UGANDA GAVE THE WORLD NEVIRAPINE

UGANDA@60 INNOVATIONS

As Uganda celebrates 60 years of independence this year, the *New Vision* is highlighting the country's contribution to the world. There are many innovations and inventions from Uganda, which have had an impact on the world. Today, **Hilary Bainemigisha** brings you Uganda's research which saved the world from HIV infection among babies.

Nevirapine played a huge role in reducing mother-to-child transmission of the HIV virus

NEVIRAPINE ROLL OUT

In September 2001, Uganda agreed to make it mandatory for all pregnant women living with HIV to receive Nevirapine. Government was ready to provide the drug for free.

In March 2002, the study was declared by Hopkins University scientists and their colleagues at both University of Washington and Makerere University as a major public health advance in resource-poor settings.

The drug's manufacturer, Boehringer Ingelheim, Inc. announced that it will continue to offer the drug to developing countries as part of its donation programme.

On December 14, 2004, Hopkins University revealed that no deaths, serious reactions or serious adverse effects reported.

All centres for disease control concluded that nevirapine was safe, appropriate and effective.

Nevirapine is a medication that was used to prevent mothers from transmitting HIV to their babies during birth. It was approved for medical use in the US and got listed on the World Health Organisation's (WHO) List of Essential Medicines.

Although it was not invented by Ugandan scientists, the first clinical studies of the drug were done in Uganda.

After a follow up study in Thailand, WHO endorsed the use of single-dose nevirapine in many developing world settings as a cost-effective way of reducing mother-to-child transmission.

Nevirapine was discovered by Karl D. Hargrave and colleagues at Boehringer Ingelheim Pharmaceuticals, Inc.

After the proof of concept, it needed to be tried among humans. Uganda offered to try the drug at the Joint Clinical Research Centre (JCRC), by its director and co-founder, Dr Peter Ndimbirwe Mugyenyi.

Mugyenyi was then quoted as saying the implications of the treatment could change everything for children born with HIV.

JCRC was established in 1991 as a joint-venture between the ministries of health, defence and Makerere College of Health Sciences.

The centre collaborated with various institutions and organisations, such as USAID, the World Health Organisation, Case Western Reserve University (CWRU), FHI, NIH, European and Developing Countries Clinical Trials Partnership (EDCTP), Medical Research Council (MRC), to study HIV, tuberculosis (TB), malaria and other tropical diseases.

It was the first recipient of

Mugyenyi

PEPFAR funding in December 2013 for ARVs.

Between December 2003 and June 2010, JCRC established 52 ART sites and 25 outreaches across the country and became the largest provider of ART in Africa, before transitioning these sites to Ministry of Health for mainstreaming into the national HIV care network.

Currently, JCRC headquarters are located at Lubowa Complex, off Entebbe Road, Wakiso district, with a regional network of six regional centres of excellence strategically located at Kakira, Mbale, Gulu, Fort Portal, Mbarara, and Kabale.

After the successful study in Uganda, Nevirapine became the first non-nucleoside reverse transcriptase inhibitors (NNRTI) to be approved by the US Food and Drug Administration (FDA), under US Patent 5,366,972.

WHERE IS NEVIRAPINE NOW?

Nevirapine is no longer recommended as a preferred option for first-line antiretroviral treatment because new, better and more effective ARVs came on the market.

The World Health Organisation recommended its phasing out after it was discovered that 17.5% who used it developed resistance to the drug and 16.3% reduced tolerability.

It was approved on June 21, 1996 for adults and September 11, 1998, for children. It was also approved in Europe in 1997.

HISTORY

By the 1990s, HIV was ravaging the world and mother-to-child transmission (MTCT) was the largest source of HIV infection in children under the age of 15.

When countries started to screen blood products regularly, mothers infecting their children became the only source of HIV in young children.

In 1997, an estimated 600,000 infants worldwide were infected with the virus from their mothers, bringing the total number of young children living with HIV to over 1 million at the end of the year.

Of the three million infants infected with HIV since the beginning of the pandemic, about 90% were born in Africa.

The virus was transmitted during pregnancy, labour, delivery, or after the child's birth, especially during breastfeeding.

In sub-Saharan Africa, MTCT was contributing substantially to rising child deaths and there were no means of preventing MTCT. Yet the probability that an HIV positive woman's baby will become infected ranged from 15% to 25% in developed countries and 25% to 35% in developing countries.

In 1994, a regimen using the antiretroviral drug zidovudine (AZT) was shown to reduce MTCT by about two-thirds in the absence of breastfeeding. However, it was expensive and had serious side effects.

And when Nevirapine treatment came up, it was costing just $4 per patient, 70 times cheaper than the AZT! The world lauded Uganda!

THE STUDY

The joint project between the Ugandan Government and the US National Institute of Allergy and Infectious Diseases followed an 18-month study on pregnant women at Mulago Hospital.

The study, known as HIVNET 012, began in 1997 and the results were published two years later.

All subjects continued in long-term follow-up to collect information on the state of their health.

The results, published in the British medical journal, *The Lancet*, in 1999, showed that the drug could reduce HIV transmission from a mother by up to 50%.

Giving one dose of Nevirapine to the mother at the time of delivery and one dose to the infant after birth, potentially could save many of the approximately 600,000 infants worldwide who are infected by HIV every year.

The new antiretroviral nevirapine was cheap, innocuous, easy to prescribe, and remarkably effective, reducing by half the rate of infection of babies. It was called a "magic bullet," which seemed particularly adapted to the African AIDS epidemic.

Suddenly, Uganda stormed into the news and the exposure earned the country many offers of collaborative research.

However, being new to clinical trials, many countries and bodies doubted Uganda's study and opted to conduct their own investigations into HIVNET 012 clinical trials of nevirapine.

But the Uganda trial was the first to demonstrate the safety and efficacy of nevirapine in preventing MTCT of HIV.

Eventually, one by one, the sceptical entities accepted Uganda's study findings and Nevirapine.