

CANADIAN PBC SOCIETY FUNDED RESEARCH

This year, the Canadian PBC Society has allocated funding to two specific research studies.

1. The Use of Grapefruit Juice to Reduce Pruritis



Drs. Kelly Burak (Principal Investigator), Kerri Novak, Mark Swain and colleagues of the University of Calgary Liver Unit will conduct a study to determine if grapefruit can reduce the itch and improve the quality of life of PBC patients with pruritis. While pharmacologic interventions to date are not always successful or have side effects limiting their use, recent case-report data suggest that grapefruit juice may reduce itch. If grapefruit juice is found to reverse or reduce cholestasis-associated itch, it may be a readily available and non-toxic adjunctive therapy used to control this disabling symptom. The data to support the use of grapefruit juice is uncontrolled and based on only two reports and ten patients. This study will be a randomized, cross-over trial, in which they hope to recruit 15 patients. Patients must have mild pruritis and be able to stop other therapies for itching for one week before beginning the study. They will be randomly assigned to receive first either yellow or pink grapefruit juice. After two weeks of once-daily ingestion of juice, the groups will undergo two weeks without any juice. They will then cross over to the other type of juice for an additional two weeks. We will be sharing the results of the study with you on its completion next year.

2. Diagnostic Applications to Detect Betaretrovirus Infection in Patients with PBC



Dr. Andrew Mason of the Division of Gastroenterology, Center of Excellence for Gastrointestinal Inflammation and Immunity Research at the University of Alberta, Edmonton, is conducting research into the role of the Human Betaretrovirus (HBRV) in PBC. Most patients with PBC have evidence of viral infection, and patients in clinical studies using combination anti-retroviral therapy showed significant, although not substantial, improvements, leading to a search for better antiviral regimens. This study will address the hypothesis that patients with PBC make antibody responses to HBRV proteins. It aims to set up an effective enzyme-linked immunosorbent assay (ELISA) to screen for prevalence of HBRV specific antibody in PBC patients. The development of a sensitive assay for detection of HBRV infection will aid the critical evaluation of HBRV's influence in PBC pathogenesis and help the researchers to conduct epidemiological studies to understand its role in the development of chronic liver disease.



OUR CONTRIBUTION ACKNOWLEDGED

On November 10, 2011, the three PBC Society directors, Barbara Badstober (President), Esther Schwartz and Lenore Bennett, attended a meeting with Dr. Jenny Heathcote, a pioneer in research into autoimmune liver disease, Francis Family Chair in Liver Research at the University Health Network and head of Patient-Based Clinical Research at the Toronto Western Research Institute. Dr. Heathcote presented the PBC Society with an Upper Canada Medal, which honours those who have made significant contributions to the Toronto Western Hospital. The Society was thanked for its "generosity and for the vital role you have played in supporting our work and the success of the entire team. Specifically, your generous contributions to PBC research have led to a major breakthrough in the field."



Left to Right: Lenore, Esther, Barbara & Dr. Jenny Heathcote

The Upper Canada medal has an interesting history. Initially created by the Loyal and Patriotic Society of Upper Canada to recognize distinguished service and bravery by volunteer soldiers in the War of 1812, the Society recognized a greater need when it later reduced the medals to gold bullion which was then used to fund the first general hospital in Canada.

FUNDRAISING

Sunday June 10, 2012 will be our next Woodbine Day at the Races. Yes, we know it's early, but hold the date for another fun day! We are dedicating the proceeds of the day to further Dr. Jenny Heathcote's research at the Francis Family Liver Clinic at Toronto Western Hospital. Dr. Heathcote will be our guest speaker giving us the latest news about relevant research.

OVERVIEW OF CLINICAL TRIALS IN PBC RESEARCH



Dr. Gideon Hirschfield gave this overview at the Toronto Area meeting on October 29.

There remains considerable interest globally in developing new treatments for PBC. A number of approaches are presently being actively investigated in different ways around the world. The first approach is the continued development of obeticholic acid (Intercept) and this bile acid therapy will hopefully be entering Phase 3 studies in 2012. (See following article) The next approach has been spurred forward by the recent genetic discoveries into why people get PBC. Stelara (Johnson & Johnson) is a medicine that works for patients with

psoriasis and appears very safe. It blocks an immune pathway thought potentially relevant to patients with PBC. Phase 2 trials are now underway looking to see if this specific immune system blocking drug can help patients with PBC. Finally, fenofibrate is a drug that is widely used for treating patients with high cholesterol. It also drops the liver biochemistry in patients with PBC, but doctors don't know if this is helpful or not. There are efforts in the US to do a proper clinical trial of this drug, and the limiting step is getting sufficient resources to back the study long term.

So there is a lot of hope that we can develop new treatments for patients with PBC. It just takes time and effort!

INTERCEPT PHARMACEUTICALS TO START PHASE III STUDY OF OBETICHOLIC ACID (INT-747) IN PBC

Last March, Intercept Pharmaceuticals, Inc. announced positive results from a Phase II clinical study of obeticholic acid (OCA; previously called INT-747) given alone as a monotherapy to 59 patients with PBC. The study evaluated the effects of 10 mg and 50 mg of OCA compared with placebo in patients with elevated alkaline phosphatase (AP). AP is a liver enzyme routinely used to evaluate the clinical status and disease progression of PBC patients.

At the end of the 12 week treatment period, both doses of OCA produced highly significant reductions in AP, the primary endpoint, compared with the patients receiving placebo. Pruritus (itch) was reported more commonly in the OCA-treated patients and increased with dose; otherwise, all other adverse events (i.e., potential side effects) were generally similar across the different treatment groups. Lower doses of OCA will be tested in upcoming Phase III trials, which, it is hoped, will be associated with less itch.

These data have been presented at both of the major European (EASL) and American (AASLD) liver disease conferences this year. The above study is Intercept's second study showing positive results in PBC patients. In 2010, Intercept reported positive data from a study of OCA in PBC patients who were also being treated with UDCA. The combination of the two drugs showed a significantly greater improvement in disease markers compared to UDCA alone.

Intercept has remained committed to supporting larger follow-on trials to prove the effects of OCA in PBC. The company has submitted a protocol to the U.S. Food and Drug Administration (FDA) informing them of plans to start an international Phase III study at the beginning of 2012, and is preparing submissions in several European countries. To be eligible, patients must be on a stable dose of UDCA (or unable to tolerate UDCA) and must have an elevated alkaline phosphatase level of more than 1.67 times the upper limit of normal. In this study, patients will receive OCA or placebo (a "sugar pill") for 12 months, then may enter a long-term study extension during which they will take OCA (free of charge) for up to 5 years. Intercept plans to begin recruiting study patients at several U.S. centers in January 2012.

A list of PBC doctors participating in Intercept's Phase III PBC study will be posted at:

- Intercept's website: <http://www.interceptpharma.com>
- ClinicalTrials.gov (a registry of federally and privately supported clinical studies conducted in the United States and around the world): <http://clinicaltrials.gov/ct2/show/NCT00570765?term=Primary+Biliary+Cirrhosis&rank=19>

Our thanks as always to Cathi I. Sciacca for keeping us informed. (Executive Director, Clinical Operations, Intercept Pharmaceuticals)

INTRODUCING JAE YON JUNG AS THE CANADIAN PBC SOCIETY LAWYER



Jae-Yon Jung, principal of JYJ Law, is a litigation lawyer with a reputation for delivering stellar results. Jae has expertise in many fields of law, including civil, corporate/commercial, employment & estate cases.

Jae is fluent in English and Korean, and conversant in basic French.

Jae has a Bachelor of Arts from York University in Mass Communications and Sociology and a Bachelor of Laws from Queen's University.

She is a member of the following organizations:

Ontario Bar Association, Canadian Bar Association, Korean Canadian Lawyers Association, International Association of Korean Lawyers, and the Federation of Asian Canadian Lawyers.

In addition, Jae is a section executive for two of the Ontario Bar Association committees: Civil Litigation and Sole, Small Firm and General Practice Committee.

We appreciate her willingness to help us in any legal matter that arises.

ATLANTIC CANADA

The Atlantic Group held an annual meeting, followed by a nice lunch, on November 9, 2011, at the Ramada Inn, Dartmouth. Six members attended. The current officers agreed to continue in their positions: Judi Pemberton, President; Pat Berrigan, Secretary; Ellen Hearn, Social and Phone Committee; and Barb Pollard, Social and Cards Committee. One member of the group is recovering from a liver transplant and expected home within the week. They had had one request for information about liver transplant from a lady in Newfoundland. Judi reported that Dr. Peltikian is now head of GI Medicine. Pat was asked to liaise with the Liver Foundation contact to find out their plans for a LiveRight conference or other activities.

The next meeting will be the spring Bingo Bowling social on Wednesday, May 23, 2012, when Judi will give each person 10 flyers to distribute for PBC Awareness Day on May 30, 2012.

For information about the group, please contact Judi Pemperton: atlantic@pbc-society.ca or 902-798-5554.



The Canadian PBC Society is not responsible and cannot be held liable for the accuracy of any medical or treatment information printed here, which is not necessarily representative of the views and opinions of the Society. Please consult your own health care provider before making any changes in your daily living or treatment plan.

TORONTO & GTA

An information meeting was held on Saturday, October 29, 2011, at 8 Covington Road. Dr. Gideon Hirschfield gave an overview of current research on treatments for PBC (see Page 3) to an interested audience of about 20 people. Barbara Badstober thanked Dr. Hirschfield, who will be joining the Liver Centre, University of Birmingham in the UK before the end of the year, for his work and involvement with the Society. She presented him and his Research Coordinator, Catalina Coltescu, with gift certificates in appreciation of their efforts. The talk was followed by a draw for two \$25 gift certificates donated by Diana Ponte of "Call Me Cupcake". Thanks to Katherine Fuerst for arranging the room and coffee.

For information, please contact the Society: info@pbc-society.ca

MANITOBA

I have been dealing with some minor medical issues (unrelated to PBC), so we have not met as a group since the spring. We do keep in touch to some degree using e-mail, telephone calls and Facebook. There are 19 members, but many of us have yet to meet. A family picnic was planned for September 11 at a local park but no-one was able to attend due to previous commitments, etc. Perhaps a Christmas gathering will materialize this year and there will be more activity in 2012.

Members have requested more brochures and I have placed several in medical clinics.

May you all enjoy a wonderful celebration with family and friends. For information about the group, please contact Carol Seburn: manitoba@pbc-society.ca or 204-254-5226.