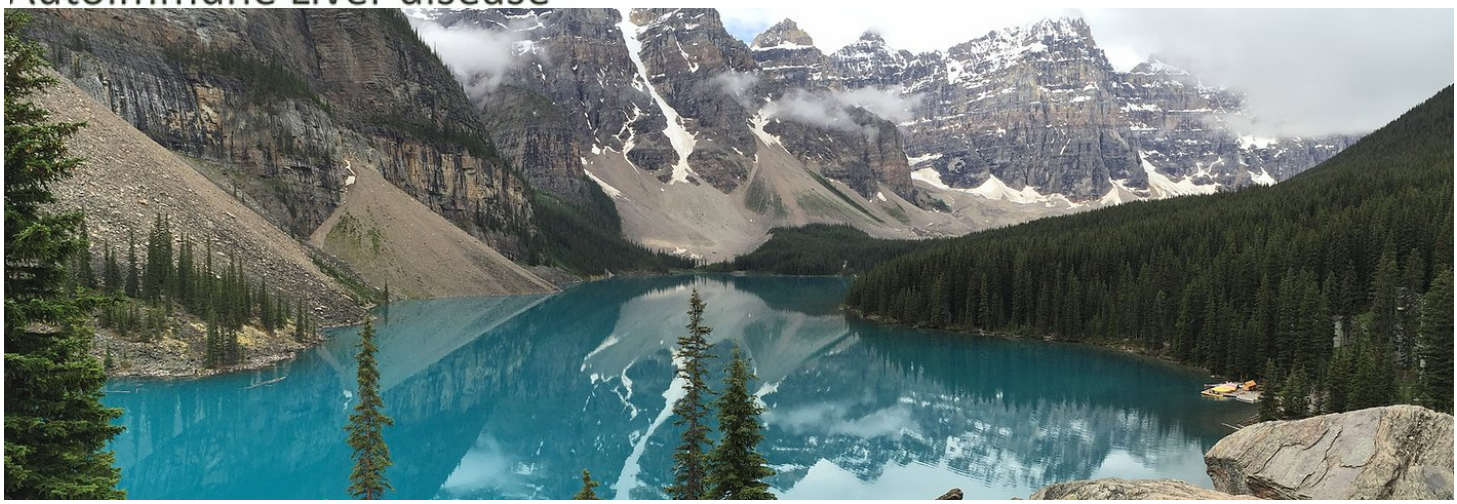
CaNAL

Canadian Network for Autoimmune Liver disease

IN THIS ISSUE:



PROJECT UPDATES:

- 10 Active Sites
- 5 Sites With Activation in Progress
- Current Patient Cohort: 3690

ABOUT CANAL

The Canadian Network for Autoimmune Liver disease (CaNAL) is a longitudinal observational cohort study of patients diagnosed with Primary Biliary Cholangitis (PBC), Autoimmune Hepatitis (AIH), or overlap syndrome. This nationwide registry focuses on high quality long-term follow-up of individual patients from major Canadian centres including The Toronto Centre for Liver Disease (TCLD).

The primary goal of CaNAL is to build a Canadian registry of patients with PBC, AIH, and overlap syndrome in order to allow new insights into autoimmune liver diseases. As these illnesses are rare and slow progressing, this type of large-scale approach will help enhance our understanding by providing information about disease development, and identifying risk factors associated with important outcomes.

Variables such as patient demographics, quality of life, and patient outcomes are collected to allow for the identification of biomarkers. This can help predict disease progression or non-response to therapy, as well as aid in the earlier diagnosis of autoimmune liver disease to ensure timely treatment and prevent disease progression.

STEERING COMMITTEE:

Andrew Mason
Bettina Hansen
Harry Janssen
Gideon Hirschfield
Aldo Montano-Loza
Mark Swain
Catherine Vincent
Hin Hin Ko
Eric Yoshida

RECENT PUBLICATION SUMMARY

Real-World Effectiveness of Obeticholic Acid in Patients with Primary Biliary Cholangitis. Hepatology Communications.

Ursodeoxycholic Acid (UDCA) is the standard therapy for patients with primary biliary cholangitis (PBC), but ~40% of patients do not respond adequately to it. These patients remain in need of additional treatment, and so Obeticholic Acid (OCA) was approved for use in Canada in May 2017 based on evidence from a phase 3 randomized control trial (POISE).

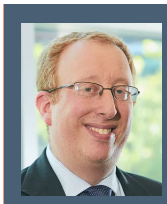
This retrospective cohort study describes the effectiveness of OCA in a real-world setting at two Canadian liver clinics: Toronto Centre for Liver Disease (TCLD) and Centre Hospitalier de l'Université de Montréal. This study included adults with an established clinical diagnosis of PBC who were started on OCA based on their Hepatologist's discretion.

Electronic medical records were abstracted for clinical data. Changes were assessed in serum alkaline phosphatase (ALP), total bilirubin (TB), and gamma-glutamyl transferase (GGT) over the duration of the OCA therapy. Other assessments included changes in alanine aminotransferase (ALT), aspartate aminotransferase (AST), immunoglobulin M (IGM), platelets and albumin, achievement of the POISE primary endpoint, treatment discontinuations, dose reductions, and tolerability. Mixed effects regressions were employed to examine the association between duration of OCA therapy and changes in blood values.

64 patients were initiated on OCA between August 2017 and June 2019. Median age at initiation of OCA was 54.6 years and patients were on OCA therapy for a median of 13 months. A significant reduction in ALP of 55 U/L, GGT of 138U/L, and in ALT of 11.9U/L over 12 months of OCA treatment was observed. Reductions were already visible within 3 months of treatment. AST and IgM values also declined significantly during therapy while total bilirubin, albumin, and platelet levels remained stable. The most common tolerability concern was pruritus (itching) and it was reported in 41% of patients. In total 17% (11 patients) discontinued the OCA treatment, 6 of whom stopped due to a insufficient response to OCA after 1 year. The remaining 5 patients discontinued treatment due to pruritus.

Furthermore, OCA was also effective in patients who did not meet the inclusion criteria of the POISE trial. Due to strict inclusion and exclusion criteria, patients enrolled in clinical trials often differ from patients being treated in a real-world setting. The fact that effectiveness of OCA was observed in these patients as well highlights that OCA is effective in a broader range of patients. In summary, the findings suggest that OCA is effective in real-world patients regardless of whether or not they resemble patients in clinical trial

Reference: Roberts SB, Ismail M, Kanagalingam G, Mason AL, Swain MG, Vincent C, Yoshida EM, Tsien C, Flemming JA, Janssen HL, Hirschfield GM., Hansen BE, Gulamhusein AF. **Real-World Effectiveness of Obeticholic Acid in Patients with Primary Biliary Cholangitis**. Hepatology communications. 2020 Sep;4(9):1332-45. doi: 10.1002/hep4.1518.



CLINICIAN MESSAGE

Dr. Gideon Hirschfield

Staff Physician, Toronto Centre for Liver Disease

Lily and Terry Horner Chair in Autoimmune Liver Disease Research

What impact has COVID-19 had on the CaNAL project and the care provided at the Liver Clinic?

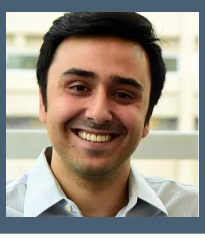
"COVID-19 is and will continue to be a challenge for all of us. We have pivoted to an entirely remote work flow. Our clinic recognised in March 2020, that we could contribute to keeping everyone safe by using remote tele-medicine. Since many of our patients come far to clinic, for many this was actually a bonus! Sick patients are of course seen in person as needed, but we now use telephone and Webcam visits very effectively. The CaNAL project is important to us, so we adapted rapidly as well, thanks to everyone working hard, and in new ways. This meant the consenting and follow-up process for the study had to be done distantly, along with setting up virtual or phone appointments for the Liver Clinic. It was a tough battle at first, but now we have an effective and simple system in place. I am incredibly grateful to the team for being so industrious and committed to the project, and thankful that our patients continue to value participation in this study."

Remote consent vs. in person

"Both processes have their pros and cons. A pro to remote consent is that patients who do not have time after their appointment are contacted at a later date. The downside is that it is sometimes difficult reaching patients. Obtaining consent also takes more time as you explain the study, then send the consent form, set up another call, etc. Consenting patients in-person in the clinic setting is done on the spot after their appointment and all questions can be answered by the coordinators. However, since implementing the remote consent, we have received positive feedback from the patients and have streamlined our process. Paradoxically our new (in fact now since March 2020 dare I remind us all) entirely virtual programme, except for very sick patients, has meant clinic timekeeping is in fact better, and we hope ultimately access to our research studies are equally so. We can see the end in sight for COVID-19 but fully intend to learn and continue from the new approaches to care and research we have implemented."

Current status of study

"The study is going well. Right now we have 10 active sites across Canada. We are still in the process of getting more sites on board and enrolling more patients to build our database. We are hoping to get a good representation of the population across the country to conduct more analyses. We currently have one published manuscript and a number of conference abstracts looking at the data we have."



Surain Roberts
PhD Candidate

Why are studies like CaNAL important?

"Registry studies like CaNAL are an important part of studying PBC (and any rare chronic disease for that matter). In order to learn more about PBC, we first need to collect information from a large number of patients over time. However, because patients with PBC are uncommon, this is difficult! Our registry approach allows us to reach all over Canada and includes as many patients as possible, so that we have a large enough sample to do meaningful research that can impact the greater population of patients with PBC."

"Another great aspect of registry studies like CaNAL is that we collect information about a wide variety of topics that are important to patients. While clinical trials are narrow in their focus and retrospective studies only use pre-existing data from medical charts, CaNAL follows patients in real time and collects medical chart data from the past. This provides CaNAL a unique opportunity to ask questions directly to patients and document important information including symptoms, lifestyle, and quality of life that other studies are less equipped to address."