Clinical trial results:
A Double-blind, Placebo-controlled, Randomized, Multicenter Proof-of-principle Trial of Adjunctive Minocycline for Patients With Treatment Resistant Unipolar Major Depressive Disorder (MDD)

Summary

EudraCT number	2015-001456-29
Trial protocol	DE
Global end of trial date	07 August 2020

Results information

Result version number	v1 (current)
This version publication date	21 May 2022
First version publication date	21 May 2022

Trial information

Trial identification

Sponsor protocol code	Mino-TRD(OptiMD)

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Charité University Medicine Berlin
Sponsor organisation address	Hindenburgdamm 30, Berlin, Germany, 12203
Public contact	Charité - Campus Benjamin Franklin, Institut Klinik für Psychiatrie und Psychotherapie, +49 30450 517522, isabella.heuser@charite.de
Scientific contact	Charité - Campus Benjamin Franklin, Institut Klinik für Psychiatrie und Psychotherapie, +49 30450 517522, isabella.heuser@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	07 August 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	07 August 2020
Global end of trial reached?	Yes
Global end of trial date	07 August 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Change in the MADRS value from starting point (week 1) to last visit (week 7), with weekly visits
Time point of determination of primary target parameters (objective): week 1-6, 7, 6 week after and 6 months after last visit

Protection of trial subjects:

Routine lab safety measurements were performed in addition to clinical interviews, where AEs were assessed

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 August 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: 168
Worldwide total number of subjects	168
EEA total number of subjects	168

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)	168
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was conducted at 9 study centers in 1 country,7. Januar 2016 - 7. August 2020

Pre-assignment

Screening details:

A total of 253 subjects entered the screening period, of whom 85 withdrew before randomization. The remaining 168 subjects were randomized.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Minocycline

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Minocycline Hydrochloride dihydrate
Investigational medicinal product code	10118-90-8
Other name	Udima
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

Subjects Minocycline Hydrochloride dihydrate capsule orally for 7 weeks (daily, weekly...??)

Arm title	Placebo

Arm description: -

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

6 weeks 2X2 200mg Placebo

Number of subjects in period 1	Minocycline	Placebo
Started	81	87
Completed	69	75
Not completed	12	12
Adverse event, serious fatal	1	1
Consent withdrawn by subject	6	2

Physician decision	3	2
N/A	-	4
Adverse event, non-fatal	1	1
Protocol deviation	1	2

Baseline characteristics

Reporting groups	
Reporting group title	Minocycline
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	

Reporting group values	Minocycline	Placebo	Total
Number of subjects	81	87	168
Age categorical			
Units: Subjects			
In utero			0
Preterm newborn infants (gestational age < 37 wks)			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)			0
From 65-84 years			0
85 years and over			0
Age continuous			
Units: years			
arithmetic mean	44.8	47.3	
standard deviation	± 13.6	± 12.5	-
Gender categorical			
Units: Subjects			
Female	31	48	79
Male	50	39	89
MADRS			
MADRS=Montgomery–Åsberg Depression Rating Scale			
Units: Score			
arithmetic mean	26.4	26.6	
standard deviation	± 4.8	± 5.1	-
HAMD-17			
AM-D-17=Hamilton Depression Rating Scale			
Units: Score			
arithmetic mean	20.0	20.3	
standard deviation	± 3.5	± 3.5	-
BDI II			
BDI-II=Beck Depression Inventory			
Units: Score			
arithmetic mean	32.3	32.9	
standard deviation	± 9.0	± 10.4	-
SCL-90-RGSI			
SCL-90-R= Symptom Checklist-90-R			
Units: Score			

arithmetic mean	68.7	66.9	
standard deviation	± 6.8	± 6.9	-
CGI			
GSI Global Severity Index			
Units: Score			
arithmetic mean	4.8	4.9	
standard deviation	± 0.6	± 0.7	-
TMT-A			
TMT = trail making test			
Units: Score			
arithmetic mean	34.7	35.1	
standard deviation	± 16.6	± 14.3	-
TMT-B			
Units: Score			
arithmetic mean	77.5	76.1	
standard deviation	± 32.7	± 32.3	-
CRP			
C-reactive protein			
Units: milligram(s)/litre			
arithmetic mean	1.21	0.6	
full range (min-max)	0.02 to 22.10	0.05 to 7.30	-
SCL-PSDI			
Positive Symptom Distress Index			
Units: Score			
arithmetic mean	66.3	66.1	
standard deviation	± 4.9	± 6.0	-
SCL-PST			
Positive Symptom Total			
Units: Score			
arithmetic mean	64.4	62.2	
standard deviation	± 6.6	± 6.0	-

End points

End points reporting groups

Reporting group title	Minocycline
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	

Primary: Change of MADRS baseline - week 7

End point title	Change of MADRS baseline - week 7
End point description:	
End point type	Primary
End point timeframe:	
MADRS scores were assessed at baseline and throughout week 7, change in MADRS score was calculated for the 6 week treatment period	

End point values	Minocycline	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	69	75		
Units: points				
arithmetic mean (standard deviation)	17.6 (± 7.8)	18.7 (± 9.0)		

Statistical analyses

Statistical analysis title	Change of the MADRS sum score
Comparison groups	Minocycline v Placebo
Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	t-test, 2-sided
Confidence interval	
level	95 %

Secondary: Post-treatment BDI

End point title	Post-treatment BDI
End point description:	
BDI II = Beck’s depression inventory Version II	
End point type	Secondary

End point timeframe:
6 weeks

End point values	Minocycline	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	66	72		
Units: Score				
arithmetic mean (standard deviation)				
BDI	21.6 (± 12.0)	23.6 (± 13.2)		

Statistical analyses

No statistical analyses for this end point

Secondary: Post-treatment CGI

End point title	Post-treatment CGI

End point description:
clinical global impression scale

End point type	Secondary

End point timeframe:
6 weeks

End point values	Minocycline	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	69	75		
Units: Score				
arithmetic mean (standard deviation)				
CGI	3.9 (± 1.1)	4.0 (± 1.2)		

Statistical analyses

No statistical analyses for this end point

Secondary: Post-treatment HAMD 6

End point title	Post-treatment HAMD 6

End point description:
HAMD = Hamilton Depression Rating Scale

End point type	Secondary

End point timeframe:
6 weeks

End point values	Minocycline	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	69	71		
Units: Score				
arithmetic mean (standard deviation)				
HAMD6	7.4 (± 3.5)	7.6 (± 6.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: Post-treatment HAMD 17

End point title	Post-treatment HAMD 17

End point description:

End point type	Secondary

End point timeframe:

6 weeks

End point values	Minocycline	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	68	71		
Units: Score				
arithmetic mean (standard deviation)				
HAMD 17	13.1 (± 5.9)	14.2 (± 6.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: Post-treatment SCL-90

End point title	Post-treatment SCL-90

End point description:

End point type	Secondary

End point timeframe:

6 weeks

End point values	Minocycline	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	66	72		
Units: Score				
arithmetic mean (standard deviation)				
GSI	62.3 (± 10.7)	62.0 (± 10.1)		
PSDI	60.2 (± 8.3)	60.2 (± 8.9)		
PST	60.5 (± 10.1)	59.5 (± 8.9)		

Statistical analyses

No statistical analyses for this end point

Secondary: Post-treatment trail making test

End point title	Post-treatment trail making test

End point description:

End point type	Secondary

End point timeframe:

6 weeks

End point values	Minocycline	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	69	74		
Units: Score				
arithmetic mean (standard deviation)				
TMT-A	29.9 (± 12.2)	30.4 (± 14.1)		
TMT-B	68.1 (± 27.6)	68.8 (± 29.1)		

Statistical analyses

No statistical analyses for this end point

Secondary: Post-treatment Log CRP

End point title	Post-treatment Log CRP

End point description:

End point type	Secondary

End point timeframe:
4 weeks

End point values	Minocycline	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	66	69		
Units: milligram(s)/litre				
arithmetic mean (standard deviation)				
CRP	1.77 (± 0.29)	1.82 (± 0.28)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
6 weeks	
Assessment type	Systematic

Dictionary used	
Dictionary name	own
Dictionary version	1

Reporting groups	
Reporting group title	Minocycline
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	

Serious adverse events	Minocycline	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 81 (7.41%)	8 / 87 (9.20%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Investigations			
Colon-Ca; CEA- Increase			
subjects affected / exposed	0 / 81 (0.00%)	1 / 87 (1.15%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tumormarkerbefund			
subjects affected / exposed	0 / 81 (0.00%)	1 / 87 (1.15%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
cheekbone fracture			
subjects affected / exposed	1 / 81 (1.23%)	0 / 87 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
drunk bicycle accident			

subjects affected / exposed	0 / 81 (0.00%)	1 / 87 (1.15%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Vascular disorders			
Zerebrale Aneurysmablutung			
subjects affected / exposed	1 / 81 (1.23%)	0 / 87 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Eosinophilie			
subjects affected / exposed	1 / 81 (1.23%)	0 / 87 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Cholezystektomie			
subjects affected / exposed	0 / 81 (0.00%)	1 / 87 (1.15%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
biliäre Pankreatitis			
subjects affected / exposed	0 / 81 (0.00%)	1 / 87 (1.15%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Depression			
subjects affected / exposed	3 / 81 (3.70%)	2 / 87 (2.30%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Suicidal behaviour			
subjects affected / exposed	0 / 81 (0.00%)	1 / 87 (1.15%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	1 / 1	

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

Non-serious adverse events	Minocycline	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	67 / 81 (82.72%)	63 / 87 (72.41%)	
Nervous system disorders			
Headache			
subjects affected / exposed	17 / 81 (20.99%)	27 / 87 (31.03%)	
occurrences (all)	33	43	
Dizziness			
subjects affected / exposed	15 / 81 (18.52%)	5 / 87 (5.75%)	
occurrences (all)	20	7	
Tremor			
subjects affected / exposed	3 / 81 (3.70%)	0 / 87 (0.00%)	
occurrences (all)	5	0	
General disorders and administration site conditions			
Tiredness			
subjects affected / exposed	9 / 81 (11.11%)	6 / 87 (6.90%)	
occurrences (all)	11	9	
Hyperhidrosis			
subjects affected / exposed	3 / 81 (3.70%)	6 / 87 (6.90%)	
occurrences (all)	4	6	
Gastrointestinal disorders			
Dyspepsia/Indigestion			
subjects affected / exposed	14 / 81 (17.28%)	14 / 87 (16.09%)	
occurrences (all)	25	19	
Flatulence/Diarrhoea			
subjects affected / exposed	12 / 81 (14.81%)	14 / 87 (16.09%)	
occurrences (all)	15	26	
Nausea			
subjects affected / exposed	8 / 81 (9.88%)	11 / 87 (12.64%)	
occurrences (all)	12	12	
Skin and subcutaneous tissue disorders			
Exanthem; Erythem, Akne			
subjects affected / exposed	10 / 81 (12.35%)	10 / 87 (11.49%)	
occurrences (all)	11	11	
Psychiatric disorders			
Depression/Extracerbation			

subjects affected / exposed	8 / 81 (9.88%)	9 / 87 (10.34%)	
occurrences (all)	10	10	
Insomnia			
subjects affected / exposed	2 / 81 (2.47%)	6 / 87 (6.90%)	
occurrences (all)	4	9	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	6 / 81 (7.41%)	6 / 87 (6.90%)	
occurrences (all)	6	6	
Infections and infestations			
flu-like symptoms			
subjects affected / exposed	24 / 81 (29.63%)	13 / 87 (14.94%)	
occurrences (all)	30	16	
Vaginal fungal infection			
subjects affected / exposed	3 / 81 (3.70%)	1 / 87 (1.15%)	
occurrences (all)	5	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported