-----------------|--|--|--|
| Subject group type          | Reporting group |  |  |  |
| Number of subjects analysed | 126             |  |  |  |
| Units: Polymorphismen       |                 |  |  |  |
| number (not applicable)     | 1               |  |  |  |

### Statistical analyses

No statistical analyses for this end point

## Adverse events

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

Timeframe for reporting adverse events:

31.03.2009-2011-11-30

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

### Dictionary used

|                 |       |
|-----------------|-------|
| Dictionary name | CTCAE |
|-----------------|-------|

|                    |      |
|--------------------|------|
| Dictionary version | 4.03 |
|--------------------|------|

### Reporting groups

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

Reporting group description: -

| Serious adverse events                            | Treatment       |  |  |
|---------------------------------------------------|-----------------|--|--|
| Total subjects affected by serious adverse events |                 |  |  |
| subjects affected / exposed                       | 0 / 126 (0.00%) |  |  |
| number of deaths (all causes)                     | 0               |  |  |
| number of deaths resulting from adverse events    | 0               |  |  |

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

| Non-serious adverse events                            | Treatment       |  |  |
|-------------------------------------------------------|-----------------|--|--|
| Total subjects affected by non-serious adverse events |                 |  |  |
| subjects affected / exposed                           | 0 / 126 (0.00%) |  |  |

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: Es wurde nur ein einmaliger Mundhöhlenabstrich durchgeführt.

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date          | Amendment                                                                                                                                           |
|---------------|-----------------------------------------------------------------------------------------------------------------------------------------------------|
| 12 March 2009 | Zusatz Studienprotokoll (Version 4):<br>Relevante Gene für die Wirkung von Antidementiva<br>Relevante Gene für die Pathogenese der Alzheimer Demenz |

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported