



Clinical trial results:

Phase III Study Evaluating the Efficacy and Safety of Olmesartan Medoxomil/Hydrochlorothiazide 40/12.5 mg Combination Therapy versus Olmesartan Medoxomil 40 mg Monotherapy in Patients with Essential Hypertension

Summary

EudraCT number	2006-005556-32
Trial protocol	DK DE CZ IT
Global end of trial date	28 May 2008

Results information

Result version number	v1 (current)
This version publication date	15 November 2018
First version publication date	15 November 2018

Trial information

Trial identification

Sponsor protocol code	CS866CM-B-E303
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Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Menarini Ricerche S.p.A.
Sponsor organisation address	Via Sette Santi, 1, Florence, Italy, 50131
Public contact	Corporate Clinical Sciences, Menarini Ricerche S.p.A., +39 05556809990, acapriati@menarini-ricerche.it
Scientific contact	Corporate Clinical Sciences, Menarini Ricerche S.p.A., +39 05556809990, acapriati@menarini-ricerche.it

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	28 May 2008
Is this the analysis of the primary completion data?	Yes
Primary completion date	28 May 2008
Global end of trial reached?	Yes
Global end of trial date	28 May 2008
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the anti-hypertensive effect of Olmesartan Medoxomil/Hydrochlorothiazide (OM/HCTZ) 40/12.5 mg combination therapy compared to Olmesartan Medoxomil (OM) 40 mg monotherapy in lowering sitting diastolic blood pressure (DBP) in hypertensive patients after 8 weeks of double-blind treatment (from baseline to the end of the first double-blind treatment phase of the study).

Protection of trial subjects:

If any event(s) related to the conduct of the study or the development of the IMP which affected the safety of the study participants, the sponsor and the investigator were to take appropriate urgent safety measures to protect the patients against any immediate hazard. The CAs and IRB/ECs were to be informed forthwith about these new events and the measures taken.

For patients participating in the study, Menarini Ricerche S.p.A. had stipulated an insurance policy in accordance with local regulatory requirements.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	03 July 2007
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	Poland: 152
Country: Number of subjects enrolled	Czech Republic: 161
Country: Number of subjects enrolled	Denmark: 62
Country: Number of subjects enrolled	Germany: 137
Country: Number of subjects enrolled	Italy: 76
Country: Number of subjects enrolled	Romania: 145
Country: Number of subjects enrolled	Israel: 53
Country: Number of subjects enrolled	Croatia: 60
Worldwide total number of subjects	846
EEA total number of subjects	793

Notes:

Subjects enrolled per age group

In utero	0
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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)	665
From 65 to 84 years	181
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Patients were to be screened for eligibility. Eligible patients were entered into a two-phase pre-randomisation period consisting of

- a) 2 weeks for tapering off the current anti-hypertension treatment and a
- b) 2 weeks single-blinded placebo run-in phase.

Period 1

Period 1 title	Phase A
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	OM 40 mg

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Olmesartan Medoxomil
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Tablet containing 40 mg Olmesartan, once daily for 8 weeks

Arm title	OM/HCTZ 40/12.5 mg
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Arm description: -

Arm type	Experimental
Investigational medicinal product name	Olmesartan Medoxomil/Hydrochlorothiazide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Tablet containing 40 mg Olmesartan Medoxomil and 12.5 mg Hydrochlorothiazide, once daily for 8 weeks

Number of subjects in period 1^[1]	OM 40 mg	OM/HCTZ 40/12.5 mg
Started	282	556
Completed	268	523
Not completed	14	33
BP out of specifications	2	-

Consent withdrawn by subject	7	18
unk	2	6
Adverse event, non-fatal	2	9
Lost to follow-up	1	-

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: Reported data are from ITT population. Eight patients were randomized and but did not provide efficacy data and are therefore not considered in the baseline number.

Period 2

Period 2 title	Phase B
Is this the baseline period?	No
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	OM 40 mg responders

Arm description:

Patients that received 40 mg OM in Phase A and responded to treatment

Arm type	Experimental
Investigational medicinal product name	Olmesartan Medoxomil
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Tablet containing 40 mg Olmesartan, once daily for 8 weeks

Arm title	OM 40 mg non-responders
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Arm description:

Patients that received 40 mg OM in Phase A and did not respond to treatment

Arm type	Experimental
Investigational medicinal product name	Olmesartan Medoxomil/Hydrochlorothiazide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Tablet containing 40 mg Olmesartan Medoxomil and 12.5 mg Hydrochlorothiazide, once daily for 8 weeks

Arm title	OM/HCTZ 40/12.5 mg responders
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Arm description:

Patients that received OM/HCTZ 40/12.5 mg in Phase A and responded to treatment

Arm type	Experimental
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Investigational medicinal product name	Olmesartan Medoxomil/Hydrochlorothiazide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Tablet containing 40 mg Olmesartan Medoxomil and 12.5 mg Hydrochlorothiazide, once daily for 8 weeks

Arm title	OM/HCTZ 40/12.5 mg non responders
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Arm description:

Patients that received OM/HCTZ 40/12.5 mg in Phase A and did not respond to treatment

Arm type	Experimental
Investigational medicinal product name	OM/HCTZ 40/25 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Tablet containing 40 mg olmesartan medoxomil and 25 mg hydrochlorothiazide, once daily for 8 weeks

Number of subjects in period 2	OM 40 mg responders	OM 40 mg non-responders	OM/HCTZ 40/12.5 mg responders
Started	129	139	336
Completed	128	137	333
Not completed	1	2	3
Consent withdrawn by subject	-	2	-
unk	-	-	1
Adverse event, non-fatal	1	-	1
Lost to follow-up	-	-	1

Number of subjects in period 2	OM/HCTZ 40/12.5 mg non responders
Started	187
Completed	186
Not completed	1
Consent withdrawn by subject	1
unk	-
Adverse event, non-fatal	-
Lost to follow-up	-

Baseline characteristics

Reporting groups

Reporting group title	OM 40 mg
Reporting group description: -	
Reporting group title	OM/HCTZ 40/12.5 mg
Reporting group description: -	

Reporting group values	OM 40 mg	OM/HCTZ 40/12.5 mg	Total
Number of subjects	282	556	838
Age categorical			
Units: Subjects			
18 years or older	282	556	838
Age continuous			
Units: years			
arithmetic mean	56.0	55.4	
standard deviation	± 11.5	± 10.6	-
Gender categorical			
Units: Subjects			
Female	127	264	391
Male	155	292	447
Smoking habits			
Units: Subjects			
Smoker	45	119	164
Non-smoker	186	334	520
Ex-smoker	51	103	154
Alcohol consumption			
Units: Subjects			
None	91	186	277
Sporadic	174	333	507
Regular	17	37	54
Trough sitting dBp			
sitting diastolic blood pressure at baseline			
Units: mmHG			
arithmetic mean	104.5	104.6	
standard deviation	± 4.0	± 4.2	-
Trough sitting sBP			
Sitting systolic blood pressure			
Units: mmHg			
arithmetic mean	168.0	168.5	
standard deviation	± 7.7	± 8.4	-
BMI			
Body Mass Index			
Units: kg/m²			
arithmetic mean	29.67	29.18	
standard deviation	± 4.8	± 4.7	-

End points

End points reporting groups

Reporting group title	OM 40 mg
Reporting group description: -	
Reporting group title	OM/HCTZ 40/12.5 mg
Reporting group description: -	
Reporting group title	OM 40 mg responders
Reporting group description:	
Patients that received 40 mg OM in Phase A and responded to treatment	
Reporting group title	OM 40 mg non-responders
Reporting group description:	
Patients that received 40 mg OM in Phase A and did not respond to treatment	
Reporting group title	OM/HCTZ 40/12.5 mg responders
Reporting group description:	
Patients that received OM/HCTZ 40/12.5 mg in Phase A and responded to treatment	
Reporting group title	OM/HCTZ 40/12.5 mg non responders
Reporting group description:	
Patients that received OM/HCTZ 40/12.5 mg in Phase A and did not respond to treatment	

Primary: dBP change after 8 weeks Phase A

End point title	dBP change after 8 weeks Phase A
End point description:	
Reduction in Mean Trough Sitting dBP (mmHg) from Baseline (Week 0) to Week 8	
End point type	Primary
End point timeframe:	
Eight weeks	

End point values	OM 40 mg	OM/HCTZ 40/12.5 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	282	556		
Units: mmHG				
arithmetic mean (standard deviation)	-15.8 (± 9.71)	-18.9 (± 9.32)		

Statistical analyses

Statistical analysis title	dBP change after 8 weeks (Phase A)
Comparison groups	OM 40 mg v OM/HCTZ 40/12.5 mg

Number of subjects included in analysis	838
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	ANCOVA

Primary: sBP change after 8 weeks Phase A

End point title	sBP change after 8 weeks Phase A
End point description:	Reduction in Mean Trough Sitting sBP (mmHg) from Baseline (Week 0) to Week 8
End point type	Primary
End point timeframe:	Eight weeks

End point values	OM 40 mg	OM/HCTZ 40/12.5 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	282	556		
Units: mmHg				
arithmetic mean (standard deviation)	-26.5 (± 14.56)	-31.9 (± 14.76)		

Statistical analyses

Statistical analysis title	sBP change after 8 weeks (Phase A)
Comparison groups	OM 40 mg v OM/HCTZ 40/12.5 mg
Number of subjects included in analysis	838
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	ANCOVA

Secondary: dBP change after 8 weeks Phase B

End point title	dBP change after 8 weeks Phase B
End point description:	Reduction in trough sitting diastolic blood pressure after 8 weeks of additional treatment, depending on Phase A treatment and outcome (responder/non-responder).
End point type	Secondary
End point timeframe:	Eight weeks

End point values	OM 40 mg responders	OM 40 mg non-responders	OM/HCTZ 40/12.5 mg responders	OM/HCTZ 40/12.5 mg non responders
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	129	139	336	187
Units: mmHg				
arithmetic mean (standard deviation)	-0.5 (± 6.95)	-9.3 (± 7.91)	-0.3 (± 6.68)	-8.0 (± 8.56)

Statistical analyses

Statistical analysis title	dBp change after 8 weeks (Phase B)
Comparison groups	OM 40 mg responders v OM 40 mg non-responders v OM/HCTZ 40/12.5 mg responders v OM/HCTZ 40/12.5 mg non responders
Number of subjects included in analysis	791
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	ANCOVA

Secondary: sBP change after 8 weeks Phase B

End point title	sBP change after 8 weeks Phase B
End point description:	Reduction in trough sitting systolic blood pressure after 8 weeks of additional treatment, depending on Phase A treatment and outcome (responder/non-responder).
End point type	Secondary
End point timeframe:	
Eight weeks	

End point values	OM 40 mg responders	OM 40 mg non-responders	OM/HCTZ 40/12.5 mg responders	OM/HCTZ 40/12.5 mg non responders
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	129	139	336	187
Units: mmHg				
arithmetic mean (standard deviation)	-0.5 (± 6.95)	-12.4 (± 11.64)	-0.4 (± 9.32)	-12.1 (± 12.69)

Statistical analyses

Statistical analysis title	sBP change after 8 weeks (Phase B)
Comparison groups	OM 40 mg responders v OM 40 mg non-responders v OM/HCTZ 40/12.5 mg responders v OM/HCTZ 40/12.5 mg non responders
Number of subjects included in analysis	791
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	ANCOVA

Adverse events

Adverse events information

Timeframe for reporting adverse events:

from first double-blinded study dose (start of Phase A) to EOS visit (end of Phase B)

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	11
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Reporting groups

Reporting group title	Phase B OM/HCTZ 40/12.5 mg non-responders
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Reporting group description: -

Reporting group title	Phase B OM/HCTZ 40/12.5 mg responders
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Reporting group description: -

Reporting group title	Phase B OM 40 mg non-responders
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Reporting group description: -

Reporting group title	Phase B OM 40 mg responders
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Reporting group description: -

Reporting group title	Phase A OM/HCTZ 40/12.5 mg
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Reporting group description: -

Reporting group title	Phase A OM 40 mg
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Reporting group description: -

Serious adverse events	Phase B OM/HCTZ 40/12.5 mg non- responders	Phase B OM/HCTZ 40/12.5 mg responders	Phase B OM 40 mg non-responders
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 188 (0.53%)	3 / 336 (0.89%)	0 / 139 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Uterine leiomyoma			
subjects affected / exposed	0 / 188 (0.00%)	0 / 336 (0.00%)	0 / 139 (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
Duodenal ulcer			
subjects affected / exposed	0 / 188 (0.00%)	0 / 336 (0.00%)	0 / 139 (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
Injury, poisoning and procedural complications			

Anal fissure	Additional description: worsening and surgery		
subjects affected / exposed	1 / 188 (0.53%)	0 / 336 (0.00%)	0 / 139 (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
Humerus fracture			
subjects affected / exposed	0 / 188 (0.00%)	1 / 336 (0.30%)	0 / 139 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper limb fracture			
subjects affected / exposed	0 / 188 (0.00%)	1 / 336 (0.30%)	0 / 139 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Atrial flutter			
subjects affected / exposed	0 / 188 (0.00%)	0 / 336 (0.00%)	0 / 139 (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
Nervous system disorders			
Ischaemic cerebral infarction			
subjects affected / exposed	0 / 188 (0.00%)	0 / 336 (0.00%)	0 / 139 (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
Syncope			
subjects affected / exposed	0 / 188 (0.00%)	0 / 336 (0.00%)	0 / 139 (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
Brain contusion			
subjects affected / exposed	0 / 188 (0.00%)	1 / 336 (0.30%)	0 / 139 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Gastritis			

subjects affected / exposed	0 / 188 (0.00%)	0 / 336 (0.00%)	0 / 139 (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
Small intestinal obstruction			
subjects affected / exposed	0 / 188 (0.00%)	0 / 336 (0.00%)	0 / 139 (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
Vomiting			
subjects affected / exposed	0 / 188 (0.00%)	0 / 336 (0.00%)	0 / 139 (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
Incontinence			
subjects affected / exposed	0 / 188 (0.00%)	0 / 336 (0.00%)	0 / 139 (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
Palpitations			
subjects affected / exposed	0 / 188 (0.00%)	1 / 336 (0.30%)	0 / 139 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chest pain			
subjects affected / exposed	0 / 188 (0.00%)	1 / 336 (0.30%)	0 / 139 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Osteoarthritis			
subjects affected / exposed	0 / 188 (0.00%)	0 / 336 (0.00%)	0 / 139 (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
Infections and infestations			
Diverticulitis			
subjects affected / exposed	0 / 188 (0.00%)	0 / 336 (0.00%)	0 / 139 (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

Pneumonia viral			
subjects affected / exposed	0 / 188 (0.00%)	0 / 336 (0.00%)	0 / 139 (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
Parotid abscess			
subjects affected / exposed	0 / 188 (0.00%)	0 / 336 (0.00%)	0 / 139 (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
Erysipeloid	Additional description: Erysipel B / Erysipel Crus Left		
subjects affected / exposed	0 / 188 (0.00%)	0 / 336 (0.00%)	0 / 139 (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

Serious adverse events	Phase B OM 40 mg responders	Phase A OM/HCTZ 40/12.5 mg	Phase A OM 40 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 129 (1.55%)	4 / 561 (0.71%)	5 / 285 (1.75%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Uterine leiomyoma			
subjects affected / exposed	0 / 129 (0.00%)	1 / 561 (0.18%)	0 / 285 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Duodenal ulcer			
subjects affected / exposed	0 / 129 (0.00%)	0 / 561 (0.00%)	1 / 285 (0.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Anal fissure	Additional description: worsening and surgery		
subjects affected / exposed	0 / 129 (0.00%)	0 / 561 (0.00%)	0 / 285 (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
Humerus fracture			

subjects affected / exposed	0 / 129 (0.00%)	0 / 561 (0.00%)	0 / 285 (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
Upper limb fracture			
subjects affected / exposed	0 / 129 (0.00%)	0 / 561 (0.00%)	0 / 285 (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
Cardiac disorders			
Atrial flutter			
subjects affected / exposed	0 / 129 (0.00%)	0 / 561 (0.00%)	1 / 285 (0.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Ischaemic cerebral infarction			
subjects affected / exposed	0 / 129 (0.00%)	1 / 561 (0.18%)	0 / 285 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	0 / 129 (0.00%)	0 / 561 (0.00%)	1 / 285 (0.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Brain contusion			
subjects affected / exposed	0 / 129 (0.00%)	0 / 561 (0.00%)	0 / 285 (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			
Gastritis			
subjects affected / exposed	0 / 129 (0.00%)	1 / 561 (0.18%)	0 / 285 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Small intestinal obstruction			
subjects affected / exposed	0 / 129 (0.00%)	0 / 561 (0.00%)	1 / 285 (0.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Vomiting			
subjects affected / exposed	0 / 129 (0.00%)	0 / 561 (0.00%)	1 / 285 (0.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Incontinence			
subjects affected / exposed	0 / 129 (0.00%)	0 / 561 (0.00%)	1 / 285 (0.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Palpitations			
subjects affected / exposed	0 / 129 (0.00%)	0 / 561 (0.00%)	0 / 285 (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
Chest pain			
subjects affected / exposed	0 / 129 (0.00%)	0 / 561 (0.00%)	0 / 285 (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
Musculoskeletal and connective tissue disorders			
Osteoarthritis			
subjects affected / exposed	1 / 129 (0.78%)	0 / 561 (0.00%)	0 / 285 (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
Infections and infestations			
Diverticulitis			
subjects affected / exposed	0 / 129 (0.00%)	1 / 561 (0.18%)	0 / 285 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia viral			
subjects affected / exposed	0 / 129 (0.00%)	0 / 561 (0.00%)	1 / 285 (0.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Parotid abscess			
subjects affected / exposed	0 / 129 (0.00%)	0 / 561 (0.00%)	1 / 285 (0.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Erysipeloid	Additional description: Erysipel B / Erysipel Crus Left		
subjects affected / exposed	1 / 129 (0.78%)	0 / 561 (0.00%)	0 / 285 (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

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

Non-serious adverse events	Phase B OM/HCTZ 40/12.5 mg non- responders	Phase B OM/HCTZ 40/12.5 mg responders	Phase B OM 40 mg non-responders
Total subjects affected by non-serious adverse events			
subjects affected / exposed	24 / 188 (12.77%)	38 / 336 (11.31%)	21 / 139 (15.11%)
Vascular disorders			
Hypertension			
subjects affected / exposed	2 / 188 (1.06%)	2 / 336 (0.60%)	0 / 139 (0.00%)
occurrences (all)	2	2	0
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 188 (0.00%)	0 / 336 (0.00%)	0 / 139 (0.00%)
occurrences (all)	0	0	0
Headache			
subjects affected / exposed	1 / 188 (0.53%)	2 / 336 (0.60%)	2 / 139 (1.44%)
occurrences (all)	1	2	2
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	0 / 188 (0.00%)	1 / 336 (0.30%)	0 / 139 (0.00%)
occurrences (all)	0	1	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 188 (0.00%)	0 / 336 (0.00%)	0 / 139 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	2 / 188 (1.06%)	1 / 336 (0.30%)	0 / 139 (0.00%)
occurrences (all)	2	1	0
Infections and infestations			

Bronchitis subjects affected / exposed occurrences (all)	2 / 188 (1.06%) 2	2 / 336 (0.60%) 2	0 / 139 (0.00%) 0
Nasopharyngitis subjects affected / exposed occurrences (all)	0 / 188 (0.00%) 0	2 / 336 (0.60%) 2	2 / 139 (1.44%) 2
Metabolism and nutrition disorders			
Hypercholesterolaemia subjects affected / exposed occurrences (all)	2 / 188 (1.06%) 2	2 / 336 (0.60%) 2	1 / 139 (0.72%) 1
Hypertriglyceridaemia subjects affected / exposed occurrences (all)	0 / 188 (0.00%) 0	4 / 336 (1.19%) 4	1 / 139 (0.72%) 1

Non-serious adverse events	Phase B OM 40 mg responders	Phase A OM/HCTZ 40/12.5 mg	Phase A OM 40 mg
Total subjects affected by non-serious adverse events subjects affected / exposed	22 / 129 (17.05%)	41 / 561 (7.31%)	42 / 285 (14.74%)
Vascular disorders			
Hypertension subjects affected / exposed occurrences (all)	0 / 129 (0.00%) 0	0 / 561 (0.00%) 0	0 / 285 (0.00%) 0
Nervous system disorders			
Dizziness subjects affected / exposed occurrences (all)	0 / 129 (0.00%) 0	10 / 561 (1.78%) 10	0 / 285 (0.00%) 0
Headache subjects affected / exposed occurrences (all)	1 / 129 (0.78%) 1	9 / 561 (1.60%) 9	6 / 285 (2.11%) 6
Gastrointestinal disorders			
Abdominal pain upper subjects affected / exposed occurrences (all)	2 / 129 (1.55%) 2	0 / 561 (0.00%) 0	0 / 285 (0.00%) 0
Respiratory, thoracic and mediastinal disorders			
Cough subjects affected / exposed occurrences (all)	0 / 129 (0.00%) 0	2 / 561 (0.36%) 2	5 / 285 (1.75%) 5
Musculoskeletal and connective tissue disorders			

Arthralgia subjects affected / exposed occurrences (all)	0 / 129 (0.00%) 0	0 / 561 (0.00%) 0	0 / 285 (0.00%) 0
Infections and infestations			
Bronchitis subjects affected / exposed occurrences (all)	2 / 129 (1.55%) 2	6 / 561 (1.07%) 6	3 / 285 (1.05%) 3
Nasopharyngitis subjects affected / exposed occurrences (all)	2 / 129 (1.55%) 2	14 / 561 (2.50%) 14	5 / 285 (1.75%) 5
Metabolism and nutrition disorders			
Hypercholesterolaemia subjects affected / exposed occurrences (all)	1 / 129 (0.78%) 1	0 / 561 (0.00%) 0	0 / 285 (0.00%) 0
Hypertriglyceridaemia subjects affected / exposed occurrences (all)	0 / 129 (0.00%) 0	0 / 561 (0.00%) 0	0 / 285 (0.00%) 0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
12 October 2007	Non-substantial amendment: to detail the electronic SUSAR reporting to the EMEA and to all CAs where electronic submission was in place.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported