hiv prevention

highlights

- Aurum began preparations for preventive HIV vaccine trials in the Matlosana District in 2003, and the first HIV vaccine trial, a phase 2 trial to assess the safety and immune response to two candidates HIV vaccines (HVTN 204), is to begin in April 2006.
- The new world-class Aurum HIV Vaccine Research and Treatment Centre was established in Klerksdorp, the hub of the Matlosana District in the North West Province. These facilities include an HIV vaccine research clinic, a pharmacy for preparing trial vaccines for administration to trial participants, and a laboratory for processing specimens.
- The Community Education and Outreach Programme continued in 2005. The World HIV Vaccine Day event, organised in collaboration with the KOSH Community Advisory Group (CAG) and held on 18 May 2005, was well supported by the community and local business.
- A survey was conducted to determine the prevalence of adenovirus antibodies, and in particular high-titre adenovirus antibodies among people living in the Matlosana District. Testing for adenovirus antibodies is useful in planning for HIV vaccine trials.
- In November 2005, Aurum submitted an application for renewed funding from SAAVI for HIV vaccine research activities in the three-year period beginning April 2006. Provisional approval has been given for this proposal to be funded.

OVERVIEW

The HIV Prevention Programme, the newest of Aurum's four programmes, is actively preparing to embark upon several new research projects and is likely to expand considerably during the course of 2006. The HIV Prevention Programme has a research focus and its current major activity is preventive HIV vaccine trials in the Matlosana District, an area that includes the towns of Klerksdorp and Orkney in the North West Province.

Bringing the HIV pandemic under control requires continued use of existing methods of HIV prevention that have proven effective (such as correct and consistent condom use), as well as the introduction of additional methods of prevention. Currently the HIV Prevention Programme focusses on two possible methods of prevention that have the potential to significantly affect the HIV pandemic, namely HIV vaccines and microbicides.

REVIEW OF PROGRESS – 2005

HIV vaccine trials: Currently, there is no vaccine available to prevent HIV infection, but there are many candidate HIV vaccines in the development pipeline. A preventive HIV vaccine is considered to be the best long-term hope of controlling the HIV epidemic. Ideally a preventive vaccine should block HIV infection completely, but it is perhaps more realistic to hope for a vaccine that will boost the body's immune response and limit the progression of HIV disease following infection. As HIV infection normally progresses to AIDS over the course of five to ten years, it will take a long time to establish whether or not a candidate HIV vaccine that is partially effective, is worth licensing. The first preventive vaccine trials in South Africa started in November 2003. Early trials were all phase one trials to assess the safety and best dosage of candidate HIV vaccines. In November 2005, the first phase 2 HIV vaccine trial started in South Africa.

The preventive HIV vaccine trial planned for April 2006 will test two different candidate HIV vaccines used in combination, drawing on the "prime-boost concept" whereby two vaccines used sequentially can potentially have a complementary effect and cause a better immune response than either vaccine used alone. The final stage in testing preventive HIV vaccines is an efficacy trial, which involves evaluating whether people who have been vaccinated have a lower incidence of HIV infection than those who receive a placebo injection. The first HIV vaccine efficacy trial in South Africa (HVTN 503) is due to start towards the end of 2006. The Aurum HIV Vaccine Research Centre has been chosen as one of between three and five sites countrywide to conduct this study.

To date, HIV vaccine trials have focused on preventive HIV vaccines. In recent years, there has been increasing interest in developing therapeutic HIV vaccines, that is vaccines given to people who are already infected with HIV in order to limit the progression of the disease. Therapeutic vaccines could potentially prolong survival following HIV infection, reduce the need for ART, and limit the transmission of HIV infection to others. No therapeutic HIV vaccine trials have yet been conducted in South Africa, but there are at least two groups planning such trials. The first therapeutic HIV vaccine trial in South Africa will begin in 2006, and Aurum plans to be part of that initiative.

Community Education and Outreach Programme: The Community Education and Outreach Programme was established in 2003 to prepare the population of the Matlosana District for HIV vaccine trials. Notable accomplishments during 2005 included greater engagement with the mineworker community, increased participation in the global community advisory board established by the HIV Vaccine Trials Network (HVTN) as well as increased collaboration and engagement with local health and civic authorities.

Adenovirus sero-prevalence survey: Testing for adenovirus antibodies has no clinical value per se, but is useful in planning for HIV vaccine trials (such as HVTN 204) that use adenoviral vector vaccines, as the presence of pre-existing adenovirus antibodies may affect the immune response to the vaccine. Left-over serum specimens were obtained from 135 people in 2005 (who retained their anonymity) attending hospitals in the Matlosana District, and sent to the Vaccine Research Center at the National Institutes of Health (NIH) in Bethesda, Maryland, USA for adenovirus antibody testing. The results of specimens analysed to date indicate high titres of neutralising antibodies to adenovirus strains, findings that are similar to studies conducted in Soweto and Cape Town.

GRANT APPLICATIONS

As the HIV Prevention Programme is a programme with much potential for growth, considerable time and energy was spent in 2005 on writing grant applications, either for the renewal of support for existing projects, or for the initiation of new research. The programme applied for ongoing funding for its HIV vaccine trial site in the Matlosana district as part of the multi-site clinical trial unit application submitted by the Centre for AIDS Prevention Research in South Africa (CAPRISA). In this funding application, we applied for the scope of the work to be expanded to include HIV treatment optimisation trials (also an HIV Treatment Programme activity). The South African AIDS Vaccine Initiative (SAAVI) has continued to fund the Community Education and Outreach Programme in the Matlosana district and the salaries of HIV Prevention Programme staff. SAAVI also agreed to co-fund the HVTN 204 HIV vaccine trial at the Matlosana site. In November 2005 we submitted an application for renewed funding from SAAVI for our HIV vaccine research activities in the three-year period beginning April 2006. Provisional approval has been given for this proposal to be funded.

Applications for awards to fund new research included an application to IAVI to fund the development of a new HIV vaccine trial site in Rustenburg, and an application to the International Partnership for Microbicides (IPM) to fund the development of a microbicide trial site at a location still to be determined. Discussions with IAVI and IPM are looking very promising. An application was also submitted for the Matlosana site to be included as a Center for AIDS Vaccine Immunology (CHAVI) site. CHAVI, a major new initiative, is to undertake an in-depth study of immune responses to HIV infection with a view to informing the development of new candidate HIV vaccines. The Matlosana site is

one of three clinical trial sites in South Africa chosen for inclusion in the CHAVI consortium and funding for this initiative will begin in 2007.

As the Aurum HIV Vaccine Research and Treatment Centre District is affiliated both with the SAAVI and the HVTN, we enjoy significant collaboration with South African and foreign scientists involved in HIV vaccine research from a range of disciplines. In 2005, we strengthened our collaboration in the South African AIDS Immunology Laboratory (SAIL) at the National Institute for Communicable Diseases (NICD) and entered into an agreement to jointly manage the research laboratory at our Centre. We also committed the programme to a long-term collaboration with the Centre for AIDS Prevention Research in Southern Africa (CAPRISA), based at the University of KwaZulu-Natal, and included the Centre as part of their clinical trial unit funding application. The Centre was also included in CAPRISA's proposal to become part of the new CHAVI consortium, further strengthening our ties with CAPRISA.

FUTURE PLANS AND OPPORTUNITIES

Microbicide trials: As it will take many years before an effective preventive HIV vaccine becomes available, and success in finding an effective vaccine is by no means guaranteed, scientists are seeking alternative new strategies for preventing HIV infection. In South Africa, young women are at particular risk of acquiring HIV infection, so devising additional prevention strategies for young women is a high priority. Substances known as "microbicides" designed to prevent HIV transmission, applied either into the vagina or the rectum, are also being tested at several trial sites in South Africa, and are showing a lot of promise as a potential new "woman-controlled" method of HIV prevention. There is currently no microbicide available that has been shown to be safe and effective in the prevention of HIV infection, but there are multiple promising candidate microbicides in development. Microbicides are not proposed as an alternative to condoms as they are unlikely to be as effective at blocking HIV transmission as condoms, however, they could be a useful adjunct to condoms, in providing protection to women whose male partners refuse to use condoms. The timeline for microbicide development is shorter than the timeline for HIV vaccine development, and if all goes well, an effective microbicide could be available in as little as the next five years. Aurum plans to set up a new microbicide trial site during 2006 with a view to embarking on its first trial in 2007.

Other plans:

- In 2005 the major sources of funding for the programme were the SAAVI and the HVTN. In 2006 we hope to attract funding from additional sources, including IAVI and IPM.
- In 2006 the programme plans to expand both its scope of research and its geographic focus. We plan to embark on site development activities for a second HIV vaccine trial site. Aurum's HIV Prevention Programme hopes to host a trial site for therapeutic HIV vaccines and to commence its first therapeutic HIV vaccine trial in 2007 or 2008.
- The programme also plans to expand its HIV vaccine research to include research in support of HIV vaccine development, as well as non-trial research to support the planning of future HIV vaccine efficacy trials. Laboratory-orientated studies include a study which investigates circulating HIV strains, and a study of the immune response to acute HIV infection (acquired through natural means such as sexual transmission).
- The SAAVI Socio-behavioural Working Group, based at the University of Stellenbosch, is planning to second a social scientist to the HIV Vaccine Research and Treatment Centre to conduct social science research to assist with preparations for HIV vaccine efficacy trials. We also plan to colaborate with the HIV/AIDS Vaccine Ethics Group (HAVEG) at the University of KwaZulu-Natal on research relating to improving the informed consent process.

- A major focus in 2006 will be to conduct HIV vaccine trials at the Centre. A generic pre-screening protocol will be implemented to assist with recruitment of participants for HIV vaccine trials. This pre-screening protocol includes vaccine discussion groups to prepare potential participants for HIV vaccine trials. We plan to begin enrolling participants in the first vaccine trial, a phase 2 trial, in April 2006. We aim to recruit approximately 70 participants over a six-month period and to conduct follow up visits on each participant over a one-year period.
- We hope to begin enrollment for a phase 2b HIV vaccine trial (HVTN 503) towards the end of 2006. This will be the first HIV vaccine efficacy trial conducted in South Africa. For the HVTN 503 trial, we will aim to recruit approximately 1 000 participants over 18-months and to conduct follow up visits over a three year period. This is both an opportunity and a challenge. We are honoured at having been chosen as a site for the first HIV vaccine efficacy trial in South Africa, but are cognisant of the challenges of enrolling such a large number of participants and retaining their participation over the long period that it will take to complete the trial.
- We intend to expand the scope of the Community Education and Outreach Programme in the Matlosana district to include an Adolescent Programme which will engage adolescents and people who work with adolescents (including parents and teachers) in preparation for future HIV vaccine trials among adolescents from the age of 15 years.
- We hope to work closely with Masikhulisane, SAAVI's Community Involvement Programme, in engaging communities in HIV vaccine trials. As we move into the area of microbicide trials, we will establish collaborative relationships with researchers already active in this field and learn from their experience. This will also entail finding opportunities to conduct research on barriers to HIV testing, in order to facilitate recruitment for future HIV vaccine and microbicide trials.

PROGRAMME CHALLENGES

- The programme is in a growth phase, so currently needs additional staff and funding to develop the programme to its full potential. In particular we require a data manager to develop data management infrastructure for the expansion of the programme activities, and a social scientist to oversee social and behavioural research in support of HIV vaccine trials and microbicide trials, particularly efficacy trials.
- A major challenge to recruitment into efficacy trials is addressing the common phenomenon of widespread reluctance to undergo HIV testing. As all participants in HIV prevention efficacy trials (including HIV vaccine trials and microbicide trials) are required to be HIV-negative and willing to undergo repeated HIV testing while participating in the trial, we will need to address this reluctance to be tested in order to achieve our recruitment targets.
- Development of new trial sites is a time-consuming and expensive endeavour. Sponsors of HIV prevention trials are usually able to provide only limited support for the development of new research facilities and infrastructure, so we will need to find additional sources of funding for site development.