



Hit hard, hit early

The big news of the year on the HIV front is the swing in the “when to start treatment” pendulum back to “hit hard, hit early.” The consensus is now that treatment should be started when CD4 cell counts fall below 350 cells/mm³, not 200 as previously recommended. This is based on a number of factors and pieces of evidence that have come together in the last few years.

- The results of the Strategies for Management of Antiretroviral Therapy (SMART) study, involving almost 5500 HIV+ participants, showed that taking highly active antiretroviral therapy (HAART) continuously (as opposed to taking HAART intermittently, just enough to maintain a CD4 count between 250 and 350 cells/mm³) reduces the risk of getting sick or dying not only from AIDS-related conditions, but also from non-AIDS related conditions such as heart, liver and kidney disease.
- Results of a sub-study of SMART showed that blood levels of inflammatory markers increase when HAART is interrupted and decrease again when HAART is restarted. These markers indicate that HIV infection is causing chronic inflammation, a major driver of non-AIDS conditions such as heart disease. Being on HAART decreases this chronic inflammation.
- New antiretroviral drugs that have less long-term side effects than the older drugs make it safer to start HAART early and remain on it for a longer time.

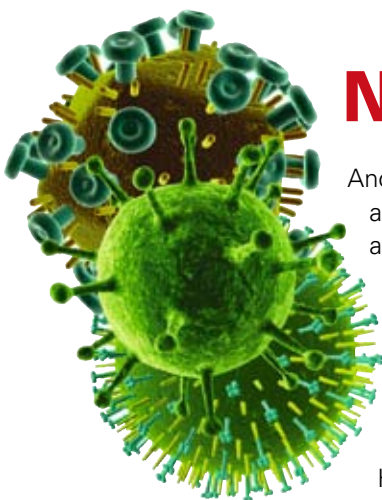
As a result, the main HIV treatment guidelines issued by the United States Department of Health and Human Services (DHHS) (available at <http://AIDSinfo.nih.gov>) and the International



AIDS Society — USA Panel (S Hammer et al., *JAMA* 2008) have now changed their recommendations to say that HAART should be started earlier in HIV disease, when the CD4 falls below 350 cells/mm³, instead of below 200 cells/mm³ as before.

Guidelines on treatment options were also updated:

- Kaletra® (lopinavir/r) can now be dosed either once or twice daily in people who have not been on ARVs before.
- Co-formulated Epzicom® (abacavir and lamivudine) has been demoted from a ‘preferred’ NRTI combination to an ‘alternative’ one because of data suggesting that it may be insufficiently potent in people with high viral loads and also because of other data linking its use to possible increased risk of heart attacks.
- Two triple-drug combinations — ddl, FTC plus unboosted atazanavir, as well as tenofovir, FTC plus nevirapine — have been flagged as ones to avoid or to use with caution because some studies have demonstrated poor efficacy.



New drug class for resistant virus

Another important development is the availability of raltegravir (Isentress®), the first agent in a new class of drugs called integrase inhibitors. Since it was approved for use in Canada late in 2007, raltegravir has been used by many people whose virus had developed resistance to the previously-available drugs, with excellent results. It combines well with other HAART agents to suppress the virus effec-

tively and so far it appears to be remarkably well tolerated.

Raltegravir has been a real boon for people who had to take T20 (enfuvirtide or Fuzeon®), another drug that is effective for drug-resistant HIV but has to be given by injection twice daily. Many of these people were able to replace T20 with raltegravir, which is given by mouth, thus eliminating the need for injections while maintaining control of their HIV infection.