Efficacy and Safety of Quadruple Therapy in Eradication of H. Pylori: A Comparison to Triple Therapy

ClinicalTrials.gov Identifier: NCT00669955

Recruitment Status : Completed
First Posted : May 1, 2008
Results First Posted : August 5, 2010
Last Update Posted : March 16, 2017

Sponsor:
Forest Laboratories

Information provided by (Responsible Party):
Forest Laboratories

Study Type:	Interventional
Study Design:	Allocation: Randomized; Intervention Model: Parallel Assignment; Masking: None (Open Label); Primary Purpose: Treatment
Condition:	Helicobacter Infections
Interventions:	Drug: Omeprazole, amoxicillin, clarithromycin Drug: Pylera (Bismuth subcitrate potassium, metronidazole, tetracycline) given in combination with omeprazole

Participant Flow

Hide Participant Flow

Recruitment Details

Key information relevant to the recruitment process for the overall study, such as dates of the recruitment period and locations
First patient in: 11 June 2008 Last patient out: 22 June 2009 Patients were recruited from clinics and hospitals located in seven European Countries: Germany, Poland, Italy, France, Ireland, Spain, United Kingdom.

Pre-Assignment Details

Significant events and approaches for the overall study following participant enrollment, but prior to group assignment
If patient was on any contraindicated medications, such as H2 antagonists, sucralfate, or proton pump inhibitors, a washout period of 2 weeks began following informed consent signature, and patient returned to the clinic to perform the endoscopy and the C-13 UBT. Presence of H. pylori needed to be confirmed by C-13 UBT and RUT at least.

Reporting Groups

	Description
Quadruple Therapy (OBMT) 10 Days	Omeprazole 20 mg BID (twice a day), and the 3 in 1 capsule, Pylera, containing Bismuth Subcitrate potassium 140 mg, metronidazole 125 mg and tetracycline 125 mg, administered as 3 capsules QID (four times day)
Triple Therapy (OAC) 7 Days	Omeprazole 20 mg BID, Amoxicillin 500 mg 2 capsules BID and Clarithromycin 500 mg 1 tablet BID

Participant Flow: Overall Study

	Quadruple Therapy (OBMT) 10 Days	**Triple Therapy (OAC) 7 Days**
STARTED	**218** [1]	**222**
COMPLETED	**204**	**195**
NOT COMPLETED	**14**	**27**
Adverse Event	**3**	**5**
Death	**0**	**1**
Withdrawal by Subject	**2**	**3**
Lost to Follow-up	**5**	**7**
Protocol Violation	**2**	**7**
Investigator Sponsor Judgement	**0**	**1**
not compliant with study drug/visit	**2**	**3**

[1] 216 patients received study drug. 2 patients were dispensed study drug but did not take it

Baseline Characteristics

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
No text entered.

Reporting Groups

	Description
Quadruple Therapy (OBMT) 10 Days	Omeprazole 20 mg BID (twice a day), and the 3 in 1 capsule, Pylera, containing Bismuth Subcitrate potassium 140 mg, metronidazole 125 mg and tetracycline 125 mg, administered as 3 capsules QID (four times day)
Triple Therapy (OAC) 7 Days	Omeprazole 20 mg BID, Amoxicillin 500 mg 2 capsules BID and Clarithromycin 500 mg 1 tablet BID
Total	Total of all reporting groups

Baseline Measures

	Quadruple Therapy (OBMT) 10 Days	Triple Therapy (OAC) 7 Days	Total
Overall Participants Analyzed [Units: Participants]	**218**	**222**	**440**
Age [Units: Participants] Count of Participants			
<=18 years	**0** 0.0%	**0** 0.0%	**0** 0.0%
Between 18 and 65 years	**184** 84.4%	**194** 87.4%	**378** 85.9%
>=65 years	**34** 15.6%	**28** 12.6%	**62** 14.1%
Age [Units: Years] Mean (Standard Deviation)	**48.53 (14.64)**	**47.95 (14.52)**	**48.24 (14.58)**
Sex: Female, Male [Units: Participants] Count of Participants			
Female	**105** 48.2%	**100** 45.0%	**205** 46.6%
Male	**113** 51.8%	**122** 55.0%	**235** 53.4%
Region of Enrollment [Units: Participants]			
Italy	**10**	**10**	**20**
Spain	**7**	**6**	**13**
France	**15**	**17**	**32**
Germany	**92**	**91**	**183**
Poland	**91**	**93**	**184**
United Kingdom	**3**	**5**	**8**

Outcome Measures

1. **Primary: Helicobacter Pylori Eradication Confirmed by Urea Breath Test [Time Frame: Week 6 and week 10 follow-up visits]**

Measure Type	Primary
Measure Title	Helicobacter Pylori Eradication Confirmed by Urea Breath Test
Measure Description	H. pylori Eradication defined as a negative C13-UBT (urea breath test) result at both Week 6 and Week 10 follow-up visits.
Time Frame	Week 6 and week 10 follow-up visits

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
No imputation method used, as this is the per protocol population, which excludes patients with missing values, or with protocol violations.

Reporting Groups

	Description
Quadruple Therapy (OBMT) 10 Days	Omeprazole 20 mg BID (twice a day), and the 3 in 1 capsule, Pylera, containing Bismuth Subcitrate potassium 140 mg, metronidazole 125 mg and tetracycline 125 mg, administered as 3 capsules QID (four times day)
Triple Therapy (OAC) 7 Days	Omeprazole 20 mg BID, Amoxicillin 500 mg 2 capsules BID and Clarithromycin 500 mg 1 tablet BID

Measured Values

	Quadruple Therapy (OBMT) 10 Days	**Triple Therapy (OAC) 7 Days**
Participants Analyzed [Units: Participants]	**178**	**161**
Helicobacter Pylori Eradication Confirmed by Urea Breath Test [Units: Participants]	**166**	**112**

No statistical analysis provided for Helicobacter Pylori Eradication Confirmed by Urea Breath Test

2. **Secondary: Number of Patients Experiencing Treatment Emergent Adverse Events. [Time Frame: at the end of treatment (day 8-14), week 6 and wek 10 follow-up visits.]**

Measure Type	Secondary
Measure Title	Number of Patients Experiencing Treatment Emergent Adverse Events.
Measure Description	A treatment-emergent adverse event is defined as an event not present prior to exposure to the study medication or any event already present that worsens in either intensity or frequency following exposure to study medication up to 30 days after study discontinuation. All safety analysis based on the safety population.
Time Frame	at the end of treatment (day 8-14), week 6 and wek 10 follow-up visits.

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Safety population, described as all randomized patients having received at least one dose of study medication

Reporting Groups

	Description
Quadruple Therapy (OBMT) 10 Days	Omeprazole 20 mg BID (twice a day), and the 3 in 1 capsule, Pylera, containing Bismuth Subcitrate potassium 140 mg, metronidazole 125 mg and tetracycline 125 mg, administered as 3 capsules QID (four times day)
Triple Therapy (OAC) 7 Days	Omeprazole 20 mg BID, Amoxicillin 500 mg 2 capsules BID and Clarithromycin 500 mg 1 tablet BID

Measured Values

	Quadruple Therapy (OBMT) 10 Days	**Triple Therapy (OAC) 7 Days**
Participants Analyzed [Units: Participants]	**216**	**222**
Number of Patients Experiencing Treatment Emergent Adverse Events. [Units: Participants]	**101**	**112**

No statistical analysis provided for Number of Patients Experiencing Treatment Emergent Adverse Events.

3. Secondary: H. Pylori Eradication and Presence or Past History of Peptic Ulcers [Time Frame: Week 6 and week 10 follow-up visits]

Measure Type	Secondary
Measure Title	H. Pylori Eradication and Presence or Past History of Peptic Ulcers

Measure Description	Eradication rates in the subset of patients with peptic ulcer (current or past history) at baseline are reported based on the per protocol population. Eradication must be confirmed at week 6 and week 10 by a negative Urea Breath Test conducted within the allocated windows.
Time Frame	Week 6 and week 10 follow-up visits

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Per protocol population.

Reporting Groups

	Description
Quadruple Therapy (OBMT) 10 Days	Omeprazole 20 mg BID (twice a day), and the 3 in 1 capsule, Pylera, containing Bismuth Subcitrate potassium 140 mg, metronidazole 125 mg and tetracycline 125 mg, administered as 3 capsules QID (four times day)
Triple Therapy (OAC) 7 Days	Omeprazole 20 mg BID, Amoxicillin 500 mg 2 capsules BID and Clarithromycin 500 mg 1 tablet BID

Measured Values

	Quadruple Therapy (OBMT) 10 Days	**Triple Therapy (OAC) 7 Days**
Participants Analyzed [Units: Participants]	**19**	**18**
H. Pylori Eradication and Presence or Past History of Peptic Ulcers [Units: Participants]	**18**	**15**

No statistical analysis provided for H. Pylori Eradication and Presence or Past History of Peptic Ulcers

4. Secondary: Clarithromycin Resistance [Time Frame: Measured at baseline]

Measure Type	Secondary
Measure Title	Clarithromycin Resistance
Measure Description	Eradication rates in subset of patients infected with a bacterial strain confirmed as resistant to clarithromycin at baseline. Resistance to clarithromycin defined as Minimum Inhibitory Concentration (MIC) of 1 ug/ml and above
Time Frame	Measured at baseline

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Per protocol analysis population

Reporting Groups

	Description
Quadruple Therapy (OBMT) 10 Days	Omeprazole 20 mg BID (twice a day), and the 3 in 1 capsule, Pylera, containing Bismuth Subcitrate potassium 140 mg, metronidazole 125 mg and tetracycline 125 mg, administered as 3 capsules QID (four times day)
Triple Therapy (OAC) 7 Days	Omeprazole 20 mg BID, Amoxicillin 500 mg 2 capsules BID and Clarithromycin 500 mg 1 tablet BID

Measured Values

	Quadruple Therapy (OBMT) 10 Days	Triple Therapy (OAC) 7 Days
Participants Analyzed [Units: Participants]	**33**	**25**
Clarithromycin Resistance [Units: Participants]	**30**	**2**

No statistical analysis provided for Clarithromycin Resistance

5. Secondary: Metronidazole Resistance [Time Frame: Measured at baseline]

Measure Type	Secondary
Measure Title	Metronidazole Resistance
Measure Description	Eradication rates in subset of patients infected with a bacterial strain confirmed as resistant to metronidazole at baseline. Resistance to metronidazole defined as Minimum Inhibitory Concentration (MIC) above 8 ug/ml
Time Frame	Measured at baseline

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Per protocol population

Reporting Groups

	Description
Quadruple Therapy (OBMT) 10 Days	

	Omeprazole 20 mg BID (twice a day), and the 3 in 1 capsule, Pylera, containing Bismuth Subcitrate potassium 140 mg, metronidazole 125 mg and tetracycline 125 mg, administered as 3 capsules QID (four times day)
Triple Therapy (OAC) 7 Days	Omeprazole 20 mg BID, Amoxicillin 500 mg 2 capsules BID and Clarithromycin 500 mg 1 tablet BID

Measured Values

	Quadruple Therapy (OBMT) 10 Days	Triple Therapy (OAC) 7 Days
Participants Analyzed [Units: Participants]	**42**	**41**
Metronidazole Resistance [Units: Participants]	**38**	**28**

No statistical analysis provided for Metronidazole Resistance

6. Secondary: Overall Compliance to Study Medications [Time Frame: At the end of the treatment phase (days 8-14)]

Measure Type	Secondary
Measure Title	Overall Compliance to Study Medications
Measure Description	Overall compliance: number of capsules dispensed - number of capsules returned/Number of prescribed capsules X 100. Percentages based on safety population
Time Frame	At the end of the treatment phase (days 8-14)

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Safety population.

Reporting Groups

	Description
Quadruple Therapy (OBMT) 10 Days	Omeprazole 20 mg BID (twice a day), and the 3 in 1 capsule, Pylera, containing Bismuth Subcitrate potassium 140 mg, metronidazole 125 mg and tetracycline 125 mg, administered as 3 capsules QID (four times day)
Triple Therapy (OAC) 7 Days	Omeprazole 20 mg BID, Amoxicillin 500 mg 2 capsules BID and Clarithromycin 500 mg 1 tablet BID

Measured Values

	Quadruple Therapy (OBMT) 10 Days	Triple Therapy (OAC) 7 Days

Participants Analyzed [Units: Participants]	**216**	**218**
Overall Compliance to Study Medications [Units: Participants] Mean (Standard Deviation)	**97.58 (10.71)**	**97.47 (14.91)**

No statistical analysis provided for Overall Compliance to Study Medications

7. Secondary: Number of Patients With Bismuth Plasma Concentrations Above the Toxic Level [Time Frame: Baseline (both arms), end of treatment (Day 11-14) and end of study (Day 70) OBMT arm only]

Measure Type	Secondary
Measure Title	Number of Patients With Bismuth Plasma Concentrations Above the Toxic Level
Measure Description	Tolerability of OBMT with respect to plasma bismuth concentrations: number of patients with bismuth concentrations above the toxic level (50 ug per liter)
Time Frame	Baseline (both arms), end of treatment (Day 11-14) and end of study (Day 70) OBMT arm only

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Plasma bismuth concentrations were analysed in the OBMT arm only. The goal was to determine whether bismuth plasma concentrations would be of 50 ug/l or above at end of treatment, or at the end of study. The results report the number of patients having reached 50 ug/l in the OBMT arm at either of these timepoints.

Reporting Groups

	Description
Quadruple Therapy (OBMT) 10 Days	Omeprazole 20 mg BID (twice a day), and the 3 in 1 capsule, Pylera, containing Bismuth Subcitrate potassium 140 mg, metronidazole 125 mg and tetracycline 125 mg, administered as 3 capsules QID (four times day)
Triple Therapy (OAC) 7 Days	Omeprazole 20 mg BID, Amoxicillin 500 mg 2 capsules BID and Clarithromycin 500 mg 1 tablet BID

Measured Values

	Quadruple Therapy (OBMT) 10 Days	**Triple Therapy (OAC) 7 Days**
Participants Analyzed [Units: Participants]	**216**	**0**
Number of Patients With Bismuth Plasma Concentrations Above the Toxic Level [Units: Participants]	**0**	

No statistical analysis provided for Number of Patients With Bismuth Plasma Concentrations Above the Toxic Level

Serious Adverse Events

Time Frame	Adverse events were recorded starting at the signing of the informed consent until the final visit (Day 70) or early withdrawal visit. Serious adverse events were followed until 30 days after the patient had stopped study participation.
Additional Description	Systematic assessment done for laboratory evaluations and bismuth plasma levels.

Reporting Groups

	Description
Quadruple Therapy (OBMT) 10 Days	Omeprazole 20 mg BID (twice a day), and the 3 in 1 capsule, Pylera, containing Bismuth Subcitrate potassium 140 mg, metronidazole 125 mg and tetracycline 125 mg, administered as 3 capsules QID (four times day)
Triple Therapy (OAC) 7 Days	Omeprazole 20 mg BID, Amoxicillin 500 mg 2 capsules BID and Clarithromycin 500 mg 1 tablet BID

Serious Adverse Events

	Quadruple Therapy (OBMT) 10 Days	**Triple Therapy (OAC) 7 Days**
Total, Serious Adverse Events		
# participants affected / at risk	**4/216 (1.85%)**	**3/222 (1.35%)**
Cardiac disorders		
Ventricular extrasystoles [*1]		
# participants affected / at risk	**0/216 (0.00%)**	**1/222 (0.45%)**
# events	**0**	**1**
Gastrointestinal disorders		
Pancreatitis [*1]		
# participants affected / at risk	**0/216 (0.00%)**	**1/222 (0.45%)**
# events	**0**	**1**
Vomiting [*1]		
# participants affected / at risk	**0/216 (0.00%)**	**1/222 (0.45%)**
# events	**0**	**1**
General disorders		
Condition aggravated [*1]		
# participants affected / at risk	**0/216 (0.00%)**	**1/222 (0.45%)**

# events	0	1
Pyrexia [*1]		
# participants affected / at risk	0/216 (0.00%)	1/222 (0.45%)
# events	0	1
Infections and infestations		
Appendicitis [*1]		
# participants affected / at risk	0/216 (0.00%)	1/222 (0.45%)
# events	0	1
Proteus infection [*1]		
# participants affected / at risk	1/216 (0.46%)	0/222 (0.00%)
# events	1	0
e coli urinary tract infection [*1]		
# participants affected / at risk	1/216 (0.46%)	0/222 (0.00%)
# events	1	0
Metabolism and nutrition disorders		
Dehydration [*1]		
# participants affected / at risk	0/216 (0.00%)	1/222 (0.45%)
# events	0	1
Malnutrition [*1]		
# participants affected / at risk	0/216 (0.00%)	1/222 (0.45%)
# events	0	1
Neoplasms benign, malignant and unspecified (incl cysts and polyps)		
Gastrointestinal carcinoma [*1]		
# participants affected / at risk	1/216 (0.46%)	0/222 (0.00%)
# events	1	0
Nervous system disorders		
Vascular dementia [*1]		
# participants affected / at risk	0/216 (0.00%)	1/222 (0.45%)
# events	0	1
Psychiatric disorders		
Schizophrenia [*1]		
# participants affected / at risk	1/216 (0.46%)	0/222 (0.00%)
# events	1	0
Renal and urinary disorders		
Renal artery stenosis [*1]		
# participants affected / at risk	1/216 (0.46%)	0/222 (0.00%)
# events	1	0
Renal failure acute [*1]		
# participants affected / at risk	1/216 (0.46%)	0/222 (0.00%)
# events	1	0

Skin and subcutaneous tissue disorders		
Eczema * 1		
# participants affected / at risk	**1/216 (0.46%)**	**0/222 (0.00%)**
# events	**1**	**0**

* Events were collected by non-systematic assessment

1 Term from vocabulary, PT

Other Adverse Events

Time Frame	Adverse events were recorded starting at the signing of the informed consent until the final visit (Day 70) or early withdrawal visit. Serious adverse events were followed until 30 days after the patient had stopped study participation.
Additional Description	Systematic assessment done for laboratory evaluations and bismuth plasma levels.

Frequency Threshold

Threshold above which other adverse events are reported	5%

Reporting Groups

	Description
Quadruple Therapy (OBMT) 10 Days	Omeprazole 20 mg BID (twice a day), and the 3 in 1 capsule, Pylera, containing Bismuth Subcitrate potassium 140 mg, metronidazole 125 mg and tetracycline 125 mg, administered as 3 capsules QID (four times day)
Triple Therapy (OAC) 7 Days	Omeprazole 20 mg BID, Amoxicillin 500 mg 2 capsules BID and Clarithromycin 500 mg 1 tablet BID

Other Adverse Events

	Quadruple Therapy (OBMT) 10 Days	**Triple Therapy (OAC) 7 Days**
Total, Other (not including serious) Adverse Events		
# participants affected / at risk	**98/216 (45.37%)**	**105/222 (47.30%)**
Gastrointestinal disorders		
Dyspepsia * 1		
# participants affected / at risk	**22/216 (10.19%)**	**30/222 (13.51%)**
Diarrhea * 1		
# participants affected / at risk	**14/216 (6.48%)**	**28/222 (12.61%)**
Nausea * 1		

# participants affected / at risk	**14/216 (6.48%)**	**2/222 (0.90%)**
Headache * 1		
# participants affected / at risk	**18/216 (8.33%)**	**7/222 (3.15%)**
Nervous system disorders		
Dysgeusia * 1		
# participants affected / at risk	**12/216 (5.56%)**	**22/222 (9.91%)**
Vascular disorders		
Abdominal pain upper * 1		
# participants affected / at risk	**18/216 (8.33%)**	**16/222 (7.21%)**

* Events were collected by non-systematic assessment

1 Term from vocabulary, PT

Limitations and Caveats

Limitations of the study, such as early termination leading to small numbers of participants analyzed and technical problems with measurement leading to unreliable or uninterpretable data
No text entered.

More Information

Certain Agreements:

Principal Investigators are **NOT** employed by the organization sponsoring the study.

There **IS** an agreement between Principal Investigators and the Sponsor (or its agents) that restricts the PI's rights to discuss or publish trial results after the trial is completed.

The agreement is:

☐ The only disclosure restriction on the PI is that the sponsor can review results communications prior to public release and can embargo communications regarding trial results for a period that is **less than or equal to 60 days**. The sponsor cannot require changes to the communication and cannot extend the embargo.

☐ The only disclosure restriction on the PI is that the sponsor can review results communications prior to public release and can embargo communications regarding trial results for a period that is **more than 60 days but less than or equal to 180 days**. The sponsor cannot require changes to the communication and cannot extend the embargo.

Other disclosure agreement that restricts the right of the PI to discuss or publish trial results after the trial is completed.

☑ **Restriction Description:** Restrictions vary in accordance with the agreement with investigators. Axcan will allow publication after a multi-centre publication or after an agreed period, subject to review by Axcan for confidentiality and intellectual protection.

Results Point of Contact:

Name/Title: Monique Giguere, PhD, Programs Director,
Organization: Axcan Pharma Inc.
phone: 1-800-565-3255 ext 2078

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Responsible Party:	Forest Laboratories
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