AIDS BRIEFS

NEW TREATMENT FOR ORAL THRUSH IN HIV

A new treatment for oral candidiasis is as effective as the current standard of care and may be even better at preventing relapse in HIV-positive individuals, according to an international study published in *Clinical Infectious Diseases*.

Oral thrush is the most common opportunistic infection seen in HIV-positive individuals. The current standards of care are fluconazole or itraconazole, but resistance to these drugs can develop.

Laboratory studies have shown that the orally administered posaconazole is effective against the species of *Candida* that cause oral candidiasis, leading investigators to design a study comparing the efficacy and safety of posaconazole with fluconazole. The primary aim was to compare the proportion of HIV-positive patients with oral *Candida* who experienced an improvement in or cure of their oral *Candida* after 14 days of treatment. The investigators also assessed the durability of the 2 therapies and looked at rates of relapse in the 2 treatment arms after 42 days. The effects of the 2 drugs on *Candida* cultured from patients enrolled in the study were assessed at day 14 and again at day 42.

A total of 350 individuals were recruited to the study at 47 world-wide sites between late 1998 and late 1999. Only a third of patients were taking antiretroviral therapy of any kind and the median CD4 cell count on entry to the study was 134 cells/mm^3, showing a high risk of opportunistic infections, including oral candidiasis.

Patients were equally randomised into the 2 treatment arms. Therapy with a 200 mg oral suspension of their allocated study drug was provided on day 1 followed by 14 days of treatment consisting of a once-daily 100 mg oral dose. After 14 days, clinical signs of *Candida* were no longer present in 92% of patients treated with posaconazole and 93% of individuals who received fluconazole. The investigators then looked at culture results. These showed a 68% success rate in both treatment arms at day 14. By day 42, however, significantly more patients who received posaconazole had negative culture results (41%) than those who received fluconazole (26%), suggesting that posaconazole has greater long-term effects on oral candidiasis.

Vazquez JA, *et al. Clin Infect Dis* 2006; **42:** 1179 - 1186.
Klotz SA. *Clin Infect Dis* 2006; **42:** 1187 - 1188.

HAART FAILURE RATE DECREASING

The risk of an initial antiretroviral combination failing more than halved between 1996 and 2002, according to an international retrospective observational study published in the *Archives of Internal Medicine*. This may be because of more potent drugs, treatment guidelines emphasising maximal viral suppression, and a better understanding of resistance and adherence.

It is important that patients respond well to initial treatment with triple combination highly-active antiretroviral therapy (HAART), which has been the standard of care in well-resourced countries for a decade, since early virological failure may lead to the emergence of resistance, compromising future treatment choices. Since 1996, however, more powerful and better-tolerated antiretrovirals have been developed and resistance and adherence issues are better understood.

Investigators from 5 HIV clinic cohorts in Barcelona, Frankfurt, London, Calgary and Nice examined trends in the risk of initial virological and immunological failure in antiretroviral-naïve individuals from 1996 to 2002.

A total of 3 825 individuals were included in the analysis. Compared with earlier years, people initiating HAART in later years were less likely to have been infected through sex between men; more likely to be older; have a lower median CD4 cell count; and use a ritonavir-boosted protease inhibitor or non-nucleoside reverse transcriptase inhibitor. Throughout the study period, the most common nucleoside backbone remained AZT (zidovudine) and lamivudine (3TC).

The investigators used the first viral load measurement obtained 6 - 12 months after starting HAART to look at virological failure (a viral load measurement of more than 500 copies/ml). From 1996 to 2002, the overall risk of virological failure fell from between 38.9% and 8.2%. Heterosexual men and women and those infected via injecting drug use (IDU) had a higher risk of virological failure. Risk of failure was lower among older people and higher among people with a previous AIDS diagnosis. A higher pre-therapy viral load was associated with a higher risk of failure in certain categories.

Compared with other single non-boosted protease inhibitors (PIs), regimens containing hard-gel saquinavir tended to be associated with a higher risk of failure. In contrast, boosted PI regimens and those containing efavirenz tended to be associated with lower risk.

Trends in virological failure per calendar year did not differ significantly by age group (under 30 v. over 30), previous AIDS, baseline CD4 count (under 200 v. over 200 cells/mm^3), or baseline viral load (under 5 v. over 5 log_{10} copies/ml). However, gay men had less risk of failure than other risk groups.

Similar trends were seen for immunological failure, defined as a CD4 count increase from baseline of less than 50 cells/mm^3 between 6 and 12 months after commencing HAART.

Overall, 290 individuals had a new clinical AIDS diagnosis or died within the first year of initiating HAART, with no significant trend over time.

These results suggest a large improvement in the initial treatment success of people started on HAART for the first time. For people now starting HAART for the first time, the initial failure risk is very low and, according to researchers, may be as low as is 'realistically possible'.

Lampe FC, *et al. Arch Intern Med* 2006; **166:** 521-528.

RISK OF GRAVES' DISEASE IN PATIENTS STARTING ANTIRETROVIRALS

Patients who start HIV treatment with a very low CD4 cell count and then experience a rapid and substantial increase in their CD4 cell count should be monitored for Graves' disease, according to investigators writing in *AIDS*. This warning follows 5 cases of Graves' disease in patients who started antiretrovirals with a low CD4 count. Researchers think that this should be considered an immune reconstitution inflammatory syndrome (IRIS).

Researchers noted that 4 of the 5 cases involved people who started potent antiretroviral therapy with a CD4 cell count below 25 cells/mm^3 or less. The fifth patient had a CD4 cell count of 472 cells/mm^3 when HIV treatment was started. Within 12 - 25 months of starting HIV treatment, the patients had experienced an increase in their CD4 cell counts of between 130 and 200 cells/mm^3. However, symptoms of Graves' disease developed at around this time and 2 patients also developed eye problems – 1 having compression of the optic nerve and the other retraction of an upper eyelid.

The patients were treated for Graves' disease, including thyroidectomy in 1 case, and symptoms largely resolved, although the eye problems remained. There have been 23 additional cases of IRIS-related Graves' disease reported in HIV-positive individuals in the literature. The median age was 39 years, and 57% of cases involved women. The mean CD4 cell increase after starting HIV therapy was 355 cells/mm^3 and symptoms of Graves' disease, which typically included tremor, weight loss, palpitations, insomnia and eye problems, occurred 21 months after starting antiretroviral therapy. Researchers suggest that this late presentation may be as a result of naïve cells migrating from the thymus in the second phase of CD4 cell increase.

They suggest that HIV physicians should remain alert for thyroid disorders and Graves' disease among patients taking antiretroviral therapy, and consider testing for thyroid disorders among patients with consistent clinical findings.

Crum NF, *et al. AIDS* 2006; **20:** 466 - 469.

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SINGLE SUTURE

FAMILY SUPPORT CURES TB

In the foothills of Nepal, communities are fighting TB effectively, not with a vaccine or a new drug, but simply with family support that makes sure that someone with TB completes the 6-month course of treatment. Until now, it has been health workers who have checked that patients take their treatment in the DOTS approach. But a trial by James Newell, University of Leeds, shows that the regimen works just as well when a family member takes responsibility for the patient completing the treatment. Of 358 patients observed by family members, 89% were cured, which is a 4% improvement on the cure rate of the 539 patients looked after by health workers on the same trial. This could be the key to dealing with TB in remote areas or, in our case, in areas where it is unsafe for health care workers to venture, such as the gang-ridden Cape Flats.

Newell J, *et al. Lancet* 2006 ; **367:** 903.