



## Clinical trial results:

### Effects of mineralocorticoid receptor stimulation on cognitive bias and social cognition in patients with major depression and healthy controls: what's the role of NMDA receptors?

#### Summary

EudraCT number	2014-005239-15
Trial protocol	DE
Global end of trial date	11 February 2019

#### Results information

Result version number	v1 (current)
This version publication date	14 May 2021
First version publication date	14 May 2021
Summary attachment (see zip file)	MISO_summary (EudraCT_synopsis_MISO.pdf)

#### Trial information

##### Trial identification

Sponsor protocol code	MISO
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##### Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03062150
WHO universal trial number (UTN)	-

Notes:

#### Sponsors

Sponsor organisation name	Charité - Universitätsmedizin Berlin
Sponsor organisation address	Hindenburgdamm 30, Berlin, Germany,
Public contact	Christian Otte, Klinik für Psychiatrie und Psychoth, Charité - Universitätsmedizin Berlin, +49 30450 517531, christian.otte@charite.de
Scientific contact	Christian Otte, Klinik für Psychiatrie und Psychoth, Charité - Universitätsmedizin Berlin, +49 30450 517531, christian.otte@charite.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	11 February 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	11 February 2019
Global end of trial reached?	Yes
Global end of trial date	11 February 2019
Was the trial ended prematurely?	No

Notes:

## General information about the trial

Main objective of the trial:

The primary objective of the study is to investigate the effects of fludrocortisone versus placebo on the attention bias in a pooled group of depressive patients and healthy control subjects (measured by the „Attentional bias index“ in the emotional dot probe paradigm)

Protection of trial subjects:

Safety: Blood pressure, heart rate, measures of subjective well-being (Visual Analogue Mood Scales, VAMS), adverse events (AE), serious adverse events (SAE), serious adverse reactions (SAR)

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	21 September 2016
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	Germany: 232
Worldwide total number of subjects	232
EEA total number of subjects	232

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)	230
From 65 to 84 years	2
85 years and over	0

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

Diagnosis and main criteria for inclusion:

- Age 18-65 years
- Depressed male and female patients according to DSM-V & minimum of 17-items Hamilton Depression Score of 18
- healthy controls

### Period 1

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

### Arms

Are arms mutually exclusive?	Yes
<b>Arm title</b>	Fludrocortisone + Placebo

Arm description:

Fludrocortisone: pill, Astonin H 0,1gm, single dose, Merck Serono GmbH Placebo: pill, 8mm, single dose, Lichtenstein, Winthrop Arzneimittel GmbH.

Arm type	Experimental
Investigational medicinal product name	Fludrocortisone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Fludrocortisone: pill, Astonin H 0,1gm, single dose, Merck Serono GmbH Placebo: pill, 8mm, single dose, Lichtenstein, Winthrop Arzneimittel GmbH.

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Placebo: pill, 8mm, single dose, Lichtenstein, Winthrop Arzneimittel GmbH.

<b>Arm title</b>	Placebo + D-Cycloserine
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Arm description:

Placebo: pill, 8mm, single dose, Lichtenstein, Winthrop Arzneimittel GmbH. D-Cycloserine: capsule, Cycloserine 250mg, single dose, King Pharmaceuticals Ltd

Arm type	Experimental
Investigational medicinal product name	D-Cycloserine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:	
D-Cycloserine: capsule, Cycloserine 250mg, single dose, King Pharmaceuticals Ltd	
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use
Dosage and administration details:	
Placebo: pill, 8mm, single dose, Lichtenstein, Winthrop Arzneimittel GmbH.	
<b>Arm title</b>	Fludrocortisone+D-Cycloserine
Arm description:	
Fludrocortisone: pill, Astonin H 0,1gm, single dose, Merck Serono GmbH D-Cycloserine: capsule, Cycloserine 250mg, single dose, King Pharmaceuticals Ltd	
Arm type	Experimental
Investigational medicinal product name	Fludrocortisone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use
Dosage and administration details:	
Fludrocortisone: pill, Astonin H 0,1gm, single dose, Merck Serono GmbH Placebo: pill, 8mm, single dose, Lichtenstein, Winthrop Arzneimittel GmbH.	
Investigational medicinal product name	D-Cycloserine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use
Dosage and administration details:	
D-Cycloserine: capsule, Cycloserine 250mg, single dose, King Pharmaceuticals Ltd	
<b>Arm title</b>	Placebo + Placebo
Arm description:	
Placebo: pill, 8mm, single dose, Lichtenstein, Winthrop Arzneimittel GmbH.	
Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use
Dosage and administration details:	
Placebo: pill, 8mm, single dose, Lichtenstein, Winthrop Arzneimittel GmbH.	

Number of subjects in period 1	Fludrocortisone + Placebo	Placebo + D-Cycloserine	Fludrocortisone+D-Cycloserine
Started	58	58	58
Completed	58	58	58

<b>Number of subjects in period 1</b>	Placebo + Placebo
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Started	58
Completed	58

## Baseline characteristics

### Reporting groups

Reporting group title	Fludrocortisone + Placebo
Reporting group description:	
Fludrocortisone: pill, Astonin H 0,1gm, single dose, Merck Serono GmbH Placebo: pill, 8mm, single dose, Lichtenstein, Winthrop Arzneimittel GmbH.	
Reporting group title	Placebo + D-Cycloserine
Reporting group description:	
Placebo: pill, 8mm, single dose, Lichtenstein, Winthrop Arzneimittel GmbH. D-Cycloserine: capsule, Cycloserine 250mg, single dose, King Pharmaceuticals Ltd	
Reporting group title	Fludrocortisone+D-Cycloserine
Reporting group description:	
Fludrocortisone: pill, Astonin H 0,1gm, single dose, Merck Serono GmbH D-Cycloserine: capsule, Cycloserine 250mg, single dose, King Pharmaceuticals Ltd	
Reporting group title	Placebo + Placebo
Reporting group description:	
Placebo: pill, 8mm, single dose, Lichtenstein, Winthrop Arzneimittel GmbH.	

Reporting group values	Fludrocortisone + Placebo	Placebo + D-Cycloserine	Fludrocortisone+D-Cycloserine
Number of subjects	58	58	58
Age categorical			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	57	58	58
From 65-84 years	1	0	0
85 years and over	0	0	0
Gender categorical			
Units: Subjects			
Female	40	48	54
Male	18	10	4

Reporting group values	Placebo + Placebo	Total	
Number of subjects	58	232	
Age categorical			
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)	57	230	
From 65-84 years	1	2	
85 years and over	0	0	
Gender categorical			
Units: Subjects			
Female	40	182	
Male	18	50	

## End points

### End points reporting groups

Reporting group title	Fludrocortisone + Placebo
Reporting group description: Fludrocortisone: pill, Astonin H 0,1gm, single dose, Merck Serono GmbH Placebo: pill, 8mm, single dose, Lichtenstein, Winthrop Arzneimittel GmbH.	
Reporting group title	Placebo + D-Cycloserine
Reporting group description: Placebo: pill, 8mm, single dose, Lichtenstein, Winthrop Arzneimittel GmbH. D-Cycloserine: capsule, Cycloserine 250mg, single dose, King Pharmaceuticals Ltd	
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Reporting group title	Placebo + Placebo
Reporting group description: Placebo: pill, 8mm, single dose, Lichtenstein, Winthrop Arzneimittel GmbH.	

### Primary: Emotional dot probe

End point title	Emotional dot probe
End point description:	
End point type	Primary
End point timeframe: 1 hour	

End point values	Fludrocortisone + Placebo	Placebo + D-Cycloserine	Fludrocortisone +D-Cycloserine	Placebo + Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	58	58	58	58
Units: Effect	0	0	0	0

### Statistical analyses

Statistical analysis title	Emotional Dot Probe
Comparison groups	Fludrocortisone + Placebo v Placebo + D-Cycloserine v Fludrocortisone+D-Cycloserine v Placebo + Placebo
Number of subjects included in analysis	232
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	ANOVA
Parameter estimate	Mean difference (final values)





## Adverse events

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

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Timeframe for reporting adverse events:

Day of assessment

Assessment type	Non-systematic
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### Dictionary used

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Dictionary name	own system
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Dictionary version	1
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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: No AE, SEA SAR reported.

## **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