



Clinical trial results:

A Placebo-controlled, double-blind, Randomized, dose finding phase II study on OMT-28 in Maintenance of Sinus rhythm after Electrical cardioversion in patients with persistent Atrial Fibrillation (PROMISE-AF)

Summary

EudraCT number	2018-001626-26
Trial protocol	CZ BG HU
Global end of trial date	08 April 2020

Results information

Result version number	v1 (current)
This version publication date	31 December 2020
First version publication date	31 December 2020

Trial information

Trial identification

Sponsor protocol code	OMT28-C0201
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Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	OMEICOS Therapeutics GmbH
Sponsor organisation address	Robert-Rössle-Straße 10, Berlin, Germany, 13125
Public contact	Sponsor's medical expert, OMEICOS Therapeutics GmbH, +49 30948948 10, r.fischer@omeicos.com
Scientific contact	Sponsor's medical expert, OMEICOS Therapeutics GmbH, +49 30948948 10, r.fischer@omeicos.com

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	17 August 2020
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	08 April 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the efficacy of three different doses of OMT-28 administered once daily versus placebo in the maintenance of normal sinus rhythm after electrical direct current cardioversion (DCC) in patients with persistent AF treated with an appropriate anticoagulant therapy.

Protection of trial subjects:

The study aims to minimize potential risks to patients based on the proposed inclusion/exclusion criteria and safety monitoring, including use of the insertable cardiac monitor (ICM), and by establishing an internal Data Monitoring Committee (DMC) responsible for ensuring patient safety.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	19 March 2019
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	Bulgaria: 12
Country: Number of subjects enrolled	Czechia: 15
Country: Number of subjects enrolled	Hungary: 16
Country: Number of subjects enrolled	Ukraine: 93
Worldwide total number of subjects	136
EEA total number of subjects	43

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)	74

From 65 to 84 years	61
85 years and over	1

Subject disposition

Recruitment

Recruitment details:

There were 25 enrolling sites across Ukraine, Bulgaria, Hungary, and Czech Republic. Patients were screened at 21 sites. Four sites were activated but did not recruit any patients.

Pre-assignment

Screening details:

The first patient for study OMT28-C0201 was screened into the study on 19 Mar 2019 and the last patient completed the study on 08 Apr 2020. There were 167 patients screened for the study at 21 centers (3 in Bulgaria, 2 in Czech Republic, 4 in Hungary, and 12 in Ukraine).

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, Data analyst, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Participants received once-daily Placebo from Visit 3 (Day 1) to Visit 8 (Day 99 ± 3 days): 102 days

Arm type	Placebo
Investigational medicinal product name	Placebo for OMT 28
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Patients will take from Visit 3 (Day 1) to Visit 8 (Day 99 ± 3 days): 102 days

Arm title	4 mg OMT-28
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Arm description:

Participants received once-daily 4 mg OMT-28 from Visit 3 (Day 1) to Visit 8 (Day 99 ± 3 days): 102 days

Arm type	Experimental
Investigational medicinal product name	OMT-28 / 4 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Patients are taking from Visit 3 (Day 1) to Visit 8 (Day 99 ± 3 days): 102 days 4 mg OMT-28 per day

Arm title	12 mg OMT-28
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Arm description:

Participants received once-daily 12 mg OMT-28 from Visit 3 (Day 1) to Visit 8 (Day 99 ± 3 days): 102 days

Arm type	Experimental
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Investigational medicinal product name	OMT-28 / 12 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use
Dosage and administration details:	
Patients will take from Visit 3 (Day 1) to Visit 8 (Day 99 ± 3 days): 102 days 12 mg per day	
Arm title	24 mg OMT-28

Arm description:

Participants received once-daily 24 mg OMT-28 from Visit 3 (Day 1) to Visit 8 (Day 99 ± 3 days): 102 days

Arm type	Experimental
Investigational medicinal product name	24 mg OMT-28
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Patients will take from Visit 3 (Day 1) to Visit 8 (Day 99 ± 3 days): 102 days

Number of subjects in period 1^[1]	Placebo	4 mg OMT-28	12 mg OMT-28
Started	31	33	34
Completed	28	31	31
Not completed	3	2	3
Adverse event, serious fatal	1	-	-
Consent withdrawn by subject	-	-	1
Physician decision	-	-	1
Adverse event, non-fatal	1	1	-
Lost to follow-up	1	-	-
Sponsor decision	-	1	1

Number of subjects in period 1^[1]	24 mg OMT-28
Started	34
Completed	30
Not completed	4
Adverse event, serious fatal	-
Consent withdrawn by subject	1
Physician decision	1
Adverse event, non-fatal	2
Lost to follow-up	-
Sponsor decision	-

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: 4 patients were randomised but did not receive investigational treatment:

Placebo:

Reason: inclusion/exclusion criteria not met: 2:

4 mg OMT-28:

Reason: withdrawal by patient: 1

12 mg OMT-28: -

24 mg OMT-28 :

Reason: withdrawal by patient: 1

Baseline characteristics

Reporting groups

Reporting group title	Placebo
Reporting group description:	
Participants received once-daily Placebo from Visit 3 (Day 1) to Visit 8 (Day 99 ± 3 days): 102 days	
Reporting group title	4 mg OMT-28
Reporting group description:	
Participants received once-daily 4 mg OMT-28 from Visit 3 (Day 1) to Visit 8 (Day 99 ± 3 days): 102 days	
Reporting group title	12 mg OMT-28
Reporting group description:	
Participants received once-daily 12 mg OMT-28 from Visit 3 (Day 1) to Visit 8 (Day 99 ± 3 days): 102 days	
Reporting group title	24 mg OMT-28
Reporting group description:	
Participants received once-daily 24 mg OMT-28 from Visit 3 (Day 1) to Visit 8 (Day 99 ± 3 days): 102 days	

Reporting group values	Placebo	4 mg OMT-28	12 mg OMT-28
Number of subjects	31	33	34
Age categorical Units: Subjects			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age continuous Units: years			
arithmetic mean	65.0	62.6	61.3
standard deviation	± 9.14	± 8.85	± 9.59
Gender categorical Units: Subjects			
Female	11	13	12
Male	20	20	22
Race Units: Subjects			
White	31	33	34
Other	0	0	0
Ethnicity Units: Subjects			
Not Hispanic or Latino	29	33	33
Unknown	1	0	1

Hispanic or Latino	1	0	0
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Height Units: cm arithmetic mean standard deviation	174.3 ± 9.92	172.5 ± 10.77	172.6 ± 7.60
Body Weight Units: kg arithmetic mean standard deviation	89.12 ± 16.839	94.88 ± 20.731	93.02 ± 19.491
Body Mass Index Units: kg/m2 arithmetic mean standard deviation	29.11 ± 3.695	31.74 ± 5.914	31.21 ± 6.079
Left Ventricular Ejection Fraction Units: percent arithmetic mean standard deviation	57.7 ± 5.96	55.6 ± 7.65	54.9 ± 7.58
Left Atrium Size Units: mm arithmetic mean standard deviation	44.0 ± 5.27	45.5 ± 2.97	45.4 ± 4.47

Reporting group values	24 mg OMT-28	Total	
Number of subjects	34	132	
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 standard deviation	63.8 ± 10.17	-	
Gender categorical Units: Subjects			
Female	13	49	
Male	21	83	
Race Units: Subjects			
White	34	132	
Other	0	0	
Ethnicity			

Units: Subjects			
Not Hispanic or Latino	34	129	
Unknown	0	2	
Hispanic or Latino	0	1	
Height			
Units: cm			
arithmetic mean	172.4		
standard deviation	± 9.91	-	
Body Weight			
Units: kg			
arithmetic mean	92.81		
standard deviation	± 17.795	-	
Body Mass Index			
Units: kg/m ²			
arithmetic mean	31.18		
standard deviation	± 5.253	-	
Left Ventricular Ejection Fraction			
Units: percent			
arithmetic mean	56.7		
standard deviation	± 8.48	-	
Left Atrium Size			
Units: mm			
arithmetic mean	44.9		
standard deviation	± 4.95	-	

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description:	
Participants received once-daily Placebo from Visit 3 (Day 1) to Visit 8 (Day 99 ± 3 days): 102 days	
Reporting group title	4 mg OMT-28
Reporting group description:	
Participants received once-daily 4 mg OMT-28 from Visit 3 (Day 1) to Visit 8 (Day 99 ± 3 days): 102 days	
Reporting group title	12 mg OMT-28
Reporting group description:	
Participants received once-daily 12 mg OMT-28 from Visit 3 (Day 1) to Visit 8 (Day 99 ± 3 days): 102 days	
Reporting group title	24 mg OMT-28
Reporting group description:	
Participants received once-daily 24 mg OMT-28 from Visit 3 (Day 1) to Visit 8 (Day 99 ± 3 days): 102 days	

Primary: Primary endpoint: Post-DCC Daily Mean AF Burden (%)

End point title	Primary endpoint: Post-DCC Daily Mean AF Burden (%)
End point description:	
Post-DCC Daily Mean AF Burden (%), defined as individual mean of all daily AF burden values per patient recorded from the day after the first DCC up to and including the day of last dose.	
End point type	Primary
End point timeframe:	
Assessment of AF Burden was done continuously from Visit 2 (implantation of ICM device) to Last Follow-up Visit (or extrapolation of the device, when it occurred).	

End point values	Placebo	4 mg OMT-28	12 mg OMT-28	24 mg OMT-28
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	24	19	21	21
Units: percent				
median (standard deviation)	12.3 (± 39.3)	57.8 (± 41.4)	80.7 (± 44.6)	91.3 (± 45.5)

Statistical analyses

Statistical analysis title	OMT-28 4 mg vs. Placebo
Comparison groups	Placebo v 4 mg OMT-28

Number of subjects included in analysis	43
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Median difference (final values)
Point estimate	11.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.0294
upper limit	55

Statistical analysis title	OMT-28 12 mg vs. Placebo
Comparison groups	Placebo v 12 mg OMT-28
Number of subjects included in analysis	45
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Median difference (final values)
Point estimate	3.33
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.578
upper limit	71.1

Statistical analysis title	OMT-28 24 mg vs. Placebo
Comparison groups	Placebo v 24 mg OMT-28
Number of subjects included in analysis	45
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Median difference (final values)
Point estimate	14.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.00662
upper limit	79.2

Secondary: Secondary Endpoint: Recurrence of Persistent AF (Yes/No)

End point title	Secondary Endpoint: Recurrence of Persistent AF (Yes/No)
End point description:	
Recurrence of Persistent AF (Yes/No), defined as at least 1 instance of persistent AF from the day after the first DCC up to and including the day of the last dose.	
End point type	Secondary

End point timeframe:

The DMC met 4 times, ie, when 10%, 25%, 50%, and 75% of patients completed the 3-month treatment phase, and reviewed the data in an unblinded manner.

End point values	Placebo	4 mg OMT-28	12 mg OMT-28	24 mg OMT-28
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	24	19	21	21
Units: subjects				
Yes	9	12	11	13
No	15	7	10	8

Statistical analyses

No statistical analyses for this end point

Secondary: Secondary endpoint: Recurrence Rate (RecR) of Persistent AF (%)

End point title	Secondary endpoint: Recurrence Rate (RecR) of Persistent AF (%)
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End point description:

Recurrence Rate (RecR) of Persistent AF (%), defined as percentage of patients with recurrence of persistent AF

End point type	Secondary
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End point timeframe:

The DMC met 4 times, ie, when 10%, 25%, 50%, and 75% of patients completed the 3-month treatment phase, and reviewed the data in an unblinded manner.

End point values	Placebo	4 mg OMT-28	12 mg OMT-28	24 mg OMT-28
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	24	19	21	21
Units: percent				
number (not applicable)				
Yes	37.5	63.2	52.4	61.9
No	62.5	36.8	47.6	38.1

Statistical analyses

No statistical analyses for this end point

Secondary: Secondary endpoint: Time to Recurrence (TTR) of Persistent AF (days)

End point title	Secondary endpoint: Time to Recurrence (TTR) of Persistent AF (days)
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End point description:

Time to Recurrence (TTR) of Persistent AF (days), defined as time from successful DCC on Visit 4 to the first recurrence of persistent AF.

End point type	Secondary
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End point timeframe:

The DMC met 4 times, ie, when 10%, 25%, 50%, and 75% of patients completed the 3-month treatment phase, and reviewed the data in an unblinded manner.

End point values	Placebo	4 mg OMT-28	12 mg OMT-28	24 mg OMT-28
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	24	19	21	21
Units: day				
median (confidence interval 95%)				
days	88.5 (36.0 to 91.0)	37.0 (8.00 to 91.0)	55.0 (14.0 to 89.0)	15.0 (4.00 to 91.0)

Statistical analyses

No statistical analyses for this end point

Secondary: Secondary pharmacokinetic (PK) endpoints: Plasma concentration of OMT-28 and its metabolites

End point title	Secondary pharmacokinetic (PK) endpoints: Plasma concentration of OMT-28 and its metabolites ^[1]
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End point description:

Plasma concentration of OMT-28 (at each timepoint; Visit 3 to Visit 9) and its metabolites (specific timepoints; Visit 3 and Visit 6, 1 to 2 hours post-dose).

Next to OMT-28, plasma concentration of metabolites were measured at the same time points, but these results are not reported here.

End point type	Secondary
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End point timeframe:

Visits 3 to 8 trough levels (pre-dose), Visit 3 (first dose) and Visit 6 (steady state) within 15-45 minutes, 1-2 hours, and 2.5-8 hours post-dose. Visit 9 (Follow-up).

Notes:

[1] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Placebo arm not reported for PK data

End point values	4 mg OMT-28	12 mg OMT-28	24 mg OMT-28	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	33	34	34	
Units: ng/ml				
arithmetic mean (standard deviation)				
Visit 3 (post-dose, 1-2 h)	283 (± 153)	930 (± 492)	2020 (± 886)	
Visit 4	319 (± 299)	672 (± 443)	1590 (± 1230)	
Visit 5	274 (± 160)	869 (± 566)	1700 (± 1030)	
Visit 6	332 (± 177)	1020 (± 726)	2190 (± 1390)	
Visit 6 (post-dose, 1-2 h)	561 (± 255)	1770 (± 771)	4180 (± 2020)	

Visit 7	319 (± 205)	768 (± 511)	1860 (± 1280)	
Visit 8	293 (± 172)	791 (± 665)	2150 (± 1360)	
Visit 9	9.60 (± 24.2)	76.2 (± 309)	154 (± 634)	

Statistical analyses

No statistical analyses for this end point

Secondary: Secondary pharmacokinetic (PK) endpoints: Plasma concentration of OMT-28 and its metabolites - Population Pharmacokinetic Analysis of Exposure (AUC)

End point title	Secondary pharmacokinetic (PK) endpoints: Plasma concentration of OMT-28 and its metabolites - Population Pharmacokinetic Analysis of Exposure (AUC) ^[2]
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End point description:

Briefly, a 2-compartmental popPK model with first-order absorption and lag time was successfully developed. The OMT-28 exposure after oral dosing was characterized by a moderately fast but variable absorption, followed by a clear 2-compartmental curvature and slow accumulation of concentrations.

End point type	Secondary
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End point timeframe:

Visits 3 to 8 trough levels (pre-dose), Visit 3 (first dose) and Visit 6 (steady state) within 15-45 minutes, 1-2 hours, and 2.5-8 hours post-dose. Visit 9 (Follow-up).

Notes:

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Placebo arm not reported for PK data

End point values	4 mg OMT-28	12 mg OMT-28	24 mg OMT-28	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	33	34	34	
Units: mg*h/L				
number (not applicable)				
AUC	9.11	28.6	64	

Statistical analyses

No statistical analyses for this end point

Secondary: Secondary pharmacokinetic (PK) endpoints: Plasma concentration of OMT-28 and its metabolites - Population Pharmacokinetic Analysis of Exposure (Cmax)

End point title	Secondary pharmacokinetic (PK) endpoints: Plasma concentration of OMT-28 and its metabolites - Population Pharmacokinetic Analysis of Exposure (Cmax) ^[3]
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End point description:

Briefly, a 2-compartmental popPK model with first-order absorption and lag time was successfully developed. The OMT-28 exposure after oral dosing was characterized by a moderately fast but variable absorption, followed by a clear 2-compartmental curvature and slow accumulation of concentrations.

End point type	Secondary
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End point timeframe:

Visits 3 to 8 trough levels (pre-dose), Visit 3 (first dose) and Visit 6 (steady state) within 15-45 minutes, 1-2 hours, and 2.5-8 hours post-dose. Visit 9 (Follow-up).

Notes:

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Placebo arm not reported for PK data

End point values	4 mg OMT-28	12 mg OMT-28	24 mg OMT-28	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	33	34	34	
Units: ng/mL				
number (not applicable)				
Cmax	558	1770	3898	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Day 1 Visit 3, Day 8 (± 3 days) Visit 4, Day 15 (± 3 days) Visit 5, Day 43 (± 3 days) Visit 6, Day 71 (± 3 days) Visit 7, Day 99 (± 3 days) Visit 8, Follow-up/ ET (28 ± 3 days after last dose of study drug) Visit 9

Adverse event reporting additional description:

All clinical AEs occurring after the patient signed the ICF and up to 30 days after the last dose of study medication, whether observed by the Investigator or reported by the patient, were recorded on the AE eCRF page.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
Dictionary version	21.1

Reporting groups

Reporting group title	Placebo
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Reporting group description:

Participants received once-daily Placebo from Visit 3 (Day 1) to Visit 8 (Day 99 ± 3 days): 102 days

Reporting group title	4 mg OMT-28
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Reporting group description:

Participants received once-daily 4 mg OMT-28 from Visit 3 (Day 1) to Visit 8 (Day 99 ± 3 days): 102 days

Reporting group title	12 mg OMT-28
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Reporting group description:

Participants received once-daily 12 mg OMT-28 from Visit 3 (Day 1) to Visit 8 (Day 99 ± 3 days): 102 days

Reporting group title	24 mg OMT-28
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Reporting group description:

Participants received once-daily 24 mg OMT-28 from Visit 3 (Day 1) to Visit 8 (Day 99 ± 3 days): 102 days

Serious adverse events	Placebo	4 mg OMT-28	12 mg OMT-28
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 31 (9.68%)	0 / 33 (0.00%)	4 / 34 (11.76%)
number of deaths (all causes)	1	0	0
number of deaths resulting from adverse events	0	0	0
Cardiac disorders			
Hypertension			
subjects affected / exposed	1 / 31 (3.23%)	0 / 33 (0.00%)	1 / 34 (2.94%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure			

subjects affected / exposed	0 / 31 (0.00%)	0 / 33 (0.00%)	2 / 34 (5.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure chronic			
subjects affected / exposed	0 / 31 (0.00%)	0 / 33 (0.00%)	1 / 34 (2.94%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sinus arrest			
subjects affected / exposed	0 / 31 (0.00%)	0 / 33 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anemia			
subjects affected / exposed	1 / 31 (3.23%)	0 / 33 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemorrhagic stroke			
subjects affected / exposed	1 / 31 (3.23%)	0 / 33 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial fibrillation			
subjects affected / exposed	0 / 31 (0.00%)	0 / 33 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Colorectal adenocarcinoma			
subjects affected / exposed	1 / 31 (3.23%)	0 / 33 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Upper respiratory tract infection			
subjects affected / exposed	1 / 31 (3.23%)	0 / 33 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Pneumonia			
subjects affected / exposed	1 / 31 (3.23%)	0 / 33 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Liver injury			
subjects affected / exposed	0 / 31 (0.00%)	0 / 33 (0.00%)	1 / 34 (2.94%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	24 mg OMT-28		
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 34 (5.88%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Cardiac disorders			
Hypertension			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac failure			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac failure chronic			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Sinus arrest			
subjects affected / exposed	1 / 34 (2.94%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Anemia			

subjects affected / exposed	0 / 34 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Haemorrhagic stroke			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Atrial fibrillation			
subjects affected / exposed	1 / 34 (2.94%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Colorectal adenocarcinoma			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Upper respiratory tract infection			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pneumonia			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Liver injury			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 1.5 %

Non-serious adverse events	Placebo	4 mg OMT-28	12 mg OMT-28
Total subjects affected by non-serious adverse events subjects affected / exposed	2 / 31 (6.45%)	5 / 33 (15.15%)	8 / 34 (23.53%)
Investigations			
Blood uric acid increased subjects affected / exposed occurrences (all)	0 / 31 (0.00%) 0	2 / 33 (6.06%) 2	0 / 34 (0.00%) 0
INR increased subjects affected / exposed occurrences (all)	0 / 31 (0.00%) 0	0 / 33 (0.00%) 0	0 / 34 (0.00%) 0
Cardiac disorders			
Atrioventricular block first degree subjects affected / exposed occurrences (all)	1 / 31 (3.23%) 1	0 / 33 (0.00%) 0	3 / 34 (8.82%) 3
Bradycardia subjects affected / exposed occurrences (all)	1 / 31 (3.23%) 1	0 / 33 (0.00%) 0	2 / 34 (5.88%) 2
Tachycardia subjects affected / exposed occurrences (all)	0 / 31 (0.00%) 0	0 / 33 (0.00%) 0	0 / 34 (0.00%) 0
Gastrointestinal disorders			
Diarrhoea subjects affected / exposed occurrences (all)	0 / 31 (0.00%) 0	0 / 33 (0.00%) 0	0 / 34 (0.00%) 0
Infections and infestations			
Nasopharyngitis subjects affected / exposed occurrences (all)	0 / 31 (0.00%) 0	0 / 33 (0.00%) 0	2 / 34 (5.88%) 2
Metabolism and nutrition disorders			
Hyperkalaemia subjects affected / exposed occurrences (all)	0 / 31 (0.00%) 0	1 / 33 (3.03%) 1	1 / 34 (2.94%) 1
Glucose tolerance impaired subjects affected / exposed occurrences (all)	0 / 31 (0.00%) 0	2 / 33 (6.06%) 2	1 / 34 (2.94%) 1

Non-serious adverse events	24 mg OMT-28		
Total subjects affected by non-serious adverse events			

subjects affected / exposed	12 / 34 (35.29%)		
Investigations			
Blood uric acid increased			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences (all)	0		
INR increased			
subjects affected / exposed	2 / 34 (5.88%)		
occurrences (all)	2		
Cardiac disorders			
Atrioventricular block first degree			
subjects affected / exposed	1 / 34 (2.94%)		
occurrences (all)	1		
Bradycardia			
subjects affected / exposed	2 / 34 (5.88%)		
occurrences (all)	2		
Tachycardia			
subjects affected / exposed	2 / 34 (5.88%)		
occurrences (all)	2		
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	2 / 34 (5.88%)		
occurrences (all)	2		
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	2 / 34 (5.88%)		
occurrences (all)	2		
Metabolism and nutrition disorders			
Hyperkalaemia			
subjects affected / exposed	3 / 34 (8.82%)		
occurrences (all)	3		
Glucose tolerance impaired			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences (all)	0		

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