Background: Antiretroviral therapy (ART) suppresses HIV RNA and prevents viral transmission. Genital HIV RNA shedding occurs in 2-20% of individuals on standard 3-drug ART. The incidence of genital HIV RNA shedding with the novel two-drug regimen of DTG+3TC is unknown.

Methods: Virologically suppressed participants randomized to either arm of the ASPIRE study (switch to DTG+3TC versus continue standard 3-drug ART) and ART-naïve participants who initiated DTG+3TC in the single-arm ACTG A5353 study were eligible for this genital substudy. Participants provided genital samples (semen or vaginal swabs) at week 24 and/or later timepoints through 48 weeks after study initiation to quantify genital HIV RNA, herpes simplex virus (HSV) and cytomegalovirus (CMV) DNA by real-time PCR. HIV genotyping and urine analysis for Gonorrhea and Chlamydia were performed in genital HIV shedders. Plasma HIV RNA results were obtained from parent studies.

Results: Fifty-one participants (ASPIRE DTG+3TC arm (N=16); ASPIRE 3-drug ART arm (N=22); and A5353 (N=13)) contributed 90 samples (77 semen, 13 vaginal swabs) at weeks 24-36 (N=41) and 48 (N=49). Median (range) time on ART before ASPIRE entry was 5.8 (1.3-17.6) years, and the pre-randomization regimens included a protease inhibitor (32%), non-nucleoside reverse transcriptase (RT) inhibitor (26%) or integrase inhibitor (42%). HIV RNA was not detected in any of the vaginal swabs. During the 48 weeks of follow-up, three participants had seminal HIV shedding: 1/22 (4.5% [95%CI:0.1%,22.8%]) in the ASPIRE 3-drug ART arm, 1/16 (6.3% [0.2,30.2]) in the ASPIRE DTG+3TC arm and 1/13 (7.7% [0.2,36.3]) in the A5353 study (table 1). For participant #2, no integrase drug-resistance mutation was detected in seminal HIV RNA (RT sequencing unsuccessful). Genital HSV and bacterial infection were not detected in the three participants with seminal HIV RNA shedding, while high CMV levels were detected in participant #2 at both assayed time-points. Overall, genital CMV was detected in 17/51 (33%) and HSV was detected in 5/51 (9.8%) participants.

Conclusions: In this study, we detected genital HIV RNA shedding in virologically suppressed individuals who switched to DTG+3TC and ART-naïve participants treated with DTG+3TC at similar rates as 3-drug ART. Dual-drug regimen appears to be safe to use but more testing is needed.