A Phase 3, Randomized, Double-Blind, Double-Dummy Study to Compare the Efficacy and Safety of Lefamulin (BC 3781) Versus Moxifloxacin (With or Without Adjunctive Linezolid) in Adults With Community-Acquired Bacterial Pneumonia

Published: 12-10-2015
Last updated: 19-04-2024

The Primary Objectives for the study are:* Demonstrate the non-inferiority (NI) of lefamulin versus comparator with respect to the Early Clinical Response (96 ± 24 hours after the first dose of study drug) in the Intent to Treat (ITT) Analysis Set (...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Respiratory tract infections
Study type	Interventional

Summary

ID

NL-OMON43840

Source
ToetsingOnline

Brief title
Nabriva: NAB-BC-3781-3101

Condition

- Respiratory tract infections

Synonym
A lung infection obtained in your daily life, such as at school or work

Research involving
Human

Sponsors and support

Primary sponsor: Nabriva Therapeutics AG
Source(s) of monetary or material Support: by the sponsor Nabriva

Intervention

Keyword: Community-Acquired Bacterial Pneumonia, Lefamulin, Moxifloxacin

Outcome measures

Primary outcome

The Primary Endpoints are:

* Proportion of Responders for ECR at 96 ± 24 hours following the first dose of study drug in the ITT Analysis Set (FDA)

* Proportion of subjects with an IACR of Success at TOC in the mITT and CE-TOC Analysis Sets (Primary for EMA and secondary for FDA)

Timepoint(s) of evaluation of this end points are:

- 96 ± 24 hours following the first dose of study drug

- 5-10 days post last dose - test of cure

Secondary outcome

The Secondary Endpoint is:

* Efficacy will be assessed by ECR, IACR and by Microbiological Response, 5-10 days post last dose - test of cure.

Study description

Background summary

Community-acquired bacterial pneumonia (CABP) is a commonly occurring serious infection that requires systemic antibiotic therapy and is associated with substantial morbidity, mortality, and considerable healthcare costs. In Europe, there are 44 cases of CABP for every 1000 patients treated in a single general practice.

The emergence of pathogens resistant to antimicrobials has become an increasingly complicating factor in the selection of empiric therapy for CABP. S. aureus, including methicillin-resistant S. aureus (MRSA), has emerged as an important pathogen in CABP. Optimal management for patients with CABP caused by MRSA is not yet clear, and even the best available treatment may still result in poor outcomes.Therefore, there is a need for more treatment options for CABP caused by MRSA.

Lefamulin is a potent, semi-synthetic antibacterial belonging to a novel class known as the pleuromutilins. Both the intravenous (IV) and oral dosage forms of lefamulin are under investigation in this study.

Study objective

The Primary Objectives for the study are:

* Demonstrate the non-inferiority (NI) of lefamulin versus comparator with respect to the Early Clinical Response (96 ± 24 hours after the first dose of study drug) in the Intent to Treat (ITT) Analysis Set (FDA endpoint).
*Demonstrate the NI of lefamulin versus comparator with respect to the Investigator*s Assessment of Clinical Response at Test of Cure (TOC) (i.e., 5-10 days after the last dose of study drug) in the modified-ITT (mITT) and Clinically Evaluable at TOC (CE-TOC) Analysis Sets (EMA endpoint).

Study design

A multicenter, multinational, randomized, double-blind, double-dummy, active controlled efficacy and safety study in subjects with community-acquired bacterial pneumonia (CABP) to be conducted at approximately 125 centers.

Intervention

Lefamulin IV 150 mg of lefamulin in 15 mL of 0.9% saline, to be further diluted in 10mM citrate buffered 0.9% saline
PO 600 mg of lefamulin as a yellow oval film coated immediate-release tablet
Moxifloxacin IV 400 mg of moxifloxacin in a ready-to-use latex-free flexibag
PO 400 mg of moxifloxacin as an over-encapsulated film-coated tablet
Linezolid IV 600 mg of linezolid in a ready-to-use flexible plastic (latex-free) infusion bag
PO 600 mg of linezolid as an over-encapsulated film-coated tablet

Study burden and risks

There are possible side effects and discomforts associated with the procedures and study treatment. Patients may experience some, all, or none of these effects. The possible side effects and discomforts associated with study procedures and study treatment are described in an addendum (Side effects) of the Patient Information Leaflet.

There may be side effects or discomforts from the study treatment that are not yet known.

Pregnancy Risks:
If you are pregnant or become pregnant, there may be risks to the foetus which are currenfly unknown.

Contacts

Public
Nabriva Therapeutics AG

Leberstraße 20
Wenen 1110
AT
Scientific
Nabriva Therapeutics AG

Leberstraße 20
Wenen 1110
AT

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

- Have an acute illness (7 days or less duration) with at least 3 of the following symptoms consistent with a lower respiratory tract infection (new or worsening):
* Dyspnea
* New or increased cough
* Purulent sputum production
* Chest pain due to pneumonia;- Have at least 2 of the following vital sign abnormalities:
* Fever (body temperature >38.0°C) or hypothermia (body temperature <35.0°C)
* Hypotension (systolic blood pressure <90 mmHg)
* Tachycardia (heart rate >100 beats/min)
* Tachypnea (respiratory rate >20 breaths/min);- Have at least 1 other clinical sign or laboratory finding of CABP:
* Hypoxemia
* Auscultatory and/or percussion findings consistent with pneumonia
* White blood cell count >10,000 cells/mm3 or <4500 cells/mm3 or >15% immature neutrophils (bands) regardless of total WBC count

Exclusion criteria

- Subject must not have received more than a single dose of a short-acting oral or IV antibacterial for CABP *24 hrs before randomization (for exceptions, see the study protocol).;- Subject should not require concomitant systemic antibacterial therapy potentially effective against CABP pathogens.;- Subject should not have been hospitalized for *2 days within 90 days prior to the onset of symptoms or have resided in a nursing home or long-term healthcare facility within 30 days prior to the onset of symptoms.

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	22-02-2017
Enrollment:	12
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	AVELOX
Generic name:	moxifloxacin
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	NA
Generic name:	lefamulin
Product type:	Medicine
Brand name:	Zyvox
Generic name:	Linezolid
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	12-10-2015
Application type:	First submission
Review commission:	METC Maxima Medisch Centrum (Veldhoven)
Approved WMO Date:	12-01-2016
Application type:	First submission
Review commission:	METC Maxima Medisch Centrum (Veldhoven)
Approved WMO Date:	05-04-2016
Application type:	Amendment
Review commission:	METC Maxima Medisch Centrum (Veldhoven)
Approved WMO Date:	09-05-2016
Application type:	Amendment
Review commission:	METC Maxima Medisch Centrum (Veldhoven)
Approved WMO Date:	30-05-2016
Application type:	Amendment
Review commission:	METC Maxima Medisch Centrum (Veldhoven)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR2014-005169-63-NL

Register	ID
ClinicalTrials.gov	NCT02559310
CCMO	NL54955.015.15