



## CHAP Summer 2002 Newsletter

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## **News**

Baby section:

Laura: is starting her maternity leave. While she is away, Tony Antoniou (tantoniou@smh.toronto.on.ca) will continue to work as the HIV pharmacist at the 410 clinic of St. Michael's Hospital. She expects to return to work next fall (August 2003), and will be checking her email fairly infrequently until then.

Kathy is also about to be Mom again.

Good luck to both of you and enjoy your new challenging gift of life.

## **Communications**

### ***Distribution of CDs from the last CHAP annual meeting***

A CD containing the presentations from our last annual meeting in Winnipeg was mailed in June to the working group members. The CD also includes posters distributed by Dr M Robinson from Abbott Laboratories. Anybody who would like to have access to the documents may do so by communicating with me. The files may be sent by e-mail or by mail on a CD.

## **CHAP Working Group**

A **call for candidates** for open spots in the working group took place in May. This resulted in 2 new members:

Nancy Sheehan, HIV pharmacy specialty resident at the Toronto General Hospital / St. Michael's Hospital. As of this summer, she plans to work in Montreal with Dr Lalonde at the CHESS where she intends to focus on TDM.

Linda Akagi, outreach Pharmacy Services coordinator at the BC Centre for Excellence in HIV/AIDS.

On behalf of all the members, congratulation! Both of you will be extraordinary additions. I am delighted to see the growing dynamism of the group.

Unfortunately, as a consequence of the reshuffle, Ann decided to continue her involvement in CHAP in the e-mail list only. However, she would be more than happy to participate in any projects that she can. In addition, I was unable to contact directly Glenda and my e-mail has not yet been returned. Consequently, in accordance with CHAP convention, I had to change her membership to the general membership. In the interim, I will leave her position open until this fall. Until then, this decision may be reversed should the required statement of the commitment obtained.

## Project Updates

### **Poster for the International AIDS Conference**

The abstract entitled **Development of a National HIV/AIDS Pharmacists Network in Canada** was accepted for publication in the abstract book.

Abstract E11553

I would also like to congratulate the members of the network who were actively present in Barcelona and had poster presented:

[MoPpB2007] J. Ananworanich, P. Cardiello, T. Monhaphol, A. Mahanontharit, **R. van Heeswijk**, D. Burger, K. Ruxrungtham, J. Lange, D. Cooper, P. Phanuphak. Pharmacokinetics of once daily saquinavir-hard gel caps and saquinavir-soft gel caps boosted with ritonavir in HIV-1+ Thai patients.

MoPeB3215] R.H. Glazier, (L Park-Wyllie). Patient support and education for promoting adherence to highly active antiretroviral therapy for HIV/AIDS: A systematic review of controlled trials

[TuPeB4515] **P. Giguère**, L. McGregor, J.B. Angel, J. Clinch. Lack of an association between protease inhibitors use and sexual dysfunction in patients with HIV infection.

[TuPeB4572] **R.P.G. van Heeswijk**, C. Cooper, K.D. Gallicano, G. Carignan, Y. Khaliq, I. Seguin, N. Hawley, J. Angel, A.D. Badley, G. Garber, D.W. Cameron. The pharmacokinetics of saquinavir/ritonavir 400/400 mg bid before, and after short- and long-term co-administration of efavirenz 600 mg qd

### **Publications/Research**

- a) Pregnancy survey: The results of the survey were compiled and a report was presented at the CHAP annual meeting. At this time, we have decided to keep the report as an internal document. Because of time constraints, decisions with regards to possible future publication will be assessed later by the research sub-group.
- b) HIV Drug Interactions website paper: Alice, Debbie, Christine and Lizanne are currently finalizing the research project. Laura & Nancy worked on the statistical analysis and a draft document should be available soon. 17 members of the group returned the evaluation of the proposed sites. Thanks to all of you! The Stat Team had the assistance of Dr Kirsteen Woodend, Director, Research, Canadian Pharmacist's Association. On behalf of CHAP, I will personally express our sincere gratitude to Dr Woodend for her contribution to the paper.

## **Conferences:**

### ***Summary of past conferences:***

#### XIV International AIDS Conference (Barcelona)

Information available on:

<http://www.medscape.com/viewprogram/1943>

<http://www.hivpharmacology.com/>

<http://www.hiv-druginteractions.org/>

### **Upcoming conferences:**

September 22-25, 2002

4th International Workshop on Adverse Drug Reactions and Lipodystrophy in HIV  
San Diego, CA

September 27-30, 2002

42nd Interscience Conference on Antimicrobial Agents and Chemotherapy  
San Diego, CA

October 24-27, 2002

40th Annual Meeting of the Infectious Diseases Society of America  
Chicago, Illinois

July 13-17, 2003

The 2nd IAS Conference on HIV Pathogenesis and Treatment  
Paris, France

Abstract deadline March 15, 2003

## **Drug Updates:**

### ***Atazanavir EAP***

The expanded access program for atazanavir is now opened. Enrollment of centers is now in process. No details available with regards to inclusion criteria.

### ***Valganciclovir (Valcyte)***

Valcyte has received the notice of compliance from Health Canada on May 3, 2002 and is now widely available. Roche sent a letter to everybody involved in the EAP (see below).

Dear Doctor,

Hoffman-LaRoche Ltd is pleased to announce the availability of Valcyte (valganciclovir HCL) tablets as of July 16, 2002. A general notice has been sent to all retail pharmacies, hospital pharmacies and drug wholesalers providing them with this information.

Valcyte tablets are approved for the treatment of CMV retinitis in patients with AIDS. The dose for induction therapy is 900mg (2 tablets) twice daily for three weeks; the dose for maintenance therapy is 900mg once daily. Valcyte tablets are available in bottles of 60 tablets at a price of \$22.41 per 450mg tablet. The price of Valcyte 900mg (2 tablets) daily is \$44.82 which is approximately 10% below the price of Cytovene (ganciclovir) capsules 3 grams per day (\$49.80).

Previously, Valcyte tablets have been available from Hoffman-La Roche as a service under our EAP. This EAP is now closed. We are contacting prescribers who have obtained Valcyte for their patients under this program, and are advising them that future prescriptions should be filled at the usual retail or hospital locations.

[...]

For complete prescribing information, please refer to the enclosed Valcyte product monograph. For any questions regarding our EAP, please contact myself [Parneet Charma] at 1-800-561-1759, extension 5063). For further information on Valcyte, please contact the drug information and safety department at 905 542-5537 or 1-888-762-4388.

### ***Efavirenz (Sustiva) 600mg tablets***

No official words yet.... but I heard through the grape vines that it would shortly receive its NOC. Stay on your toes....

## **Clinical Pearls:**

### ***Rapid HIV tests:***

Debbie

I'm preparing a talk on PEP, and wanted to get a feel of whether any sites are using the rapid HIV test kits in practice. The U.S. guidelines recommend the use of these tests for the source patient, however to my knowledge, we have only one brand available in Canada (the Fast Check HIV-1/2), which was recalled last month due to the false negative rate. Could you let me know what is happening in your institution regarding the use of rapid HIV testing for PEP decision? Also, if anyone knows of another rapid HIV test available in Canada, I am interested in that info, too. Thanks,

Pierre

In our clinic, we don't use the rapid test. We continue to do ELISA on the source patient. I am not aware of any other rapid tests available.

Linda.

In BC we do not recommend use of the rapid test. I know that there were possibly a few labs in outlying areas that were using them prior to the recall, but the CFE never recommended that they be used for this

purpose. As an aside, we have been randomly testing patients (HIV+ve) who come to the clinic for various reasons and have found a false negative rate of around 15%.

Jeff

I'm curious...were these HIV +ve patients on therapy and suppressed at the time of the testing??

Linda

Most of the patients were on therapy at the time and most had a pVL that was <50 or undetectable. There were only a couple patients that had high pVLs.

Also, we've checked almost 40 patients now and when you include the number of patients who had indeterminate readings the number of false negative results is about 50%. We're in the process of getting more specific information ie exact therapies and pVLs for the CDC.

Jinell

Here is the response I got from the coordinator in our main lab in Calgary. I did a PEP talk with her assistance 3 months ago for all our

ER staff at each acute care hospital.

I hope this helps. If there is anything else you need, please ask....

We use Biochem fast check serum HIV kit. Biochem makes Rapid HIV kits for whole blood and serum.

The issue is mainly to do with the whole blood kits. We are still permitted to test for rapid HIV because all of our specimens are confirmed by Prov Lab, using another method. We have been using the rapid HIV kit over a year now (approx 200 - 250) and have not found any false negative or positives results. The other brands of rapid HIV kits have worse error rates.

Christine

Good question! I know we were testing the rapid HIV test at one of our hospitals (mostly for pregnant women delivering who were not previously tested). Anyways, since the recall of this test, one of our doctors has recently learned of another rapid HIV test available in Canada and wants our lab to use it. I will contact him to see if he remembers the name and let you know.

Debbie

Thanks everyone for your responses!

### ***Tenofovir – DDI interaction***

Kathy

I can't seem to wrap my head around the potential mechanism for this interaction. Does anyone have any thoughts on this ie increase in AUC of DDI??

Linda.

The Gilead group has suggested that the increase may be due to competition for renal elimination. (41st ICAAC conference- Abstract I-1729, 2001). Has anyone seen any other proposed mech?

Michelle

I am also wondering what you guys are recommending on spacing with ddl and tenofovir? ddl buffered tabs vs ddl EC?

The letter that I circulated suggests the following:

\*\*\*\*\*EC caps:

ddl and TNF taken together with a light meal- 60% increase in ddl AUC

ddl ac and TNF with food 1 hour later- 50% increase in ddl AUC it appears that taking ddl EC with food (and TNF) is ok and does not impair ddl absorption. So in this case, can you simplify the schedule and recommend that both drugs can be given together with food (rather than ddl ac and TNF with food)?  
- any dosing modifications for ddl in light of the 50-60% increase?

\*\*\*\*\*ddl buffered:

ddl ac and TNF ac taken 1 hour later- 44% increase in ddl AUC

no data on ddl buffered given at the same time as TNF with food or fasting(too bad).....

- Is there any need to space these out because of buffers in ddl?

- I guess we do not have the info required to make a decision about giving ddl buffered with TNF and food, right?

In contrast to the product monograph, the letter suggests that dosing modifications would be considered with the combo (ddl formulation and food restrictions not alluded to), but provides no guidelines.

Is anyone as confused as I am?????? Any comments would be appreciated.

P.S. I also found a post ICAAC comment that talks about IC conc.

<http://www.natap.org/2001/ICAAC/day12.htm>

DDI and Tenofovir Interaction excerpted from ICAAC PK & Drug-Interaction report posted to NATAP site written by S Piscitelli

An interaction between didanosine and tenofovir was reported at the IAS meeting earlier this year in Buenos Aires.<sup>9</sup> Tenofovir increased DDI exposure in healthy volunteers by approximately 40%. Trough levels, peak concentrations and half-life were not significantly changed. There was much debate as to the clinical relevance of this data. Plasma levels of nucleoside RT inhibitors generally do not correlate with efficacy or toxicity since they are prodrugs that must be phosphorylated intracellularly to their active form. In an extension of this study, data from two, 24-week placebo-controlled tenofovir trials, which included 197 subjects receiving DDI, were examined.<sup>10</sup> Comparisons in toxicity between groups receiving DDI+TDF and DDI+placebo showed no difference in the incidence of pancreatitis, neuropathy, or increase in amylase. While this analysis does not rule out the possibility of increased DDI toxicity from higher levels with TDF, it does provide some reassurance that there is not an obvious safety problem from this combination. Additional data from Phase IV studies will add additional insight into this interaction and its clinical relevance. Clinicians should not decrease the dose of DDI when using tenofovir unless signs and symptoms of DDI toxicity are present.

ddl-Tenofovir interaction; ddl-Ribavirin-Interferon interaction; 3TC-ribavirin interaction; elevated glucose & diabetes in HCV/HIV coinfecting patients

Written for NATAP by Stephen Piscitelli, Pharm.D., Associate Director, Clinical Pharmacology, Tibotec-Virco and Jules Levin, NATAP

#### BRIEF SUMMARY OF THIS REPORT.

The studies reported on below found PMPA (Tenofovir) increased ddl blood levels by 40% but we are unsure if this is clinically significant because intracellular levels and not blood levels are correlated with NRTI toxicities. The study authors did not look at intracellular levels. And they reported on a relatively short-term study in humans who received ddl + PMPA which did not show an increase in key ddl-related toxicities (neuropathy, pancreatitis). Clearly, this is a question that needs further research attention. Second, ribavirin + interferon is the treatment for HCV. Preliminary in vitro (in the test tube) studies find that ribavirin alone and interferon alone may increase the amount of exposure to ddl a patient may see. And when using interferon plus ribavirin the ddl exposure may increase more than when either drug is used alone. Interferon has activity against HIV. Several preliminary studies show interferon can reduce HIV viral load. A study at ICAAC (abstract I-1938) found the Peg-Intron reduced HIV viral load from 0.25 to 0.43 log varying by the Peg-Intron dose used. This suggests that the triple therapy of ddl+interferon+ribavirin may offer an effective treatment for both HIV and hepatitis C. Further studies are needed to address this. Third, a small study of 22 patients was reported at ICAAC finding that patients receiving ddl+d4T and HCV therapy with IFN+RBV were more likely to experience clinical pancreatitis.



And perhaps taking d4T or ddl alone could increase the risk for pancreatitis when also taking HCV therapy. Another study found ribavirin reduced 3TC levels in vitro. Taken together it is reasonable to ask what could these data mean towards effects on cholesterol, triglycerides and sugar (metabolic abnormalities) and perhaps lipodystrophy.

At ICAAC a researcher reported study findings that HCV/HIV coinfecting patients receiving HAART may be more likely to experience develop diabetes, insulin resistance, and elevated glucose than patients who had HIV alone. Most of the coinfecting patients who experienced diabetes were on a PI regimen. This was a small study and there were a few factors in the study that confound the study findings such as there were more Hispanics in the coinfecting group of patients (60% vs 38%) and Hispanics are prone to have diabetes. But I think it's certainly fair to presume that coinfecting patients may be more likely to experience metabolic abnormalities and lipodystrophy (as was reported from a study reported at the Retrovirus Conference in Feb. 2001). Further research is needed on this question.

Linda

I can tell you what we have been doing with patient's thru Dr. Montaner's clinic. Please note that this is based on the very limited pharmacokinetic data presented so far and not any evidence of clinical outcomes. We have been dosing DDI-EC and tenofovir at the same time, with food. We have not been modifying the dose of DDI in light of the increased DDI levels.

However, these are mostly all salvage patients on multiple antiretrovirals. So, I can't say that we would take the same approach for a patient using a much simpler combination of medications.

We currently do not have any patients taking buffered DDI and tenofovir together. If we had patients on this combo, we would suggest staggering doses.

### ***QD PIs with NNRTIs***

Michelle

Hi I am wondering if any of you have tried giving a once daily PI regimen in combination with EFV or NVP? The doses are a concern and I am worried about low Cmins with the combo even with higher PI doses to compensate. some of our DOT patients who need more complex drug regimens due to resistance (yet once daily tx) it is something we are looking at. I have not seen intx data/ doses on the triple combos in a once daily format. i.e. NVP or EFV with

- APV/RTV
- IDV/RTV
- LPV/RTV- we are particularly interested in this agent for one patient
- NFV/RTV
- SQV/RTV

Any insights or experience would be appreciated.

Pierre

I am not aware of data on once daily PI plus NNRTI. At last CAHR, Rolf presented interim data on the PK of the ERASE study (abstract 201) suggesting that efavirenz has no effect on RTV-SQV PK dosed at 400/400 BID. The usual once daily regimen includes 100mg of RTV... except if you go with Kaletra (RTV=200mg). The story may change then.

I heard he has more patients for the analysis... maybe the conclusions are somewhat changed now.

Rolf, do you have a scoop for us ???

Rolf

Hi Michelle,

At the 8th European AIDS Conference (Athens 2001) Kurowski et al presented PK data on SQV-SGC/RTV 1,600/200 mg QD plus EFZ. This was a randomized, one-way cross-over study in 24 healthy volunteers. Coadministration of EFZ resulted in a non-sign. decrease of the SQV AUC (-19%), and trough concentrations remained unchanged (troughs with/without EFZ were 129 and 124 ng/mL respectively, mean or median?? not mentioned in the abstract).

At the last PK workshop Aarnoutse et al presented data from a PK study in healthy volunteers on the effect of NVP on the PK of NFV/RTV QD (NFV 2000 or 2500 mg plus RTV 200 mg). You can find the abstract and presentation on hivpharmacology.com (abstract 7.5). Conclusion of this study: AUC and Cmin of NFV + M8 were not affected by coadministration of NVP 400 mg QD.

If you plan to use once-daily boosted PIs plus NNRTI, I would suggested to study full PK profiles, for patient care as well as research purposes.

Regards

Christine

I do not recall any data specifically, but looked back to the recent CID article on once daily dosing of HAART (CID 2002;34:686-92). That article references a small study by Hsieh et al. (J Acquir Immune Defic Syndr 2000; 24:287-8)- they studied ddl + efavirenz + IDV 1200 mg + RTV 400 mg. Not sure if they looked at PKs but they have outcome data in terms of VL.

I think several studies (not once daily) have shown little effect of efavirenz when given with ritonavir 200 mg. If you can't find any other data, you could try a regimen with 200 mg ritonavir and perhaps use TDM??

Lizanne

Hi Michelle:

(Study from GSK - Study APV10009; N= 32; I am not sure if the study has been published)

GW433908 (pro-drug of APV)1395 mg OD + RTV 200 mg OD: Cmin = 1.45; AUC = 69.4; Cmax = 7.24  
GW433908 1395 mg OD + RTV 200mg OD + EFV 600 mg OD : Cmin = 1.00; AUC = 66.4; Cmax = 8.10  
GW433908 1395 mg OD + RTV 300mg OD + EFV 600 mg OD: Cmin = 1.46; AUC = 70.1 ; Cmax = 7.78

In this drug regimen, a dose of RTV 300 mg OD is necessary to counteract EFV induction, and achieve adequate Cmin levels.

When the GW433908 is given 700 mg bid with RTV bid (plus EFV 600 mg OD), RTV 100mg bid suffices and gives similar (although lower - AUC 17% lower) GW levels as when RTV 200 mg bid is given(9th Retro, Poster 431).

### ***Once daily antiretrovirals***

Kathy

Just wondering if any one is routinely using once a day ARV.

Obviously DDI, Sustiva but what about 3TC and nevirapine and amprenavir plus ritonavir (ie 1200mg/200mg). Just wondering if people were doing this routinely and also if there are any other enhanced PI once a day combinations that you may be using.

Rolf

Once-daily PIs are not routinely used in Ottawa. There are a few other options that you can consider. Recently data from a small study on QD Kaletra were presented (9th CROI), there are also data on SQV/r 1,600/100 mg and IDV/r 1,200/400 mg. It is important to realize that for all once-daily boosted-PIs the Cmins are lower than for BID regimens. The question is of course if it is still enough, and preliminary data (small numbers of patients, short follow-up) suggest yes (at least for PI-naive patients). The same is true for NVP 400 mg QD (AUC for QD and BID is the same, but Cmax is higher and Cmin is lower for the QD regimen compared to BID). 3TC has been used in a QD regimen in several studies. At the last PK workshop there were a few presentations on QD PIs (APV/r and NFV/r), you can find the slides of most presentations in [www.hivpharmacology.com](http://www.hivpharmacology.com). Kind regards,

Alice

Tenofovir is also a good option to add into a regimen if you are trying for QD dosing. We're not really doing much here at Toronto General yet, maybe 1-2 people on the 1600/100 mg SQV/rit, but that's it. I agree with Rolf that it would be a bit more risky in pts with possible resistant virus. Re:NVP QD, I seem to recall that there was an abstract from last year's PK workshop that suggested that PI levels were a bit lower when people switched their concomitant NVP 200 mg BID to 400 mg QD. I haven't seen anything else on this topic, though. I'm still waiting for atazanavir

Deborah

We're not doing once daily ARVs routinely at St.Mikes either, although I don't know if its happening at 410 Sherbourne with the DOT/methadone program. I think we wanted more clinical evidence of success before going that route. Some of the PK results (ie. lower Cmins for once daily regimens) Rolf spoke of were of concern to us so we've opted to stick with BID regimens for now.

Christine

I had the same question! We don't tend to use once daily PIs and can't think of anyone off-hand who is on one. We had one patient in mind who we thought may benefit from a once daily regimen (res to NNRTI, PI naive) however when you count up the pill burden (even if efficacy was equivalent) it is a lot of pills to take at once. If the patient has compliance problems (like this patient does), it is hard to balance the convenience of once daily with the increased pill burden for the one dose and also the consequences of missing this one dose.

Linda

In BC (especially in the Lower Mainland), we have been routinely using once daily regimens, especially in the marginalized populations, patients with compliance problems or in patients on salvage-type regimens. We have many patients taking 3TC and nevirapine once daily as well as many on SQV/RTV (1600/100mg) once daily. The most common starting combination used in the MAT programs which link methadone with ARVs is DDI/3TC/NVP once daily. The CFE does not advise the use of APV/RTV once daily, but I know of a few people on this combination (in the IVDU group). I am also aware of a few patients in this group who are taking Kaletra and abacavir once daily as well. Of course, we are also using a lot of tenofovir ..present count is around 180 patients for Dr. Montaner and around 10 patients for Dr. Conway's site.

## **TDM**

Michelle

Bonjour,

Just wondering if you have access to TDM assays in your institution or elsewhere in Canada? We have been sending limited samples down to Mayo clinic at a cost of \$130 US which seems pretty pricey. If you do have access to assays in Canada, do they do samples from other institutions and are they an accredited lab (or is it just for research purposes)? What type of assays are they using (HPLC, Mass Spec?)

Thanks

### **ALR beepers**

Alice

Hi everyone,

If people are still interested in using the ALR beepers for their patients, Merck still has a supply left (the ALR company went out of business, but Merck still has a stock of beepers in their warehouse). Also, we figured out what type of batteries the beepers need (two Maxell or Sony LR44 lithium batteries), and Merck will be able to supply fresh batteries as well.

If you are interested, you can e-mail Wildred DeSouza, one of the Toronto reps. His e-mail is: [wilfred\\_desouza@merck.com](mailto:wilfred_desouza@merck.com)

Jinell

Thanks Alice....

We get most of our "free" supplies from Merck (beepers and dosettes).

We also get dosettes from Glaxo (big white ones). Do any of you have any other pharmaceutical company supported supplies for patients? Those ALR beepers are handy, but not always reliable to work (I am glad you got the info on the batteries)

Alice

Hi Jinell, Yes, I'm quite happy about the batteries for the beepers. I just tried replacing a few, and they really work.

I used to get these really nice big pillboxes from Roche (the Fortopak), but I don't think we even have a Roche rep anymore, so I haven't had them in ages.

Pierre

Hi Alice,

I met last month my new Roche Rep. Her name is Shelley Dee. She covers one part of Toronto area but I don't know if it is yours. Try to contact her, she may be able to help you.

I had too the FortoPaC but I think they were 'slightly' too big, looking more like fishing box than pillbox.... I still have 5 here, if you send a courier, I will give them to you....

I am also happy for the batteries, I will try my Merck rep...

Hasta la vista !

### **Efavirenz teratogenicity**

Michelle

Allo all, I am wondering if any of you have had patients who received efavirenz in the first trimester of pregnancy (prior to dx of pregnancy), and what the outcome to the baby was? I have a patient who is in this situation and is quite concerned.

I have only found one case report with human infant toxicity. I am aware of the animal data.

Here is a link with some recent updates on teratogenicity.

<[http://www.hivatis.org/guidelines/perinatal/May23\\_02/STMay23.pdf](http://www.hivatis.org/guidelines/perinatal/May23_02/STMay23.pdf)>

Thanks

Pierre

Hi guys,

We have not had a good experience in 1 patient who was found out to be pregnant (6 wks) while on Kaletra-3TC-Sustiva. She was switched to RTV-IDV-CBV for the rest of her pregnancy. She was expecting twins but one died intrauterine and the other one is being investigated for possible malformation.

CHEO is leading the investigation analyzing the tissue sample from the stillborn to detect any sign of teratogenicity. I have to admit that the patient was already at risk for her advanced age (40 y.o.). As we obtain more information, I will keep you posted on future developments.

Michelle

Thanks Pierre, Did both of the twins die or just the one in utero?

Pierre

Hi Michelle,

A bit more of info...

The twins were heterozygous. One died in utero from what the pathologist believe is trisomy 18 (not drug related...). However, the pathologist was not able to perform an autopsy to confirm it. Analysis of the placenta is still pending.

The second infant is alive. She has some subtle differences consistent with one of the oral-facial-digital syndrome. More specifically, she has some hyperplasia in one hand and both feet. Also, she has abnormalities to her gums with premature eruption of her teeth and a lump on her tongue.

The development of teeth, limbs and tongue take place between week 4-8 of gestation. The mother took efavirenz until week 4 of the gestation. In addition to that, the fetuses were likely exposed for 1-2 more weeks given the long half-life of EFV. All this together make us believe that this is EFV-related.

This case will likely be reported in the near future.

### ***Diabetes and switch studies***

Christine

Is anyone aware of any studies showing improvement of diabetes following d/c of a PI (i.e. switch to NNRTI or triple nucs)? I know there are a couple of case reports of diabetes resolving after d/c a PI but wondered if there was any trial data. From what I have seen with switch studies, the usual endpoints are lipids, lipodystrophy and markers of insulin sensitivity, but the patients are not generally diabetic per se.

Thanks

## **New References**

### ***New Treatment Guidelines:***

Perinatal Guidelines –

DHHS: February 4, 2002; available on [www.hivatis.com](http://www.hivatis.com)  
European Consensus: June 2002; AIDS 2002; vol 16 (supp 2).