

10TH ANNIVERSARY EDITION

PBC connections

A Canadian PBC Society Newsletter

2013 • VOLUME ONE

UPDATES

INTERCEPT PHARMACEUTICALS COMPLETES ENROLLMENT INTO ITS PHASE III TRIAL OF OBETICHOLIC ACID (OCA) IN PBC

Enrollment in the Phase III 'POISE Trial' was successfully completed by the end of December 2012. A total of 217 patients at 59 centers in 13 countries entered the trial. The double-blind phase of the study lasts 12 months after which patients will enter a long-term extension phase for several years. Typically, Phase III is the last stage of a drug's development before gaining regulatory approval. Results from the double-blind phase of the trial are expected before the middle of next year. In Canada, the study is being conducted at the University of Toronto by Dr. Hemant Shaw and at Hôpital Saint-Luc/CHUM in Montreal by Dr. Catherine Vincent.

The long term phase of one of Intercept's earlier Phase II trials of OCA is currently ongoing with 19 patients continuing to receive OCA, about half of whom have been on OCA for over 3 years. Longer-term therapy with OCA continues to appear safe and tolerable in PBC patients and as previously reported, significant improvements in liver enzyme tests, including alkaline phosphatase, have been maintained.

Intercept remains committed to proving the effects of OCA in PBC and remains in communication with the U.S. Food and Drug Administration (FDA) and other regulatory authorities with plans to proceed into a confirmatory Phase 3 trial.

More information about the ongoing Phase III POISE trial and Intercept can be found at:

- 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/NCT01473524?intr=%22INT-747%22&rank=4>
- Intercept's website: www.interceptpharma.com

RESEARCH INTO PBC AND GRAPEFRUIT

Our initial criteria were revised to enable us to recruit more patients and to date we have successfully enrolled three subjects. Our aim is to recruit at least five patients before starting the administration of the grapefruit and have every intention of reaching our goal in the near future. However, because at this point we have refrained from administering the juice, there are no outcome results to give at this time.

Itsabo John Oshiomogho, *Clinical Research Assistant*
Liver Unit
University of Calgary



UPDATES

RESEARCH INTO RETROVIRAL INFECTION IN PATIENTS WITH PBC

The Canadian PBC Society has kindly provided funds to our PBC research program at the University of Alberta. This particular project is geared towards constructing a "Diagnostic application to detect betaretrovirus infection in patients with PBC". The aim of this undertaking is to make a reliable and reproducible kit that can detect antibodies to the human betaretrovirus in patients' serum. For this project, we have expressed the human betaretrovirus Surface protein in a human cell line in culture. The viral protein is collected and the coated onto a 96 well plate to make an ELISA assay for detecting betaretrovirus antibodies in patients' serum (<http://en.wikipedia.org/wiki/ELISA>). Once we have constructed a reliable diagnostic assay, we can then screen a large collection of samples to determine who has evidence of betaretrovirus infection.

This virus was first characterized in patients with PBC in 2003 in a report from my laboratory and our collaborators in the United Kingdom. Since then we have been studying the relationship of betaretrovirus infection with PBC in various clinical and laboratory investigations. In our original studies, our collaborators at the University of Glasgow observed virus like particles by electron microscopy in PBC patients' biliary epithelial cells provided from researchers at the University of Birmingham. At the same time my laboratory had obtained the viral genomic DNA sequences from PBC patients' samples. Then we found that most patients with PBC had evidence of viral infection in their tissues. Subsequently, we have isolated the virus in culture as a proof that patients have a retrovirus infection. Now we are now trying to make diagnostic tools to detect antibody responses to the betaretrovirus.

However, the hypothesis that patients with PBC have a retrovirus infection is controversial because other laboratories have been unable to find the virus in patients with PBC. There are good explanations for the different observations from other laboratories. Nevertheless, it is up to us to provide better data to support our notion that PBC is a retroviral disease. Accordingly, we are identifying DNA junction sequences within the human genome where the human betaretrovirus has inserted. These studies are being conducted to provide incontrovertible evidence that the viral infection is at the site of disease within the bile ducts from patients with PBC.

In the clinic, we have conducted several pilot studies over the years using anti-retroviral therapy. We found that PBC patients treated with Combivir anti-retroviral therapy experienced significant reduction in their liver blood tests as well as inflammation in their liver biopsies. These data provide some circumstantial evidence for a retroviral infection in PBC. Although we could show significant improvements in these anti-retroviral pilot studies, the changes were not substantial. So we continue to look for better antiviral regimens.

Fortunately, we found several of the PBC mouse models also have evidence of betaretrovirus infection that resembles the virus found in patients with PBC. Notably, the NOD.c3c4 mouse model of PBC develops spontaneous inflammatory bile duct disease associated with betaretrovirus infection in the bile ducts. So we have used this model to show that different combinations of antiviral therapy block the development of bile duct inflammation in this mouse. In order to find better treatment regimens for patients with PBC, we continue to use this model to assess different antiretroviral combinations for the betaretrovirus infection.

Recently, some encouraging data has emerged to suggest that one particular combination of anti-retroviral treatment may provide some benefit for patients with PBC. In 2011, Dr. Gabriel Schembri reported one case in *The Lancet* of a man with HIV infection who developed PBC and human betaretrovirus infection. He was treated with the antiretroviral combination of Kaletra and Truvada and he developed a marked reduction of his liver tests. Subsequently, he received Ursodiol treatment and then normalized his liver studies. At the University of Alberta, I have treated a young patient with the same combination of anti-retroviral medications over the last 3 years for the development of severe recurrent PBC after liver transplantation. She experienced a reduction in her liver tests that normalized at one point. More importantly, her serial liver biopsies showed a reversal of PBC from stage III disease to no obvious signs of PBC on her last biopsy. She also reported a marked improvement in energy levels and other symptoms.

Encouraged by these results, we are conducting more antiretroviral pilot studies at the University of Alberta. However, we have found that many patients with PBC find it difficult to tolerate Kaletra as they develop abdominal complaints, such as nausea, cramping and diarrhea. Nonetheless, we continue to study other combination therapies. Once we have found a well-tolerated regimen that shows clear and substantial benefit for patients with PBC, we plan to invite other sites to join in with these treatment studies in a randomized controlled trial. In the mean time, we hope to create a clinically useful diagnostic kit to detect the presence of human betaretrovirus infection in blood soon.

For further information, read A Viral Debate, International Innovation, 2013
http://cegiir.med.ualberta.ca/forms/p43-45_Andrew_Mason.pdf



Andrew L. Mason *MBBS MRCPI*,
Professor of Medicine, University of Alberta
Senior Scholar, Alberta Heritage Foundation for Medical Research

IT'S OUR 10TH ANNIVERSARY!

BRING THE FAMILY AND ENJOY A FUN DAY IN AID OF A GOOD CAUSE

If you're within striking distance of Toronto, don't miss our annual fundraising **Day at the Races at Woodbine Racetrack** on **Sunday, June 9, 2013**.

Watch the action on the track from the elegant Northern Dancer Room while enjoying a fabulous buffet, silent auction and 50/50 draw.

Betty Van Luven, Coordinator of the South West Chapter, will be our Guest MC and Speaker.

Arrival 12:15 pm | Buffet Opens 12:30 pm.

Tickets cost \$90 per adult and \$25 per child 5-12 years. No charge for children under 5 years.

Deadline to buy tickets is May 31, 2013. Don't miss it!

TORONTO WESTERN HOSPITAL ANNOUNCEMENTS

Dr. Jenny Heathcote Retiring

We are both happy and sad to announce that Dr. Heathcote is now officially retiring after 34 years of service at the Toronto Western Hospital. Her retirement is effective July 2013. She will continue to run the Autoimmune Liver Clinic, every Wednesday at Toronto Western Hospital until that time.

Dr. Harry Janssen, Professor of Hepatology from the Netherlands has arrived and is now the Head of Hepatology for Toronto Western and Toronto General Hospitals as well as the Francis Family Chair in Hepatology Research. He has just recruited one of our very best trainees to take over the Autoimmune Liver Disease clinic – her name is Dr. Angela Cheung.

Dr. Heathcote graduated from the Royal Free Hospital School of Medicine, London, UK in 1968. She was the first Hepatologist to be hired at TWH, where she has built an internationally recognized clinical liver research unit, with a major interest in viral hepatitis and autoimmune liver disease. She has been a Professor at the University of Toronto since 1995. The American, European as well as the Canadian Liver Associations have presented her with their distinguished Awards in honor of her sustained scientific contributions to the field of liver disease and the scientific foundations of hepatology. These are only three of many awards she has been given over the last 34 years.

We wish her all the best and a great retirement (back living in the 'country' as she did as a child – but this time in Canada).

International Leader in Liver Research Recruited to University Health Network

We are delighted to announce that **Dr. Harry Janssen** has been appointed as the Francis Family Chair in Liver Research at University Health Network (UHN), succeeding Dr. Jenny Heathcote in her role. Dr. Janssen is also Head of the Liver Clinic at UHN.



Dr. Janssen, an internationally renowned physician and liver researcher, was previously Head of the Liver Unit at Erasmus University Medical Centre in the Netherlands. With Dr. Janssen's recruitment, UHN will remain at the vanguard of liver research, and continue to transform the way we care for people and their families in our hospitals, and in healthcare organizations around the world.

Dr. Janssen plans to enhance the treatment continuum for patients with every form of liver disease through further integration of clinical care, research and education at both Toronto Western Hospital and Toronto General Hospital.

Dr. Janssen's full profile can be seen on the website of Toronto Western Hospital.

ANNUAL GENERAL MEETING

The Annual General Meeting was held at 8 Covington Road, Toronto on Saturday, April 13, 2013 with nine members in attendance. Proxies held by the President completed and surpassed the required quorum. Thanks go to Katherine Fuerst for arranging the meeting room.

The meeting opened at 10:00 a.m. and adjourned at 11:30 a.m. Members approved the minutes of the previous meeting, the financial statement, which showed a healthy year-end balance, and the President's report, which is reproduced below. Mark Wolansk was retained as accountant. An unchanged slate of officers was approved by a show of hands. New Business prompted some discussion about disbursement of funds for research before the meeting adjourned for a more informal exchange of ideas and information.

SAD NEWS

We are sorry to inform you that two members of the Society have died this year. In January, **Andrea Armstrong** died of PBC; the BC Group will miss her upbeat presence.

Marion Frances Amirault of Yarmouth, NS, died peacefully on April 26 after a long battle with cancer. Her daughter wrote to the Atlantic group on behalf of Marion's family: *Mum was proud to be a member of your group and often referred to some of the stories and information that you shared. We thank you for supporting her throughout her illness with PBC and cancer.*

regional connections

ATLANTIC CANADA

Annual meeting, October 17, 2012

The meeting was called to order by the president, Judi Pemberton. There were 10 members and one husband present.

The minutes of the meeting of November 9, 2011 were approved as circulated. Judi stated that we have \$176.58 in the bank. It was moved by Judi Pemberton, and seconded by Pat Berrigan that \$100.00 be sent to the PBC Society for research. MOTION CARRIED.



Judi asked if those who are committee chairpersons were willing to stay on in their present capacity. Judi will continue as president, Pat Berrigan will remain as secretary, and Ellen Hearn and Barb Pallard will continue to look after the social committee, and the sending out of cards. It was suggested that we hold the spring social at a later time of day so that those who have a distance to travel will be able to attend. There being no further business, the meeting adjourned.

Notice of Spring Social Gathering, May 15, 2013

Please meet at 11:30 for Bingo Bowling at the Fairlanes Bowling Alley, Halifax Shopping Centre. We will have lunch around 1pm in the food court upstairs. That will give us plenty of time to socialize. Bragging about bowling scores is encouraged! It's a fun game and experience is not necessary for participation (points are awarded for gutter balls). We need someone to keep score.

Each person is asked to donate a small \$1 or \$2 prize or two for the occasion.

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

SOUTH WEST ONTARIO

Hello, Fellow PBC'ers!!



Now that the weather is beautiful, I can hardly wait for the get-togethers, all across the regions.

Here are some photos of the South-west Ontario and Niagara Regions' Easter get-together, held in Burlington, Ontario. Although our numbers were few, we had a great time! We ate, shared stories, and laughed at each other's jokes! Did I mention the chocolate??

For information about the group, please contact **Betty Van Luven:** bvanluven@rogers.com or 519-954-3765.

QUEBEC

For information about the group, please contact **Francine Lamontagne:** QuebecRep@pbc-society.ca. Pour y assister, n'hésitez pas à contacter **Francine Lamontagne:** QuebecRep@pbc-society.ca

MANITOBA

Meeting, November 12, 2012

We had lunch together at a Pizza Hut and enjoyed a time of sharing and laughter. Derrick, husband of one of the liver ladies, helped us to keep our sense of humour. We welcomed a new friend, Valerie, and were happy to see Candice from Dauphin, MB. Others attending were Kathy, Karen, Sandra and myself.

Once again Ruth from the CLF joined us. We truly appreciate her input. I will be speaking briefly at a special event sponsored by Nygard Canada called "What A Girl Wants". There will be a fashion show, silent auction, entertainment and refreshments. Proceeds will go to the work of the Canadian Liver Foundation. I will put in a good word for the PBC Society as I tell my story.

Meeting, April 26, 2013

Our group has not met for some time but today nine out of a possible 20 had lunch together at The Olive Garden. Three new members were with us. A number of our Manitoba contacts live outside the city of Winnipeg so cannot attend unless they make a special trip. As is the case with much of Canada, we here in

Winnipeg were experiencing a long, cold and snowy spring. That is one of my excuses for not calling a meeting but today was beautiful. Also, I was in Toronto for two weeks in Feb/March for my youngest grandson's 3rd birthday, very important since all my other grandkids are adults. While there I experienced some extreme fatigue and heart symptoms, eventually discovering that my haemoglobin was only 68, so I required two units of blood. The doctors and staff at Toronto Western were great. I feel normal now (whatever normal is) and am back to my usual busy schedule. Something to think about; be sure to have your haemoglobin checked regularly as the fatigue level was unbelievable. Ruth Magnuson of the Canadian Liver Foundation provided more invaluable information, particularly for those trying to procure disability payment.



For information about the group, please contact **Carol Seburn:** manitoba@pbc-society.ca or 204-254-5226.

ALBERTA NORTH

1. Sunday September 15th is the date set aside for our 6th annual BBQ & Silent Auction.
2. On Monday February 4th, 2013 Dr. Arya Sharma spoke to our group about obesity assessment and management for patients of PBC.

Dr. Sharma was curious as to why our group would be interested in what he had to say, since our condition is not marked by weight gain; in fact, with advanced PBC weight loss can be a problem. Our answer to him is that managing other areas of health enables us to better manage the effects of our primary condition.

The lecture given by Dr. Sharma underscored the fact that there is management, but no cure for obesity. (Where have PBC patients heard that before?) On the upside he gave some simple, but effective tips and some highlights are:

- eat at home
- eat before you get hungry (since overeating results from becoming overly hungry)
- stop the gain, even if you don't lose weight

Dr. Sharma is founder and Scientific Director of the Canadian Obesity Network, a network of over 8000 obesity researchers, health professionals and other stakeholders. He is also the Past-President of the Canadian Association of Bariatric Physicians and Surgeons.

For information about the group, please contact **Shauna Vander Well:** alberta@pbc-society.ca or 780-962-6217.

BRITISH COLUMBIA

There is really not much to report from us this year. We will be having a spring luncheon in May, date unknown yet.

For information about the group, please contact **Kathryn Swift:** kswift@pbc-society.ca or 604-988-4030.

CANADA HELPS

What We Do CanadaHelps is a registered charity with a goal to make giving simple. Through CanadaHelps.org, anyone can donate online to any registered Canadian charity. We have proudly facilitated over \$100 million in charitable donations through our website since it was launched in 2000. **For Donors** CanadaHelps is a one-stop-shop for giving. We made donating online easy and secure.



CONTACT US

Canadian PBC Society

4936 Yonge Street, Suite 221, Toronto, Ontario M2N 6S3

Toll free: 1-866-441-3643

E-mail: info@pbc-society.ca

www.pbc-society.ca

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