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Abstract title: Pharmacokinetic Assessment of an Anti-HIV Dapivirine Vaginal Microbicide Gel (Gel-002)

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Background: Dapivirine (TMC 120) is a non-nucleoside reverse transcriptase inhibitor that is currently in development for prevention of HIV transmission. Dapivirine has been formulated as a gel for daily vaginal dosing. Formulations that allow non-coital use of microbicides can increase the choices of products available to women.

Methodology: Dapivirine was formulated into a predominately Carbopol®-based gel and packaged in pre-filled applicators delivering 2.5 mL of gel. Three gel concentrations were tested: [0.001% (10 µg/mL), 0.002% (20 µg/mL) and 0.005% (50 µg/mL)]. Plasma levels and other pharmacokinetics of Dapivirine Gel-002 were evaluated in a single centre, double-blind, randomized 18 participant phase I study. Healthy female participants applied the gels intravaginally once daily on Day 1 and Day 10, and twice daily on Days 2-9. Eighteen women completed the study with 6 each in the three gel concentration groups. Plasma, vaginal biopsies and vaginal fluid samples were collected at sequential time points over a 24-hour period on Day 1 and Day 10 and evaluated for Dapivirine levels. Safety was evaluated by adverse events (AEs), clinical laboratory tests, colposcopy, vital signs and physical examinations at Days 1 and 10.

Results:
Dapivirine Gel-002 Cmax and AUC values increased with increasing dose with a tendency to dose linearity. The mean t½ for day 10 was approximately 87 hours and was similar for all 3 doses. No serious or drug-related treatment-emergent AEs (TEAEs) were reported. TEAEs reported were all graded as minor with no clinical significant laboratory findings. There were no significant differences between groups with regard to colposcopic examination or genital infection findings.

Conclusions: Dapivirine appeared safe and well tolerated in healthy HIV-negative women. Pharmacokinetic data supports future testing of Dapivirine gel as a once-daily microbicide.