

AIDS 2008: Is the HIV drug pipeline drying up?

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The conference heard promising reports about the newer HIV treatments designed to help treat people with advanced and drug-[resistant](#) [1]HIV which has mutated and is less susceptible to the effects of one or more anti-HIV drugs is said to be resistant. HIV, all of which are now available in Australia on [PBS](#) [2][Pharmaceutical Benefits Scheme] The federal government program which subsidises medication costs in Australia. Anti-HIV drugs are part of a special part of the PBS called Section 100 (S100) which is used for expensive, highly specialised drugs. or compassionate access.

These drugs are the protease darunavir (Prezista, TMC-114), the NNRTI etravirine (TMC-125) and the new classes, the CCR5 inhibitor maraviroc and the integrase inhibitor raltegravir. There were also presentations about new agents in [trial](#) [3]A clinical trial is a research study to answer specific questions about vaccines or new therapies or new ways of using known treatments. Clinical trials are used to determine whether new drugs or treatments are both safe and effective. Carefully conducted clinical trials are the fastest and safest way to find treatments that work in people. Trials are in four phases: Phase I tests a new drug or treatment in a small group; Phase II expands the study to a larger group of people; Phase III expands the study to an even larger group of people; and Phase IV takes place after the drug or treatment has been licensed and marketed. and discussions about [gene](#) [4]The most basic unit of genetic information. therapy – see Treatments Briefs articles linked in the right sidebar.

The newer drugs have been a great boon for treatment-experienced people who had developed resistance to older drugs and many of these people have now been able to put together treatment regimens with two or more fully active drugs. For some people who have treated HIV for a long time or had difficulties with available treatments, it has been the first time they have been able to get an undetectable [viral load](#) [5]A measurement of the quantity of HIV RNA in the blood. Viral load blood test results are expressed as the number of copies (of HIV) per milliliter of blood plasma. in their treatment history.

Resistance to the new classes

Writing on thebody.com, Paul Dalton from Project Inform though sounds a word of caution as to whether the of new HIV drug pipeline is drying up as people start to develop resistance to the new drugs as well. He quotes Dr Steven Deeks, a prominent HIV physician and researcher who says that he is following a [cohort](#) [6]In epidemiology, a group of individuals with some characteristics in common. A cohort study is a special kind of clinical trial which looks at a treatment or treatment strategy in a cohort of people. with about 25 individuals who have already failed all six [drug classes](#) [7]A group of anti-HIV drugs with the same target of action. Anti-HIV drug classes include *nucleoside analogue reverse transcriptase inhibitors*, *protease inhibitors* and *non-nucleoside analogue reverse transcriptase inhibitors*, as well as several others. Combining drugs from three or more classes is the basis of Highly Active Antiretroviral Therapy (HAART).. “The key (for these people) is to design regimens which maintain immunologic and [clinical](#) [8]Pertaining to or founded on observation and treatment of participants, as distinguished from theoretical or basic science. stability while we wait for more drugs ... We desperately need a second generation integrase inhibitor that works against [viruses](#) [9]A small infective organism which is incapable of reproducing outside a host cell. resistant to raltegravir,” says Deeks.

There are some drugs in development that show promise such as rilpivirine (TMC-278), which is being studied as a first line treatment against efavirenz (Stocrin), as well as anew CCR5 inhibitor vicriviroc (being developed by Schering) and a maturation inhibitor called bevirimat from Panacos Pharmaceuticals.

Difficulty getting trial volunteers?

Dalton points to a lack of people with treatment experience willing to go on trials in the US and argues that the [FDA](#) [10]The U.S. Department of Health and Human Services agency responsible for ensuring the safety and effectiveness of all drugs, biologics, vaccines, and medical devices, including those used in the diagnosis, treatment, and prevention of HIV infection, AIDS, and AIDS-related opportunistic infections. The FDA also works

with the blood banking industry to safeguard the nation's blood supply. The Australian equivalent is the Therapeutic Goods Administration (TGA). has made the model for drug trials for these people (using optimised background therapy based on resistance results) too stringent for drug companies to really be able to prove the worth of new drugs for people in this situation. He uses as an example the difficulty Gilead had trialling volunteers for their [experimental](#) [11](Of a drug) Not licensed for use in humans, or as a treatment for a particular condition. Experimental drugs are studied in clinical trials to determine their safety and efficacy, and are sometimes made available via Special Access Schemes prior to their approval. integrase inhibitor, elvitegravir because of the lack of treatment-experienced volunteers. Eventually the FDA allowed Gilead to trial the drug using the more robust model allowed for first line therapies.

Bill Whittaker, NAPWA Health, Treatments and Research Co-Convenor, is more confident of the possibility of new therapies being produced in the near future and that there should be enough people available to participate in the necessary trials. "The treatment pipeline ebbs and flows over time, and we may not have quite as many new treatments over the next few years. So it's really important that the new drugs we do have are used wisely. However, as I see it, there are a number of companies who have promising drugs in development that are designed to have unique resistance profiles, new ways of attacking the virus and better tolerability. If rates of clinical trial participation become a problem, then the system may need to be adjusted to reflect this reality. But Australia still has a wonderful record of participation in clinical research and I think this can continue, and I'm sure there are many patients in developing countries who are failing therapy who would be very interested to take part in such trials as well."

Drug companies withdraw from HIV

There have been some major pharmaceutical companies who have decided to withdraw their research efforts in the HIV field, with Roche and GSK both recently deciding to discontinue with the development of new HIV drug developments. But new players, such as Panacos. Schering Plough and Pfizer have entered the field and Whittaker suggests that there are good opportunities for drug companies who can develop the right drugs at the right prices for emerging economies in the Asia Pacific region, for instance, as well as in developed countries like Australia.

"My greatest concern for the future," says Whittaker, "is that the involvement in treatment and research advocacy by community activists continues to decline. Without the close scrutiny of advocates, clinical trials and compassionate access programs may not be delivered in the way they should be. There is also a need for continuing and savvy pressure to be applied by activists on governments and pharmaceutical companies on drug pricing to ensure the ongoing availability of the drugs required."

"Finally, we must ensure that HIV research and drug development doesn't stop with people having to be on lifetime daily treatment, even if drugs are well tolerated and potent. Research momentum needs to continue until HIV is effectively able to be managed with intermittent treatment and ultimately cured."

- [bevirimat \(PA-457\)](#)
- [clinical trials](#)
- [darunavir](#)
- [elvitegravir \(GS-9137\)](#)
- [etravirine \(TMC-125\)](#)
- [HIV treatments](#)
- [maraviroc](#)
- [raltegravir](#)
- [rilpivirine \(TMC 278\)](#)

Links:

[1] <http://www.napwa.org.au/glossary/term/109>

[2] <http://www.napwa.org.au/glossary/term/121>

[3] <http://www.napwa.org.au/glossary/term/89>

[4] <http://www.napwa.org.au/glossary/term/126>

[5] <http://www.napwa.org.au/glossary/term/416>

[6] <http://www.napwa.org.au/glossary/term/477>

[7] <http://www.napwa.org.au/glossary/term/124>

[8] <http://www.napwa.org.au/glossary/term/475>

[9] <http://www.napwa.org.au/glossary/term/125>

[10] <http://www.napwa.org.au/glossary/term/492>

[11] <http://www.napwa.org.au/glossary/term/491>