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Abstract title: Clinical Safety and Tolerability Assessment of an Anti-HIV Dapivirine Vaginal Microbicide Gel (Gel-002)

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Background: A number of antiretroviral-based microbicides are currently in development for prevention of HIV transmission. Dapivirine (TMC120) is a non-nucleoside reverse transcriptase inhibitor that is formulated as a gel for daily vaginal dosing. Gel formulations are an acceptable microbicide dosage form and offer promise as a means of preventing HIV transmission.

Methods: Dapivirine was formulated into a predominately Carbopol®-based gel and packaged in pre-filled applicators delivering 2.5 mL of gel. Three concentrations were tested, 0.001% (10 µg/mL), 0.002% (20 µg/mL) and 0.005% (50 µg/mL). The safety and tolerability of Dapivirine Gel-002 was evaluated in a multi-center, randomized, double-blind placebo-controlled 42 day Phase I/II study comparing twice daily dosing of dapivirine gel and a "universal" placebo. A total of 111 healthy HIV-negative women in Rwanda, South Africa and Tanzania completed the study with 32 each in the 0.001% and 0.002% groups, 31 in the 0.005% group, and 16 in the placebo group. Safety was evaluated by adverse events (AEs), clinical laboratory tests, colposcopy, vital signs and physical examinations. A follow-up visit occurred at Day 56.

Results: No drug-related serious AEs were reported. AEs reported in four women indicated macroscopic damage to the vulval or vaginal epithelium or cervical mucosa (2 from the 0.001% group and 1 each from the placebo and 0.002% groups). Two women each in the 0.001% and 0.002% treatment groups, and one woman each in the 0.005% and placebo groups reported laboratory values graded as Grade 3 or Grade 4 according to the Division of Acquired Immunodeficiency Syndrome (DAIDS) grading scale. There were no significant differences between groups with regard to colposcopic examination or urogenital infection findings.

Conclusions: Dapivirine (TMC120) Gel-002 administered twice daily for 42 consecutive days in healthy HIV-negative women was safe and well tolerated, suggesting that continued development of Dapivirine is warranted.