Managing HIV in a Modern World

Thirteenth Annual HIV Pharmacy Education Day – April 16, 2021

Introduction

This year marks the 25th Anniversary of the Ontario HIV Professional Specialty Group, which was launched in 1996. This period was a medical turning point in the treatment of HIV when the first effective triple therapies became available and the role of an HIV pharmacist was born to support these very complex regimens. In her opening remarks, Linda Robinson noted and celebrated the contributions of two visionary young women Alice Tseng and Michelle Foisy, in founded the group. She also acknowledged and thanked the event's corporate sponsors, Gilead Sciences, Viiv Healthcare, Merck, AbbVie, and AstraZeneca for their support.

COVID-19 Special Sessions

Vaccines – update and focus/challenges in HIV

Dr. Abdu Sharkawy

Dr. Sharkawy has become a leading voice for public education in the pandemic. He spoke about:

- Where we are in the epidemic from an epidemiological standpoint including variants
- Relative efficacy and appropriateness of different vaccines
    - Dosing intervals
    - Thrombogenesis

The numbers defining the COVID epidemic in Canada continue to change constantly, and Canada recently crossed the million-infection threshold. The first wave was a bunny hill compared to the current third wave of infections, and although Ontario is testing more widely and effectively than it did in the first and second waves (50,000 tests/day), the current wave is not contained.

Efficacious vaccines that target the spike protein mediating attachment to the host cell are now rolling out, but it is unclear when, or how well vaccination will contain the epidemic. We are already beginning to see virus mutations in the receptor binding domain (RBD.) The RBD is the primary target for neutralizing antibodies (both natural immunity and vaccine drive immunity), and the emergence of RBD mutations may undermine vaccine efficacy.

Dr. Sharkawy briefly review the most prominent variants, emphasizing the impact on vaccine success. He noted that an escape mutation, E484K, now known to be associated with both B.1.351 and P.2 appears to reduce the capability of neutralizing antibodies and thus vaccine efficacy:

- **D614G** was one of the earliest variants detected (first in Germany) became the dominant strain worldwide. It may enhance RBD-ACES binding, compared to wild type virus.
- **B.1.1.7** was first identified in the UK and is now a dominant variant in many places, with many cases in Ontario. It has higher RBD binding than other mutations, which increases the virus' "stickiness" making it more infectious and increased mortality. There is minimal impact on neutralizing antibodies. UK evidence shows it's susceptible to AstraZeneca (AZ) vaccine.
- **B.1.351** was first detected in South Africa. It does not appear to increase disease susceptible, but does escape neutralizing antibodies from prior infection. Data suggests that Jansen vaccine efficacy reduced to 57% from 72% and AZ vaccine only about 10% effective in South Africa.
- **P.1** was first describe in Brazil and Japan. It harbours RBD and spike mutations so that is more transmissible and able to evade protective immunity (only 25-61% response from previous infection!!)

These variants are appearing in Canada with many cases of B.1.1.7 in Ontario. Modelling suggests these variants are having an increasing impact. See https://art-bd.shinyapps.io/covid19canada/ for detailed Canadian data and modelling. Dr. Sharkawy observed that the vaccine rollout is not happening fast enough to counter infections, with only the northern territories approaching 50% of adults fully vaccinated.

He briefly compared the efficacy of the vaccines:

Vaccine	Type	Trial Efficacy	Real life notes
Pfizer-BioNTech (Pf)	mRNA	95%	72% one dose, 85% two doses
Moderna (M)	mRNA	94%	
AstraZeneca Oxford (AZ)	viral vector	62%/90%	Single dose 95% effective to prevent hospitalization
Janssen (J&J)	viral vector	72%	Down to 57% in South Africa (variant?)
Novavax	protein + adjuvant	96% original	86% for B.1.1.7 60% for B.1.351

Two other protein sub-unit + adjuvant vaccines will be manufactured in Canada (Medicago and Sanofi/GSK), which will be important if we need boosters. This is likely.

Dosing interval - The National Advisory Committee on Immunization (NACI) has recommended that the dosing interval be extended to up to 4 months in Canada to allow more people to receive first vaccine doses. Deferring the second dose has shown little loss of efficacy with hepatitis and shingles (DNA vaccines). A longer interval might facilitate more effective T cell deployment with an initial (durable) B-cell response, but the only firm evidence is with the AZ vaccine. The multi-tiered design of the trial comparing boost intervals, showing that waiting more than 12 weeks had a stronger response than six weeks. This was statistically significant!

Data on Pf vaccine shows immunity around 14 days with no increase in infections until 90-100 days after that first dose, but not true for the elderly or immune compromised (see Pimenta D. BMJ 2021 March.) Another UK study (still in preprint) suggest that delaying the second dose potentially leaves most solid and haematological cancer patients wholly or partially unprotected.

Clotting – The rare clotting effects of vaccines appear to be a vaccine induced immune mediate thrombocytopenia (VIIT). The hypothesis is that the immune response to the spike protein and ACE receptor binding triggers a platelet factor 4 antibody complex with B cells and that leads to an aggregation of cells and platelets that ultimately leads to a clot. These clots are similar to heparin induced clots and can occur in unusual locations. They are much more common in COVID-19 infections than in vaccine treated patients. The relative risk of vaccine clots versus COVID infection is higher in younger people but is still quite low. **COVID infection in any age group is worse than vaccine.**

One emerging treatment for COVID-19 is showing promise. Inhaled budesonide (STOIC trial) shows only 3% of treated patient required urgent care versus 15 of usual care patients. (Ramakrishnan S et al, Lancet, Resp Med, 2021 Apr.)

Dr. Sharkawy concluded by highlight some important future directions for Canadian health policy prompted by COVID-19:

- Domestic vaccine production
- Diversifying rapid testing programs
- Enhancing early detection systems
- Integration of regional Public Health policies
- Consensus building across scientific, social, financial, political sectors

Is HIV a Risk Factor for Worse COVID 19 Outcomes?

Alice Tseng

There has been some debate in the literature about the impact of COVID-19 on people living with HIV.

Why it might be worse?	Why it might be better?
• Immunodeficiency/immune dysregulation • Comorbidities • Social determinants of disease • Accelerated aging	• Immunological factors proposed to be protective, but no evidence • ART might affect outcomes, but no evidence for a protective effect

Some initial reports from New York suggested that HIV might actually be protective for COVID infection; subsequent case reports suggested that those on effective ART were not at higher risk of infection or poorer outcomes. Now a large meta-analysis (Mellor MM et al. AIDS 2021 March) has shown that being HIV positive doubles the risk of death! The risk was associated with:

- Older age
- Chronic lung disease
- Low CD4+
- Racial and income disparities (Weiser JK et al. JAIDS, 2021 March)

Ultimately it is still unknown, whether or not there is an absolute increased risk for a person on effective ART with suppressed viral load.

Treatment Effects - There have also been multiple conflicting studies about the impact of HIV treatments. The meta-analysis above captures observational cohorts that suggest protective effects for tenofovir (TAF), and other literature with worse outcomes.

- PrEP use does not appear to protect against COVID-19 infection (Ayerdi O et al, OFID, 2020 Nov)
- COVID-19 infection does not appear to adversely affect CD4+ counts or viral load as long as patient continues meds
- There is a cascade of indirect COVID-19 impacts on people living with HIV and their access to treatment and ability to manage HIV
- The COVID-19 pandemic is associated with declines in new PrEP starts and refill rates (Krakower D et al. IAS abstract OACLB0104, 2020)

Ultimately the pandemic has led to a higher rate of diagnosis associated with acute HIV infection but increased odds of not being virally suppressed for those living with HIV and more admissions due to AIDS-defining conditions. More people are falling through the cracks and have limited access to social supports. Alice recommended the resource, Responding to HIV care challenges presented by COVID-19, from the British Psychological Society.

COVID testing and vaccines in pharmacies

Ben Gunter

Community pharmacist Ben Gunter described his experience participating in COVID-19 testing programs:

1. **Ontario's free public asymptomatic COVID Testing Program** - The criteria for testing via this program change frequently, which is a significant challenge for test delivery. Initially most clients were testing to gain access to Long Term Care, but much of this testing is now done at LTC facilities. Pharmacies are now testing more school related populations (only asymptomatic,) as well as those traveling to Indigenous communities, as well as farm workers and international students.

International travelers cannot use this public program. The testing uses an anterior nasal swab (just in the nose, bilateral) and the laboratory comes once a day to pick up specimens. Clients can log in with OHIP card for results, which take 48-72 hours, or longer when demand is high.

2. **Private Pay Asymptomatic International Travel Testing –** This option emerged when public support for this international travel testing was shut down. Travelers now pay for this service and the pharmacy books appointments through LifeLabs. Testing results take 24-48 hours and use the same anterior nasal swabs.
3. **Rapid Antigen Test (Panbio/Abbott device)** – This uses the same sample collection as other tests but tests with a rapid 15-minute test kit. This is a screening test. Any positive has to be sent to an assessment centre for confirmatory testing.

Questions for COVID Special Sessions

What is the evidence of using different vaccine technology for initial vs boost dose (viral vector + mRNA)?
There is a trial ongoing right now for combined AZ and Pfizer in the UK. There is plausibility to this concept and a practical role if there are supply limitations of one vs another vaccine.

People who receive AZ ask "when are they in the clear" of not worrying about clots post vaccine?
All of the serious VIIT clots have been reported from 4-22 days post first dose only. If you get through that window, you are almost certainly "free and clear"

How do we address vaccine hesitancy re: AZ. Do you have tips?
The situation has been complicated by serious adverse events and communication challenges. Trust is very easily lost. Side effects are rare and the concept of choice has limitations. If people hunkered down at home, they can wait, but that doesn't apply to most. Those at higher risk should be encouraged as possible. People should be warned that the booking systems can be a nightmare. They may wish to call.

What about ASA prophylaxis (some family doctors are recommending 2 weeks of ASA post A/Z vaccine?)
There is no data for this and it is definitely not recommended. No evidence that ASA would prevent VIIT. No role for ASA pre-vaccine to prevent thromboses and a definite risk of ulcers, GI bleeds etc.

Health Canada just approved a Rapid Response Test device for home use. Are they accurate?
Home tests are limited in terms of sensitivity 70-75%, and particularly problematic for asymptomatic folks don't usually have a high enough VL. They are useful in higher risk environments – factories, schools, where people need to make rapid decisions about how much exposure they should have to others.

There is lots of misinformation about mRNA vaccine.
mRNA vaccines do not change DNA or make any permanent alterations to cells.

Other common questions about vaccine side effects?
Allergy questions in screening may be misleading. Shellfish allergies etc have no correlation with risk of allergy to the vaccine. An allergic reaction to PEGG during a colonoscopy is relevant because it is the most immunogenic element of vaccine.
Serious adverse events of any vaccine all happen in the first 45 days. All trials waited for 50% of participants to have second dose 60 days. Clots happen in the first three weeks. If you do not have side effects in these windows, there are no long-term consequences.
Patients should not have other vaccines 2-3 weeks before or after.

If a patient tests positive for COVID and self treats at home after how many days could they get the vaccine. Is it 14 days after the positive COVID test?
Probably 2-3 weeks if asymptomatic, or a similar period after symptoms (fatigue, flulike not cough.)

Can the adenovirus play a role in VIIT?
Probably not, adenovirus infection doesn't cause this.

Modernizing Therapy

Modernizing ART: Resistance reminder

Linda Robinson

HIV prescribing has come a long way in terms of offering patients simple dosing schedules with low pill burden and few side effects. We now spend a lot of time trying to simplify regimens in clinic. These discussions need to be ground in engaging clients in their care, and understanding what kind of changes will make their treatments work better for them – including making very complex regimens slightly less complex. Linda presented three cases:

Patient A – patient has been HIV+ for 8 years, still on their first regimen, (RTV boosted Darunavir and TDF/FTC) and undetectable, asking about one pill regimens

- This is a simple switch – the baseline genotype is pristine with no resistance
- Use the modern guidelines and consider an integrase-based 2-3 drug regimen
- In this case, no reason not to consider a two-drug suppression regimen

Patient B – also suppressed for 8 years, this time on a regimen of RTV boosted Darunavir BID + Raltegravir BID + Eltravirine BID. Patient has been HIV+ for 24 years, this is their fifth regimen! The patient would like a daily regimen and less pills.

- Need to become a resistance detective (complicated if patient treated in other clinics/countries)
- Break possible resistances into three columns + NRTI, PI, integrase
- Piece together:
  1. Today's current mutations, if VL is detectable
     - can do with a VL as low as 250 copies
  2. Previous mutations from any previous genotyping
     - if the patient's complete history is not with your site, contact PHOL with patient name/health card
     - can also contact BC for genotyping history in other provinces (but many provincial systems use initials, and some (Quebec) don't use BC lab; contact Chanson Brumme cbrumme@bccfe.ca
     - remember the year of diagnosis matters, no genotypes possible pre-1999
  3. Document patient treatment history, particularly prior to available genotyping
     - Try and get a full history including location of other treaters
     - Mutations from pre-1999 drugs relatively easy to predict, drugs were rarely fully suppressive and resistance should be assumed (ddC or 3TC = M184V or predict TAMS and PRAMS in early protease failures); these mutations do impact modern drugs
  4. Put into an online calculator (Stanford) including your predicted mutations https://hivdb.stanford.edu/. This tool will tell you all currently available drugs and offers commentary, which is a great way to learn to be a better predictor.

> Proviral DNA testing of virus in latent cells is a possible tool, which could be used for someone with undetectable VL and no history of resistance testing. However, it only samples a small selection of cells, so if a mutation is found it is there, but if it is not found, it does not prove it is not present in other cells.

This patient had a complex array of mutations, but they were able to simplify the regimen to DRV/ cDTG / DOR (based on NNRTI comments) - pills once a day (and nuke sparing).

A deep sequencing report is another tool that can be used for someone with a detectable viral load (such as a patient with switched medications who breaks through.) This detects mutations that occur in less than 20% of the sample.

Patient C – Woman diagnosed in late 90s but put off treatment until 2005. Initially started EFV + TDF + ETC but failed due to adherence. Switched and maintained on DRV/r/RAL, simplified to DRV/c/DTG. She had multiple resistances but had been suppressed on a nuke-sparing regimen for 20 years. With aging would it be possible to get her off the boosted PI to avoid future drug/drug reactions and help manage weight?

- Thought we might switch this double D (DRV/c/DTG to a new double D (DTG/DOR) but careful analysis showed a 230L which causes high level resistance to NNRTI, so always go back to basics.

Treatment experienced virus always has a past, so a strategy to uncover archived resistance is mandatory.

Weight gain/metabolic syndrome with antiretrovirals – back to the future?

Deborah Yoong

At the end of 2019, Deborah made a presentation at Pharmacy Day about ART and weight gain. We are now making switches to older drugs to avoid some of these complications. Weight gain was once seen as a sign of return to health, but by 2019 we were seeing weight gain that seemed to be an effect of treatment with INSTI and TAF, and seemed to disproportionately affect people according to their race (Black) and gender (female.) (Venter WDF et al. NEJM 2019 and Sax PE et al. CID 2019). These people were not underweight. The mechanisms, reversibility and long-term consequences were not clear.

Subsequent study has confirmed these effects:

- Change in weight for those switching from TDF to TAF is clear and dramatic in the first nine months (OPERA, Mallon P et al. JIAS 2021)
- Weight gain is also evident with INSTI drug combos, particularly DTG, and additive with the two drug classes – as much as 8 kg in the first 9 months!
- The switch to TAF has a similar impact for those on PrEP (DISCOVER, Mayer KH et al. Lancet 2020)

What about long-acting injectables?

- A gain of 1.8 kg at 48 weeks (Orkin C et al. NEJM, 2020), not big if switching to CAB from another INSTI
- May also be modest weight gain using CAB for PrEP in some populations (Landovitz R et al. CID 2020)

What do we do? – Deborah polled the room on a case of a woman who had gained weight in a switch from Stibild to Genvoya, who now had hyperlipidemia and pre-diabetes; possible solutions divided the room.

- Is there a benefit to removing TAF and keeping INSTI – TANGO study suggests not a lot of weight difference but possibly some benefits with lipids; modeling suggested TAF-treated people would have higher insulin resistance versus those that removed the TAF (Van Wyk et al, CID 2020)
- Avoid TAF, include TDF and switch back to Stibild – this study has not been done but results of including TDF in Gemini-1 and Gemini-2 studies (Cahn P et al. JAIDS, 2020), suggests choosing TDF did blunt weight gain and have beneficial lipid effects
- Avoid TAF, keep TDF, avoid INSTI - the Drive-SHIFT study (Johnson M et al. JAIDS, 2019) suggests this would improves lipid profiles and reduce lipids out to 144 weeks, however still modest weight gain (one kg to 144 weeks) so this might slow weight gain. Weight gain did not appear associated with sex, race, ethnicity, perhaps slightly less for those switching from EVG/c (Kumar P et al. JAIDS, 2021)

Deborah showed several relevant cases from her own clinic, where ART switches reuced or stabilized weight or where changes made for other reasons, like osteoporosis, increased weight.

Clinical consequences *– Sue Gill*

Sue reviewed a large cohort study (Rabeiro et al. CID, 2020), which included some Canadians, and which explored the clinical consequences of ART-associated weight and metabolic changes. Individuals starting ART with an INSTI-based ART had a 17% increased risk of diabetes compared to those starting with NNTRI based regimens (those starting with raltegravir had a 40% higher risk!). People starting with protease-based ART had a 27% increased risk over NNRTIs.

Multiple case studies have now been published linking integrase drugs to the risk of diabetes, weight gain and hyperglycemia. The Advance trial offers a rich data set describing a population which is almost entirely Black and 56% female. This data (Hindley L et al. CROI 2021 Abstract 517) suggesting a higher risk of heart attack over 10 years in the group treated with TAF/FTC + DTG vs TDF/FTC + EFZ (especially in men) and a higher risk of diabetes over 10 years for those treated with TAF/FTC + DTG vs TDF/FTC + DTG (especially in women.)

In summary:

- 1 in 6 people starting HIV treatment gain at least 10% body weight over one-two years
- Risk factors including women, Black race and low pre-treatment CD4+ counts
- Weight gain is associated with specific therapies, particularly DTG, BIC and TAF
- Mechanism for weight gain remains unclear
- Weight gain associated with HIV treatment may increase the risk of diabetes and cardiovascular disease

She suggested that pharmacists:

- Counsel patients on potential weight gain beyond health weight
- Consider alternatives when starting or switching therapy in patients with the known risk factors
- Monitor weight, abdominal girth and assess parameters or concomitant drugs that suggest cardiovascular risk

Ultra-modern Therapy

Long-acting Agents

Pierre Giguere

The simplification of therapy continues, as we begin to explore the feasibility and sustainability of long-acting agents. Currently we have monthly Cabotegravir/rilpivirine (CAB + RPV). Emerging options include:

- HIV treatment – Islatravir and MK8507, an oral weekly combo or Lenacapavir (a new class of capsid inhibitor)
- PrEP treatments – possibilities include oral Islatravir + IM CAB monthly or lenacapavir (every six months) or Islatravir (possibly replaced once a year

These options are a continuation of current simplification trends (89% of people in Pierre's Ottawa practice are now on single daily pill regimens.)

CAB + RPV – was approved in Canada last March, Canada is the first country for market approval of this drug dubbed Cabenuva. The rollout started last fall and we are now beginning to use every two months based on study data. Key trials:

- Atlas = showed the monthly regimen was non-inferior for management of stable suppressed patients
- Flair = showed the monthly regimen was non-inferior for management of naïve patients at both 48 and 96 weeks
- Atlas 2M = showed that patients already on CAB that be injected every month OR every two months, with no difference in outcomes

- FLAIR OLI = extension of Flair, which should that patients could initiate with oral drug or go directly to injection, with no difference in outcomes

FLAIR OLI also demonstrated the high tolerability of the injections – of the minority that do experience injection reactions 99% are grade one, and reactions become less frequent over time.

The failure rate of this treatment is 1-2%. A presentation at HIV Drug Therapy Glasgow (Oct 2020) suggests that the predictive factors for failure are additive, patient must have at least two of the following four factors to be at increased risk of failure:

- RPV RAM(s) mutations at baseline
- Log2 of post hoc week 8 RPV trough concentration
- Baseline HIV-1 subtype A6/A1 (more common in Russia/Asia)
- High BMI at baseline

In real world therapy, drugs are given as two IM ventrogluteal injections one on each side of the body. Eligibility is VL <50 copies, No CYP inducer therapy, >18 years of age and have coverage for this therapy. This last is critical as it is not covered under ODP!

Current dosing is daily oral CAB + RVPV for the first month, then injections in months 2 and 3, then every other month beginning at month 5.

CAB for PrEP every two months has been shown to be superior to Truveda, with three times fewer infections. Most Truveda failures had sub-optimal drug concentrations, so likely adherence issues.

New drugs

Islatravir (ISL) – is a transcriptase translocation inhibitor as well as NNRTI. It has a very long half life and is being studied in combination with DOR as a therapy, but it also has a lot of potential for PrEP. A once a month oral dose is more than adequate for PrEP, but studies are also exploring an implant modeled on Nexplanon (a contraceptive implant) which would be replaced annually. *Islatravir + MK-8507* are currently being combined in dose finding studies. That would potentially be a once a week therapy option.

Lenacapavir (LEN) – is a new class of drug, a capsid inhibitor, with no cross-resistance to PIs! A single sub-cutaneous injection will last 6 months, and sub-q is much easier that IM. The company is still exploring the best loading dose schedule in the first 3-4 weeks.

- In heavily treatment experienced patients 19/26 were able achieve a VL of <50 copies with a single shot.
- In a macaque model, a single injected dose was effective PrEP out to 25 weeks.
- LEN also appear to have little impact on other drugs (doesn't use CYP3A4)
- Safety and tolerability are good; roughly 20% of people complain of injection reactions
- A collaboration has been announced exploring a combo of LEN and ISL; would likely be oral

Practical Implementation

Andrew Schonbe

Andrew is part of the Ontario Prevention Clinic and Pharmacy, which provides PrEP and other services to people across Ontario, with the goal of meeting people where they are at.

Hospitals have some barriers to delivering injections of CAB+RPV, especially right now due to COVID. Manufacturers would like to establish injection sites and offer to patients within 5 km of the site. Another bold approach would be to use pharmacist delivery.

Pharmacists can provide injections of CAB+RPV under a medical directive. Pharmacists are well suited to handle booking and monitoring of these medications, and to manage patient safety during COVID. It is important to monitor patients pre- and post- injection, but also to do follow-up about any injection reactions in the days following treatment.

CAB+RPV seems well suited to support and treat marginalized populations and is something that could even potentially be done from an outreach van or with pop-up sites, as many provinces are doing with COVID now. However, right now Andrew's service wants to focus on development of home-based services.

There are some major barriers:

- Not covered under provincial formulary
- Private coverage can be a problem, requiring large co-pays and deductibles
- There may also be policy (PPN) barriers that require the product to be shipped directly to the patient – negotiations with insurance, manufacturer and even patient's HR departments have been necessary
- Difficult to navigate the oral supply for bridging, re: travel or other interruptions
- Lack of patient support programs

Uber-modern Therapy

This group of presentations explored some unique pharmacy practices in modern HIV treatment.

PrEP Start – *Mina Tadros, Maple Leaf Pharmacy*
Truveda got its indication for PrEP in 2016, but there have been two key barriers to its widespread use:

1. Lack of experienced providers willing to engage in the (relatively time-consuming) prescribing process; pharmacists have a role in reducing this barrier

2. Financial barriers ($100-200 a month at the end of 2017) In 2017, it became generic, ODP listed it and OHIP+ made it free for those under 25.) Although a significant number of at-risk people registered for PrEP at this time, the withdrawal of the OHIP+ program, along with the complexities of Trillium applications (and the need to pay up front), meant that many clients came to perceive payment as difficult and to delay therapy. Conversely a survey of clients accessing PrEP with Trillium support suggested that 80% were comfortable with their deductible, once payment was established. PrEPStart, was created with OHTN and industry support to address this challenge.

PrEPStart works like a free starter pack. Through the program, the client can access prevention immediately and then get support to identify the lowest cost coverage and to make Trillium applications where applicable. A phone number is provided where the client can get follow-up help with any Trillium issues (changes in income from a previous year is one frequent problem.)

To date, hundreds of individuals have registered for PrEPStart:

- About 80% continue after the initial months of free drug
- Open to new patients starting PrEP or people restarting PrEP
- Anyone with an OHIP card can apply and the program will help them find a prescriber
- If the prescriber deems that they are eligible, they complete an application on ontarioprep.ca and someone will contact them within 24 hours
- The pharmacy sends three months of meds and they are offered counselling, etc for any ongoing concerns
- Medications can be shipped anywhere or picked up in Toronto at Maple Leaf Pharmacy

Regional-based PrEP Strategy - *Andrew Schonbe, Ontario HIV Prevention Clinic + Pharmacy, The PrEP Clinic*
The Ontario Prevention Clinic is a collaborative practice combing pharmacists, pharmacy technicians, nurse practitioners and a social worker. They aim to meet people where they are at with a digital service providing PrEP remotely (in person too) from anywhere in Ontario.

- Support the care of 2000 Ontarians via testing services, PrEP starts and support
- >95% would otherwise not be on PrEP
- Many are first time testers
- Opportunity to address HIV stigma, mental health and harm reduction
- Standardized quality care processes incorporating counselling, monitoring, prescribing, STI management and harm reduction
- Can be accessed 7 days a week to midnight via text

HIV Pharmacy Testing – *Zahid Somani, Village Pharmacy, Toronto*
Many clients reported that access to HIV testing was difficult for them that sexual health clinics were crowded and that they are uncomfortable going to family doctor. Zahid called OCP and was told pharmacy-based testing was not possible, so starting working with OHTN to pilot a pharmacy approach.

- Receive training in POC testing including input from Deborah Kelly (NFLD pharmacist with testing program)
- From Dec 2019-Dec 2020, performed 835 INSTI rapid HIV tests
- 93% coming for routine testing; only 4% reported a specific exposure
- 9% had never had an HIV test
- 6 reactive tests (positivity rate 0.7%) with arrangements made to immediately link to local clinicians – clients with positive tests were literally walked over to clinic, PrEP referrals by fax, PEP mostly to St. Mikes by phone (due to COVID screening protocols)
- Most clients under 39 – attracting a diverse population including many foreign students since OHIP card note required (3 of the positive tests were in foreign students)
- Were busy during COVID when other testing centres were closed
- Tests provided by the study free of charge, workload not overwhelming

HIV Pharmacy Testing – *Ben Gunter, Shoppers Drug Mart, Ottawa*
Ben is involved in the same study as Zahid, but more corporate setting. Open for walk-in testing Monday 5-9 PM or scheduled appointments whenever possible. Is it feasible for this to be a pharmacy service:

- Clients liked easy access in a discrete environment
- Also saw many international students and clients from Quebec since OHIP card not needed
- Ben believe it would be feasible with payment of $25/per HIV test, as currently paid for COVID tests
- Opportunity to use the launch pad provided by COVID to get the OCP more onside.

Modern Issues in HIV Case Management: 3 Current Cases

Case 1: PrEP Failure with ambiguous diagnosis

Sherri Livingston

- On PrEP and reportedly adherent, with anal fissures
- Oct 2020 non-reactive HIV combo screen
- Feb 2021 combo screen reactive and suggestive of recent seroconversion, however also in Feb, viral load testing came back target not detected, CD4+ = 1023, no STIs, no acute illness
- Was taking daily PrEP until near end of Feb, off therapy VL=131 copies in early March

The discussion both at the clinic and in the room suggests the likelihood of this individual being an elite controller whose viral load was further suppressed by PrEP. PrEP therapy may also have been compromised by taking PrEP with Metamucil, which would impair drug absorption. For this patient, it is challenging to get enough viral load to genotype and start therapy. Given that many in the room believed he was an elite controller, there is minimal risk to his health or others to delay therapy until there is sufficient virus to genotype.

However, the clinic was able to genotype in early March, client started on BIC in mid-March, DOR added when genotype returned as patient virus showed several mutations including M184V, 215E and 66I.

Case 2: Salvaging a heavily treatment-experienced patient with 6-class resistance

Alissa Koop

- 57 year old man first diagnosed in 1992
- Multiple comorbidities: lipodystrophy, hypertriglyceridemia, GERD, Osteoporosis, hypertension
- Medications: Atovoquone (1500 mg daily), Amiodipine (5 mg daily), Omeprazole (20 mg daily), Fenofibrate E (145 mg daily), Alendronate (70 mg weekly) plus ART
- Complex therapy history:
    - Feb 1992- Nov 1994 – AZT
    - Nov 1994-May 1996 – AZT, ddC
    - May 1996-August 1996 – AZT, 3TC
    - Aug 1996-March 1997 – AST, 3TC, SQV
    - March 1997- Jan 1999- d4T, 3TC, IDV
    - Jan 1999-Dec 1999 – d4T, 3TC, NFV, EFV
    - Dec 1999- May 2000 - ABC, 3TC, SQV/RTV

Marked decline in CD4+ in mid 90s, which dual/triple therapy reversed

Decline in VL, from Feb 1997 to May 1999 after that a steady increase in VL to May 2000

All drugs stopped in May 2000 after genotype revealed multiple mutations

- First genotype in May 2000 – showed high-level resistance to pretty much everything available
- Started on d4T + ddI + EFV from May 2000
- In June 2001 started d4T, ABC, 3TC, LPV/RTV – VL suppressed (1000-3000 copies), CD4+ rose
- In Aug 2002, T-20 added to regimen – lower VL but still some low-level viremia
- Genotype 2004 – added multiple resistances, showed intermediate resistance to some emerging agents
- Continued on his regimen to 2004 when breakthrough began - ABC + 3TC switched to TDF + EFV (LPV/RTV + T20 continues), but broke through again in 2007 with high VL (patient admitted non-adherence to twice daily T-20)
- In 2007 switched to TDF, DRV/RTV BID, ETR BID and T20; undetectable to Apr 2008 and broke through
- Genotype in 2008 showed high-level resistance to all available agents (no integrase available)
- In 2008, RAL added but broke through in 2009, was missing evening doses
- TDF stopped in May 2012 due to elevated creatinine
- May 2013 switched to DTG BID + DRV/RTV + ETR, VL increasing
- Feb 2014 put on TPV/RTV + DTG + ETR had a large viral spike all meds stopped, no real options
- In Aug 2014 put on 3TC, DTG BID more a viral fitness approach
- In Dec 2014 put back on mega-HAART TDF/FTC + DRV/RTV BID + ETR BID + DTG BID – CD4+ kept declining added DRV 800 in March 2016, and switched to TAF in Aug 2017 all of which had little impact VL rising, CD4+ continue to decline
- High level resistance across the board with no options – **six class resistance with no active drugs remaining**

Options

1. Ibalizumab new drug to consider – unfortunately IV every two weeks, but nothing else to pair it with, not approved in Canada and company had no interest in compassionate supply
2. Fostemsavir is a new drug in a new class; studies suggest that even highly experience patients with no remaining active classes could reach undetectable (Kozal et al. NEJM 2020.) FDA approved July 2020; Viiv very open to compassionate access, but with history the clinic wanted another agent!
3. Islatravir/Doravirine – phase 3 trial emerged for heavily experienced patients – randomized for first 7 days then everyone gets ISL + DOR – were allowed to combine with Fostemsavir in trial!!

Chose option 3 and stopped existing drugs end of Dec 2019 for anticipated trial enrollment March 2020, then with COVID all research stopped!!! Screened in Aug 2020 and treatment started Oct 2020:

- VL suppressed within a month to undetectable and CD4+ cells now rising (over 100)
- Next steps – would you simplify further? (Clinician would like to do so at six months.)

Case 3: Hypercholesterolemia in Primary Prevention

Claude Charbonneau

- 64 year old female smoker (60 kg)
- Irritable bowel syndrome, osteoporosis, HIV - treated for Hepatitis C in 2017
- Suspected familial hypercholesterolemia
    - Total cholesterol = 9.65 mmol/L
    - LDL 7.16 mmol/L
    - HDL 1.49 mmol/L
    - Triglycerides 1.20 mmol/L
- Chronic pain and peripheral neuropathies related to previous ART
- Family history of cardiac disease and dyslipidemia (mother, brother, sister)

Medications

- Genvoya (once a day)
- Oxazepam 7.5 mg bedtime
- Clonidine 0.1 mg bedtime
- Risedronate 150 mg monthly
- Calcium and vitamin D supplements daily

- Seems an appropriate candidate to consider primary prevention for cardiac complications
- People with Framingham scores <10% address with lifestyle, and high-risk ≥20 initiate statin treatment but intermediate risk less clear
- 17% Framingham risk without family history (25% with) not including risk from HIV or ARV
- Doesn't want to stop smoking, limited diet/exercise interventions – should we be modifying ARV and/or treating cholesterol??
- Given her LDL this is someone we would want to treat, but patient history shows a number of unsuccessful trials of treatments:
    - Aug 2007 – atorvastatin (myopathy)
    - June 2012 – fenofibrate (myopathy)
    - May 2018 – ezetimibe (myopathy)
    - March 2020 – fluvastatin (myopathy)

- Decided to switch ART from Genvoya to Juluca (Oct 1, 2020)
- Dec 2020 initiated evolocumab (140 mg subq every 2 weeks) – lab access a challenge in her rural area

Outcome

- ARV switch improved GI symptoms = patient happy
- After evolocumab and ARV switch (no labs were available for ARV alone)
    - Total cholesterol = 3.91 mmol/L
    - LDL = 1.98 mmol/L
    - HDL = 1.38 mmol/L
    - Triglycerides 1.2
- This revises Framingham to 8% without family history (11.9 with family history)
- Don't really know that these drugs are effective primary prevention vs moving indicators
- Patient tolerates treatment really well
- LU authorization is one year – should we continue? (daunting LU process, very expensive drug $256/every 2 weeks)
- Need more trials to clarify usefulness, especially as "aging illnesses" continue to grow in our HIV populations

Closing

Sue Gill

Linda and Sue have co-chair this group for the past 17 years and partnered with the OHTN, which has helped keep this group accessible province-wide. Thanks to Linda. Thanks to OHTN. Thanks to the planning committee. SPG hopes to have a live event next year and will appreciate the return of feedback forms to help plan!