Efficacy and Safety of Quadruple Therapy by Bismuth Subcitrate Potassium, Metronidazole, and Tetracycline Given x 10 days With Omeprazole in Eradication of Helicobacter pylori: A Comparison to Omeprazole, Amoxicillin and Clarithromycin Given x 7 days

Published: 31-03-2008
Last updated: 07-05-2024

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

Summary

ID

NL-OMON32065

Source
ToetsingOnline

Brief title
PYLHp07-01

Condition

- Gastrointestinal infections
- Bacterial infectious disorders

Synonym

Gastric complaints, Helicobacter infection

Research involving
Human

Sponsors and support

Primary sponsor: Axcan Pharma
Source(s) of monetary or material Support: AXCAN Pharma

Intervention

Keyword: Bismuth, Helicobacter Pylori, Metronidazole, Tetracycline

Outcome measures

Primary outcome

Eradication rate, defined as two negative C-13 urea breath tests performed at 6

and 10 weeks following initiation of therapy.

Secondary outcome

1.

To compare eradication outcomes in patients with presence/past history of

peptic ulcers at baseline vs those without.

2.

To evaluate the effect of resistance of Helicobacter pylori to metronidazole

and clarithromycin on the efficacy of these treatments.

3.

To evaluate the rate of secondary resistance induced by these treatments.

4.

To assess the safety and tolerability of these therapeutic regimens with

respect to subject-reported and investigator-observed adverse events, clinical

laboratory abnormalities and plasma bismuth (Bi) concentrations.

5.

To evaluate compliance to treatment.

Study description

Background summary

In order to apply for authorization to market Pylera in European countries, there is a need to conduct a clinical trial comparing OBMT vs the recognized gold standard in Europe, OAC given for 7 days. It is hypothesized that OBMT given for 10 days will be comparable to OAC in terms of eradication rate. Therefore, a non-inferiority trial design was chosen.

In addition, the aim of this trial will be to further characterize the efficacy of OBMT vs OAC in bacteria strains identified as being resistant to metronidazole. Therefore, samples will be collected in order to compare eradication rates in sensitive vs resistant strains of bacteria.

Considering that bismuth salts are not commonly used in certain European countries, measuring bismuth plasma levels following treatment with OBMT will be required to confirm that they stay well below the toxic levels of 50 ug/L.

Study objective

The goal of this trial is to confirm that eradication rates obtained with Pylera are compatible to those obtained with the current European gols standard, OAC 7 days. This trial will constitute a pivotal trial leading eventually to approval of Pylera in European countries.

Study design

Multicenter, multinational, randomized, parallel group, active-controlled, open-label (but evaluator-blinded) non-inferiority trial.

Intervention

Patients with Helicobacter pylori positive status and upper gastro-intestinal symptoms will be randomly assigned to a 10-day course of OBMT using a single-triple capsule containing each bismuth subcitrate potassium (equivalent to Bi2O3) (B) 40 mg, metronidazole (M) 125 mg, and tetracycline (T) 125 mg given as 3 capsules qid with omeprazole (O) 20 mg bid or to a 7-day course of OAC, omeprazole 20 mg plus amoxicillin (A) 1g plus clarithromycin (C) 500 mg, all bid. Eradication will be confirmed by two negative urea breath tests, at 6

weeks and 10 weeks following treatment onset

Study burden and risks

During the study a maximum of 3 venous blood samples of 30 ml will be taken from a vein. This can cause some discomfort.

All patients will have to undergo at least 1, and maximum 2 gastroscopic assessments (in case the Helicobacter pylori was not eradicated). Transient complaints of sore throat, nausea, gagging, a discomfortable feeling or pain in the stomach may occur. Serious complications are rare; perforation occurs approximately in 1:20,000 procedures.

Risks regarding the medication: During previous North American studies with both treatments, complaints of the GI tract such as diarrhoea, indigestion, stomach ache and nausea were reported most frequent.

Contacts

Public
Axcan Pharma

597 Boul. Laurier
Mont St_Hilaire, Qc, J3H 6C4
Canada
Scientific
Axcan Pharma

597 Boul. Laurier
Mont St_Hilaire, Qc, J3H 6C4
Canada

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

-Male or non-pregnant, non-nursing female, 18 years of age and older
-Positive for Helicobacter pylori by both C-13 UBT and at least two of three positive results among rapid urease test, histologic examination and/or culture
-Presence of upper gastrointestinal symptoms

Exclusion criteria

-Previous surgery of the upper gastrointestinal tract (except appendectomy, polypectomy, or cholecystectomy)
-Any current or recent (within 1 month of screening) hematemesis, melena, or documented gastrointestinal bleeding or iron-deficiency anaemia of clinical significance
-Barrett*s esophagus or high-grade dysplasia
-Dysphagia or vomiting as major symptoms
-Previous attempt by a recognized antibiotic treatment to eradicate an adequately documented infection by Helicobacter pylori.

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL
Recruitment status: Recruitment stopped

Start date (anticipated):	11-03-2009
Enrollment:	16
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Amoxil Capsules 500 mg
Generic name:	Amoxicillin
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Klaricid 500
Generic name:	Clarithromycin
Product type:	Medicine
Brand name:	NA
Generic name:	Bismuth Subcitrate Potassium
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	NA
Generic name:	metronidazole
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	Tetracycline Hydrochloride
Generic name:	tetracycline
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	31-03-2008
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	12-01-2009

Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

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	EUCTR2007-006280-78-NL
CCMO	NL21853.078.08