Horizon Scanning

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DAPIVIRINE VAGINAL RING

Keywords: Dapivirine, vaginal ring, NNRTI, HIV, AIDS

SUMMARY

The first case of AIDS in Malaysia was reported from Hospital Kuala Lumpur in 1986. Initially, people living with HIV (PLHIV) in this country were predominated by males (89%). This pattern progressively shifted towards increasing infection rates in female with male to female ratio declining from 9.6 (2000) to 5.5 (2015). The epidemic in Malaysia was largely driven by people who inject drugs (PWID) at the early phase, but this pattern has shifted towards increasingly more sexual transmission with PWID/sexual transmission ratio declining from 4 (2000) to 0.2 (2015). According to data reported in 2014, amongst men, 23.7% acquired infection via injecting drug and 74.6% through sexual mode while amongst women, majority acquired through heterosexual transmission (92.4%).[1-3]

Dapivirine is a new topical microbicide which belongs to antiretroviral NNRTI group (non-nucleoside reverse transcriptase inhibitors) indicated for high risk women as a prevention to prevent sexually transmitted HIV viruses. By attaching to- and blocking the HIV enzyme (reverse transcriptase), dapivirine prevents the HIV viruses from converting its RNA into DNA; and then, prevents the viruses from replicating and spreading to other cells.[4-6]

Figure 1: Dapivirine Vaginal Ring

The novel monthly-used Dapivirine Vaginal Ring (Figure 1) was developed by International Partnership for Microbicides (IPM), a nonprofit organization in 2004 after receiving a royalty-free license from Janssen Sciences Ireland UC which was then expanded to an exclusive worldwide rights agreement in 2014. The vaginal ring is made of a flexible silicone material with dapivirine as an active ingredient dispersed throughout the matrix where it is designed to deliver the active ingredient directly to the site of potential infection with lower absorption rate at other than the targeted part in the body. With the ring type of dapivirine, it is easier for women to insert and remove the rings themselves.[4-6]

Besides, dapivirine has been studied in other dosage forms (eg: vaginal gel and film) and in combination (eg: vaginal contraceptive) but only Dapivirine Vaginal Ring has undergone clinical trials and completed two phase III clinical trials (NCT01539226 & NCT01617096) (Figure 2).[4-6]

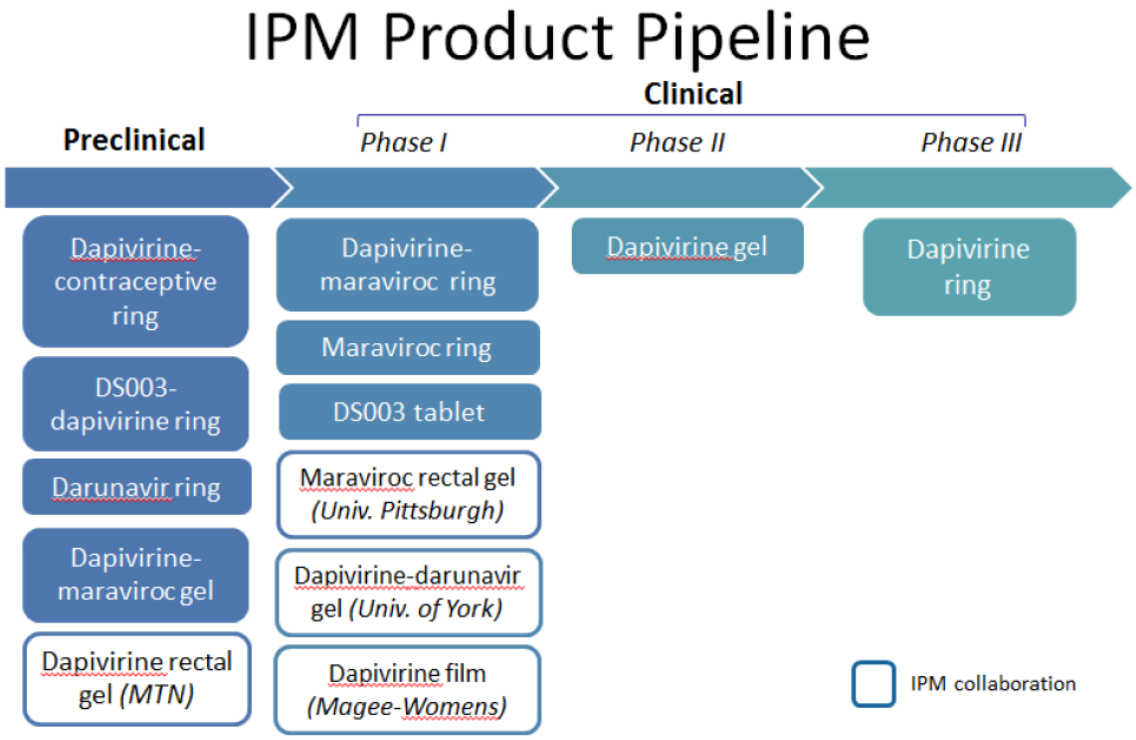

Figure 2: Stage of development for Dapivirine Vaginal Ring

POTENTIAL FOR IMPACT

Currently, using condom and practising health life style without having multiple partners may prevent HIV infection. In Malaysia, statistic showed that HIV transmission mode was higher by sexual transmission compared to other mode (Figure 3). In line with the National strategic plan for ending AIDS 2016-2030, and MOH objective to achieve zero AIDS epidemic in Malaysia by 2030, Dapivirine Vaginal Ring which can be used as preventive measures seems to have potential in reducing risk of HIV infection through sexual transmission

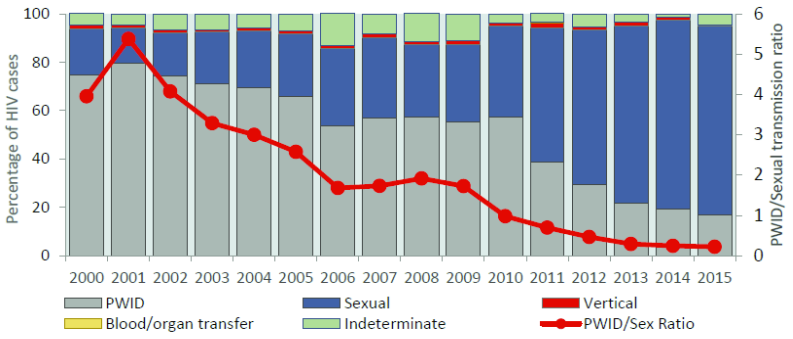

Figure 3: Trend of HIV transmission mode in Malaysia 2000-2015

among high risk women who are married to or having former drug addicts as partners. This new approach also have potential to early elimination of vertical transmission from mother to child if pregnancy occurred.[7-8]

Estimated cost of Dapivirine Vaginal Ring is around USD 107 to 115 per person per year (RM476 to 512) depending on the population sub-group. Based on the modeling analysis, cost-effectiveness estimates were below 50% of South African GDP per capita for efficacy of 25%, 50% and 75% where about 175 thousand, 364 thousand and 588 thousand HIV infections can be prevented at efficacy of 25%, 50% and at 75% respectively. This indicates that the dapivirine ring could substantially and cost-effectively prevent HIV infection among women in South Africa even under the lowest efficacy estimates. However, the cost-effectiveness of the ring may differ in other setting and factors such as user demand and adherence should be taken into account in determining the success of Dapivirine Vaginal Ring. [9]

EVIDENCE

Two Phase III clinical trials to assess the efficacy and safety of Dapivirine Vaginal Ring have been conducted and the results were described below.

Based on the results of ASPIRE and The Ring studies, two open-label trials of dapivirine ring which are called as HOPE and DREAM studies have been launched in 2016 to determine when, why, and how women use the ring, to develop effective ways to support its consistent use or adherence, and to collect additional safety and efficacy data. These continuous studies will provide a real assessment of the ring as the active dapivirine ring will be prescribed to HIV-negative women who participated in the previous studies (ASPIRE & The Ring). Moreover, IPM has plan to submit dossier for product registration in Q2 2017 based on the results of ASPIRE and The Ring studies; and if approval granted, the ring will be launched in 2018.[10]

ASPIRE (NCT01617096):[11]

This randomised, double-blind and placebo-controlled trial has been conducted from August 2012 to June 2015 at 15 research sites in Malawi, South Africa, Uganda & Zimbabwe with 2,629 healthy, sexually active, non-pregnant, HIV-1-seronegative women aged 18-45 years old were involved as participants. The results showed that the incidence of HIV-1 infection was lowered by 27% (95% CI, 1,46; P=0.046) in dapivirine group compared to placebo group. After exclusion data from two sites due to low adherence; the incidence was lowered by 37% (95% CI, 12,56; P=0.007).

Lack of HIV-1 protection along with lower adherence was seen in participants aged < 21 years old with efficacy of HIV-1 protection of -27% (95% CI, -133,31; P=0.45) but in participants aged > 21 years old the efficacy was 56% (95% CI, 31,71; P<0.001) with

rate of adherence was >70% overall. In this study, the results reported that there were no significant differences in adverse events/resistance for both groups.

The Ring Study (NCT01539226):[12-13]

This multicenter, randomised, double-blind and placebo-controlled trial has been conducted at seven research sites in South Africa and Uganda with 1,959 women underwent randomisation where 1307 were assigned to the dapivirine group and 652 were assigned to placebo group.

The results showed lower seroconversions in dapivirine group (4.1 seroconversions per 100 person-years) compared with placebo group (6.1 seroconversions per 100 person-years). The incidence of HIV-1 infection was lower by 31% in the dapivirine group compared to placebo group (Hazard ratio (HR): 0.69; 95%CI: 0.49,0.99; P=0.04). The efficacy of the dapivirine ring among women > 21 years old was reported as HR for infection of 0.63 (95% CI: 0.41,0.97) and for women < 21 years old with HR: 0.85 (95% CI: 0.45,1.60; P=0.43).

In this study NNRTI resistance mutations were detected in 14 of 77 participants in the dapivirine group (18.2%) and in nine of 56 (16.1%) in the placebo group, and serious adverse events seemed to occur more often in the dapivirine group (38 participants, 2.9%) than in the placebo group (6, 0.9%). However, none of these adverse events were identified as being product-related.

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Disclaimer: TechScan report is prepared based on information available at the time of research and a limited literature. It is not a definitive statement on the safety, effectiveness or cost effectiveness of the health technology covered. Additionally, other relevant scientific findings may have been reported since completion of this report.

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