

News	2
CHAP New Members	2
Project Updates	2
<i>Publications/Research</i>	2
Conferences:	2
Past Conferences.....	2
Upcoming conferences:	3
Drug Updates:	3
<i>Tenofovir</i>	3
Clinical Pearls:	3
<i>Pediatric DDI. different topics - tenofovir, TDM</i>	3
<i>Zidovudine for pre-meets</i>	4
<i>ddI / Tenofovir interaction</i>	5
<i>Viramune dosing in Pediatrics</i>	6
<i>Clarithromycin and EFV</i>	7
<i>MAC treatment</i>	8
<i>HMS 90</i>	8
<i>tipranavir</i>	9
<i>TPV S/E</i>	10
<i>Tablet size</i>	10
<i>sperm washing</i>	12
New References	13
<i>New Treatment Guidelines:</i>	13
<i>Other Articles of interest</i>	13
Publications from CHAP members.....	15

News

Babies

This section never ends. The recent additions: Andréanne Giguère was born few days before her time on Dec 20 in Gatineau. Mom & Dad are delighted by her continuous happiness. I also learned last March that Alice & Slava will have company soon. Alice's delivery date is in June. Congratulation to the future mom and dad.

CHAP New Members

Marie-France Goyer joined our group in April. Marie-France is a pharmacist working at Hôpital Ste-Justine in Montréal. Her expertise in Pediatric will be for sure beneficial. Her e-mail address is marie-france_goyer@ssss.gouv.qc.ca.

Welcome to CHAP.

Project Updates

Publications/Research

a) HIV Drug Interactions website paper:

A long saga which is now closed to its end. The paper has been rejected from AIDS and BMJ (more details in the minutes of the Annual Meeting). It has then been amended according to editors comments and submitted to the Annals of Pharmacotherapy. Nancy received comments from the Journal and it looks like it will be published once the comments addressed.

Congratulation to the publication group. Your hard work seems finally to give results. This is for sure a lesson and an example for the next projects.

Conferences:

Summary of past conferences:

Past Conferences

February 10-14, 2003

10th Conference on Retroviruses and Opportunistic Infections

Hynes Convention Center, Boston, MA

www.retroconference.org

Thursday March 27 - Saturday March 29, 2003

4th International Workshop on Clinical Pharmacology of HIV Therapy

CANNES, South of France
Summary available at www.hivpharmacology.com

April 10-13, 2003

12th Annual Canadian Conference on HIV/AIDS Research
World Trade and Convention Center, Halifax, Nova Scotia
The abstracts of the 2001 conference is on-line at www.cahr-acrv.ca/english/resources
Hopefully, the 2002 and 2003 abstracts will also be available eventually.

Upcoming conferences:

July 13-17, 2003
The 2nd IAS Conference on HIV Pathogenesis and Treatment
Paris, France
Deadline for late breakers: June 7, 2003
Deadline for std registration: June 15, 2003.
<http://www.ias2003.org/>

September 14-17 2003
43rd Interscience Conference on Antimicrobial Agents and Chemotherapy (ICAAC)
Chicago
Deadline for electronic abstract submission: May 8, 2003
Deadline for discounted registration: July 11, 2003.
www.icaac.org

Drug Updates:

Tenofovir

Viread received a Notice of Compliance with Conditions Mar 18/03. However, Gilead has indicated that the release of Viread in Canada will be delayed. No date was released for its commercialization.

Tenofovir will be available in a 300mg blue tablet (02247128).

Clinical Pearls:

Pediatric DDI. different topics - tenofovir, TDM

Andrea

Hi, everyone.

I was wondering if any of you have pediatric experience. I was approached today about a child who is taking DDI in the chewtabs 100mg bid. Info from the "chart" ("slip" of paper they handed me): weight 39 kg, height 147 cm and BSA ~ 1.3 meters squared.

According to dosage calculation (90-150 mg/meter squared/dose bid), this boy could take 125 mg of Videx EC bid? I am unclear as to why he is still taking the chewtabs (he also takes indinavir and d4t without problems so it doesn't make sense in terms of needing an "easier chewy" formulation). Is there any reason why children can't take the EC formulation? I can't seem to find anything that would suggest you can't. I haven't been able to get a hold of the physician yet and I am just wondering if any of you would be familiar with this.

Also, our research nurse received a fax yesterday telling us that tenofovir will no longer be supplied to us by the company after December 18th! It will be available on the market for all to use. I have to get on the horn to pharmacare tomorrow to see if they have reviewed it for coverage.

We also did drug monitoring in a patient on nevirapine and his levels were low (4 hour level was low and previous 1, 2, and 3 hour levels were below the limit of detection for the assay) and thus we are thinking he is not absorbing his drugs. I'm just wondering if any of you are using TDM often and if you find you have difficulty figuring out what to do with the info.

Thanks and hope you all get a "wee break" over the holidays! ;)

Linda

Hi Andrea,

I know that BC Children's hospital has been using the DDI-EC formulation for some time now in their pediatric patients. I'm not aware of any contraindication/precaution with pediatric patients and this formulation.

Perhaps, someone else out there can comment?

With the tenofovir, we have understood Dec 18th to be the last day that consents can be sent in for the EAP program. Gilead will still continue to provide medication for patients in the EAP program (free of charge) for now. However, the free supply of drug will stop 90 days post Gilead receiving their NOC for tenofovir.

Dom

Hi Andrea:

With regards to your question on DDI EC in kids, we have most of our older kids on this formulation once they learn to swallow tabs/caps. As in adults, this formulation has been well received. We just have a couple of kids still on the liquid suspension formulation.

Good luck.

Regards,

Zidovudine for pre-meets

Jinell

Hello everyone.

I am not sure if you have read this article, but I'd thought I would share it with all of you.... if not.

Dom

Thanks Jinell:

This is good info. We've been following the PACTG 331 dosing recommendations of AZT 1.5 mg (IV/PO) Q12h x 2 weeks; then 2 mg/kg q8h till 6 weeks. So far we've not had any preterm infants born to HIV positive mothers. But we've used the PACTG 331 dosing on a couple premature neonates born to "high risk" mothers. They received IV AZT in our Special Care Nursery until mother's status (PCR results) is determined and the AZT was discontinued.

Congrats on the engagement!

ddl / Tenofovir interaction

Nancy,

Hi,

This question goes out mostly to the pharmacists in B.C. I know at the last CHAP meeting you had discussed giving ddl and tenofovir with food to decrease the impact of the interaction (approx 50 % increase ddl AUC due to TNF and approx 25 - 50 % decrease ddl AUC when given with food). Are you still doing this and if so have you done any PK studies and are the patients still tolerating it well. I know there is a PK study done with ddl 400 EC given with TNF 300 QD with a light meal that still found a significant increase in ddl AUC. I've also recently seen recommended ddl dose adjustments when giving it with TNF in a certain clinical trial.

What are other people doing?

Thanks

Tony

Hi Nancy

Gilead has also done a study with EC ddl 250 mg and tenofovir; their results suggest that the when given with TDF, the 250 mg dose of Videx EC results in an AUC equivalent to that of the 400 mg EC ddl given on an empty stomach when given without TDF. The Videx EC 250 had to be given 2 hours before TDF to match the AUC of Videx EC 400 given alone and in a fasted state. When the 250 mg cap was given with TDF and with a light meal, the AUC was ~ 10% lower than when it was given in the staggered 2 hour apart way.

Hope that helps

Michelle

Hi Tony,

I have been awaiting more data, so thanks. Which doses are you using for the following scenarios:

- 1) BOTH FOOD and AT SAME TIME: ddl 250mg or 400mg?
- 2) DDI AC 2 hrs prior to TDF, and TDF with food: ddl 250mg or 400mg?

Also, any word on when NOC will be granted? I have several patients who need the drug but can't get it.

We have been using the 250 mg cap with tenofovir, both with food.

Lizanne

Hi Nancy:

If you call Gilead, you'll get the results of the study Tony just outlined. This issue was also addressed at the Glasgow, UK meeting. Based on this study, many centers in the UK are giving ddl EC 250 mg with tenofovir, both with food. Unfortunately, data is lacking for ddl buffered.

What we've been doing is giving ddl EC 250 mg with tenofovir, both with food. For ddl buffered, I would be inclined not to alter the dose until more data come out, in part because the impact of food is greater on ddl buffered than on ddl EC, and a dose adjustment may not be necessary.

Dom

Hi Nancy:

Here at Oak Tree Clinic we have 17 patients taking tenofovir through the EAP. We've been recommending the DDI EC and tenofovir to be administered together with food. We tend to drop the DDI EC dose down to 250 mg to minimize increased DDI levels. A couple of patients have remarked subjective decreases in peripheral neuropathy symptoms when we dropped them from the initial dose of 400 mg to 250 mg. I'll let Linda comment on what is being done with the majority of patients taking tenofovir in BC through the Centre for Excellence.

Thanks

Linda

Sorry,

I didn't forward this to the whole group. One clarification...the email below doesn't refer to the BC Children's group patients. Also, for the group of 100 patients on the higher dose of DDI-EC (400 mg), pharmacy has recommended the lower dose, but the clinician involved doesn't agree.

Dom

Hi Nancy:

I re-read my previous response and it makes it sound like we start with DDI EC 400 mg....well, we did for the first 3-4 patients. They all have been switched to the lower DDI dose. The rest of our patients were started on DDI EC 250 mg with tenofovir with food. Except we have a couple of very light (less than 60 kg) women in our clinic who are receiving 200 mg DDI EC.

Sorry about that.

Thanks.

Nancy

Hi,

Thanks to everyone who sent me an answer for the ddl and tenofovir interaction. Unfortunately, we don't have easy access to ddl EC here in Québec and my patient is forced for the moment to continue with the original buffered formulation, for which we appear to have little data with tenofovir. I have already adjusted the dose to 300 mg QD as he weighs less than 60kg and am still hesitating whether or not I should decrease the dose further based on the tenofovir. I am giving both with food hoping for some decreased bioavailability of the ddl with the food.

Thanks again for your comments,

Nancy

Sorry, an error appears in my message: ddl dose prescribed = 250 mg QD and not 300 mg QD (wt < 60 kg).

Viramune dosing in Pediatrics

Jinell

Hello everyone,

I am curious about your clinical experiences in dosing with Viramune in pediatrics as the DHHS guidelines illustrate two options (below):

Pediatric:* 120-200mg/m² q12h; initiate therapy with 120mg/m² (maximum dose 200mg) ONCE daily for 14 days, then increase to full dose (120-200mg/m²) q12h if there is no rash. *dosing from Clinical Trials Data

OR

7mg/kg q12h < eight years of age

4mg/kg q12h > eight years of age

NOTE: initiate therapy with daily dose for 14 days, then increase to full dose q12h if no rash or other untoward effects.

Dosing is based on PK data to achieve similar plasma concentrations as dosing at 150mg/m²

I am doing a project involving this with one of our pediatric ID specialists, and would like to know what the rest of Canada is doing. Thanks,

Dom

Hi Jinell:

We use the 120-200 mg/m² od x 14 days, then bid afterwards with our peds patients. For those unable to swallow the tablets, we have accessed the expanded access supply of nevirapine liquid.

Good luck.

Clarithromycin and EFV

Lizanne

Hi everyone:

We have an HIV patient who requires H. Pylori eradication. He is on an EFV-based regimen (EFV, 3TC, d4T). The regimen of choice for H. Pylori would require clarithromycin.

There is a drug interaction whereby EFV decreases clarithromycin's AUC by 39% and increases its active metabolite's AUC by 34%. This was a study done in healthy volunteers, and the dose of EFV was 400 mg. The clinical significance of the interaction is unknown. The company was not helpful in helping determine the significance of the interaction, or extrapolating data from clarithromycin given with other 3A4 inducers.

I was curious to know if you've had experience with EFV prescribed with clarithromycin.

Thanks

Michelle

We had a patient on the combo, but I did not dose adjust. We kept him on clari as part of his MAC regimen, as it is superior to azithro for tx. He ended up failing ARV therapy, but this is likely due to multifactorial reasons, as he had been previously on EFV at some time.

MAC treatment

Andrea

Hi, everyone.

We have a gentleman who has MAC (bacteremia). From all the literature that I have looked at on OI that involve MAC, MAI, the treatment is clarithro and ethambutol. There was some discussion around whether or not to add rifabutin at rounds but as far as I can tell the "only" advantage is that it decreases the chance of clarithro resistance. (I say "only" as the patient is on RTV/IND which would likely become an extremely complicated situation in combo with rifabutin). I guess my question is - is this what you all have done (etham+clarithro)? I have seen info on azithro but it looks reported to be less efficacious - are any of you using azithro for treatment?

The last question I have is with regard to stepdown - all the literature I have seen says for secondary prophylaxis for MAC/MAI you continue on the regimen that was used for treatment and for lifelong. One of the docs said there was step-down based on CD4 but I can't seem to find this data that he is talking about and I had never heard of it. Does anyone know about this?

Thanks.

Rachel

We USING BOTH with same efficacy. We also had resistance with both

Pierre

Hi Andrea,

We use the triple therapy for MAC treatment. We favor clarithro over azithro just because of the faster bacteremia clearance with clarithro (it is the same rate of MAC negative culture at 16 weeks though...). This being said, we still use azithro for patients with problem of tolerance or compliance or drug interactions.

After 12 weeks, if the symptoms resolved, we drop the RFB and continue on the macrolide+ETH. With regards to drug interactions with PI (RTV mainly), there is sufficient data to support concomitant use of RTV+RFB. You need to drop the dose of RFB to 150mg po 2x/week. We commonly do this here (we are big fans of boosted-PI).

Finally, it seems safe to stop MAC suppressive treatment once CD4 has recovered... Immune reconstitution seems to protect for PCP, TOXO, MAC and crypto meningitis.... seems good for everything!
Good luck

Christine

Hi Andrea,

We tend to use just clarithro + ethambutol for treatment. If you look at the 2001 OI guidelines (available at http://www.aidsinfo.nih.gov/guidelines/default_db2.asp?id=69), you can stop MAC treatment when the patient has completed at least 12 months of treatment, has no signs or symptoms of MAC, and has had a sustained CD4 > 100 for at least 6 months while on HAART. We have done this in a number of patients and have not experienced any relapses.

HMS 90

Michelle

Hi all,

I am wondering if you know of any of your patients on this product called "HMS 90"- It is a natural food protein whey concentrate that supplies the precursors for glutathione synthesis. The cost is about \$120/month. Regardless of lack of good data, I think he is determined to take this supplement.

I have a patient who wants this for HIV/rectal CA and cannot afford it. He was hoping our clinic could pick up the cost. I'm looking into just giving him plain old N-acetylcysteine PO as a glutathione supplement (at least this is covered by his drug plan).

Any thoughts? Have you ever tried this for patients who want to increase glutathione?

tipranavir

Debbie

Hi folks:

Just wondering if anyone has any patients involved in the tipranavir study, or has any info on how to get a patient involved in this study. We have a patient who is DESPERATE for treatment options, and it looks like she might meet the study criteria. Any info would be appreciated.

Thanks!

Pierre

Hi Debbie,

I know we will shortly have 2 studies with tipranavir in salvage patients (1 early, 1 late salvage). I do not know any details about them though as I am not involved.

You can contact our research nurse (Richard Guenette) for more specific info.(see cc)

Merci Richard....

Michelle

We have 2 protocols as well fro TPV- likely the same as Pierre. I have reviewed them, as I have patients waiting for the drug as well and wanted to see the inclusion criteria. As Pierre said, one is for deeper salvage (more mutations required) and one is comparing TPV vs other PIs that still have sensitivity for salvage (less mutations required). The protocols are approved by ethics (finally) and we are jus ironing out the legal side of it. Optimistically we think May or June may be the enrollment dates.

Of note, both protocols require that the patient be on PI therapy x at least 3 mos at the time of enrollment (i.e not on a drug holiday > 7 days). Also HU is not allowed for a month prior I think.

There are many other inclusion/exclusion criteria...If you need more info, you can contact our research nurse, Adeleine Lindemulder at: alindemu@cha.ab.ca

Debbie

Thanks Michelle and Pierre for the info. I have passed along the contact info for your research nurses to our research nurse, and have left a message for Chris Fisher at Boehringer about the tipranavir access.

TPV S/E

Marie Courchesne

Michelle,

I remembered having seen 2 patients on it. The 2 patients clearly failed Kaletra after few months of partial response. They did amazingly well on TPV. Of interest, none of them complained of serious side effects (GI being the most serious one although not too bad). Too early for LPD... but both already have S&S of it.

I met one guy from Boehringer once... his name is Michael Hoad. Tel 1-800-263-5103 ext 1602 e-mail: mhoad@bur.boehringer-ingelheim.com.

good luck

Our rep in Quebec is Chris Fisher
email: cfischer@bur.boehringer-ingelheim.com
1-800-263-5103 #1603

Tablet size

Natalie

We are in the preliminary stage of designing a salvage regimen for a 12 year girl. Can anyone help me with the size of the following

1. Tenofovir 300mg tablet
2. atazanavir 200mg capsule strength of the powder:
3. abacavir tablet (smaller than efavirenz 200mg but larger than Kaletra???)
4. tipranavir 750mg/ ritonavir 200mg capsule (oval slightly larger than 100mg ritonavir SEC capsule?)

Thanks

Dom

Hi Natalie:

Good luck with the salvage regimen for the 12 year old in your clinic.

Tenofovir tablet is oval/egg shaped about 1.2 cm in length and 1 cm wide. Abacavir tablet is 1.8 cm in length and 0.7 cm wide. By the way, how were you able to get tenofovir for a peds patient? I thought the SAP program was closed in Canada pending NOC.

Thanks.

Christine

Hi Dom,

The company (Gilead) has re-opened the expanded access program in Canada pending NOC but it has been modified. The criteria are quite a bit stricter according to our research nurses. I don't have them off-hand but I believe the CD4 had to be < 100 or something like that...

Natalie

Thank-you for your response. We have yet to secure tenofovir - we are still talking to Gilead in California. As I carefully said, we are in the preliminary stages of designing a salvage regimen. Although tenofovir

received its NOC 2 days again, I hear rumours that it will not be available for a few months (pricing issues). Hopefully tenofovir's availability will coincide with the commencing of the new regimen for our patient. Thanks alot for the detailed response. Have you seen these medication? I have that tenofovir is almond-shaped, blue coloured film-coated tablet (therefore not appropriate for cutting in half??). How does tenofovir's and abacavir's size compare to other antiretroviral tablets/capsules?

Christine

Hi Natalie,

I don't have access to the "real drugs" here in my office, however here is a chart I downloaded from the net. I can't say for sure the pictures are totally accurate but they look pretty close in terms of size. It at least gives you an idea of comparative size.

Lizanne

Hi Nathalie,

Tenofovir is not film-coated. I called Gilead last week to see if the tablet could be crushed. They could only provide me with the following info, asking that a clinical judgment be made with regards to crushing the tablets: since it is not a slow-release tablet, no dose dumping of medication expected if crushed, tenofovir soluble in water, grapefruit juice and orange, if crushed, the tablet would likely have a bitter taste. The name of the person I spoke to was Mimi 650-522-5181.

Atazanavir comes in 200 mg caps and 150 mg caps. The 200 mg caps is slightly larger (not obvious, but looks a bit longer) than Invirase and the 150 mg caps is slightly smaller than Invirase.

Dom

Thanks Christine. I just checked with our research nurse and she's just received word that the expanded access program will be reopening. You're right, the entry criteria is stricter: CD4<100 (within 3 months of screen); VL >10,000 and resistance testing documenting limited options to construct a viable combination without the inclusion of tenofovir.

Dom

Hi Natalie:

Thanks for your info. Yes, we have a few patients (adults) on tenofovir and abacavir. The tablets are not too big and their size hasn't been a problem. We've used abacavir liquid on a couple of kids who can't swallow tablets/capsules. And, so far we've not been able to use tenofovir on any of the kids because of the entry criteria > 18 years old.

Good luck.

Andrea

Hi, all.

We have the same criteria as mentioned below by Dom. We have several people we were trying to get tenofovir for before the enrollment ended and subsequently we were unable to with the new stricter criteria. We have several people who have resistance testing that indicates tenofovir is one of the last options but after talking to "Steve" with Gilead he gave me the impression that they had to meet the counts criteria as well. Also, in order to put people back into the re-opened expanded access, we would have had to gone through our ethics board at the hospital again - we decided to wait for its market arrival as the ethics process can often be drawn out.

Linda

FYI,

I was speaking with the Gilead representative for Canada on the weekend at the Whistler HIV Update. He informed me that even though tenofovir received it's NOC in Canada (he told me that this happened on March 18th), they are months away from having it commercially available. He indicated that the company still has lots of issues to deal with, with price being a big one. I asked him about the re-opened EAP program and he understood that it would still go ahead, in light of the delays with the product's launch in Canada.

Delavirdine

Michelle

Hello all,

I have few questions about delavirdine (which I have not used in 4 years now.... so I am a tad outdated!) Not the hot drug in our clinic as you can see.

- 1) Is there a newer tab strength than the 100mg's?
- 2) Prelim. data suggest using 600mg BID instead of 400TID- what have you been using?
- 3) Are any of you using DLV 600mg BID + RTV 100mg BID for extra DLV boosting? (would you use the RTV routinely if using DLV BID)?
- 4) How dependable are the GART results when there is only a G190A mutation, indicating NVP/EFV resistance and DLV sensitive (and I have even read that the presence of the G190A confers DLV hypersensitivity).

Thanks

Tony

Hey Michelle

In Canada, only the 100 mg tabs are available I believe; there is a 200 mg tab in the US (maybe SAP?). We use 600 mg bid, since nothing else is tid.

Have never used it with ritonavir for the sake of boosting the delavirdine per se, but has ended up in regimens where ritonavir was included with no real deleterious effects (in my experience).

The 190X thing - worth a shot; I have never seen clinical data (perhaps others have?) on the efficacy of delavirdine when patients have substitutions at 190, but the in vitro data does suggest either a sparing of delavirdine or increased sensitivity as you mentioned; as well, there is no evidence (yet) that this mutation is frequently accompanied by other NNRTI mutations (unlike some other mutations that "spare" individual NNRTIs), so it may be worth a try.

Later

sperm washing

Debbie

Hi everyone:

Just wondering if anyone knows of a center where they are doing sperm washing for discordant couples? I believe I threw this question out a couple of yr ago, so am looking to see if there's any news.

Thanks,

Dom

Hi Debbie:

I checked with our Ob/Gyn (Deborah Money) and she mentioned that the Italian group has the most experience with this procedure. She's not aware of any centres in Canada offering this service. I happened to notice that the London Health Sciences Centre has listed "sperm washing" on their bio listed on the second link, but their website does not mention anything about it. Our clinic has yet to establish guidelines on fertility/infertility.
Good luck.

<http://www.aidsmap.com/publications/factsheets/fs53.htm>

<http://www.familyhelper.net/iy/iyclin.html>

New References

New Treatment Guidelines:

No new treatment guidelines. We are due for an update...

Other Articles of interest

NOTICE TO PHYSICIANS

DATE: March 10, 2003

TO: HIV/AIDS Health Care Providers

FROM: Division of AIDS (DAIDS), National Institute of Allergy and Infectious Diseases,
National Institutes of Health

SUBJECT: Important Interim Results from a Phase III, Randomized, Double-Blind Comparison of Three Protease-Inhibitor-Sparing Regimens for the Initial Treatment of HIV Infection (AACTG Protocol A5095)

Dear HIV/AIDS Health Care Provider:

The purpose of this letter is to inform you of the interim results from the Adult AIDS Clinical Trials Group (ACTG) study known as A5095. A recent review of the study by the National Institute of Allergy and Infectious Diseases (NIAID) Data and Safety Monitoring Board (DSMB) found that in antiretroviral treatment-naïve patients, a combination preparation of three nucleoside analogues, Trizivir®, was inferior to two other efavirenz-containing treatment regimens being evaluated in the study. The data met pre-specified guidelines for stopping this one arm of the study based on virologic failure. There were no concerns about the toxicity of the study drugs.

Antiretroviral-naïve patients randomized to receive a combination of abacavir (ABC), lamivudine (3TC), and zidovudine (ZDV) (ABC/3TC/ZDV, Trizivir®) experienced

virologic failure earlier and more frequently than patients who were randomized to receive either of the two other treatment regimens being evaluated in the study.

The two other treatment regimens are: 1) a combination of 3TC and ZDV (Combivir.) plus efavirenz (EFV, Sustiva.), and 2) the combination ABC/3TC/ZDV plus EFV. Study drugs were given in a double-blind, placebo-matched manner.

A total of 1,147 antiretroviral-naïve patients were followed for changes in their viral load and CD4+ T cell counts. Virologic failure was defined as having an HIV RNA level in plasma above 200 copies/ml (measured by the Roche Amplicor® HIV-1 test) at least 4 months after starting study treatment. After an average of 32 weeks on study, a total of 167 study volunteers experienced virologic failure: 21% in the group receiving ABC/3TC/ZDV versus 10% in the other two groups combined. Virologic failure occurred sooner and more often in those receiving ABC/3TC/ZDV alone, regardless of their initial viral load (whether above or below 100,000 copies/mL). Although data on CD4+ T cell counts were not available at the time of the interim analysis, the DSMB felt that they would not reverse the outcome.

As a result of these data, the DSMB recommended that the ABC/3TC/ZDV treatment arm be stopped. Therefore, the study volunteers receiving ABC/3TC/ZDV have been unblinded as to what treatment they were taking, and they have been asked to remain in the study for continued follow-up. These volunteers have been offered several alternatives to the use of ABC/3TC/ZDV alone. GlaxoSmithKline, one of the pharmaceutical companies involved with this study, is also working with DAIDS and the A5095 study team to provide ABC/3TC/ZDV outside the study for patients who choose this option.

Study volunteers originally given one of the other two drug treatments will continue on the study as planned and will not yet be unblinded. They will, however, be told that they are receiving a combination treatment that contains efavirenz. All study volunteers, will continue to be followed for approximately 2 years after the last subject is enrolled – until approximately

September 2004. This follow-up period will allow a comparison of the 3TC/ZDV + EFV and ABC/3TC/ZDV + EFV groups. It also will allow more information to be collected from all three groups about how to use antiretroviral drugs.

Although we are confident of these findings, they have not been presented at a scientific meeting, peer reviewed, or published. These results will be submitted to the upcoming International AIDS Society meeting in Paris (July 2003), and further analyses (e.g., CD4+ T cell count and adherence data) will be forthcoming. A manuscript is in preparation.

It is important to consider this interim study finding in the context of published results, particularly those from prior studies that investigated either triple nucleoside regimens or EFVbased regimens. The risk of virologic failure is clearly an important factor in selecting an initial antiretroviral regimen. Other factors such as safety, toxicity, adherence, preservation of future treatment options, access, cost, and other issues also remain important in selecting the optimal first regimen for an individual patient.

Additional information about the study design and interim analysis are available on the National Library of Medicine Web site at http://www.nlm.nih.gov/databases/alerts/clinical_alerts.html and on NIAID's Division of AIDS Web site at <http://www.niaid.nih.gov/daids/default.htm>.

Publications from CHAP members

CAHR meeting:

- 1) *Magdalena A Piaseczna, **Linda Akagi**, Alistair McLeod, Cathy Lai, Michael V O'Shaughnessy. EVALUATION OF THE BRITISH COLUMBIA HIV ACCIDENTAL EXPOSURE PROGRAM*
- 2) ***T Antoniou, A Tseng, S Walker, R van Heeswijk, P Giguère, E Phillips. STEADY-STATE PHARMACOKINETICS AND TOLERABILITY OF INDINAVIR WHEN CO-ADMINISTERED WITH LOPINAVIR/R IN ANTIRETROVIRAL-EXPERIENCED SUBJECTS** (poster also presented at the 4th HIV Pharmacology Workshop).*
- 3) ***Lizanne C Béïque**, Suzie St Germain, Don Kilby. PATIENT-CENTERED ADVERSE DRUG REACTION REPORTING SOFTWARE IN OTTAWA - A PILOT PROJECT*
- 4) *MJ Turner, JB Angel, K Woodend, **P Giguère**. THE EFFICACY OF CALCIUM CARBONATE IN THE TREATMENT OF PROTEASE INHIBITOR-INDUCED PERSISTENT DIARRHEA IN HIV-INFECTED PATIENTS*
- 5) ***Rachel Therrien**, Danielle Rouleau, Pierre Côté, Sylvie Beauchamp, Sylvie Vésina, Frédéric Maari. ÉVALUATION DU PROCESSUS D'IMPLANTATION D'UNE THÉRAPIE ANTIRÉTROVIRALE DIRECTEMENT OBSERVÉ (TADO) AUPRÈS D'UTILISATEURS DE DROGUE PAR INJECTION (UDI) DE MONTRÉAL*
- 6) *Andre LaRoche, Curtis L Cooper, D William Cameron, **Rolf vanHeeswijk**, Jonathan B Angel KALETRA BASED THERAPY IN ANTIRETROVIRAL NAÏVE PATIENTS IN CLINICAL PRACTICE*
- 7) *P Akai, K Lavender, **M Foisy**. EDMONTON DIRECTLY OBSERVED THERAPY (DOT) FOR HIGHLY ACTIVE ANTIRETROVIRAL THERAPY (HAART) PROJECT I: TREATING THE UNTREATABLE IN THE INNER CITY*
- 8) ***M Foisy**, W Monahan, P Akai. EDMONTON DIRECTLY OBSERVED THERAPY (DOT) FOR HIGHLY ACTIVE ANTIRETROVIRAL THERAPY (HAART) PROJECT II: PHARMACEUTICAL CARE IN THE INNER CITY*