P044

Real-world Experience With the 2-Drug Regimen Dolutegravir and Lamivudine in Women With HIV: A Systematic Literature Review

Simona Di Giambenedetto,[1] Sharon Walmsley,[2] Beatriz Grinsztejn,[3] Maria Jesus Pérez Elías,[4] Nneka Nwokolo,[5] Madhusudan Kabra,[5] Bryn Jones,[5] Emilio Letang,[6] Michelle Kisare[7]

[1]Fondazione Policlinico Universitario Agostino Gemelli IRCCS and Università Cattolica del Sacro Cuore, Rome, Italy; [2]University Health Network, Toronto, ON, Canada; [3]Instituto Nacional de Infectologia Evandro Chagas–Fiocruz, Rio de Janeiro, Brazil; [4]Hospital Universitario Ramón y Cajal, IRYCIS, CIBERINFEC, Madrid, Spain; [5]ViiV Healthcare, Brentford UK; [6]ViiV Healthcare, Madrid, Spain; [7]GSK, Nairobi, Kenya

Key Takeaways

- **Women living with HIV are underrepresented in clinical trials, leading to gaps in the scientific understanding of treatment considerations that evolve across their life journey**
- **We conducted a systematic literature review of real-world studies of dolutegravir and lamivudine (DTG + 3TC) use in women to help compensate for underrepresentation in clinical trials**
- **Available real-world evidence for women using DTG + 3TC supports results from phase 3 clinical trials, demonstrating high virologic effectiveness in this underrepresented group**
- **There is a need to recruit women into well-designed studies that assess outcomes beyond virologic effectiveness to properly address data gaps**

Introduction

- Women and girls account for 54% of people living with HIV (PLWH) worldwide,[1] yet this important group is underrepresented in clinical trials, leading to gaps in the scientific and clinical understanding of treatment considerations for women
  - Women represented 19% of participants in HIV antiretroviral (ARV) clinical trials[2]
- Treatment considerations for women evolve throughout their lifespan and include concerns regarding drug-drug interactions with contraceptives and menopausal hormone replacement therapy, polypharmacy for comorbidities related to aging, and safety and efficacy of ARVs during pregnancy[3-5]
- In 48-week pooled analyses of phase 3 trials, women achieved or maintained high rates of virologic suppression with good tolerability on DTG + 3TC[6,7]
  - In the GEMINI-1 and -2 studies, treatment-naive women initiated the 2 drug-regimen DTG + 3TC and 88% (100/113) achieved virologic suppression (HIV-1 RNA <50 c/mL, Snapshot analysis)[6]
  - In the TANGO and SALSA studies, virologically suppressed women switched from their current antiretroviral regimen to co-formulated DTG/3TC and 91% (121/133) maintained virologic suppression (HIV-1 RNA <50 c/mL)[7]
- Real-world studies can help compensate for underrepresentation in clinical trials

Methods

- A systematic literature review was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement
- Real-world studies of DTG + 3TC (dosed separately or as a fixed-dose combination) in treatment-naive and -experienced PLWH were retrieved from January 2013 to February 2022 (Figure 1)
- Studies with <10 PLWH, case reports, reviews, editorials, and preclinical studies were excluded

Figure 1. Databases and Congresses Searched

Databases searched	Manual congress searches
Ovid MEDLINE®, Embase®, PubMed, Cochrane library	ACHA, ASHM, ASICON, BASHH, BHIVA, CAHR, CROI, European Meeting on HIV & Hepatitis, GeSIDA, HIV/HEP, HIV-NAT, IAS/IAC, ICAR, ICASA, ICID, IDWeek™, JSAR, KAP, SFLS, STI & HIV World Congress

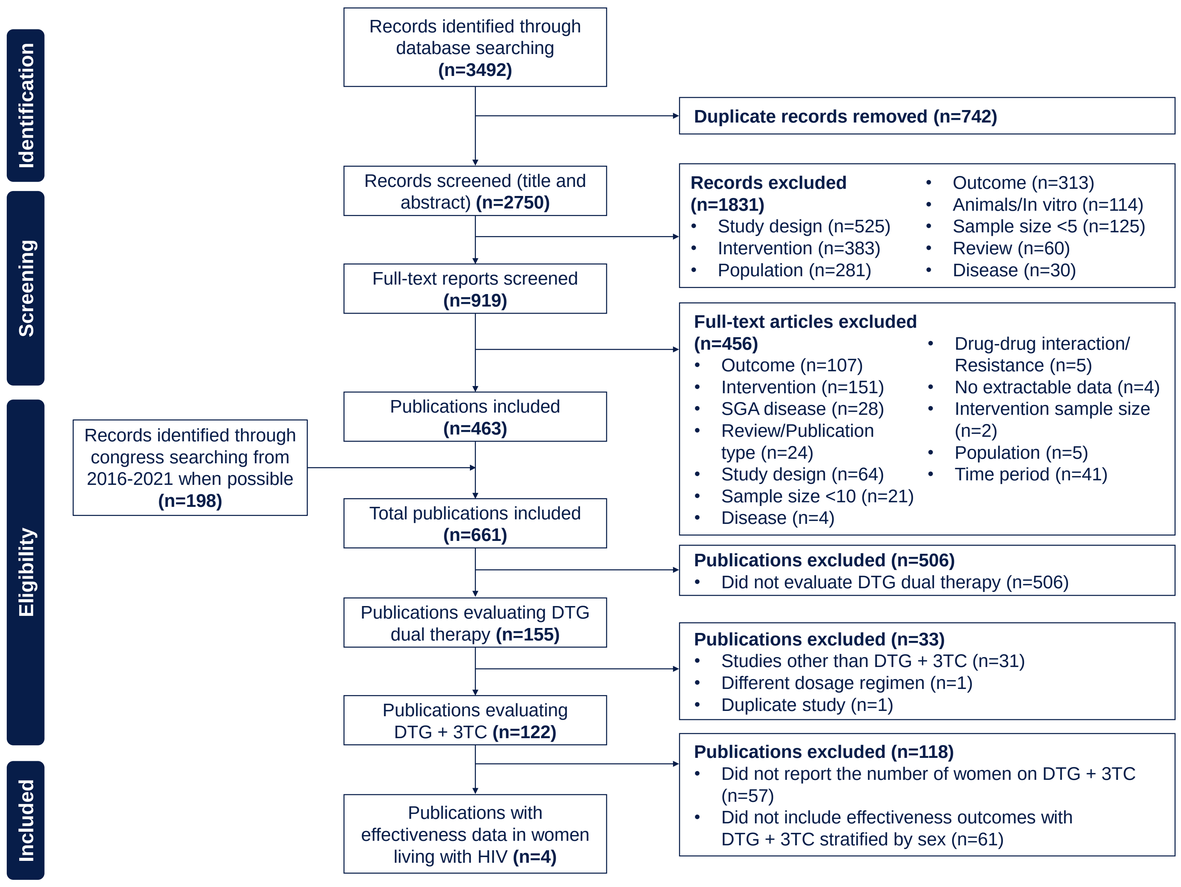
ACHA, Asian Conference on Hepatitis and AIDS; ASHM, Australasian HIV & AIDS Conference; ASICON, National Conference of AIDS Society of India; BASHH, British Association for Sexual Health and HIV; BHIVA, British HIV Association; CAHR, Canadian Conference on HIV/AIDS Research; CROI, Conference on Retroviruses and Opportunistic Infections; GeSIDA, Grupo de Estudio del SIDA-SEIMC; HIV/HEP, HIV & Hepatitis in the Americas; HIV-NAT, The HIV Netherlands Australia Thailand Research Collaboration; IAS/IAC, International AIDS Society/International AIDS Conference; ICAR, International Conference on Antiviral Research; ICASA, International Conference on AIDS and STIs in Africa; ICID, International Congress on Infectious Diseases; JSAR, Japanese Society for AIDS Research; KAP, Kenya Association of Physicians; SFLS, Société Française De Lutte Contre Le Sida; STI, sexually transmitted infection.

Results

Systematic Literature Review

- Overall, 122 publications of real-world studies from 44 unique cohorts reported on DTG + 3TC use, representing 8034 PLWH
- Of these, 31 studies reported the number of women at baseline (overall number of PLWH, 6948), representing 1658 (24%) women and 5290 (76%) men
- 4 studies reported efficacy outcomes stratified by sex (overall number of women, N=254; 240 virologically suppressed and 14 treatment-naive at DTG + 3TC initiation; Figure 2)[8-11]
- No real-world studies reported on outcomes related to weight, effectiveness and birth outcomes in pregnancy, or addressed data gaps for specific groups of women across the age or gender spectrum

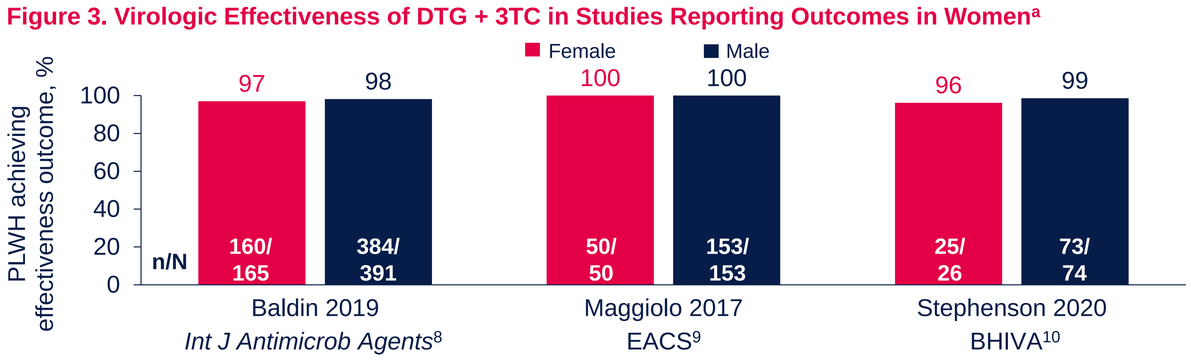
Figure 2. PRISMA Flow Diagram



Efficacy

- High rates of virologic effectiveness in women on DTG + 3TC were observed across identified studies (96%-100%; Figure 3)[8-10]
  - Results were consistent with those reported for men

Figure 3. Virologic Effectiveness of DTG + 3TC in Studies Reporting Outcomes in Women[a]

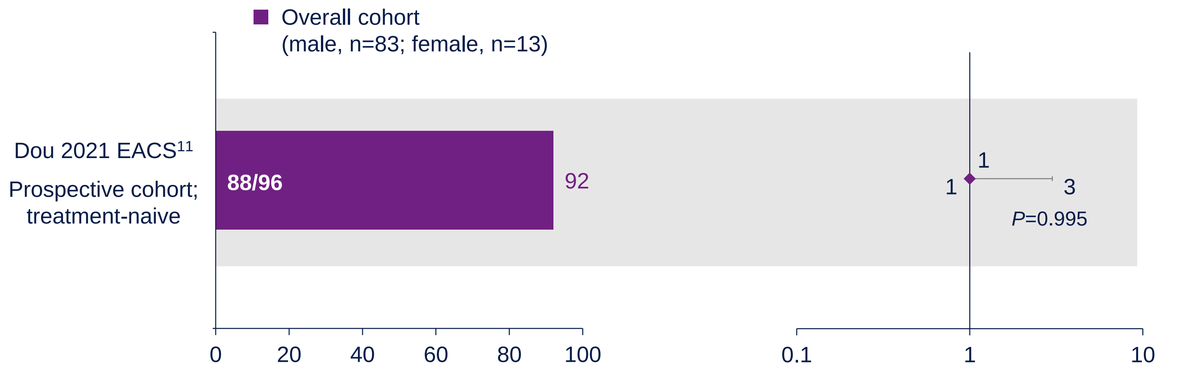


	Baldin 2019 *Int J Antimicrob Agents*[8]	Maggiolo 2017 EACS[9]	Stephenson 2020 BHIVA[10]
Study design	Retrospective observational; suppressed switch	Prospective cohort; suppressed switch	Hospital database review; treatment naive, n=4; suppressed switch, n=96[c]
Virologic effectiveness outcome	Free from VF[b] over 1020 PYFU	Free from VF over 295 PYFU	HIV-1 RNA <30 c/mL through 3-6 mo of follow-up

PYFU, person-years of follow-up; VF, virologic failure. [a]Potential overlap between patient cohorts cannot be ruled out. [b]VF defined as single HIV-1 RNA measurement ≥1000 c/mL or 2 consecutive HIV-1 RNA measurements ≥50 c/mL. [c]Among suppressed switch participants, virologic suppression was maintained in 96% (24/25) of women and 99% (70/71) of men.

- One study assessed odds of virologic suppression among treatment-naive PLWH by sex at birth and found no significant difference between sexes (odds ratio, 1; 95% CI, 1-3; Figure 4)[11]

Figure 4. Odds of Virologic Suppression by Sex at Birth



[a]VS defined as HIV-1 RNA <50 c/mL or HIV-1 RNA 50-200 c/mL with subsequent HIV-1 RNA <50 c/mL in the effectiveness set (missing = excluded).

Safety

- 2 studies reported safety outcomes, and both found higher rates of discontinuation in women vs men: 10% (5/50) vs 5% (7/153) and 15% (4/26) vs 3% (2/74), respectively (Table)[9,10]
  - In Maggiolo et al, muscle aches were the most common cause of discontinuation in women (6%; 3/50), and they were not reported in men[9]
  - Some discontinuations may have been unrelated to ART
    - In Maggiolo et al, 1 of 5 discontinuations in women was due to lost to follow-up[9]
    - In Stephenson et al, 1 of 4 discontinuations was due to pregnancy[10]

Table. DTG + 3TC Discontinuations in Women and Men

Maggiolo EACS 2017 (N=203)[9]		
Cause of discontinuation, n (%)	**Women (n=50)**	**Men (n=153)**
Discontinuations[a]	5 (10)[b]	7 (5)
Muscle aches	3 (6)	0
Headache	1 (2)	0
CNS symptoms	1 (2)	1 (<1)
Asthenia	1 (2)	0
Lost to follow-up	1 (2)	1 (<1)
Cancer-related metastasis	1 (2)	1 (<1)
Voluntary treatment interruption	0	2 (1)
Elevated liver function tests	0	1 (<1)
Alcohol-induced cirrhosis	0	1 (<1)

Stephenson BHIVA 2020 (N=100)[10]		
Cause of discontinuation, n (%)	**Women (n=26)**	**Men (n=74)**
Discontinuations	4 (15)	2 (3)
CNS intolerance	1 (4)	0
Gastrointestinal intolerance	1 (4)	0
Virologic escape	1 (4)[c]	1 (1)[d]
Pregnancy	1 (4)	0
Arthralgia	0	1 (1)

CNS, central nervous system. [a]All participants had viral load <50 c/mL at last visit. [b]2 women had multiple causes of discontinuation: 1 with muscle aches and asthenia and 1 with headache, CNS symptoms, and muscle aches. [c]Viral load was 15,135 c/mL before discontinuation. Virologic suppression achieved on BIC/FTC/TAF. [d]Viral load was 124 c/mL before discontinuation. Virologic suppression achieved on DTG + TDF/FTC.

Conclusions

- Available real-world evidence for women using DTG + 3TC supports findings from phase 3 clinical trials, demonstrating high virologic effectiveness (96%-100%) in this underrepresented group[8-11]
- 2 studies reported more discontinuations in women than men (10% vs 5% and 15% vs 3%, respectively)[9,10]
- In the 122 publications identified, 8034 PLWH were represented, only 3% (n=254) of whom were women with reported efficacy and safety outcomes, underscoring the need for greater representation of women in HIV clinical trials and real-world studies[8-11]
- The current paucity of real-world data validates the identified need to ensure that all studies investigating ART report data disaggregated by sex, recruit women, and assess outcomes beyond virologic effectiveness to properly address the unique treatment considerations for women and data gaps across the gender spectrum

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Presenting author: Michelle Kisare; michelle.o.kisare@viivhealthcare.com