CURRENT RESEARCH STUDIES
(GI and Hepatology Clinical Research Office – University of Wisconsin)

OPEN TO ENROLLMENT:

Aptima HBV Quant Assay
Collection of Plasma Samples from Individuals Initiating Therapy with Entecavir or Tenofovir for Chronic Hepatitis B Virus Infection for the Clinical Evaluation of the Aptima HBV Quant Assay
- Subject must be chronically infected with HBV; is treatment naïve and is initiating HBV antiviral therapy with either entecavir or tenofovir as indicated in the FDA approved label
- 4 study visits / $100 payment for each visit completed.

Seroprevalence of Hepatitis E in Organ Transplant subjects
Up to 300 patients who received liver, renal or small bowel transplant from 3 participating transplant centers will be recruited in the study. At least half of the cases will be liver transplant recipients. Enrollment of transplant recipients will be stratified based on number of years post-transplant, one, two and three years and by transplant center. Controls will consist of patients on the waitlist matched for age, waitlist organ and transplant center. After providing written, informed consent, subjects will undergo testing for HEV serology (HEV IgG and IgM) and HEV RNA by RT-PCR.

“InteTeam”
“Integrated Approaches for Identifying Molecular Targets in Alcoholic Hepatitis”
The purpose of this study is to collect and preserve samples of blood, urine, stool, and liver tissue from patients with alcoholic hepatitis to be used in future research studies. The purpose of future studies using these samples will be to develop new methods for diagnosing alcoholic hepatitis and its complications, to develop new markers for disease severity (how bad your disease is), and to identify new targets (treatments and/or blood tests) for improved therapy. We are offering all patients who are seen at UWHC with suspected alcoholic hepatitis the opportunity to participate in this study.

Inclusion:
- Between 18 and 70 years old
- Active alcohol abuse in the last 3 months
- Elevated AST/ALT
- Elevated total bilirubin (>3mg/dL)
- Liver biopsy or clinical picture consistent with alcoholic hepatitis
- Have they been admitted for 1 week or less

Exclusion:
- Autoimmune liver disease (ANA>1/320)
- HIV positive antibodies (if known)
- Hepatocellular Carcinoma
- Complete portal vein thrombosis
- Any extrahepatic terminal disease
- Pregnant
- Treated with prednisolone or pentoxifylline >3 days

Hepatitis C Database
This database is intended for use in tracking current treatment outcomes and future research studies about Hepatitis C.

REGNERATE: Obeticholic Acid in NASH
This is a phase 3, double-blind, randomized, long-term, placebo-controlled study evaluating the

TO REFER PATIENTS TO A TRIAL CONTACT THE RESEARCH STAFF AT 263-4185.
December 2015
safety and efficacy of Obeticholic Acid in subjects with Non-alcoholic Steatohepatitis (NASH)

Inclusion:
• NASH with evidence of fibrosis stage 2 or 3
• Stable body weight
• Stable doses of diabetic therapy, vitamin

Exclusion:
• Significant alcohol consumption
• Prior/planned bariatric surgery
• Other forms of liver disease (HCV, HBV, alcoholic liver disease, PBC, PSC, HCC)
• History of liver transplant
• Cirrhosis
• Previous exposure to obeticholic acid

M15-582 AbbVie
An Open-Label, Multicenter Study to Evaluate the Efficacy and Safety of Ombitasvir/Paritaprevir/Ritonivir and Dasabuvir with Low-Dose Ribavirin QD in Subjects with Genotype 1a Hep C Infection

Inclusion:
• HepC, genotype 1a
• Treatment naïve or previously treated
• Non-cirrhotic

Exclusion:
• Pregnant
• Other genotype other than 1a
• Positive HepB surface antigen or HIV
• Cirrhosis
• Prior or current use of investigational or commercially available anti-HCV agents
• Recent drug or alcohol abuse
• Previous solid organ transplant
Tetanus/MMR response in IBD  
PI: Freddy Caldera  
The primary objective is to compare tetanus, diphtheria, and pertussis antibody concentrations and seroprotection rates in patients with IBD treated with combination therapy to healthy individuals.

Methotrexate (MTX)/Sperm Quality in IBD  
PI: Sumona Saha  
The purpose of this study is to determine whether the treatment of IBD patients with MTX is associated with an increased risk for infertility using two different criteria for assessing male fertility: the WHO criteria for basic semen analysis and Fourier Harmonic Amplitudes. The latter will be used to describe nuclear shapes and sperm DNA staining intensity as this has been shown in animal models to correlate with male fertility. MTX-exposed male IBD patients (cases) will be compared with age-matched, non-MTX exposed patients (controls).

iPhone App in Ulcerative Colitis  
PI: Freddy Caldera  
Patients are eligible if they meet the following criteria.  
- At least 18 -65 years of age.  
- Diagnosed with ulcerative colitis established by history and biopsy confirmed by GI  
- On a stable dose of mesalamine for at least two months prior to entering the study  
- Have an Iphone (personal iPhone)  
- Patient may receive steroid or mesalamine enemas during the study only during a PRN Basis

Etrolizumab in UC  
PI: Sumona Saha  
The target population is patients with moderately to severely active UC (defined as MCS of 6-12, endoscopy subscore of ≥ 2 by central read, a rectal bleeding subscore ≥ 1, and a stool frequency subscore of ≥1), and involvement that extends a minimum of 20 cm from the anal verge.  
The study will be divided into:  
- Screening period of up to 28 days during which patient eligibility will be determined  
- Induction Phase of 14 weeks (Cohort 1: open-label etrolizumab treatment; Cohort 2: randomized to etrolizumab or placebo)  
- Randomization of etrolizumab responders prior to a double-blind Maintenance Phase of 52 weeks or continued blinded treatment with placebo Q4W for 52 weeks for placebo induction responders

Etrolizumab in Crohn  
PI: Sumona Saha  
The target population is patients who have moderate to severely active CD and have had an inadequate response, refractory response or intolerance to CS and/or IS therapy and/or anti-TNFs.  
The study will be divided into:  
- Screening period of up to 28 days during which patient eligibility will be determined  
- Induction Phase of 14 weeks (Cohort 1: open-label etrolizumab treatment; Cohort 2: randomized to etrolizumab or placebo)  
- Randomization of etrolizumab responders prior to a double-blind Maintenance Phase of 52 weeks or continued blinded treatment with placebo Q4W for 52 weeks for placebo induction responders

RHB-104 in Crohn's Disease  
PI: Mark Reichelderfer  
A Phase III Randomized, Double Blind, Placebo-controlled, Multicenter, Parallel Group Study to Assess the Efficacy and Safety of Fixed-dose Combination RHB-104 in Subjects with Moderately to Severely Active Crohn’s Disease  
- Males and females 18 to 75 years of age.

TO REFER PATIENTS TO A TRIAL CONTACT THE RESEARCH STAFF AT 263-4185.
December 2015

- Diagnosis of Crohn’s Disease confirmed by endoscopy or radiography and/or histology at least 6 months prior to randomization into the study with CD involving the ileum and/or colon.
- Subject must be intolerant or have insufficient response to conventional therapy and have moderately to severely active CD (Crohn’s Disease Activity Index (CDAI) score of ≥220 and ≤450) at baseline.
- Subjects must meet concomitant medication criteria described in the protocol.

**Salix RECD3125 (Rifaximin) in Crohn’s Disease**  
PI: Freddy Caldera  
A Double-Blind, Placebo-Controlled, Parallel-Group, Multicenter, Multiregional, One Year Study to Assess the Efficacy and Safety of Twice Daily Oral Rifaximin Delayed Release Tablets for Induction of Clinical Remission with Endoscopic Response at 16 Weeks followed by Clinical and Endoscopic Remission at 52 Weeks in Subjects with Active Moderate Crohn’s Disease  
- Males and females 18 years of age.  
- Subject has moderate, non-fistulizing Crohn’s disease in the ileum and/or colon as defined by a CDAI score of ≥220 and ≤ 450 points prior to randomization; and a SES-CD score of ≥7. The SES-CD score will be calculated using the baseline ileocolonoscopy performed during the Screening Period.  
- During the Screening Period, the subject has the following average daily scores for abdominal pain and average number of liquid/very soft stools:  
  - An average daily score of > 1.5 for abdominal pain (from CDAI Item 2); and  
  - An average daily count of > 1.5 for liquid/very soft stools (from CDAI Item 1). Liquid/very soft stool will be defined as a consistency of Type 6 or Type 7 on the BSFS.

**Exact Sciences OCEANIA for IBD**  
PI: Mark Reichelderfer  
Detection of Advanced Colorectal Neoplasia by Stool DNA in Inflammatory Bowel Disease  
- Subjects will be men and women from 18 to 84 years of age inclusive, who have diagnosed IBD with duration of at least eight years, or a diagnosis of PSC, and have either a histopathological diagnosis of advanced colorectal neoplasia (ACRN), specifically high grade dysplasia (HGD) or colorectal cancer (CRC) based on colonoscopy within the 90 days preceding enrollment or for whom a surveillance colonoscopy is indicated. Subjects enrolled with a history of ACRN must be recommended for colonoscopy (post-enrollment) or surgical intervention.

**LEGACY – Humira Registry for Ulcerative Colitis**  
PI: Freddy Caldera  
A Long-Term Non-Interventional Registry to Assess Safety and Effectiveness of HUMIRA® (Adalimumab) in Patients with Moderately to Severely Active Ulcerative Colitis (UC)  
- See protocol for specific eligibility criteria

**CCFA/NIH “MERIT-UC”**  
PI: Sumona Saha  
Randomized, double-blind, prospective trial investigating the efficacy of methotrexate in induction and maintenance of steroid free remission in UC.  
- Subjects must be between 18 and 70 y/o; UC diagnosed by routine clinical, radiographic, endoscopic, and pathological criteria; Active UC with a Mayo score of 6 to 12 points and moderate-to-severe active disease on sigmoidoscopy and at least one of the following: (1) steroid dependent UC defined by IOIBD (2) primary failure or loss of response to infliximab or (3) intolerance/failure of azathioprine/6-MP therapy.

TO REFER PATIENTS TO A TRIAL CONTACT THE RESEARCH STAFF AT 263-4185.
December 2015

**PIANO** - IBD & Pregnancy Registry (CCFA)  PI: Sumona Saha
This study is conducted to determine whether the rates of birth defects, miscarriages, premature births and other outcomes in women with inflammatory bowel disease (IBD) taking azathioprine/6MP or biologic therapy (Remicade®, Humira®, Cimzia™, Tysabri®, or Stelara®) are different from those among IBD-affected women not taking these medications. Particularly, we are interested in studying whether the level of biologic drug transferred across the placenta to the infant by the time of birth predicts the risk of infection.
- Pregnant women exposed anti-TNF therapy (Remicade®, Humira®, Cimzia™) with and without immunomodulators.
- Must be willing to give blood samples at the time of delivery
- Other optional specimen collections (see protocol)

UCB Inc – SECURE Registry  PI: Mark Reichelderfer
The objective of this registry is to track safety outcomes of patients who have taken Cimzia® for the treatment of Crohn’s Disease compared to a non- Cimzia® control population.

Cimzia® cohort
- Patient is receiving treatment with Cimzia for the first time. Patient must receive Cimzia treatment within 2 months of enrollment into the registry.
- Patient is currently receiving treatment with Cimzia for ≤12 months. Patients must also receive a Cimzia dose within 2 months following enrollment into the registry.

Comparison cohort
- Patient is switching CD treatments or beginning CD treatment for the first time. Previous Cimzia treatment is prohibited in the comparator group. Patient must receive new CD treatment within 2 months of enrollment into the registry.
- Patient is currently receiving anti-TNF treatment for ≤12 months. Patient must receive anti-TNF treatment within 2 months following enrollment into the registry.
- Patient is currently receiving immunosuppressant therapy for ≤12 months. Patient must receive immunosuppressant therapy within 2 months following enrollment into the registry.
- Patient is currently receiving systemic steroid therapy for ≤12 months. Patient must receive systemic steroid therapy within 2 months following enrollment into the registry.

Database & Registry of patients with Gastrointestinal or liver conditions  PI: Mark Reichelderfer
Registry allows research staff to notify subjects of potential eligibility in current research studies in our office. Database allows us to collect medical record information about their medical history, medication history as well as billing records.

Dysmenorrhea in IBD** (MDQ)  PI: Sumona Saha
This case-control study will screen for dysmenorrhea and assess severity of menstrual symptoms in menstruating women with CD and UC compared with healthy age-matched controls. IBD activity will be characterized using previously validated clinical disease activity indices. General and health-related quality of life will be assessed using validated measures.
**ULCERATIVE COLITIS ARM OPEN ONLY

Other Projects

NPS – Short Bowel Syndrome Registry  PI: Mark Reichelderfer
A prospective, multi-center registry for patients with Short Bowel Syndrome to evaluate the long-term safety profile for patients with short bowel syndrome (SBS) who are treated with teduglutide in a routine clinical setting. The primary safety outcome is the occurrence of colorectal cancer in SBS patients with a remnant colon taking teduglutide.

Cancer Prevention / FAP-310  PI: Jennifer Weiss
This randomized, double-blind, phase III trial will compare the efficacy, safety and pharmacokinetics of the CPP-1X/sulindac combination versus CPP-1X and sulindac as single agents over a 24 month treatment period in patients with Familial Adenomatous Polyposis (FAP).
- Diagnosis of phenotypic classical FAP, age ≥18 years, male and female gender. Must be

TO REFER PATIENTS TO A TRIAL CONTACT THE RESEARCH STAFF AT 263-4185.
December 2015

- genotyped, with an APC mutation.
- Meets eligibility criteria for at least one FAP related disease group
- If prior colorectal surgery, at least three years since colectomy with ileal-rectal anastomosis (IRA) or total proctocolectomy with ileal pouch-anal reconstruction (pouch).
- Absence of major cardiac risk factors
- Absence of clinically significant hearing loss requiring a hearing aid.
- Adequate laboratory studies (hematology, chemistry, and urinalysis) at study entry.

**Tetanus/MMR Study**

**PI: Jennifer Weiss**

This research project to determine if people with IBD on different types of therapy have a lower amount of antibodies than healthy individuals. Antibodies are proteins used by the immune system to attack viruses like tetanus and measles. Antibodies can be introduced into the body through vaccines. The fewer antibodies there are, the harder it is for the antibodies to attack a virus, meaning that the person could get sick with a virus. This research project will help us figure out whether people with IBD have fewer antibodies than people without IBD.

**Controls**
- Individual without an IBD diagnosis
- Must have documented tetanus-diptheria (Td) / tetanus-diptheria-acellular pertussis (Tdap) at least 4 weeks prior to enrollment
- Must have documented measles, mumps, and rubella (MMR) at least two injections 4 weeks prior to enrollment

**Cases**
- Diagnosis of Crohn’s or Ulcerative colitis
- Must have documented tetanus-diptheria (Td) / tetanus-diptheria-acellular pertussis (Tdap) at least 4 weeks prior to enrollment
- Must have documented measles, mumps, and rubella (MMR) at least two injections 4 weeks prior to enrollment
- Currently taking azathioprine, 6-MP, a biologic, or methotrexate

TO REFER PATIENTS TO A TRIAL CONTACT THE RESEARCH STAFF AT 263-4185.