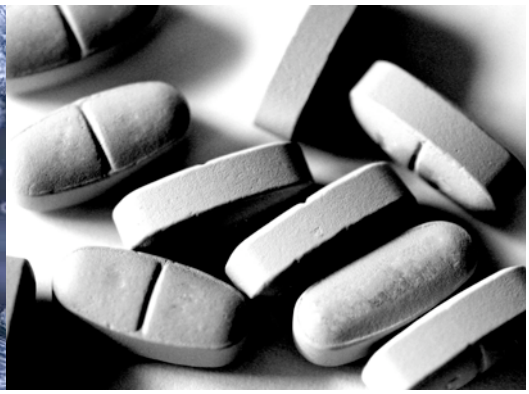
Toronto People With AIDS Foundation

# Treatment Bulletin

## Research Update: Key HIV Treatment-related research from 2010

December 2010

Disclaimer

The Treatment Resources Program at the Toronto People With AIDS Foundation provides information and resources to empower people living with HIV/AIDS to be proactive around their health by working in partnership with their health care providers. We do not recommend or promote any treatment in particular. We strongly urge those interested in any specific treatment to consult a wide range of resources, including a qualified medical and/or complementary therapy practitioner who has experience in working with HIV+ individuals.



*A guide to HIV treatment-related research from 2010 for people living with HIV/AIDS*

Every year new studies are published and conferences that focus on various aspects of the HIV/AIDS epidemic are held around the world. Scientists, researchers, physicians, community members, and many others come together and share information and every year we are learning more about HIV and how to treat it.

The amount of information released each year is vast and this treatment bulletin will highlight a few studies that were published and/or released at various conferences throughout 2010.

Terminology

There are some general terms that you may find useful to understand the information contained in this bulletin.

*In Alphabetical Order:*

*Cohort* - a group of individuals sharing a common characteristic and observed over time

*Control group:* a group of participants in a study who are similar to the treatment group in many factors but who are not receiving the intervention (e.g. treatment) being studied so that they can be used as a comparison group when results of a treatment are evaluated

*Creatinine* – A waste product produced by the body and eliminated by the kidneys. It has been shown to be an accurate indicator of kidney function

*Double-blind*: A term used to describe a research method in which neither the researcher nor the participant knows whether they are receiving the active medication or treatment or receiving a placebo. This is done in order to remove any bias (for example, if someone knows that they are receiving an experimental treatment they might unintentionally be more likely to report or feel positive results, whether they are present or not)

*Median* When all the data, or numbers, are placed in numerical order, the median is the half way point, meaning half of the numbers sit above, and half below, this particular number

*NNRTI* – Non-nucleoside Reverse Transcriptase Inhibitor. An HIV medication that stops HIV from making copies of its genetic material, but in a different way than NRTIs

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*Observational:* A type of study in which individuals are observed or certain outcomes are measured and there is no attempt to affect the outcome (e.g., no treatment is given).

*PI* – Protease Inhibitor. An HIV medication that prevents HIV from becoming active, even if it manages to make copies of itself.

*Placebo:* a substance that has no pharmacological effect

*Placebo-controlled:* A term used to describe a method of research in which a placebo is given to one group of participants, while the treatment being tested is given to another group. The results obtained in the two groups are then compared to see if the investigational treatment is more effective than the placebo.

*Randomized:* A type of study where participants are randomly assigned to be in a group either receiving an intervention or not.

19th Annual Conference on HIV/AIDS Research (CAHR) Saskatoon, Saskatchewan – May 13-16, 2010

Behaviour and Attitudes in HIV (BEAHIV): A national survey study to examine the level of agreement between physicians and patients in symptom reporting

Anita Rachlis[2] John Gill[3] Marianne Harris[4] John Macleod[5] Cathy Worthington[6] Jonathan Leith[1] Fernando Camacho[7] Daniel Turner[8] Jason Brunetta[9] Christopher Fraser[11] Albert Tsang[10] Huong Hew[1]

The BEAHIV study was a recent Canadian study presented at the CAHR conference that looked at patient-physician communication. The study was carried out at 17 sites across Canada with 42 doctors and 1000 HIV+ patients. After a regular visit and on a one-time only basis, each doctor and patient participant were asked to fill out a survey.

In the survey patients were given a list of symptoms and asked to indicate which they had experienced, how much the symptom bothered them, and whether they had discussed the symptom with their doctor during the visit. Physicians were presented with a similar questionnaire, and asked to indicate which symptoms were discussed during the visit and how much the symptoms were bothersome to the patient. The results of the two surveys were compared.

The results showed that symptoms experienced as bothersome to the patient were not well recognized as bothersome by the physician. When patients and doctors both agreed that they had discussed the symptoms, there was better agreement when it came to symptom recognition. The biggest areas of difference with respect to symptom reporting were with memory issues, sexual problems, bloating, gas, and pain.

There are some reasons why the results may have shown such discordance. The patient may have discussed the particular symptoms with another health care provider or member of the health care team, or at another visit altogether; the survey only took into account what was discussed during that single visit; and if the symptom wasn't assessed at that visit it was considered to not be present.

The results indicate that there is some need for improvement in doctor-patient communication and the importance of alerting your physician to side effects that may be problematic. There may be a tendency as well for patients to underreport symptoms that they attribute to side effects if the medication is working well and they are afraid to switch, and doctors may tend to focus more on a patient's CD4 count and viral load than symptoms affecting quality of life. In both cases, better communication can lead to a better patient quality of life.

**In Other Words**..... Doctors and patients both need to be better at communicating with each other. If you make a point of discussing an issue at your visit with your doctor and they are more likely to recognize it as a concern for you.

XVIII International AIDS Conference Vienna, Austria – July 18-23, 2010

Quadrivalent HPV vaccine efficacy against HPV 6/11/16/18 infection and disease in men

H. Jessen[1], A. Giuliano[2], J. Palefsky[3], S. Goldstone[4], E. Moreira[5], M. Penny[6], C. Aranda[7], E. Vardas[8], H. Moi[9], R. Hillman[10], Y.-H. Chang[11], D. Ferris[12], D. Rouleau[13], J. Bryan[14], J.B. Marshall[14], S. Vuocolo[14], E. Barr[14], D. Radley[13], R. Haupt[14], D. Guris[14]

This study looked at the safety and efficacy of a vaccine against human papilloma virus infection in men. The vaccine, commercially sold under the name Gardasil and currently available in Canada, is active against HPV strains 6, 11, 16, an 18.

The study was a randomized, double-blind, placebo controlled trial that enrolled participants from 95 study centres in 18 countries on 5 continents. A total of 4065 men were recruited between the ages of 16 and 26, 3,463 of whom identified as heterosexual, and 602 who identified as men having sex with men (MSM).

Those enrolled in the study received 3 doses of Gardasil or placebo at 0, 2, and 6 months and were tested to ensure that they were HPV negative for the 4 strains until the vaccinations were completed. Beginning after 7

months, when the vaccine was presumably considered to be effective, monitoring for HPV infection occurred and cases recorded. Those who did not receive all three doses (for various reasons), but returned for follow up were monitored starting on day 1.

HPV disease in men can occur in various forms:

- Latent HPV infection (meaning no clinically visible lesions are present but the person has confirmed HPV infection)
- anogenital warts (small bumps that develop on the genitals and/or around the anus)
- penile and anal intraepithelial neoplasias (pre-cancerous cells) and cancers
- cancers of the head/neck (of which 20-40% are HPV-related)
- recurrent respiratory papillomatosis (a condition caused by HPV where warty growths in the upper respiratory tract can cause obstruction and difficulty breathing)

The results showed that Gardasil was generally well tolerated and that the vaccine was highly effective (90.4%) in preventing external genital lesions when all three doses were taken as recommended. The vaccine was also effective in preventing anal intraepithelial neoplasia (AIN) and anal cancer associated with HPV 6/11/16/18 in MSM participants that did not have those particular strains when the study started.

**In Other Words**..... Gardasil is effective at preventing HPV infection in men and its associated cancers for the four strains included in the vaccine. The vaccine was generally well tolerated.

17th Conference on Retroviruses and Opportunistic Infections (CROI)
San Francisco, CA, USA – February 16-19, 2010

Single-tablet, Fixed-dose Regimen of Elvitegravir/GS-9350/Emtricitabine/Tenofovir DF (Quad) Achieves a High Rate of Virologic Suppression and GS-9350 Is an Effective Booster

Calvin Cohen[1], David Shamblaw[2], Peter Ruane[3], Richard Elion[4], Edwin DeJesus[6], Hui C. Liu[5], Lijie Zhong[6], David Warren[6], Brian P. Kearney[6], and Steven L. Chuck[6]

This study looked at the efficacy of a single tablet, four-drug pill, known as the "Quad" pill, a coformulation containing the experimental integrase inhibitor elvitegravir, the novel boosting agent GS-9350 (cobicistat), tenofovir, and emtricitabine. GS-9350 does not have HIV activity itself but acts as a booster similar to ritonavir (Norvir). In another study by the same investigators, it was shown to have similar efficacy, safety, and tolerability as ritonavir.

Subjects were required to be treatment-naïve, have a viral load over 5,000 copies/mL, have a CD4 count greater than 50, have no resistance to the 3 earliest classes of HIV medications (NRTIs, NNRTIs, and PIs), and be negative for Hepatitis B and C.

Patients were given either the Quad pill or Atripla (a three drug, once daily pill, containing efavirenz, tenofovir, and emtricitabine), which is currently available and widely used. Since both pills have Tenofovir and emtricitabine in common, the study was actually a comparison of elvitegravir/GS-9350 vs. efavirenz, the two drugs that were different between the two. The study was double-blind, and enrolled 71 patients who were randomized 2:1 to receive either the Quad pill or Atripla.

At 24 weeks, 90% of those taking the Quad pill achieved an undetectable viral load vs, 83% of those taking Atripla. The average increases in CD4+ cell count were similar for both drugs, with 123 cells/mm3 in the Quad arm and 124 cells/mm3 in the Atripla arm. There were also fewer study drug-related side effects with the Quad pill compared with Atripla.

One of the concerns with the novel booster drug GS-9350 was that there was a small increase in creatinine observed in the blood (a marker of potential kidney impairment). When looking further into this the researchers believe that the drug may inhibit one of the mechanisms for excreting creatinine from the body, but only a minor route of excretion. This is seen with other medications that are available over the counter and appears to be safe without any known kidney toxicity.

**In Other Words**.... The Quad pill was shown to work at least as well as Atripla in bringing viral load to a non-detectable level and increasing CD4 count and had fewer side effects. The booster GS-9350 did increase levels of creatinine in the blood (which may indicate kidney toxicity), but the researchers believe that this is not significant as the changes were small and other over-the-counter drugs that have similar effects have not been shown to be toxic to the kidneys.

In Print

Early versus Standard Antiretroviral Therapy for HIV-Infected Adults in Haiti.
*New England Journal of Medicine*, 363 (3), July 15, 2010, 257-65.

Patrice Severe, M.D., Marc Antoine Jean Juste, M.D. , Alex Ambroise, M.D., Ludger Eliacin, M.D., Claudel Marchand, M.D., Sandra Apollon, B.S., Alison Edwards, M.S., Heejung Bang, Ph.D., Janet Nicotera, R.N., Catherine Godfrey, M.D., Roy M. Gulick, M.D., Warren D. Johnson Jr., M.D., Jean William Pape, M.D., and Daniel W. Fitzgerald, M.D.

With the current debate on when to start treatment and the majority of studies on starting at a higher CD4 count being supported by observational cohort data, this randomized trial evaluating the optimal time to start treatment provided much needed data in support of early treatment.

This randomized study looked at whether early initiation of antiretroviral therapy (CD4 between 200-350) compared with standard timing for treatment initiation (CD4 of 200 or less or presence of an AIDS defining illness), improved survival.

A total of 816 participants were enrolled and randomized 1:1 (408 in each group) to either begin treatment within 2 weeks of the start of the study (early group) or begin once CD4 count reached 200 or an AIDS defining illness developed (standard group). Subjects were required to have a CD4 count above 200 but below 350 to be able to participate in the study, and must not have had an AIDS defining illness, or been on ART previously. Participants were followed for a median of 21 months (range from 1-44). Both groups were given the same HIV medications.

There were 23 deaths in the standard treatment group compared with 5 in the early treatment group. Only one of the deaths in the early treatment group was from an infectious disease compared with 17 in the standard treatment group. There were also 36 cases of tuberculosis in the standard treatment group and 18 in the early treatment group.

**In Other Words**.... Starting treatment when CD4 counts are between 200 and 350 decreases the rate of death and incidence of tuberculosis. This is the first randomized trial to formally show the relationship between starting treatment early and positive health outcomes in a randomized clinical trial setting (as opposed to observational cohort data).

## Acknowledgements

This treatment bulletin was written and designed by Jennifer Grochocinski, ND, Treatment Resources Coordinator at the Toronto People With AIDS Foundation (PWA)

PWA thanks Melissa Egan and the Canadian AIDS Treatment Information Exchange (CATIE) for reviewing the content of this treatment bulletin to ensure accuracy.

PWA also thanks Bristol-Myers Squibb, Gilead, ViiV Healthcare in partnership with Shire Canada, Merck, and Tibotec for supporting PWA's Treatment Bulletins.

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**Mission**

The Toronto People With AIDS Foundation exists to promote the health and well-being of all people living with HIV/AIDS by providing accessible, direct, and practical support services