Canadian HIV/AIDS Pharmacists Network (CHAP) Newsletter – December 2000

Hello Network Members!

Well this year has flown by quickly! It seems like only yesterday that it was New Years 2000 and now 2001 is just around the corner. I hope all of you have a wonderful holiday season and Happy New Year!

Good News Items….

Well I have decided to follow the lead of the previous chair and have some good news to share. My husband and I are expecting our first child at the end of May 2001. Unfortunately this means I will not be able to attend the next Network meeting at CAHR. However, I will be looking for volunteers! :-)

It seems that there is a baby epidemic in the Edmonton region. Michelle Foisy and her husband Kevin are also expecting their first child in June 2001. Congratulations Michelle!

I also wanted to congratulate Natalie Dayneka for her recent Commitment to Care Award for Hospital Pharmacy practice. Natalie is featured, along with the other award winners, in the November issue of Pharmacy Practice. Way to go Natalie!!

Upcoming Conferences

Retrovirus Conference
The 8th Retrovirus Conference will be held February 4-8, 2001 in Chicago. General registration opened December 1, 2000. Good luck to all of those who registered this year!

2nd International Workshop on Clinical Pharmacology of HIV Therapy
The second International Workshop on Clinical Pharmacology of HIV Therapy will be held April 2-4, 2001 in the Netherlands. For more information, check out the following website: http://www.virology-education.com/index2.html.

CAHR
CAHR will be held May 31- June 3, 2001 in Toronto. Get your abstracts ready – the deadline for abstracts is February 16. Check out the following website for more details: http://www.cahr-acrv.ca/cahren.htm.

Drug Availability - Updates

Sulfadiazine
(Marie)
Would any of you know if sulfadiazine tablets are still available in the States? If so which company makes it.

(Laura)
If anyone is interested....
We have a pharmacy here that is making up sulfadiazine capsules - using a compounded formulation. We have switched one guy to these capsules. They are getting the sulfadiazine from the US and then filling them into capsules.

But the capsule strength is 250 mg.

(Tony)
Along the if anyone is interested lines...

There is a tablet formulation available through HPB (special access) made by a company in the states (Harvard Medical or something like that). If you have any patients who need to be switched, you should be able to get it through this route (apparently 500 mg tabs in bottles of 100).

Zidovudine 300 mg tablets
(Laura)
I heard a rumour that AZT 300 mg tabs are being phased out.
Anyone else hear the same?

(Pierre)
I received a written note confirming the withdrawal of the 300mg tablets.
RE: low demand.

Clinical Pearls

1. Non-oxynol-9 and Risk of HIV Transmission

Health professionals who provide advice about safe sexual practices and birth control should be aware of recent studies on the use of N-9, a spermicide used widely in Canada in contraceptive products, such as foams and gels, and included in the lubricant of several brands of condoms.

Although N-9 was originally believed to also have some microbicidal properties against the human immunodeficiency virus (HIV), recent evidence indicates that the frequent use of N-9 does not reduce the risk of HIV infection and may in fact increase the risk by causing disruptions and lesions in the genital mucosal lining.

Health Canada provides the following current assessment of the available data.
· N-9 should not be promoted as an effective means of HIV prevention. In particular, individuals who cannot use a condom for HIV prevention should not be counselled to use N-9 as an alternative.
· The best STD and HIV barrier is a latex condom without N-9. However, a condom lubricated with N-9 is better than no condom at all. The protection provided by the condom appears to outweigh the potential risk of the N-9.
· Individuals who wish to use N-9 as an aid to contraception should be advised of the increased risk of genital lesions and the resulting potential for an increased risk of transmission of HIV.
The full text of the Health Canada publication is available on the Internet at: http://www.hc-sc.gc.ca/hpb/lcdc/bah/epi/nonoxynol-9_e.html

2. ddI Once Daily

The saga surrounding once versus twice daily didanosine continues….

Kazatchkine et al. compared once-daily dosing of didanosine with twice-daily dosing in 121 HIV-1-infected adults already receiving twice-daily didanosine as part of two- or three-drug antiretroviral treatment. During the study, concomitant drugs were not changed. Mean plasma HIV-1 RNA copies increased in both groups but there were no meaningful differences between the groups by week 24. CD4 cell counts declined in the once-daily and twice-daily groups, but the difference between the groups was not significant. The authors conclude that "on the basis of these findings and of previous reports in treatment-naive patients, once-daily dosing of didanosine is safe, well-tolerated, and effective at reducing the levels of plasma HIV-1 RNA. Moreover, results of our study indicate that patients currently receiving an effective antiretroviral therapy including didanosine twice daily may be switched to ddI once daily without significant change in safety or antiviral efficacy."
J Acquir Immune Defic Syndr 2000;24:418-424.

3. Nabilone for HIV-related wasting

(Alfred)
As per our conversation last week, could you please forward this query to the AIDS interest group. I did a search on the use of nabilone for AIDS related wasting and only came up with two case reports. While I am aware that Cesamet is not officially indicated for that purpose, I would be very interested in any experience, unpublished reports or studies (ongoing,

perhaps?...) on nabilone for the treatment of AIDS related wasting.

(Michelle)
The onset of action of the oral (30-60 min) is slower than the smoked (6-12 min).
The absorption with po is up to 20% (high 1st pass metab) and about 18% via inhaled. And it has a long t1/2 of several days.

Many of our patients (especially smokers) preferred the inhaled route, as they felt they could titrate the dose better and take a few drags when required. Some patients do find that they do not like the feeling on marijuana though, as it is hard to avoid the high. People who have used it recreationally in the past and liked it find it much more acceptable. Those who do not like the high feeling, may not find it all that pleasant.

Patients using it for weight gain in the end stages often found that they were able to maintain their weight (not increase it, or if so, only by a few pounds), as it really increased the appetite. However, with HAART tx, weight gain was less of an issue (in fact most wanted to lose weight as we all know). In addition, for pain control or intractable nausea, a number of patients swore by it. I think many of them had been previous recreational users.

If we used the po route, the agent on the market is nabilone (Cesamet) and it comes as 1mg pulvule (cap)- this is not as easy to titrate. The recommended dose is 1-2mg BID. What I usually did was start patients on 1mg qhs to see how they would react to it- in some this was enough to control symptoms. I would wait a few days before titrating up though, given the long t1/2 and potential for accumulation.

In others, even this dose was too high and they found the CNS S/E unbearable. You might consider a 1mg dose every 2 days given hs to see if they tolerate this at first and work your way up.

The other thing to be careful for are pharmacodynamic interactions with other drugs that impair the CNS- may need lower doses (i.e. Benzos, barbs, alcohol, narcs). This was a big issue in some of our patients with concomitant addictions.

Pharmacokinetic interactions are also a consideration. THC is a substrate of CYP2C9 and CYP3A, therefore inhibitors of these enzymes may increase THC levels (i.e. PI's, delavirdine, azoles, etc). Use the lower doses of nabilone in these patients at first to see how it is tolerated. Likewise, inducers may decrease TCH levels (nevirapine, possibly efavirenz).

3. Efavirenz

(Kathy)
Has anyone had success with taking Sustiva 200 mg tid for decreasing CNS effects. One of our pts found it extremely useful. I am however wondering if it will decrease efficacy. Does anyone have any thoughts on this.??

(Pierre)
We never tried to split the dose to TID because we have heard from Dupont that it was ineffective in reducing CNS symptoms. During the EAP, we tried in approx 5 pts 400mg HS and 200 mg AM (as per protocol) in an attempt to decrease S/E and it did not work.

I would not be worried in term of efficacy as Sustiva has a very long half life. Therefore, we should not see major fluctuations of serum levels. I would definitively not reduce the total daily dose though.

(Ann)
We have gone with 300mg BID using 1x100mg + 1x200mg caps. This seems to be fine and more user friendly.

4. KS Lesions

(Laura)
Other than good ARV therapy, are there any pharmacological treatments that will help shrink/improve the appearance of KS lesions? Something not too toxic? Is anyone doing intralesional vinblastine? Anyone using thalidomide? Any suggestions would be great.

(Kathy)
Isn't there a new Interferon Cream?? (ie non invasive/systemic) There is also Liposomal Doxorubicin. We really don't see KS any more.

(Michelle)
I remember looking into this for Dr. Stephen O'Keefe. One of his patients had a bad case. I can't remember the details, but I think it was trans retinoic acid (cis is the one for acne). At the time, the product was not yet available in Canada (only in the USA). There were some abstracts on it either at the Retrovirus conference or the World AIDS conference in 1998 I think.

(Tony)
I forgot to ask you if he was on HAART or has any associated edema.

Nonetheless, there is a product in the U.S. called Panretin gel, which, to my knowledge is the only topical preparation available. It is made by some drug company called Ligand pharmaceuticals. If I was a true friend, I suppose I could have looked into whether you could get it via special access, but I didn't. I think response rates range from 35-45%, or something along those lines.

Thalidomide is another option, but you could be looking at +++$$$$ to get it in. Celgene in the U.S supplies it, and they charge ~ $100.00 U.S for a bottle of 30 x 50 mg capsules (patients with KS are usually started at 200 mg/day, but the median dose in the best paper I have on the subject was 500 mg/d - 10 capsules).

We haven't used either in our patients; we usually go right for chemotherapy if the patient is willing with either paclitaxel or liposomal doxorubicin.

5. Amprenavir rash

(Debbie)
Does anyone have any "tricks" on managing amprenavir rash? We are seeing a few in the past little while; some can ride it out with supportive treatment (benadryl, topical treatment), while others are having a more difficult time.

Does temporarily decreasing the dose help, or spliting the dose to tid or qid? Any suggestions or shared experience would be appreciated!

(Natalie)
Sorry, we have yet to see the rash.

6. Cidofovir

(Alfred)
Has anyone prepared a topical cidofovir preparation for treatment of warts in HIV patients? If so, what concentration and base have been used? What frequency and duration of therapy? What success rate?

(Natalie)
I thought that cidofovir was removed from the Canadian market and no longer available through the Special Access program. We have made cidofovir eye drops but I thought that now we cannot even get it for our CMV patients.

(Christine)
Just to follow up on the availability of cidofovir, you can contact the TPD Special Access program to request cidofovir. Once approved the TPD forwards the request to Gilead which is the company that distributes cidofovir in the US. Billing will be directed to the ordering customer.

The contact at TPD is as follows:
Marta Caris, Acting Director of Bureau of Pharmacy Assessment
Telephone #: 613-941-2108

Here is the information that they require:
Patient's Initials, DOB, gender
Where to send vials
If patient is new to the drug
Indication
Quantity (i.e. number of vials)

(Tony)
I have used topical cidofovir for several patients with anal warts and molluscum contagiosum. I have compounded a 3% cream in an inert base (e.g. Glaxal base), and have had the patient apply it to the affected areas once daily. Most of the time, there is not 100% clearance of the warts, but patients have noted improvements in the size of the lesions or the total area affected.

Another option worth a try might be imiquimod 5% commercial prep'n (contact 3M pharmaceuticals) three times a week.

For acyclovir resistant herpes, never made up topical foscarnet; usually use the IV form. Cidofovir gel has been noted to work as well, although I've never tried it for anyone. I believe there may actually be a 1% gel available for this indication, but would have to check with Gilead on it's status/availablitiy.

7. Indinavir & Ritonavir- kidney stones

(Kathy)
Anecdotally has anyone been seeing more kidney stones when switching to BID Indinavir with BID Ritonavir?? We have had 2 cases that have recently occured both in patients who had no problems on their crixivan alone (for years) but when we added RTV 100 mg BID to IND 800mgBID they got a stone within days. Has anyone else seen this??

(Deborah)
We did have that happen to one patient this summer. He was previously on

IDV alone (not sure of duration; more than a year, I believe) with no problems. We switched him to IDV 800mg and RTV 200mg both bid, and within a couple of months he developed severe kidney stones, requiring hospitalization.

(Pierre)
We start patients on RTV-IDV very regularly since it provides better serum levels & easier scheduling. So far, we have had to my memory only one patient who experienced kidney stones. He was using RTV 200 & IDV 800mg BID.

Even it is not a consensus throughout all the physicians, we tend to use RTV 200 - IDV 600mg BID and so far, no kidney stone was reported. It makes sense as the Cmax of 200/600mg regimen is lower than 200/800mg. We used occasionally 100/800 without problems as well. Under specific circumstances such as heavily pre-treated patients with suspected multi-resistant virus, we will use RTV-IDV 200/800 keeping in mind the increase possibility of kidney stones.

It would be a good project if we could pool together our cases & determine the incidence of kidey stones....

Drug Interactions

1. Ritonavir & Bupropion

(Lizanne)
I was wondering if any of you have had patients taking bupropion and ritonavir concomitantly and if so, what were the dosages and have the patients experienced bupropion toxicity (e.g., seizures).

(Kathy)
I don't have any further information to offer. This has been a really controversial area. We often encounter it more for smoking cessation. In this situation we will not use both drugs together (ie benefit not worth the risk) Since you are using it for depression, I am assuming other antidepressants have already been tried?? It is usually a 2nd or 3rd line drug for depression. We have in rare instances used them together and had no problems but this is purely anecdotal.

(Pierre)
After discussion with our pharmacist in psychiatry, seizures induced by bupropion is overestimated. And so are the drug interactions.
I agree with Kathie that you should take into account the indication for bupropion but look also at the PI used and the dose. Only RTV could

potentially interact as it inhibits at high dose almost all CYP450 isoenzymes. However, RTV dosed at 100mg does not inhibit as much other isoenzymes other than CYP3A4 (personal info from K Gallicano).

Our position at the clinic is to allow use of regular dose of bupropion (MAX 300mg/day) with low dose RTV (<200 mg). We let patients take bupropion with all the other PIs even for smoking cessation purpose. So far, no case of seizures induced by bupropion has been noticed. This is not evidence based but it can give you a perspective of what we're doing.

(Christine)
I would have to agree with Pierre. In general we have avoided the use of buproprion in patients taking ritonavir. However, we have had a couple of patients on low dose ritonavir who took bupropion without any adverse effects.

(Ann)
We have had people on buproprion with all PIs at all doses without any problems. Many have been on buproprion prior to starting the PI and so we continued with it and monitored closely for any problems. In circumstances where the buproprion was to be added to an existing PI regimen, we to suggest that alternatives be considered but have started people on buproprion when appropriate or desired. There have been no problems to date that I am aware of.

2. Lopinavir & Amprenavir

(Christine)
I just wanted to check with all of you what dose of amprenavir and lopinavir you are using as part of salvage regimens? What about if the regimen includes efavirenz (i.e. lopinavir/amprenavir/efavirenz)? Are you still increasing lopinavir to 4 cap bid?

We have in general avoided amprenavir due to the enormous pill burden/size so I don't have any experience using the two together...

(Alice)
We usually give amprenavir 750 mg BID with usual dose lopinavir. If the regimen includes efavirenz or nevirapine, we either go up to 4 lopinavir caps BID or add 100 mg ritonavir BID to the regimen. Some MDs also like to push the amprenavir dose to 900 mg BID in this case if the patient can take the pill burden. I generally like to have at least 200 mg BID of ritonavir on board anytime there is another PI with nevirapine or efavirenz, because I don't think that 100 mg BID ritonavir (e.g., as part of lopinavir) is reliable enough to counter a strong inducer.

Reports from Working Groups

Publication Group (Sandy)
No update.

Research
The pregnancy survey is with Deb Kelly who has agreed to incorporate comments from the research committee and send it out to all pharmacists in January. Any final changes from the pharmacists to the survey should be emailed to Christine Hughes who has agreed to incorporate final changes and redistribute to pharmacists for dissemination. The pharmacists should return the surveys to Alice Tseng who has agreed to compile and analyse the results. The report will be written by Laura Park-Wyllie.

Communications
No update.

Education (Glenda)
No updates.

Additional News

Antiretroviral Fact Sheets (Rachel)
Our facts sheets for antiretroviral therapy are available free of charge on www.jag.on.ca/hiv. For the last year and a half, in Quebec, we have made them available in color. We recently did a survey to evaluate the appreciation of users and they seem to appreciate them very much. We had a professional linguist translate them in english and spanish. Do you think these tools could be useful to the other provinces? We are open to comments into ways of improving them.

May be we could ask your opinion as to whether or not these could be helpful ? We feel they are amongst the best facts sheets available: they are in color, with a picture of the drug (we have found this to be extremely useful to the patients), are updated regularly and are already available.

Updated Guidelines

The HIV/AIDS Treatment Information Services (ATIS) HIV Guidelines Working Group has updated the information in the Public Health Service Task Force Recommendations for the Use of Antiretroviral Drugs in Pregnant HIV-1 Infected Women for Maternal Health and Interventions to Reduce Perinatal HIV-1 Transmission in the United States.

The primary changes include: the addition of a new section titled, "Perinatal HIV-1 Transmission and Mode of Delivery" (pages 23-32), and the addition of information about Lopinavir (Kaletra) in Table 2.

The guidelines are available in 2 formats:

HTML format: http://hivatis.org/guidelines/perinatal/Nov_00/text/index.html

PDF format:
http://hivatis.org/guidelines/perinatal/Nov_00/text/PerinatalNov00.pdf
(requires the Adobe Acrobat Reader)

In Print

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NEJM Volume 343, Issue 11: September 14, 2000
Absence of Cardiac Toxicity of Zidovudine in Infants
S. E. Lipshultz and Others

Some food for thought….
The busier you are, the more important to stop and read this story.

One day, an expert in time management was speaking to a group of business students and, to drive home a point, used an illustration those students will never forget.

As he stood in front of the group of high-powered overachievers, he said, "Okay, time for a quiz." He then pulled out a one-gallon, wide-mouth mason jar and set it on the table in front of him. Then he produced about a dozen fist-sized rocks and carefully placed them, one by one, into the jar.

When the jar was filled to the top and no more rocks would fit inside, he asked, "Is this jar full?" Everyone in the class said, "Yes." Then he said, "Really?" He reached under the table and pulled out a bucket of gravel. Then he dumped some gravel in and shook the jar, causing pieces of gravel to work themselves down into the space between the big rocks. Then he asked the group once more. "Is this jar full?"

By this time the class was on to him. "Probably not," one of them answered. "Good!" he replied. He reached under the table and brought out a bucket of sand. He started dumping the sand in the jar and it went into all the spaces left between the rocks and the gravel. Once more he asked the question. "Is this jar full?"

"No!" the class shouted. Once again, he said, "Good!". Then he grabbed a pitcher of water and began to pour it in until the jar was filled to the brim. Then the expert in time-management looked at the class and asked, "What is the point of this illustration?"

One eager Beaver raised his hand and said, "The point is, no matter how full your schedule is, if you try really hard you can always fit some more things in it."

"No", the speaker replied, "that's not the point. The truth this illustration teaches us is this: If you don't put the big rocks in first, you'll never get them in at all.

What are the big rocks in your life? Your children. Your spouse. Your loved ones. Your friendships. Your education. Your dreams. A worthy cause. Teaching or mentoring others. Doing things that you love. Time for yourself. Your health. Remember to put these BIG ROCKS in first, or you'll never get them in at all. "If you sweat the little stuff (I.e.gravel, the sand) then you'll fill your life with little

things you worry about that don't really matter, and you'll never have the real quality time you need to spend on the big, important stuff (the big rocks).

So, tonight, or in the morning, when you are reflecting on this short story, ask yourself this question: What are the "big rocks" in my life?
Then put those in your jar first.