

MICROBICIDES DEVELOPMENT PROGRAMME

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MDP 301 Trial Results - Q&A

Q. What were some of the differences between the MDP 301 and HPTN 035 trials?

Both trials aimed to find out if PRO 2000 gel could help protect women against HIV.

The HPTN 035 trial involved 3099 women and tested a low concentration (0.5%) of PRO 2000 gel against a placebo gel and against no gel. This trial also tested a second active gel, BufferGel, and compared this to placebo and to no gel. All women in the trial were also counselled to use condoms.

The MDP 301 trial enrolled 9385 women. It was testing the same concentration of PRO 2000 gel, but against a placebo only, and all women in the trial were counselled to use condoms in addition to gel. Behavioural research was an integral part of this trial and may help scientists interpret the clinical outcome. For example, a microbicide can only work if women use it consistently. One MDP site was testing the gel in 840 mostly serodiscordant couples and all sites have carried out in-depth interviews with groups of male partners.

Q. Did the MDP 301 trial show a different result for PRO 2000 than the HPTN 035 trial?

No. The results of the HPTN 035 trial suggested PRO 2000 had an effect but the investigators recognised that this needed to be confirmed in a larger trial as the results could have been due to chance. MDP 301 was sufficiently large to demonstrate conclusively that PRO 2000 was not effective in preventing HIV infection.

Q. How do you know that women actually used the gel?

Gel use was determined in many different ways and all suggested a high level of use. Additionally, many women reported liking the gel and were disappointed when they had to stop using it.

Q. Why did you stop testing a 2% concentration of PRO 2000 in February 2008?

Our Independent Data Monitoring Committee reviewed the trial data at that point and saw that there was little chance for the 2% dose to show an effect.

Q. Why didn't you stop the entire trial at that point?

At the time of the review in February 2008 there was a good chance that the 0.5% concentration would show an effect. In addition, the HPTN 035 trial, exploring the same product, was still underway, and the Data Monitoring Committee was aware that there would be additional evidence from this smaller trial. Had we stopped our investigation of the 0.5% gel early, we would not have the definitive answer which excludes

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the possibility of a true protection of 30%. This would have left the field confused about whether or not PRO 2000 did add benefit, and there may have been pressure to mount a new and costly Phase 3 trial to answer the question.

Q. Is this the end of vaginal microbicide research?

This is certainly the end of research on PRO 2000, and products with a similar level of potency in the laboratory tests. However it does support further exploration of microbicides as women and their partners liked the gel and used it. Luckily there are two trials of a more biologically potent microbicide, tenofovir, already underway. One of these will report in 2010 and we eagerly await this result. With the continued high level of new HIV infections among women worldwide and the challenges treatment programmes are facing in taking on new patients, the search for an effective microbicide must continue.

Q. In light of the result, how can you justify the resources that were invested in this study?

The investment in MDP 301 and the preparatory research is fully justified by the robustness of the main result supported by the breadth of additional data that were collected in the trial. Negative results are as important as positive results. We now know there is no point in testing products which show only a moderate level of potency against HIV in early laboratory studies and that the experiments in monkeys which suggested efficacy for PRO 2000 did not correctly predict a protective effect in humans, so should not act as a gatekeeper in selection of products to take forward to clinical trials. We also know that laboratory safety assessments did predict the safety in real life as the trial showed that there were no concerns with genital adverse events, and that a molecule of this size was not absorbed even when the genital skin was disrupted. Importantly we know that women used the gel, and that they and their partners liked it, so this gives hope that future more potent microbicides will show protection.

The trial was a success in terms of retention, adherence, and the quality of the data collected, particularly through the integrated social science which was a unique feature of MDP 301. The preparatory studies were key to correctly setting the expectations for the sample size calculations and ensured that the power was as high as it could be to detect modest protection.

Discovery of new drugs typically takes many decades, with successive trials gradually solving different parts of the puzzle. Costs of MDP 301 were less than a third of what they would have been in a comparable industry-sponsored trial, and also compare favourably to other HIV prevention trials funded from the public sector.

MDP 301 has left an important legacy in the countries where it took place. It consolidated a vigorous African-European research partnership and built enduring research capacity in Africa. This included helping to create the foundation for a future pan-African laboratory network.

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Additionally, the trial and preceding MDP studies benefited women who took part:

- Over 20,000 women discovered their HIV status and received counselling and referrals. Many HIV positive women are now receiving ARV treatment.
- Sexually transmitted infections decreased during the trial. Treatable infections (including asymptomatic ones) were found and promptly treated.
- Reports from participants suggest that their use of condoms increased.
- Women informed us that they benefited from the regular health education and counselling services provided. These included information on both male and female condoms and training in negotiating safe sex with their partners.

See also:

IS05 - Quick Facts about MDP301 Trial

IS04 - Q&A - The MDP301 Trial