Microbicides: A promising strategy to reduce HIV infection

There are now more than 33 million people infected with HIV/AIDS worldwide and in 2008 there were 2.7 million new infections.

These daunting numbers have pushed researchers to focus more on finding prevention methods. Since the HIV/AIDS pandemic affects every region around the world, it has united researchers and institutions in the fight to prevent HIV.

Microbicides, products that can be applied topically to reduce the risk of HIV transmission during sexual intercourse, are the focus of intensive study. Research in this field has just received a considerable boost from the success of a clinical trial of one of the new generation microbicides announced at the 17th International AIDS Conference held in Vienna.

The CHAARM (which stands for Combined Highly Active Anti-retroviral Microbicides) project is showing much promise to further develop microbicides. CHAARM aims to develop combination drugs for prevention that can be used in addition to other tools and, most importantly, aiming to be accepted and widely used where condoms are not.

This large-scale collaborative project is dynamic in the sense that it involves over 30 partners from around the world- all over Europe, from South Africa to the United States, and Ukraine.

“Research on HIV/AIDS has always been a priority for the European Commission, which is mainly funded through the framework programs,” says.

Ms Alessandra Martini, Health Directorate, DG Research, at the European Commission. “A multifaceted approach has been used aiming at improving research concerning the treatment of HIV-infected people and the prevention of future infections.”

The European Commission has invested approximately 70 million euros under the framework program towards projects targeting novel therapeutic approaches and effective preventive strategies against HIV/AIDS.

“Specifically, research on microbicides has been considered a priority for the Commission research agenda, as an alternative strategy to vaccine and other preventive methodologies for HIV prevention, which would give women the possibility to protect themselves against the infection,” adds Martini. “In this context CHAARM plays a pivotal role being the main project supported in FP7 on microbicides research. “

Past Setbacks in Microbicide Research… and a new horizon

The CHAARM project builds on an earlier large-scale microbicides research project, the European Microbicides Project (EMPRO) as well as findings from other researchers in the field. “The first generation concepts were successfully tested, and I think we should not underestimate what a significant advance that was, but they appear to either lack sufficient potency or not be used appropriately enough to show statistical endpoint,” says Professor Robin Shattock, a Professor of Cellular and Molecular Infection in the Department of Cellular and Molecular Medicine at St George's University of London, UK.

These problems included ensuring adherence and making sure the drug was in an effective state and the right concentration. Another problem was with reapplication; it was impossible to use it more than once a night. These problems have led the field to move, says Shattock.

“It has also led to the field having to prioritize new formulations that maximize adherence to give the best possible chance of showing efficacy in a clinical trial,” said Professor Shattock, while giving a speech at the International Microbicide Conference 2010 in Pittsburgh, Pennsylvania, USA. “Then it has led to increasing emphasis on combination products.”

“Not only to ensure that any microbicide will hit the widest possible diversity of virus, but also potentially to reduce the risk of resistance,” he added.

The use of combination products in the project is a key aspect primarily because they will boost the barrier to resistance by increasing the required mutations to overcome all components and may also improve efficacy.

The researchers regrouped after EMPRO ended and enlisted the support of several other institutions and formed a new consortium, which is now the CHAARM project.

But concerning the future of the microbicides research, a new path has been opened in the last months. CAPRISA 004 project yielded the first clearly positive results in a microbicide efficacy trial, “providing significant momentum to the field”, said Dr Oliver Hartley, biochemist and professor in the University of Geneva’s faculty of medicine, who adds that “the CHAARM project now has the opportunity to build on this success, hopefully contributing to the development of a new microbicide product capable of making an impact on the HIV epidemic.”

Unstable Funding Sources

However, the problems are still not over for microbicide research. Funding concerns cast a dark shadow over the field as they struggle to maintain a secure funding source.

Since microbicides are considered a “public health good”, there is little economic self-interest for organizations to invest in funding for microbicide research, placing the field in a vulnerable position.

“Microbicides, like most public sector funded projects are always at a critical time point,” says Mark Mitchnick, CEO Particle Sciences, Inc., a USA based pharmaceutical company.

“Developing drugs is a hard business,” adds Mitchnick, who served on the advisory board for EMPRO.

Particle Sciences is one of four private companies involved in CHAARM. With the general lack of investment from private companies and pharmaceutical companies in microbicide research, the responsibility for funding has fallen largely on public institutions, government organizations and non-profit organisations. The CHAARM project received about 70% of their funding from the European Commission.

“Maintaining focus and the attention of funders is a real challenge since progress can, from the outside, seem slow – even when things are moving well in terms of drug development,” says Mitchnick.

With the global recession and hesitations due to the perceived setbacks from the clinical testing of first generation microbicides, despite the significant developments in the research, funding is struggling. For HIV prevention research in general, there is much reliance on public funding, which is not sufficient.

“There is no doubt that HIV prevention research could go forward more rapidly if more were made available,” says Dr Oliver Hartley.

“These funding bodies do not have infinite resources,” adds Dr Hartley. “A potential concern is that attractive new microbicide products validated through the CHAARM program might experience significant delays in clinical development because the necessary funds to move further are not available.”

Dr Hartley is also cofounder and Chief Scientific Officer of Mintaka Foundation for Medical Research based in Geneva, Switzerland, which does a lot of independent fundraising to cover the costs of its biomedical research. He suggests that the European Commission makes competitive funding available for clinical development programs that would complement the investment made in discovery and validation programs such as CHAARM.

Even though drug development is complex and expensive, the potential profit for microbicides is promising once next generation products are successfully developed.

Potential use of Microbicides

An objective of microbicide research is to fill in the gaps of prevention options in high-risk areas such as sub-Saharan Africa caused by varying cultural and social differences. One of the reasons why HIV transmission rates are high in places such as sub-Saharan Africa is that male partners refuse to wear a condom, placing women in a vulnerable position for infection.

Researchers feel microbicides are a critical prevention tool because a microbicide can be used discreetly. They could potentially give women control over contraception as well as protection against HIV, unlike most widely available options. However, non-contraceptive microbicides are currently the main focus as they are more likely to be accepted in targeted regions.

Previous studies have shown promising acceptability among target communities, and the CHAARM project will conduct acceptability studies in the clinical trials.

However, microbicides will be distributed as prescription only products initially because users will have to be tested for HIV to make sure they are not already infected with the virus since the product will not benefit infected individuals. Nonetheless, researchers are making sure that any product will be inexpensive to make sure it can be distributed widely.

"The CHAARM consortium members are fully aware that it would not make sense to develop a product, which, even if it had highly promising activity, could not be made available at a cost and scale appropriate for use worldwide," says Dr Hartley.

Project website:
www.chaarm.eu

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