Call Toll-free 1-800 856-7842 or 828-254-0881 with Extension listed

Name of Study: **A Randomized, Double-blind, Placebo-controlled, Trial of IW-3718 for 8 Weeks in Patient with Symptomatic GERD-(Ironwood Pharmaceuticals)**

LINK: https://clinicaltrials.gov/ct2/show/NCT02637557?term=ironwood+GERD&rank=2

PI: Andrew Dukowicz, MD

Study Coordinator: Ann Jones #3397 or Direct-828-350-3697

Summary: ICP-3718-202: A Phase 2b, Randomized, Double-blind, Placebo-controlled, Parallel-group, Dose-range-finding Trial of IW-3718 (colesevelam) Administered Orally for 8 Weeks to Patients with Symptomatic Gastroesophageal Reflux Disease Not Completely Responsive to Proton Pump Inhibitors

Main Inclusion Criteria:

- Patient is an ambulatory, community-dwelling male or nonpregnant female and is at least 18 years old at the Screening Visit.
- Lactating females must agree not to breastfeed.
- Patient has a diagnosis of GERD and reports experiencing GERD symptoms (heartburn or regurgitation) on ≥ 4 days per week during the 8 weeks before the Screening Visit while taking standard QD PPI therapy.
- Patient has been receiving individually optimized, standard labeled dose, QD, PPI therapy (treatment that, according to the investigator's judgment, could not be further improved by changing the brand or timing of PPI administration) for a minimum of 8 weeks before the Screening Visit.
- An EGD followed by approximately 48 to 96 hours of pH monitoring (with a Bravo® device) during the Screening Period (while the patient continues taking their PPIs) demonstrates 1 or more of the following:
    - Erosive esophagitis (Grade A or greater based on the Los Angeles classification of esophagitis on EGD
    - Evidence of pathological acid reflux (pH is < 4 for ≥ 4.2% of the recording time) during at least 1 of the 24-hour time intervals of pH testing with the Bravo device
    - Patient reports heartburn severity (HS, Item #1 on RESQ-eD) ≥ 3 (moderate) on at least 2 days and has an average HS of ≥ 2 (mild) during the last 7 days before randomization.
    - Sexually active female patients of childbearing potential (i.e., women who are not postmenopausal or who have not had a bilateral oophorectomy, hysterectomy, or tubal ligation) must agree to use

1 of the following methods of birth control from the date they sign the ICF until 24 hours after their final dose of study drug:
    - Hormonal contraception (i.e., oral contraceptive, contraceptive implant, or injectable hormonal contraceptive)
    - Double-barrier birth control (e.g., condom plus intrauterine device, diaphragm plus spermicide, etc.)
    - Maintenance of a monogamous relationship with a male partner who has been surgically sterilized by vasectomy
- Females of childbearing potential must have a negative serum pregnancy test at the Screening Visit and a negative urine pregnancy test at the Randomization Visit prior to dosing.
- Patient agrees not to make any changes to their usual diet during the study.
- Patient is compliant with eDiary completion; that is, they have adequately completed the eDiary questions on at least 5 days each week during the 14 calendar days before the start of the Treatment Period.
- Patient is compliant with QD PPI dosing during the 14 calendar days before the start of the Treatment Period. Patients are considered compliant if, as reported in the eDiary, they take their PPI on at least 5 days each week.
- Patient is fluent and literate in English or Spanish.
- Patient is able to operate the eDiary adequately and agrees to adhere to the study requirements.
- For patients who are receiving supplementation of a fat-soluble vitamin in order to correct or avoid a fat-soluble vitamin deficiency, the patient is willing to take the vitamin supplement at least 4 hours before taking study medication.

Main Exclusion Criteria

- Patient has a history of complete lack of GERD symptom response to PPIs in the past.
- Patient reports epigastric pain or burning as his or her predominant symptom at the Screening Visit.
- Patient has a history of gastroparesis, bowel obstruction, or is at risk for a bowel obstruction (e.g., patient has an organic gastrointestinal [GI] motility disorders or a history of major GI surgery).
- Patient has a history of serum triglycerides concentrations > 500 mg/dL, or has serum triglycerides concentrations > 500 mg/dL at Screening or any time during the Pretreatment Period.
- Patient has a history of hypertriglyceridemia-induced pancreatitis.
- In the investigator's opinion, a patient susceptible to a deficiency of fat-soluble vitamins (especially vitamin D deficiency; e.g., the patient is African American or Hispanic or has osteoporosis, osteomalacia) will be put at risk by receiving colesevelam for 8 weeks.
- Patient has a history of swallowing disorders.
- Patient has any alarm symptoms including but not limited to GI bleeding, anemia, vomiting, dysphagia, or unexpected weight loss any time during the Screening or Pretreatment Periods
- Patient has undergone surgery that meets any of the following criteria:
    - Surgery of the GI tract (including gastric banding) other than an appendectomy, cholecystectomy, minor oral or rectal surgery (e.g., tonsillectomy, hemorrhoidectomy, rectocele repair) at any time before the Screening Visit

    - An appendectomy during the 3 months before the Screening Visit or a cholecystectomy during the 6 months before the Screening Visit or minor oral or rectal surgery during the 30 days before the Screening Visit
    - Non-GI surgery of the abdomen, pelvis, or retroperitoneal structures during the 6 months before the Screening Visit
    - Thoracic surgery during the 6 months before the Screening Visit
    - Other major non-GI surgery during the 30 days before the Screening Visit
- Patient has previously undergone thoracic or abdominal radiotherapy
- Esophagogastroduodenoscopy, conducted during the Screening Period, reveals that the patient has long-segment Barrett's esophagus or definite dysplastic changes in the esophagus, peptic ulcer disease, active GI bleeding, presence of esophageal strictures, presence of esophageal or fundic varices, erosive gastritis, or eosinophilic, herpetic or Candida esophagitis.
- Patient has Gilbert's disease, Crohn's disease, diabetes mellitus, Zollinger-Ellison syndrome, pancreatitis, cholecystitis, or systemic sclerosis.
- Patient has elevated (defined as > 1.5 times the upper limit of normal by the laboratory) levels of serum bilirubin at Screening or any time during the Pretreatment Period.
- Patient has a history of clinically significant hypersensitivity or allergies to any of the excipients contained in the study medication (active or placebo).
- Patient has a history of cancer (resected basal cell or squamous cell carcinoma is acceptable). Note: patients with a history of cancer are allowed provided that the malignancy has been in complete remission for at least 5 years before the Screening Visit. A complete remission is defined as the disappearance of all signs of cancer in response to treatment.
- Patient has history of active alcoholism or drug addiction during the 12 months before Screening
- Patient has any clinically significant finding on a physical exam, 12-lead electrocardiogram (ECG), or clinical laboratory test after signing the ICF but before receiving the first dose of study medication. (Note: The investigator will determine if a particular finding is clinically significant. In making this determination, the investigator will consider whether the particular finding could prevent the patient from performing any of the protocol-specified assessments, could represent a condition that would exclude the patient from the study, could represent a safety concern if the patient participates in the study, or could confound the study-specified assessments of safety or efficacy.)Patient reports using a prohibited medication during the Screening or Pretreatment Periods, or is not willing or able to abide by the restrictions regarding use of prohibited medications as defined.
- Patient has received an investigational drug during the 30 days before the Screening Visit, or is planning to receive another investigational drug or use an investigational device at any time during the studyPatient has an acute or chronic condition that, in the investigator's opinion, would limit the patient's ability to complete or participate in this clinical study.
- Patient has previously entered the Treatment Period of a study in which IW-3718 is a treatment.
- Patient has previously entered the Pretreatment Period of this study.
- Patient is enrolled in this study at another clinical study site; is an employee of the Institution or Ironwood Pharmaceuticals; or is a first-degree family member, significant other, or relative residing with an employee of the Institution or Ironwood Pharmaceuticals.