TALICIA : A NEW DRUG FOR HELICOBACTER PYLORI INFECTION - REVIEW

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ABSTRACT

Infection with Helicobacter pylori (H. pylori) is a major pathogenic factor for gastro duodenal ulcer disease and gastric carcinoma, as well as for other types of gastric and extra gastric diseases. Individuals infected with H. pylori have at least a 2-fold increase in risk of gastric cancer development, though only a small proportion of infected individuals will ultimately develop this malignancy. An effective "test and treat" strategy, diagnosis and therapy are both important. Because the infection is usually asymptomatic, patient selection is a critical issue for timely diagnosis and many clinical and demographic factors should be considered. However, these are mostly preventable by eradication therapy. If the proper eradication of bacteria is not carried out ,there is a chance for further exposure to infection. Resistance of *H pylori* to the limited range of antibiotics that have efficacy in its treatment can severely affect attempts to eradicate the bacteria. Commonly used therapy for H. pylori infection is a combination therapy of a proton pump inhibitor and two antibiotics. However, there exist H. pylori strains that show resistance against these antibiotics.A new drugs has been introduced by Red Hill Biopharma, which has been approved by FDA, named TALICIA for H.pylori infection. This drug helps to reduce the drug resistant bacteria and maintain the effect of Talicia and other antibacterial drugs. Talicia is eligible for a total of eight years of U.S. market exclusivity under its Qualified Infectious Disease Product (QIDP) designation, in addition to patent protection extending until at least 2034.

KEYWORDS

Helicobacter pylori infection, Talicia, carcinoma, antimicrobial resistance.

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INTRODUCTION

Helicobacter pylori is a gram negative bacteria that enter into our body and causes infection in the digestive tract. Helicobacter pylori , previously known as Campylobacter pylori. It is the main cause of peptic ulcers, gastritis and stomach cancer. A peptic ulcer causes a dull or burning pain in stomach, especially when an empty stomach between meals and in the early morning hours, but it can also occur at other times. Less common ulcer symptoms includes, nausea, vomiting, and loss of appetite. . If bleeding is heavy, hematemesis, hematochezia, or melena may occur. It lasts for minutes to hours, and it may come and go for several days or weeks. *H. pylori's* helical shape is thought to have evolved to penetrate the mucoid lining of the stomach. It may also cause other symptoms, such as bloating, nausea and weight loss. H. pylori infection is commonly seen. About two-thirds of the world's population has it in their bodies [(1)]. It was identified in 1982 by Australian doctors Barry Marshall and Robin Warren, who found that it was present in a person with chronic gastritis and gastric ulcers, conditions not previously believed to have a microbial cause. H. pylori is usually acquired in childhood, whereas acute infection with the bacterium is rarely diagnosed. Instead, chronic gastritis develops in almost all persistently colonized individuals, 90% of whom will remain asymptomatic. The clinical course of H. pylori infection is highly variable depending on bacterial and host (genetic and immune) factors. Recent studies have supported the possible role of bone marrow-derived cells (i.e., gastric stem cells) in tumor progression. Patients with increased acid secretion are more likely to have antral-predominant gastritis, which predisposes to duodenal ulcers. Patients with low acid secretion will more likely develop gastritis in the body of the stomach and are thus more likely to develop gastric ulcer, leading to gastric atrophy, intestinal metaplasia, dysplasia and, finally, in rare cases, gastric carcinoma. This sequence of events is more frequent in people of advanced age. H. pylori infection induces the formation of mucosa-associated lymphoid tissue (MALT) in the gastric mucosa and MALT lymphoma is another rare complication of H. pylori infection [(2).] There are blood breath, and stool tests to check for H. pylori. In some cases, you may need an upper endoscopy, often with a biopsy [(3)]. Helicobacter pylori are contagious, although the exact route of transmission is not known. Transmission is either through oral-oral or fecal-oral route. So that the bacteria have been isolated from feces, saliva, and dental plaque of some infected people. Findings suggested that H. pylori is more easily transmitted by gastric mucus than saliva. *H. pylori* may also be transmitted orally by means of fecal matter through the ingestion of waste-tainted water, so a hygienic environment could help decrease the risk of *H. pylori* infection. Rising antibiotic resistance increases the need to search for new therapeutic strategies; this might include prevention in the form of vaccination. The presence of bacteria in the stomach may be beneficial, reducing the prevalence of asthma, rhinitis, atopic dermatitis, inflammatory bowel disease, gastroesophageal reflux disease, and esophageal cancer by influencing systemic immune responses. Clarithromycin-resistant *H. pylori* was formally categorized by the World Health Organization (WHO) as a pathogen for which there is a high priority, that need to develop new treatments.

TREATMENTS

- Proton pump inhibitors (PPIs) -These drugs stop acid from being produced in the stomach. Some examples of PPIs are omeprazole, esomeprazole, lansoprazole and pantoprazole.
- Histamine (H-2) blockers- These medications block a substance called histamine, which triggers acid production. One example is cimetidine.
- Bismuth subsalicylate- More commonly known as Pepto-Bismol, this drug works by coating the ulcer and protecting it from stomach acid.[4]
- The people who are allergic to penicillin, amoxicillin is replaced with metronidazole.
- For the treatment of clarithromycin-resistant strains of H. pylori, the use of levofloxacin as part of the therapy has been suggested.
- The substance sulforaphane, which occurs in broccoli and cauliflower, has been proposed as a treatment.
- Ingesting lactic acid bacteria exerts a suppressive effect on *H. pylori* infection in both animals and humans, and supplementing with Lactobacillus- and Bifidobacterium-containing yogurt improved the rates of eradication of *H. pylori* in humans .[5]

SIDE EFFECTS

Nausea, vomiting, diarrhea, headache, vaginal itching or discharge, unusual or unpleasant taste in the mouth, black or "hairy" tongue [6].

A new drug, Talicia has been introduced for the treatment of Helicobacter pylori infection.

TALICIA

FIG 1: TALICIA CAPSULES

The FDA approved a three-drug, delayed-release capsule for the treatment of *Helicobacter pylori* infection in adults. The drug, omeprazole magnesium-amoxicillin-rifabutin (Talicia, RedHill Biopharma), is the only rifabutin-based therapy approved for the treatment of *H. pylori* infection. To reduce the development of drug-resistant bacteria and maintain the effectiveness of Talicia and other antibacterial drugs, Talicia should be used only to treat or prevent infections that are proven or strongly suspected to be caused by bacteria.

The drug is designed to address the high resistance of *H. pylori* bacteria to regimens containing clarithromycin used in current standard-of-care therapies and the imperative need for new treatments. It is a delayed-release capsule 10 mg/250 mg/12.5 mg is a novel, fixed-dose, all-in-one oral capsule combination of two antibiotics (amoxicillin and rifabutin) and a proton pump inhibitor (PPI) (omeprazole), approved by the U.S

HISTORY

Talicia for H.pylori Infection on December 3, 2018. RedHill Biopharma Submits New Drug Application for Talicia for H. pylori Infection on May 7, 2019. RedHill Biopharma announces FDA acceptance of new drug application for Talicia on July 3 , 2019. FDA Approves Talicia for the treatment of H. pylori infection in adults on November 4, 2019.

MECHANISM OF ACTION

Rifabutin: Elicits antibacterial effects by inhibiting DNA-dependent RNA polymerase

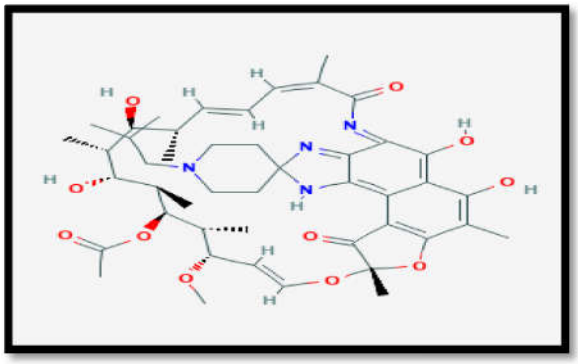

FIG 2: STRUCTURE OF RIFABUTIN

Omeprazole: Proton pump inhibitor; binds to H+/K+-exchange ATPase (proton pump) in gastric parietal cells resulting in blocking acid secretion.

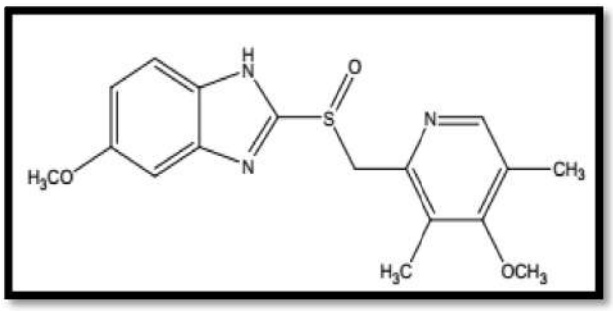

FIG 3: STRUCTURE OF OMEPRAZOLE

Amoxicillin: Ampicillin derivative; elicits antibacterial effect by inhibiting biosynthesis of cell wall mucopeptide

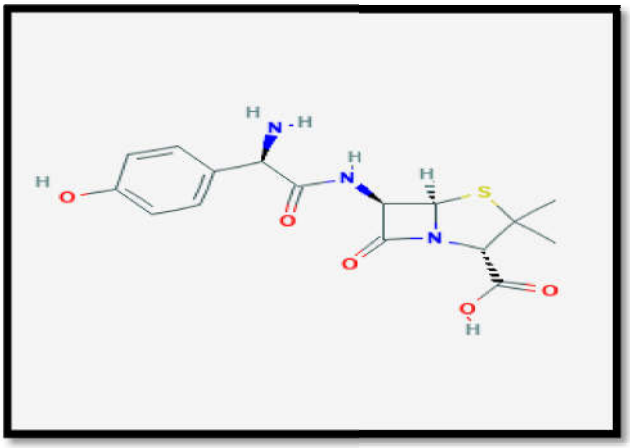

FIG 4: STRUCTURE OF AMOXICILLIN

PHARMACOKINETICS

AMOXICILLIN

Absorption

- Rapidly absorbed
- Bioavailability: 74-92%
- Peak plasma time: 2hr (capsule)

Distribution

- Most body fluids and bone, CSF <1%
- Protein bound: 17-20%

Metabolism

- Hepatic

Elimination

- Excretion: Urine
- 0.7-1.4 hr (adults)

OMEPRAZOLE

- Absorption
  - Bioavailability: 30-40%

- Onset of action: 1 hr (antisecretory effect)
- Duration: 73 hr
- Peak plasma time: 0.5-3.5 hr
- Peak response (PUD): 2 hr (initial); 5 days (peak)

- Distribution
  - Protein bound: 95-96%
  - Vd: 0.39 L/kg
- Metabolism
  - Metabolized extensively by hepatic CYP2C19; slow metabolizers are deficient in CYP2C19 enzyme system; plasma concentration can increase by 5-fold or higher in comparison with that found in persons with the enzyme
  - Metabolites: Hydroxyomeprazole, omeprazole sulfone, omeprazole sulfide (inactive)
  - Enzymes inhibited: CYP2C19
- Elimination
  - Half-life: 0.5-1 hr; increases to 3 hr with hepatic impairment
  - Dialyzable: No
  - Total body clearance: 500-600 mL/min
  - Excretion: Urine (77%); feces (16-19%; mainly in bile)

RIFABUTIN

- Absorption
  - Readily absorbed: 53%
  - Bioavailability, absolute (HIV infected individual): 20%
  - Peak plasma time: 2-4 hr
- Distribution
  - Distributed in body tissues including the lungs, liver, spleen, eyes, & kidneys
  - Vd: 9.32 L/kg
  - Protein bound: 85%
- Metabolism
  - Metabolized by hepatic CYP3A4 to active and inactive metabolites
- Elimination
  - Half-life: 45 hr (range: 16-69 hr)
- Excretion
  - Urine: 10% as unchanged drug, 53% as metabolites
  - Feces: 10% as unchanged drug, 30% as metabolites

ADMINISTRATION

Oral Administration

Swallow capsules whole with a full glass of water (8 ounces); do not crush or chew capsules
Do not take with alcohol
Missed dose: Continue normal dosing schedule until medication is completed; do not take two doses at one time to make up for a missed dose[7]

Dosage Forms & Strengths

Amoxicillin/ Omeprazole / Rifabutincapsule (delayed release)

- 250mg/10mg/12.5mg per capsule

Helicobacter Pylori Infection

Administer 4 capsules PO (orally) with food q8hr for 14 days
Each dose (4 capsules) include 1000 mg amoxicillin, 40 mg omeprazole, and 50 mg rifabutin

ADVERSE EFFECTS

Most common adverse reactions (≥1%) include diarrhea, headache, nausea, abdominal pain,

chromaturia, rash, dyspepsia, oropharyngeal pain, vomiting, and vulvovaginal candidiasis.

CONTRAINDICATIONS

- Known hypersensitivity to omeprazole, amoxicillin or any other beta-lactam antibacterial drugs, rifabutin or any other rifamycin, or any component of Talicia
- Rilpivirine-containing products.
- Delavirdine.
- Voriconazole[8]

CONCLUSION

As compared to the previous treatments, Talicia produce antimicrobial resistance property . The drug Talicia approved by FDA also have side effects similar to the previous treatment which is used Helicobacter pylori infection plays a critical role in pathogenesis of gastric ulcer and gastric cancer. Thus, the eradication of H. pylori could prevent the onset of these diseases. At present, the standard therapy against H. pylori infection is a combination of a proton pump inhibitor and two antibiotics. Talicia, a delayed-release capsule for the treatment of *Helicobacter pylori* infection in adults. To reduce the development of drug-resistant bacteria and maintain the effectiveness of Talicia and other antibacterial drugs, Talicia should be used only to treat or prevent infections that are proven or strongly suspected to be caused by bacteria.

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CONFLICT OF INTEREST REPORTED: NIL ; SOURCE OF FUNDING: NONE REPORTED