



## Clinical trial results:

### A Phase II, Randomized, Double-Blind, Multicenter, Comparative Study to Determine the Safety, Tolerability, Pharmacokinetics and Efficacy of Oral Nafithromycin Versus Oral Moxifloxacin in the Treatment of Community-Acquired Bacterial Pneumonia (CABP) in Adults

#### Summary

EudraCT number	2016-001246-26
Trial protocol	LV BG
Global end of trial date	08 July 2017

#### Results information

Result version number	v1 (current)
This version publication date	18 April 2019
First version publication date	18 April 2019

#### Trial information

##### Trial identification

Sponsor protocol code	W-4873-201
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##### Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02903836
WHO universal trial number (UTN)	-

Notes:

#### Sponsors

Sponsor organisation name	Wockhardt Bio AG
Sponsor organisation address	Grafenauweg 6, Zug, Switzerland, 6300
Public contact	Associate Vice President Clinical Research Europe, Wockhardt , +48 221105473, piwanowski@wockhardt.com
Scientific contact	Senior Vice President, Global Clinical Development Study Director, Wockhardt , +91 2271596830, abhatia@wockhardt.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:

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**Results analysis stage**

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Analysis stage	Final
Date of interim/final analysis	13 April 2018
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	08 July 2017
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:

- To assess the overall safety and tolerability of oral nafithromycin;
- To assess the clinical response in the Intention-to-Treat (ITT) population at Day 4;

Protection of trial subjects:

An internal, blinded Data Monitoring Committee reviewed the accumulated safety data on an ongoing basis.

Background therapy:

None

Evidence for comparator:

Moxifloxacin was selected as the optimal comparator for this Phase II CABP study, given its long history of efficacy and tolerability in this infection. The proposed dose regimen and treatment scheme (400 mg once daily for 7 days) was selected for consistency purposes worldwide as this study was planned to be conducted in different regions, such as Europe, US and South Africa.

Actual start date of recruitment	18 November 2016
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**

Country: Number of subjects enrolled	United States: 16
Country: Number of subjects enrolled	Georgia: 25
Country: Number of subjects enrolled	Romania: 15
Country: Number of subjects enrolled	Serbia: 58
Country: Number of subjects enrolled	South Africa: 60
Country: Number of subjects enrolled	Bulgaria: 41
Country: Number of subjects enrolled	Latvia: 9
Worldwide total number of subjects	224
EEA total number of subjects	65

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)	150
From 65 to 84 years	73
85 years and over	1

## Subject disposition

### Recruitment

Recruitment details:

Subjects were screened and enrolled at 36 study sites in Bulgaria, Georgia, Latvia, Romania, Serbia, South Africa, and the United States. Subjects were recruited from November 2016 to June 2017.

### Pre-assignment

Screening details:

Adult subjects ( $\geq 18$  years) with CABP were screened. Enrollment of PORT Risk Class II (PORT score 51 to 70) was capped at 50% and enrollment of subjects with allowed prior systemic antibiotic use (receipt of 1 or more dose(s) of a potentially effective systemic antibacterial treatment for treatment of the index CABP) was capped initially at 25%.

### 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, Carer, Assessor

Blinding implementation details:

Double dummy technique used to maintain the blind. Subjects in the nafithromycin arms also received placebo capsules matching moxifloxacin. Subjects in the moxifloxacin arm also received placebo tablets matching nafithromycin. Subjects in the nafithromycin 3-day treatment arm received matching placebo tablets on Days 4 through Day 7. Subjects in the nafithromycin 5-day treatment arm received matching placebo tablets on Days 6 and 7.

### Arms

Are arms mutually exclusive?	Yes
<b>Arm title</b>	Nafithromycin 3 Days

Arm description:

Nafithromycin 800 mg PO q24h for 3 days

Arm type	Experimental
Investigational medicinal product name	nafithromycin
Investigational medicinal product code	WCK 4873
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Nafithromycin 800 mg (two 400 mg tablets) PO q24h for 3 days

<b>Arm title</b>	Nafithromycin 5 Days
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Arm description:

Nafithromycin 800 mg PO q24h for 5 days

Arm type	Experimental
Investigational medicinal product name	nafithromycin
Investigational medicinal product code	WCK 4873
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Nafithromycin 800 mg (two 400 mg tablets) PO q24h for 5 days

<b>Arm title</b>	Moxifloxacin
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Arm description:

Moxifloxacin 400 mg PO q24h for 7 days

Arm type	Active comparator
Investigational medicinal product name	moxifloxacin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Moxifloxacin 400 mg (one 400 mg capsule) PO q24h for 7 days

<b>Number of subjects in period 1</b>	Nafithromycin 3 Days	Nafithromycin 5 Days	Moxifloxacin
Started	74	73	77
Completed	71	69	73
Not completed	3	4	4
Adverse event, serious fatal	-	-	1
Consent withdrawn by subject	2	4	1
Lost to follow-up	1	-	2

## Baseline characteristics

### Reporting groups

Reporting group title	Nafithromycin 3 Days
Reporting group description: Nafithromycin 800 mg PO q24h for 3 days	
Reporting group title	Nafithromycin 5 Days
Reporting group description: Nafithromycin 800 mg PO q24h for 5 days	
Reporting group title	Moxifloxacin
Reporting group description: Moxifloxacin 400 mg PO q24h for 7 days	

Reporting group values	Nafithromycin 3 Days	Nafithromycin 5 Days	Moxifloxacin
Number of subjects	74	73	77
Age categorical Units: Subjects			
Adults (18-64 years)	49	48	53
From 65-74 years	17	13	15
75 years and over	8	12	9
Age continuous Units: years			
arithmetic mean	57.0	54.9	56.1
standard deviation	± 15.73	± 16.90	± 15.18
Gender categorical Units: Subjects			
Female	37	32	35
Male	37	41	42

Reporting group values	Total		
Number of subjects	224		
Age categorical Units: Subjects			
Adults (18-64 years)	150		
From 65-74 years	45		
75 years and over	29		
Age continuous Units: years			
arithmetic mean	-		
standard deviation	-		
Gender categorical Units: Subjects			
Female	104		
Male	120		

## End points

### End points reporting groups

Reporting group title	Nafithromycin 3 Days
Reporting group description: Nafithromycin 800 mg PO q24h for 3 days	
Reporting group title	Nafithromycin 5 Days
Reporting group description: Nafithromycin 800 mg PO q24h for 5 days	
Reporting group title	Moxifloxacin
Reporting group description: Moxifloxacin 400 mg PO q24h for 7 days	

### Primary: Clinical Response in the ITT Population

End point title	Clinical Response in the ITT Population <sup>[1]</sup>
End point description:	
End point type	Primary
End point timeframe: Day 4	

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: This was an exploratory study and, therefore, was not powered for inferential statistical analyses. No comparative statistical analyses for any endpoint were performed. The 95% confidence interval for the response was obtained using the Clopper-Pearson method.

End point values	Nafithromycin 3 Days	Nafithromycin 5 Days	Moxifloxacin	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	74	73	77	
Units: Clinical Responders (%)				
arithmetic mean (confidence interval 95%)	91.9 (83.2 to 97.0)	89.0 (79.5 to 95.1)	87.0 (77.4 to 93.6)	

### Statistical analyses

No statistical analyses for this end point

### Secondary: Clinical Response in the Micro-ITT Population

End point title	Clinical Response in the Micro-ITT Population
End point description:	
End point type	Secondary
End point timeframe: Day 4	

<b>End point values</b>	Nafithromycin 3 Days	Nafithromycin 5 Days	Moxifloxacin	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	22	27	20	
Units: Clinical Responders (%)				
arithmetic mean (confidence interval 95%)	95.5 (77.2 to 99.9)	96.3 (81.0 to 99.9)	90.0 (68.3 to 98.8)	

### Statistical analyses

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No statistical analyses for this end point



## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

From signing of Informed Consent Form to Follow up Visit

Assessment type	Systematic
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### Dictionary used

Dictionary name	MedDRA
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Dictionary version	19
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### Reporting groups

Reporting group title	Nafithromycin 3 Days
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Reporting group description:

Nafithromycin 800 mg PO q24h for 3 days

Reporting group title	Nafithromycin 5 Days
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Reporting group description:

Nafithromycin 800 mg PO q24h for 5 days

Reporting group title	Moxifloxacin
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Reporting group description:

Moxifloxacin 400 mg PO q24h for 7 days

Serious adverse events	Nafithromycin 3 Days	Nafithromycin 5 Days	Moxifloxacin
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 74 (1.35%)	1 / 72 (1.39%)	2 / 76 (2.63%)
number of deaths (all causes)	0	0	1
number of deaths resulting from adverse events	0	0	1
Congenital, familial and genetic disorders			
Cor pulmonale			
subjects affected / exposed	1 / 74 (1.35%)	0 / 72 (0.00%)	0 / 76 (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
Hypertrophic cardiomyopathy			
subjects affected / exposed	1 / 74 (1.35%)	0 / 72 (0.00%)	0 / 76 (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
Nervous system disorders			
Cerebral ischaemia			
subjects affected / exposed	0 / 74 (0.00%)	1 / 72 (1.39%)	0 / 76 (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

Epilepsy			
subjects affected / exposed	0 / 74 (0.00%)	0 / 72 (0.00%)	1 / 76 (1.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ischaemic stroke			
subjects affected / exposed	0 / 74 (0.00%)	0 / 72 (0.00%)	1 / 76 (1.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	0 / 74 (0.00%)	0 / 72 (0.00%)	1 / 76 (1.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Frequency threshold for reporting non-serious adverse events: 3 %

<b>Non-serious adverse events</b>	Nafithromycin 3 Days	Nafithromycin 5 Days	Moxifloxacin
Total subjects affected by non-serious adverse events			
subjects affected / exposed	9 / 74 (12.16%)	8 / 72 (11.11%)	7 / 76 (9.21%)
Vascular disorders			
Hypertension			
subjects affected / exposed	3 / 74 (4.05%)	1 / 72 (1.39%)	2 / 76 (2.63%)
occurrences (all)	3	1	2
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	2 / 74 (2.70%)	2 / 72 (2.78%)	3 / 76 (3.95%)
occurrences (all)	2	3	3
Nausea			
subjects affected / exposed	3 / 74 (4.05%)	5 / 72 (6.94%)	2 / 76 (2.63%)
occurrences (all)	3	5	2
Vomiting			
subjects affected / exposed	3 / 74 (4.05%)	1 / 72 (1.39%)	0 / 76 (0.00%)
occurrences (all)	4	1	0

## 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

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

None
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Notes: