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Product Development Workshop 2013: HIV and Multipurpose Prevention Technologies

A workshop entitled "Product Development 2013: HIV and Multipurpose Prevention Technologies," was organized by CONRAD, a division of the Obstetrics and Gynecology Department of Eastern Virginia Medical School, on 20–21 February, 2013 in Arlington, Virginia. This workshop was a follow-on to one entitled "Trends in Microbicide Formulations" held in Arlington in January, 2010 (Friend, 2010). The recent workshop was attended by a wide range of scientists from academia, industry and government staff. The workshop covered a range of topics, addressing both microbicide (topical pre-exposure prophylaxis, PrEP) development and the latest developments in Multipurpose Prevention Technologies (MPTs). MPTs are products that, if successfully developed, will address two or more reproductive health needs of women from a single product. The first day of the workshop focused primarily on microbicides while day two focused exclusively on MPTs.

Following the 2010 Workshop, the results of CAPRISA-004 were announced that tenofovir (TFV) 1% gel was effective at reducing sexual transmission of HIV-1 to women, although the effects were modest (39% reduction compared with placebo) (Abdool Karim et al., 2010). This was the first study to report effectiveness of a microbicide and provided support to a field that until then had experienced several clinical trial failures. The TFV 1% gel was tested in a once-daily dosing regimen in the VOICE study (CAPRISA-004 used an on-demand dosing regimen wherein gel was dosed within 12 h prior to and within 12 h after coitus). While the gel showed a beneficial effect in the VOICE study, it was not statistically significant (Marrazzo et al., 2013). The most important finding of this study was the remarkably low adherence (between 20% and 30%). The conclusion was that women enrolled in this (and probably other microbcide trials) are not using the product consistently enough to demonstrate effectiveness.

These critical findings are causing a shift better monitoring to increase adherence and to design products that women are willing to use, particularly in efficacy trials. All these points were addressed in the workshop, including development of more potent compounds, more convenient on-demand dosage forms such as fast-dissolve vaginal films and tablets, long-acting dosage forms, and MPTs that can provide protection against unintended pregnancy as well as prevention of HIV-1 transmission. These MPT products are being evaluated as both on-demand and long-acting dosage forms. It is a commonly held belief that products with two indications, particularly if one is to prevent unintended pregnancy, will be better accepted than a microbicide-only product. Another is that long-acting dosage forms such as intravaginal rings (IVRs) will be better accepted than on-demand or once-daily products.

This supplemental issue of *Antiviral Research* is a collection of review articles based on several presentations from the 2013 workshop. A range of experts were asked to present recent findings in development of innovative microbicide and MPT products. Topics presented included a critical view of the field of prevention products (P. Kiser, University of Utah), new understanding about HIV transmission (T. Hope, Northwestern University), and novel endpoints in nonclinical and early clinical evaluation of prevention products (G. Doncel, CONRAD). Several papers were presented on microbicides in clinical development or nearing clinical development. Novel dosage forms, including IVRs and rapidly-disintegrating tablets of tenofovir (M. Clark, CONRAD) and development of the dapivirine IVR (B. Devlin, International Partnership for Microbicides) (Devlin et al., 2013) were summarized. Recent advances in dosage forms (gels and IVRs) containing MIV-150 and other biologically active compounds such as zinc acetate were presented (T. Zydowsky, Population Council) along with data using a newer non-nucleoside reverse transcriptase inhibitor IQP-0528 (A. Ham, Imquest). Electrospun fibers offer the potential to create a range of vaginal products capable of distinct drug release rates and duration of release. Woodrow and coworkers (University of Washington) present their findings and address some of the challenges facing the use of this technology for HIV prevention (Blakney et al., 2013). Rectal microbcides have been an area of considerable interest. Recent developments and issues associated with rectal PrEP products are reviewed by Rohan and coworkers (Magee-Womens Research Institute) (Rohan et al., 2013). Long-acting pre-exposure prophylaxis (PrEP) using a new integrase inhibitor GSK744 was presented (W. Spreen, GlaxoSmithKline/ViiV Healthcare). Two other presentations covered novel dosage forms [vaginal tablets based on osmotic pump technology (R. Rastogi, University of Utah) (Rastogi et al., 2013b) and mucoadhesive/pH sensitive microspheres (B.-B.C. Youan, University of Missouri-Kansas City)].

The second half of the workshop focused on various aspects of MPTs. Several talks were presented on lessons learned from family planning and other reproductive health fields (J. Manning, United States Agency for International Development [USAID]; J. Halliday, Ferring), including regulatory strategies (M. Brady, Population Council) (Brady and Manning, 2013). A framework for MPT developmental priorities has been the on-going work of the Scientific Agenda Working Group of the Initiative for Multipurpose Prevention Technologies. Romano and colleagues have identified MPT products with the highest public health impact potential

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necessary to serve as the basis of coordinated investment of supporting agencies in the development of such products (Romano et al., 2013). A review of recent activities in the area of MPT product development was presented (D. Friend, CONRAD) (Friend et al., 2013). The development of antibody-based products targeting HIV, HSV, and sperm was also reviewed (K. Whaley, Mapp-Biopharmaceuticals) (Whaley and Zeitlin, 2013). The cost-effectiveness of microbicides was presented by S. Blower (UCLA). Finally, a review of the important issues of acceptability and adherence of MPTs during clinical trials was presented (B. Tolley, FHI 360) (Tolley et al., 2013). Improving adherence in on-going and future clinical trials involving microbicides and MPTs may well be the single most important breakthrough in the field.

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