

Effects of Bacterial Vaginosis Associated Bacteria, Endogenous *Lactobacillus* and Sociodemographic Factors on Vaginal Colonization with the Probiotic *Lactobacillus crispatus* CTV-05: A Study of the Intervention Cohort in a Phase IIA Clinical Trial of LACTIN-V[®] in San Francisco, USA

Benjamin Mbiyu Ngugi

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ABSTRACT

Several fastidious bacteria have been associated with bacterial vaginosis (BV), but their role in lactobacilli recolonization failure is unknown. This study examined the effect of seven BV-associated bacterial species and two *Lactobacillus* species on vaginal colonization with *L. crispatus* CTV-05 (LACTIN-V). Twenty four women with BV were treated with metronidazole vaginal gel and then randomized 3:1 to receive either LACTIN-V or placebo. Vaginal swabs for *L. crispatus* CTV-05 culture and 9-bacterium specific 16S rRNA gene quantitative PCR assays were analyzed on several study visits for the 18 women receiving LACTIN-V. Vaginal colonization with CTV-05 was achieved in 61% of the participants receiving LACTIN-V at either the day 10 or the 28 visit and 44% at day 28. Participants not colonized with CTV-05 had generally higher median concentrations of BV-associated bacteria compared to those who colonized. Between enrollment and day 28, the median concentration of *Gardnerella vaginalis* minimally reduced from $10^{4.5}$ to $10^{4.3}$ 16S rRNA gene copies per swab in women who colonized with CTV-05 but increased from $10^{5.7}$ to $10^{7.3}$ in those who failed to colonize ($p=0.19$). Similarly, the median concentration of *Atopobium* spp. reduced from $10^{2.7}$ 16S rRNA gene copies per swab to below limit of detection (375 rRNA gene copies per swab) in women who colonized with CTV-05 but increased from $10^{2.7}$ to $10^{6.6}$ in those who failed to colonize ($p=0.04$). The presence of endogenous *L. crispatus* at enrollment was found to be significantly associated with a reduced odds of colonization with CTV-05 on day 28 ($p=0.003$) and vaginal intercourse during the study significantly impaired successful CTV-05 colonization ($p=0.018$). These results suggest that vaginal concentration of certain BV-associated bacteria, vaginal intercourse during

treatment and presence of endogenous *L. crispatus* at enrollment predict failure of colonization with probiotic lactobacilli.