

HIV drug remains unproven without placebo trial

Ethical concerns over use of a placebo weaken evidence for the benefits of nevirapine.

Sir—While raising concerns about “standards of record keeping” in the HIVNET 012 trial in Uganda, in your News story “Activists and researchers rally behind AIDS drug for mothers” (*Nature* **432**, 935; 2004), you overlook a greater flaw. None of the available evidence for nevirapine comes from a trial in which it was tested against a placebo. Yet, as the study’s senior author has said (see www.hopkinsmedicine.org/hmn/S01/feature.html), a placebo is the only way a scientist can assess a drug’s effectiveness with scientific certainty.

The HIVNET 012 trial abandoned its placebo group in early 1998 after only 19 of the 645 mothers randomized had been

treated, under pressure of complaints that the use of a placebo was unethical.

The HIV transmission rate reported for nevirapine in the HIVNET 012 study was 13.1%. However, without antiretroviral treatments, mother-to-child transmission rates of HIV vary from 12% to 48%. The HIVNET 012 outcome is higher than the 12% transmission rate reported in a prospective study of 561 African women given no antiretroviral treatment (J. Ladner *et al.* *J. Acquir. Immun. Def. Syndr. Hum. Retrovirol.* **18**, 293–298; 1998).

There are also reports of placebo-group transmission rates that vary within the same hospital and between hospitals, as

well as during different time periods of the same study. One study reported a lower transmission rate in the placebo group than with no treatment.

On what basis can it be claimed that “there’s nothing that has in any way invalidated the conclusion that single-dose nevirapine is effective for reducing mother-to-child transmission”? Without supporting evidence from a placebo-controlled randomized trial, such statements seem unwarranted.

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