Abstract Number:
THPEB048

22nd International AIDS Conference

July 23 - 27, 2018
Amsterdam, The Netherlands

Genital HIV-1 Shedding with Dolutegravir (DTG) plus Lamivudine (3TC) Dual Therapy

S. Gianella[1], V.C. Marconi[2], B. Berzins[3], C.A. Benson[1], P. Sax[4], C.J. Fichtenbaum[5], T. Wilkin[6], M. Vargas[1], Q. Deng[1], M.F. Oliveira[1], C. Moser[7], B.O.Taiwo[3].

[1]Division of Infectious Diseases & Global Public Health, University of California San Diego, La Jolla, California, [2]Emory University, School of Medicine and Rollins School of Public Health, Atlanta, Georgia., [3]Division of Infectious Diseases, Northwestern University, Chicago, [4]Division of Infectious Diseases Brigham and Women's Hospital Boston, Massachusetts, [5]University of Cincinnati Medical Center, Cincinnati Division of Infectious Diseases, [6]Weill Cornell Medicine, New York, [7]Department of Biostatistics, Center for Biostatistics and AIDS Research, Harvard TH Chan School of Public Health, Boston, Massachusetts.

Sara Gianella, MD
University of California, San Diego
9500 Gilman Drive
San Diego, CA 92093-0679, USA
E-mail: gianella@ucsd.edu
Web: http://gianella.ucsd.edu

Background

- Genital HIV shedding occurs in 2-20% of individuals on standard three-drug antiretroviral therapy (ART).
- The incidence of genital HIV RNA shedding with the investigational two-drug regimen of DTG+3TC is unknown.

Objective

To determine the frequency and magnitude of genital HIV RNA shedding in men and women virologically suppressed on DTG+3TC, an investigational two-drug regimen currently in phase 3 clinical trials, as compared to three-drug ART.

Cohort and Sampling

- Participants were recruited from two ongoing clinical trials:
  - **ASPIRE**: Virologically suppressed participants randomized to continuation of three-drug ART or switch to DTG+3TC.
  - **A5353**: ART-naïve participants, who initiated DTG+3TC in a single-arm phase 2 pilot study.
- At week 24 (or 36) and at week 48 after study initiation, genital secretions were collected to quantify genital HIV RNA (self-collected vaginal swab for women and semen for men).

Data Generated

- Genital HIV RNA, herpes simplex virus (HSV) and cytomegalovirus (CMV) DNA were quantified by real-time PCR.
- HIV genotyping and urine PCR for gonorrhea and chlamydia were performed if genital HIV RNA was detected.

Tables

Table 1. Demographics and clinical characteristics for ASPIRE study and A5353 study.

Characteristics	ASPIRE (DTG+3TC) (n=18)	ASPIRE (3-drug) (n=20)	A5353 (DTG+3TC) (n=13)
Age (years)			
Median (IQR)	43 (35-56)	47 (41-52)	29 (25-40)
HIV RNA level at Baseline(copies/ml)			
Median (IQR)	<20	<20	29138 (13365-67968)
CD4+ at Baseline (cells/μL)			
Median (IQR)	663 (528-812)	710 (484-872)	458 (336-671)
Time on ART at Baseline (Years)			
Median (IQR)	5.4 (3.5-7.6)	6.2 (3.8-7.8)	ART- Naive
Self-reported ART Adherence*, n (%)			
No missed doses	11 (61%)	11 (55%)	11 (85%)
Missed some doses	7 (40%)	9 (45%)	2 (15%)
Sex, n (%)			
Female	3 (17%)	2 (10%)	1 (8%)
Male	15 (83%)	18 (90%)	12 (92%)

Legend: IQR: Interquartile Range, ART: antiretroviral therapy, n: number, , *Self-reported ART Adherence during study follow-up

Table 2. Summary of HIV RNA Genital Shedders (N=3)

Parent study	Study week	ART regimen	Last missed doses	Genital HIV RNA (copies/ml)	Plasma HIV RNA* (copies/ml)	CMV DNA (copies/ml)	HSV DNA (copies/ml)	Gonorrhea RNA	Chlamydia RNA
ASPIRE #1	48	RPV/TDF/FTC	1-2 weeks	42	179	Not detected	Not detected	Not detected	Not detected
ASPIRE #2**	36	DTG+3TC	> 3 months	488	<20	314607	Not detected	Not detected	Not detected
	48	DTG+3TC	Never	79	31	86090	Not detected	Not detected	Not detected
A5353	24	DTG+3TC	Never	48	<40	NA***	NA***	Not detected	Not detected

Legend: RPV: Rilpivirine, TDF: Tenofovir, FTC: emtricitabine, DTG: Dolutegravir, 3TC: Lamivudine. NA = not available. *Plasma HIV RNA at the same rime of genital HIV RNA shedding **ASPIRE participant #2 had detectable HIV RNA at two consecutive time-points, ***not enough semen sample to run these additional tests

Results

- Demographics and clinical characteristics for ASPIRE study and A5353 study are summarized in **Table 1**.
- Three participants had seminal HIV RNA shedding (**Table 2**):
  - 1/20 (5% [95%CI: 0.1%, 25%]) in the ASPIRE three-drug ART arm.
  - 1/18 (5.6% [0.1%, 27%]) in the ASPIRE DTG+3TC arm.
  - 1/13 (7.7% [0.2%, 36%]) in A5353 (DTG+3TC).
  - No women had detectable genital HIV RNA.
- HIV genotyping was unsuccessful in genital secretions except integrase sequencing in one participant, which revealed no resistance mutations.
- HSV, gonorrhea or chlamydia was not detected in any participant with concomitant detectable genital HIV RNA. One participant had concurrent HIV and CMV genital shedding.

Conclusions

- **Genital HIV RNA shedding was comparable between virologically suppressed individuals receiving initial or maintenance DTG+3TC and those on three-drug ART.**
- **These results suggest that DTG+3TC may confer similar transmission prevention benefits as triple therapy.**
- **It is unknown if HIV RNA in genital secretions represent replication competent or transmissible virus.**

Acknowledgments

We are grateful to the study participants and the ASPIRE and A5353 clinical research staff at Northwestern University (Sherrie Wolfe), Emory University (Kishna Outlaw), University of Cincinnati (Eva Whitehead), Cornell (Todd Stroberg), University of California at San Diego (Edward Seefried) whose commitment and cooperation made this study possible.

This work was supported by an Investigator Sponsored Study grant "Virologic Activity of DTG +3TC in the Genital Compartment: Substudy of ASPIRE and A5353" from ViiV Healthcare to Northwestern University. ViiV Healthcare/GlaxoSmithKline provided funding and study drugs. Additional support was provided from the National Institute of Allergy and Infectious Diseases of the National Institutes of Health under Award Number UM1 AI068634, UM1 AI068636 and UM1 AI106701, the San Diego Center for AIDS Research Translational Virology Core (P30AI036214) as well as the Third Coast Center for AIDS Research (P30AI117943), and Emory Center for AIDS Research (P30AI050409). The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health or ViiV Healthcare."

CFAR CENTER FOR AIDS RESEARCH University of California San Diego

ACTG AIDS CLINICAL TRIALS GROUP

ViiV Healthcare