01059

A COMBINED ESTROGEN/PROGESTIN VAGINAL RING IMPROVES MICROBIAL COMMUNITIES

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BACKGROUND

During use of an ethinyl estradiol (EE)/ etonogestrel (ENG) intravaginal ring (IVR) over 3 weeks

- Efavirenz-based ART (EFV) significantly decreased EE levels by 53% and ENG levels by 76%
- Atazanavir/ritonavir-based ART (ATV/r) decreased EE levels by 29% , but increased ENG levels by 71%[1]

We explored the role of the IVR on

- vaginal microbial communities and
- vaginal short chain fatty acids (SCFA)

We explored the role of vaginal microbes/SCFA

- on EE/ENG concentrations

METHODS

Of the 74 PK-evaluable participants

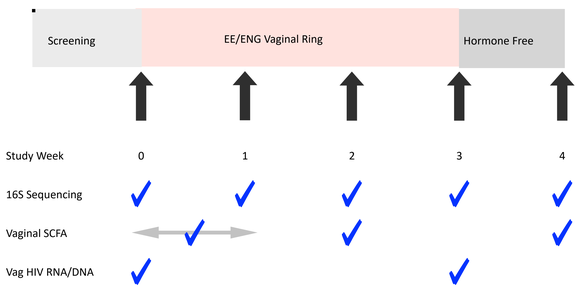
- 25 ART Naïve, 25 EFV, 24 ATV

64 were vaginal environment evaluable

- 19 ART Naïve, 21 EFV, 24 ATV/r

IVR was placed at Entry (week 0) and removed at week 3

- 16S rRNA sequencing of the V4 region was performed. Sequences were processed using DADA2, species assigned using SPINGO with SILVA database, and Lactobacillus classified using BLAST.
- Vaginal aspirate SCFA were measured by Metabolon®
- Negative binomial and linear regression models identified differentially abundant microbiome and SCFA features
- Spearman correlation assessed relationships between microbiome relative abundance and weekly EE/ENG concentrations



REFERENCES

1. Scarsi KK, Lancet HIV, 2019

ACKNOWLEDGEMENTS

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RESULTS

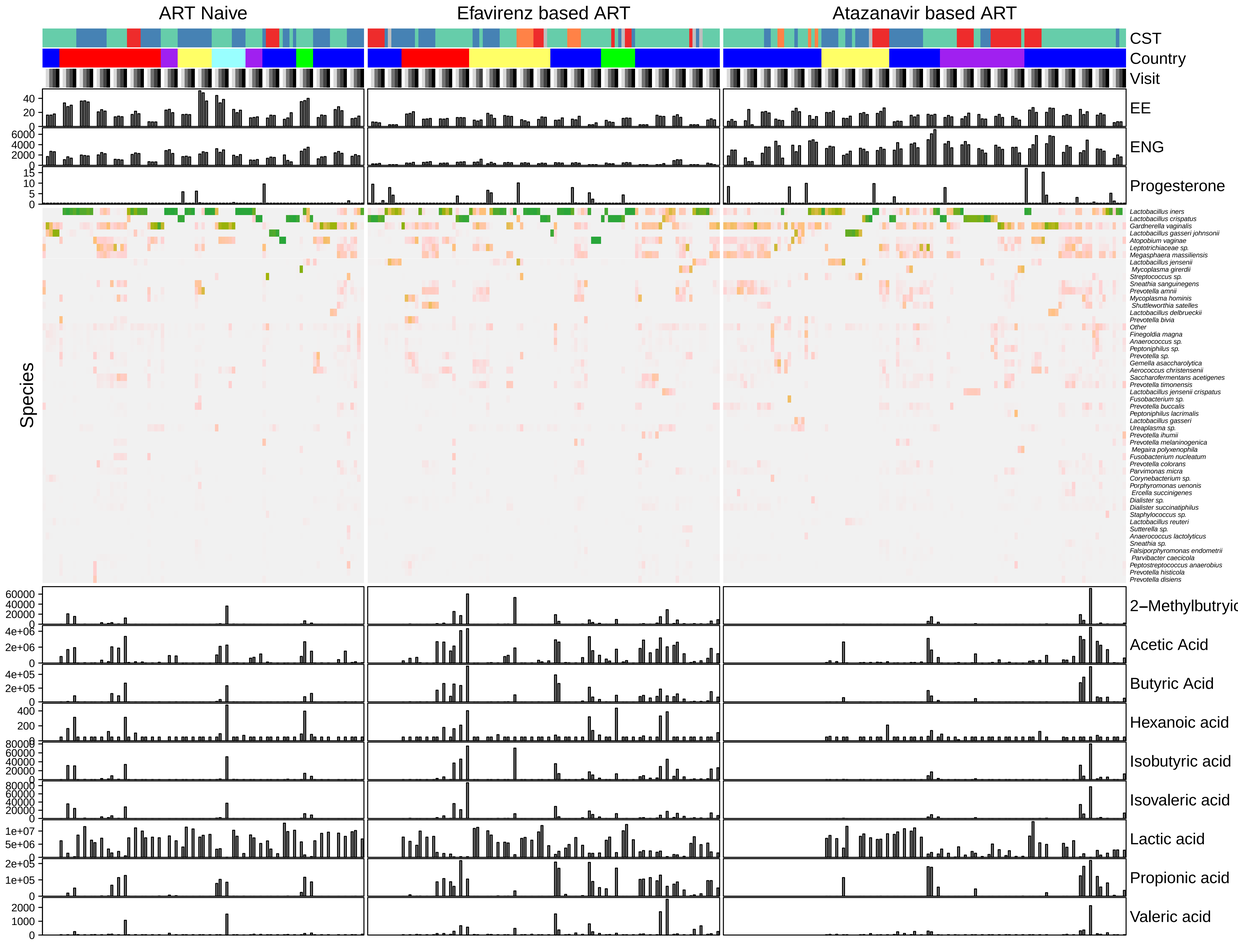


Figure 1: Heatmap of vaginal microbiome Community State Type (CST), Country, Visit week, Hormone concentrations, Progesterone Levels, Bacterial species and Short chain fatty acid levels for 64 subjects by treatment arm and participant

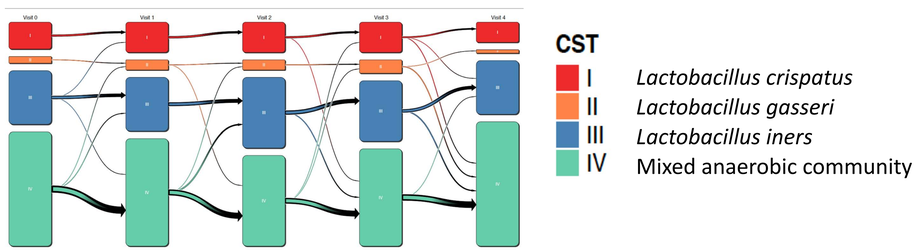


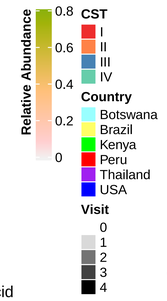
Figure 2: Community State Type (CST) transitions during the course of the study. Start of IVR was associated with transitions to CST I-III. IVR removal was associated with a shift to CST IV

CLINICAL CHARACTERISTICS

	ART-Naïve	EFV-based ART	ATV/r-based ART	p
N	19	21	24	
Age (years)	31 [27, 34]	36[28, 45]	37.0 [32, 42.5]	<0.001
BMI (kg/m2)	27.1 [23.7, 33.2]	25.4 [24.1, 32.3]	26.6 [23.5, 29.3]	0.825
EE (pg/mL)	19.6 [14.7, 28.3]	10.4 [6.4, 13.1]	16.0 [10.9, 19.8]	<0.001
ENG (pg/mL)	1900 [1390, 2420]	430 [278, 534]	3405 [2748, 4023]	<0.001
Plasma HIV RNA (log10)	3.42 [2.87, 4.20]	undetectable	undetectable	<0.001
CD4 count (cells per ul)	623 [477, 909]	752 [603, 866]	671 [494, 933]	0.109

Data shown as median, [IQR]

LEGEND



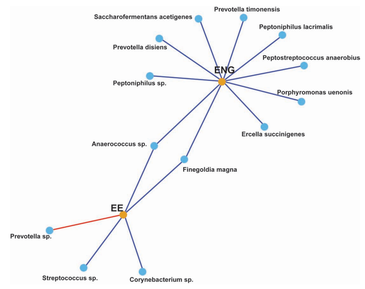


Figure 3: Associations between bacterial species and plasma hormonal concentrations (blue line = negative correlation, red line = positive correlation)

SUMMARY

- Use of the IVR was associated with an increased probability of transitioning to Lactobacillus-dominant (CST I-III) community types (p=0.09), suggesting a potential therapeutic role
- Removal of the IVR was associated with
  - a shift from CST I-III to CST IV (p=0.13)
  - a decrease in lactic acid levels (p<0.003)
  - no differences in species-level abundances
- Vaginal shedding of HIV-1 RNA/DNA was assessed at weeks 0 and 3 and will be presented in Themed Discussion 15
- Lactic acid levels are highly correlated with *Lactobacillus species* (p<0.001)
- Levels of all other SCFA are highly correlated with non-Lactobacillus mixed anaerobes (p<0.001)
- Specific microbes are associated with lower levels of EE and ENG (see Figure 3)
- For women on ATV-based regimens, higher levels of *Saccharofermentans acetigenes* and *Sneathia sanguinegens* are associated with lower levels of EE
- Further investigation is needed to fully assess the interactions and safety of vaginal hormonal contraception in women living with HIV