HIV, Not Integrase Inhibitor-Based ART, Modifies Gut Microbiota Composition in MSM

330

Marta Rosas Cancio-Suárez[1,2], Jorge Díaz-Álvarez[1,2], Luis Miguel Nieto-Salas[1,2], **Claudio Díaz-García**[1,2], Alejandro G. García-Ruiz de Morales[1,2], Clara Crespillo-Andújar[1,2], Laura Luna[1,2], Elena Moreno[1,2], Laura Martín-Pedraza[1,2], María Fons[1,2], Javier Martínez-Sanz[1,2], Raquel Ron[1,2], Santiago Moreno[1,2], Matilde Sánchez-Conde[1,2], Sergio Serrano-Villar[1,2]

1. Infectious Diseases Department, Hospital Universitario Ramón y Cajal, Universidad de Alcalá, IRYCIS, Madrid, Spain 2. CIBERINFEC, Instituto de Salud Carlos III, Madrid, Spain

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BACKGROUND

Understanding gut microbiota variations in HIV is confounded by factors like antiretroviral therapy (ART), immune status, and sexual orientation.

We aimed to isolate the **impact of integrase strand transfer inhibitor (INSTI)-based ART** on gut microbiota among men who have sex with men (MSM) across varying conditions of **HIV status** and **immune recovery**.

METHODS

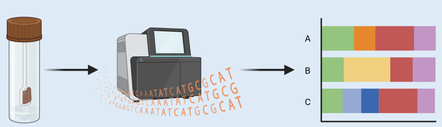
We conducted an observational study with **three cohorts of men who have sex with men (MSM)**:

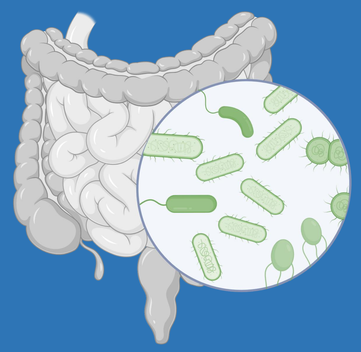


HIV	Without HIV	Advanced HIV	Controlled HIV
ART	Post-exposure prophylaxis	INSTI-based ART	Long-term ART (avg.* 9.5 years)
Immune status	Normal	< 350 CD4+ cells	> 500 CD4+ cells
Samples	0 and 28 days	0 and 48 weeks	One sample

*avg.: average

DNA was extracted from stool samples to perform **16S rRNA gene sequencing** (V3-V4 regions). QIIME2 workflow was used for data analysis. Amplicon Sequence Variants were inferred with DADA2 and assigned to taxons with a Silva-based classifier. Differential abundance testing was done with ANCOM-BC2.





INSTI-based ART has a **neutral** effect on gut microbiota composition

RESULTS

We included 22 MSM HIV-, 23 MSM HIV+ <350 CD4, and 17 MSM HIV+ >500 CD4 participants. Pairwise comparisons were performed to delineate the effects of ART, HIV status, and immune function on microbiota composition.

- Alpha diversity:

Alpha diversity **varied significantly** between specific groups (Figure 1A), with higher values in HIV+ MSM compared to HIV- MSM.

- Beta diversity:

Weighted UniFrac, which considers the total abundance of each taxa (Figure 1B), showed that the overall **microbiota structure differed across groups**. Regardless of ART, MSM HIV- formed a cluster clearly differentiated from MSM HIV+ >500 CD4.

- Differential abundance analysis (Figure 2):

Leuconostoc genera was more abundant in MSM HIV- preART (p=4.2e-5). **Alloprevotella** was significantly higher in MSM HIV+ <350 CD4 preART (p=5.5e-5) than in MSM HIV-. ART itself showed **little impact** on microbiota composition across all cohorts.

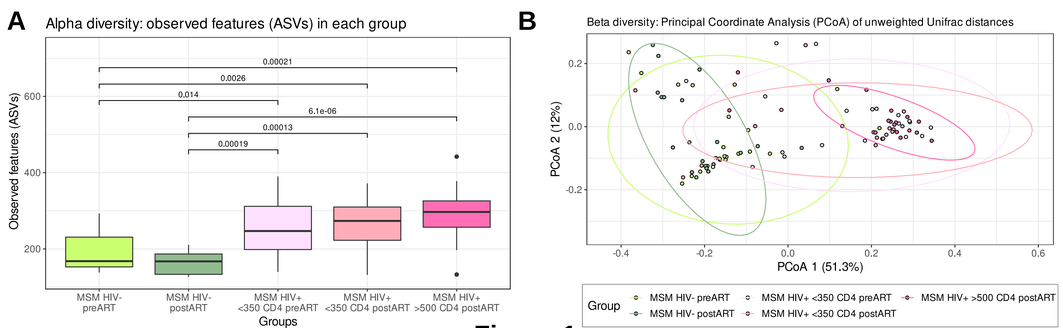
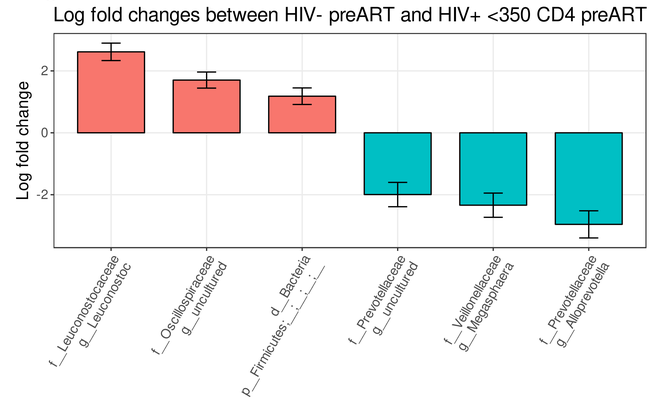


Figure 1

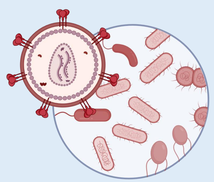
Figure 2



CONCLUSIONS

Our findings suggest that **INSTI-based ART is neutral** with respect to its impact on gut microbiota. The primary differences in microbiota composition seem to be driven more by **HIV infection** rather than ART or immune status, especially when controlled for possible confounders such as MSM condition.

This insight adds a new dimension to our understanding of HIV's impact on gut health and may guide future therapeutic strategies aimed at mitigating **HIV-related gut dysbiosis**.



Author Contact Information
Marta Rosas Cancio-Suárez: marta.rosas@salud.madrid.org
Claudio Díaz García: claudio.diaz@salud.madrid.org

Acknowledgements
We would like to thank all the participants in this study, and the support and collaboration of the infectious diseases team of the Hospital Ramón y Cajal.

Funding
This study has been financed by MSD (Investigator Studies Program IIS#59181).

Hospital Universitario Ramón y Cajal
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