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

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Background: Currently, there are a number of anti-retroviral based microbicides 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 0.02% gel (500 µg drug/dose,). Clinical evaluation of safety and tolerability was achieved in a single center, randomized, double-blinded placebo controlled 42 day phase I/II study comparing twice daily dosing of dapivirine gel and the "universal" placebo. Twenty four women received the active gel and twelve received placebo. Safety was evaluated by adverse events (AEs), clinical laboratory tests, colposcopy, vital signs and physical examinations and dapivirine levels in plasma assessed at Days 7, 28 and 42. A follow-up visit occurred at Day 56.

Results: There were no clinically significant laboratory findings, drug related SAEs or any subjects who had AEs indicating macroscopic damage to the vulval or vaginal epithelium or cervical mucosa. There were no significant differences between groups with regard to colposcopic examination or genital infection results. Mean plasma dapivirine concentrations were 0.45, 0.47 and 0.43 ng/mL on Days 7, 28, and 42 respectively, suggesting that steady-state concentrations had been reached by at least Day 7.

Conclusions: The study demonstrated that dapivirine gel administered twice daily for 42 consecutive days in healthy HIV negative women was safe and well tolerated, suggesting that continued development is warranted.