

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 María Jesús Pérez Elías,⁴ Nneka Nwokolo,⁵ Madhusudan Kabra,⁵ Bryn Jones,⁵ Emilio Letang,⁶ Michelle Kisare⁷

¹Fondazione Policlinico Universitario Agostino Gemelli IRCCS and Università Cattolica del Sacro Cuore, Rome, Italy; ²University Health Network, Toronto, ON, Canada;

³Instituto Nacional de Infectología Evandro Chagas–Fiocruz, Rio de Janeiro, Brazil; ⁴Hospital Universitario Ramón y Cajal, IRYCIS, CIBERINFEC, Madrid, Spain;

⁵ViiV Healthcare, Brentford UK; ⁶ViiV Healthcare, Madrid, Spain; ⁷GSK, 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 trials²
- 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 pregnancy³⁻⁵
- 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-naïve 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-naïve 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

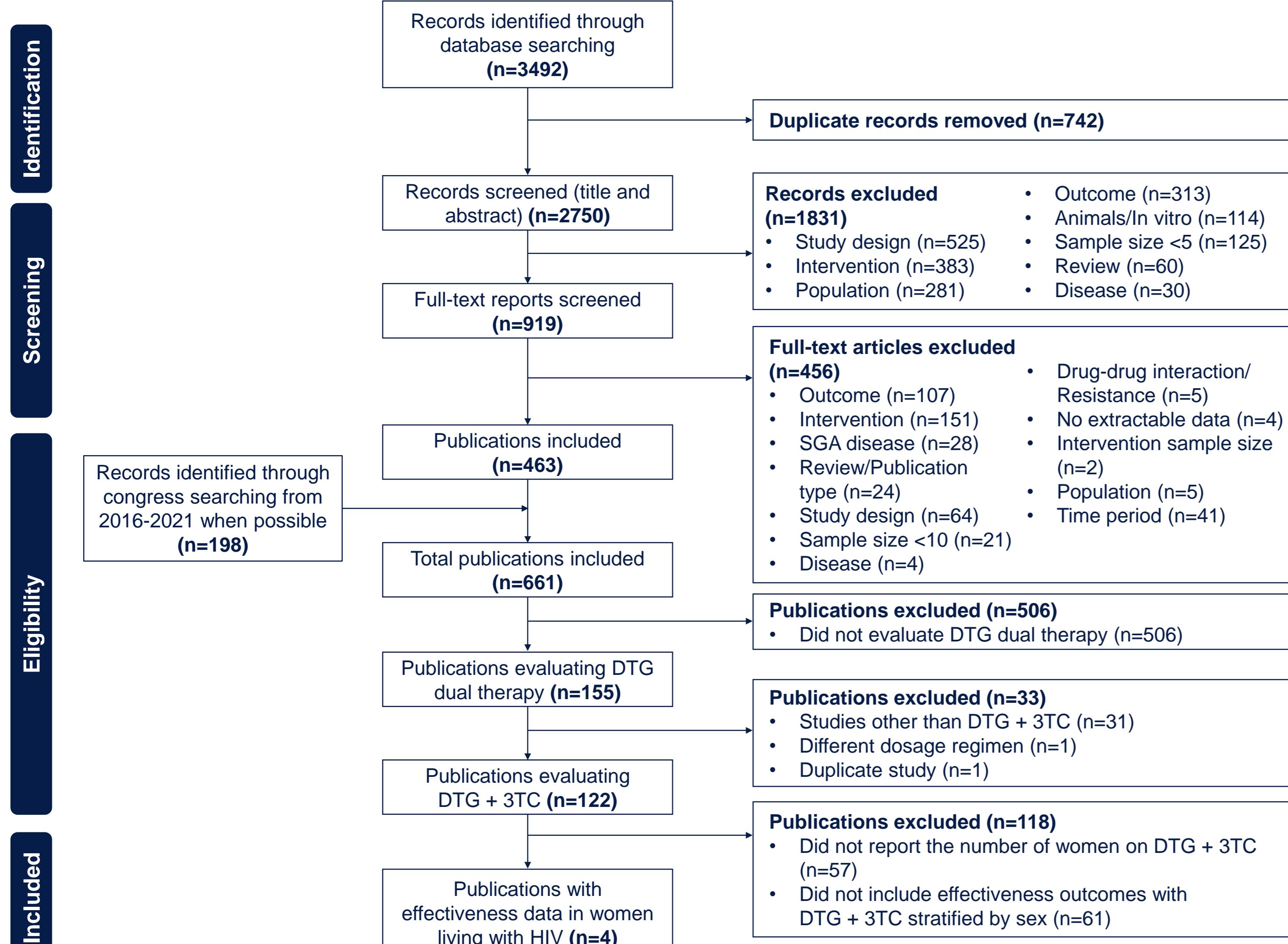
ACHA, Asian Conference on Hepatitis and AIDS; ASHM, Australasian HIV & AIDS Conference; ASICON, National Conference of AIDS Society of India; BASHH, British Association for Sexual Health and HIV; BHIVA, British HIV Association; CAHR, Canadian Conference on HIV/AIDS Research; CROI, Conference on Retroviruses 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-naïve 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

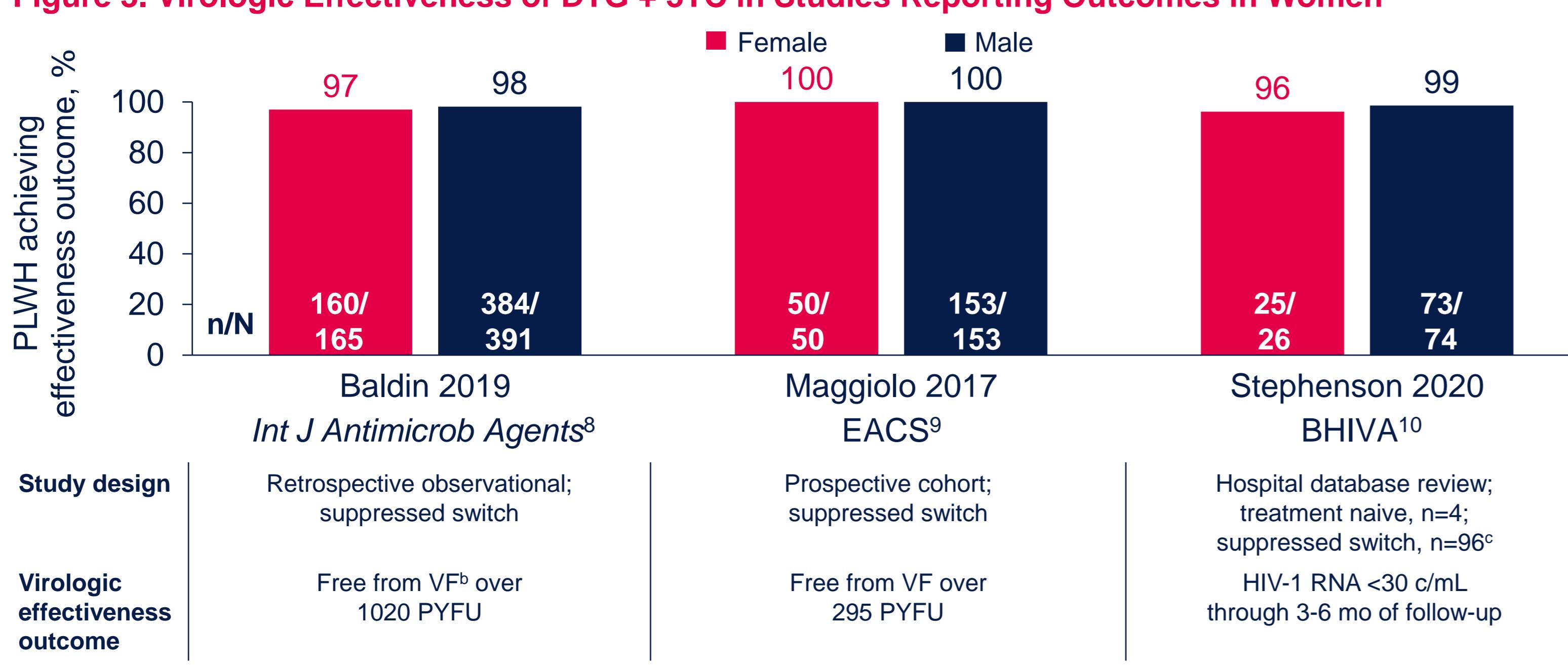
Figure 2. PRISMA Flow Diagram



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

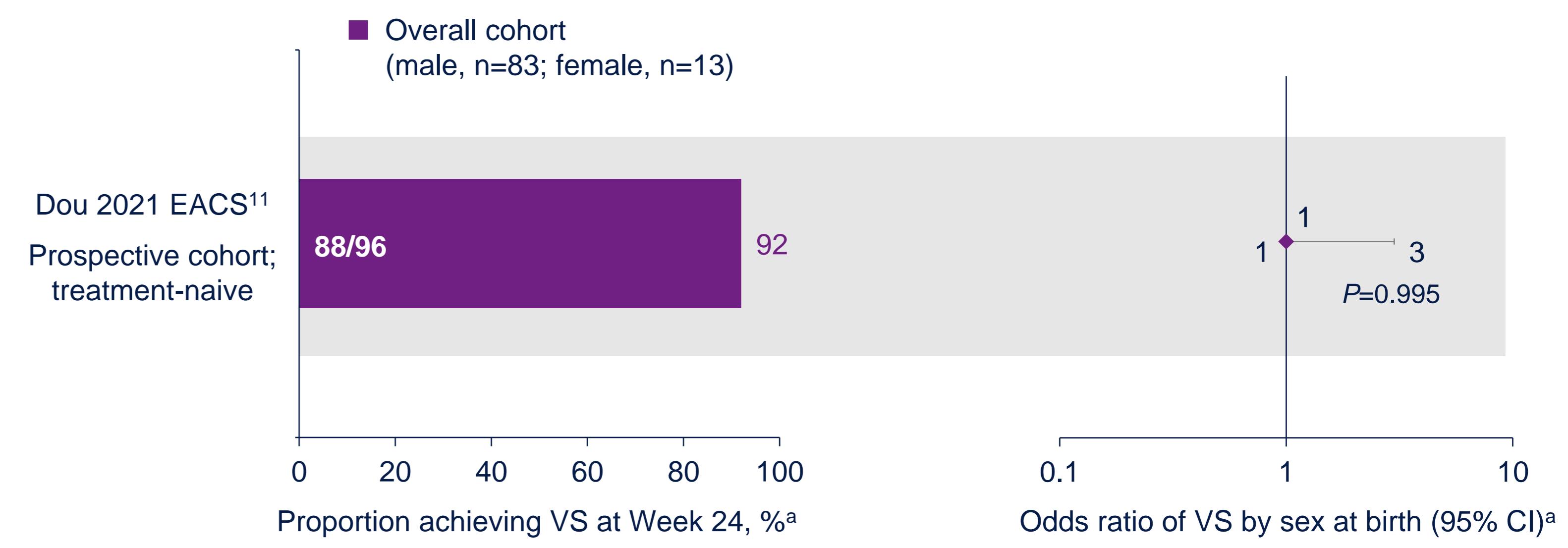
Figure 3. Virologic Effectiveness of DTG + 3TC in Studies Reporting Outcomes in Women^a



PYFU, person-years of follow-up; VF, virologic failure. ^aPotential overlap between patient cohorts cannot be ruled out. ^bVF defined as single HIV-1 RNA measurement ≥1000 c/mL or 2 consecutive HIV-1 RNA measurements ≥50 c/mL. ^cAmong 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-naïve 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



^aVS 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 Maggioli et al, muscle aches were the most common cause of discontinuation in women (6%; 3/50), and they were not reported in men⁹
- Some discontinuations may have been unrelated to ART
 - In Maggioli et al, 1 of 5 discontinuations in women was due to lost to follow-up⁹
 - In Stephenson et al, 1 of 4 discontinuations was due to pregnancy¹⁰

Table. DTG + 3TC Discontinuations in Women and Men

Maggioli 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. ^aAll participants had viral load <50 c/mL at last visit. ^b2 women had multiple causes of discontinuation: 1 with muscle aches and asthenia and 1 with headache, CNS symptoms, and muscle aches. ^cViral load was 135 c/mL before discontinuation. Virologic suppression achieved on BIC/FTC/TAF. ^dViral load was 124 c/mL before discontinuation. Virologic suppression achieved on DTG + TDF/TAF.

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 group⁸⁻¹¹
- 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 studies⁸⁻¹¹
- 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

This content was acquired following an unsolicited medical information enquiry by a healthcare professional. Always consult the product information for your country, before prescribing a ViiV medicine. ViiV does not recommend the use of our medicines outside the terms of their licence. In some cases, the scientific Information requested and downloaded may relate to the use of our medicine(s) outside of their license.