HIV Gender & Ethnicity - Implications for Toxicity and Altered Pharmacology

David Back, PhD
University of Liverpool
Liverpool
United Kingdom

HIV Gender & Ethnicity:

Implications for Toxicity & Altered Pharmacology

David Back

University of Liverpool, UK.

Disclosures

- Honoraria received for advisory boards and lectures from AbbVie, BMS, Gilead Sciences, Merck, ViiV Healthcare.
- Educational grants for www.hiv-druginteractions.org, www.hep-druginteractions.org, www.cancer-druginteractions.org and www.covid19-druginteractions.org from AbbVie, BMS, Gilead Sciences, Janssen, Merck, ViiV Healthcare, Astellas, AstraZeneca, Boehringer Ingelheim, BMS, Ipsen, Janssen, Pfizer, Roche, Sanofi, Sobi.

Overview

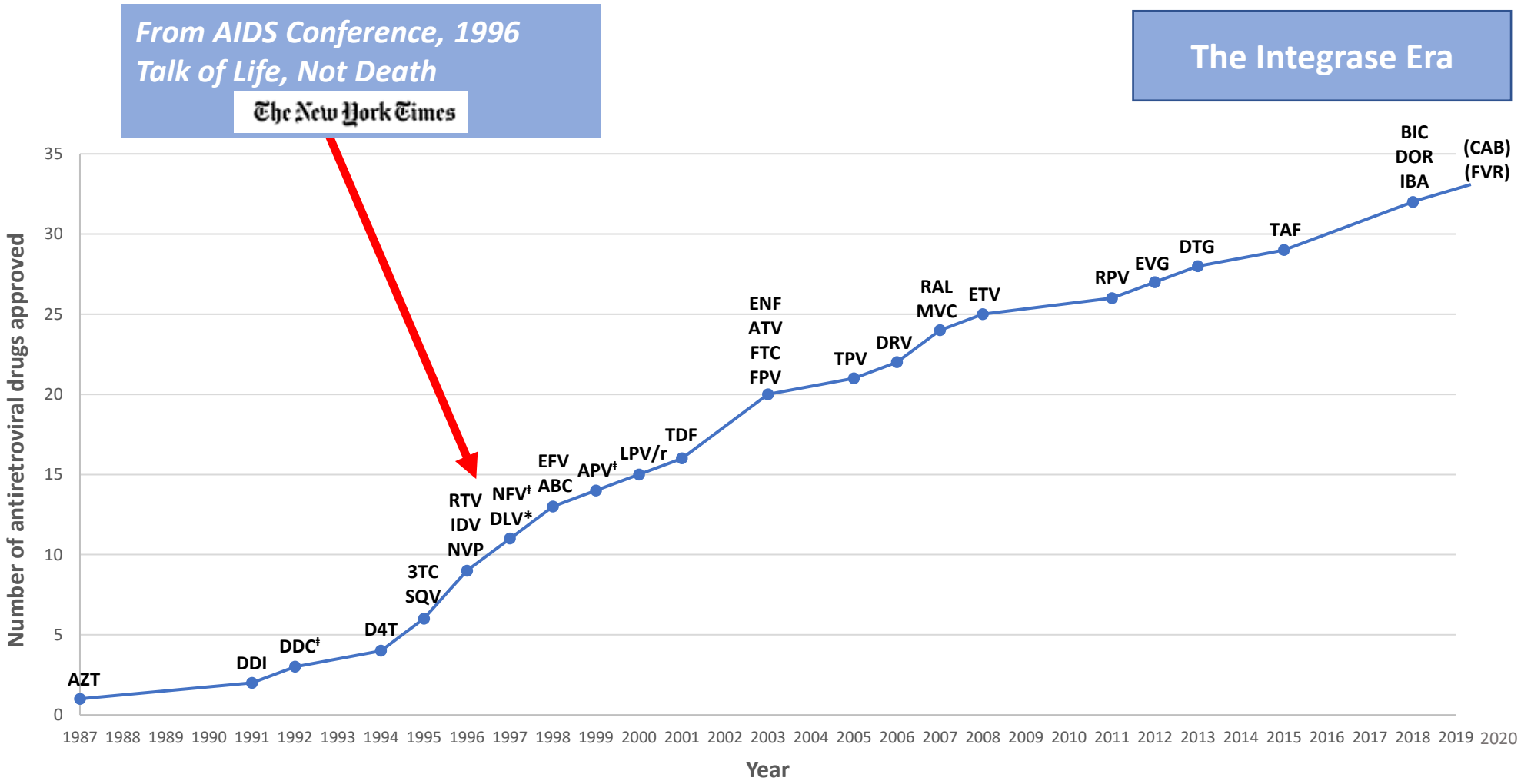
1. Antiretroviral Therapy: Where are we?
2. Antiretroviral Therapy & Gender: PK differences?
3. Antiretroviral Therapy & Gender: DDI Issues.

Overview

1. Antiretroviral Therapy: Where are we?
2.
3.

Antiretroviral Drug Approval 1987 - 2020

AZT; Azidothymidine (zidovudine)
DDI; Dideoxyinosine
DDC; Dideoxycytidine‡
D4T; Stavudine
3TC; Lamivudine
SQV; Saquinavir
RTV; Ritonavir
IDV; Indinavir
NVP; Nevirapine
NFV; Nelfinavir‡
DLV; Delavirdine*
EFV; Efavirenz
ABC; Abacavir
APV; Amprenavir‡
LPV/r; Lopinavir/ritonavir
TDF; Tenofovir disoproxil fumarate
ENF; Enfuvirtide
ATV; Atazanavir
FTC; Emtricitabine
FPV; Fosamprenavir
TPV; Tipranavir
DRV; Darunavir
RAL; Raltegravir
MVC; Maraviroc
ETV; Etravarine
RPV; Rilpivirine
EVG; Elvitegravir
DTG; Dolutegravir
TAF; Tenofovir alafenamide
BIC; Bictegravir
DOR; Doravirine
IBA; Ibalizumab
CAB; Cabotegravir
FVR; Fostemsavir



Based on US approval dates.
*Not licensed in the EU; ‡No longer available in the EU.

Adapted from: DHHS. FDA Approval of HIV Medicines. Available at: https://files.aidsinfo.nih.gov/images/infographics/FDAMedTimeline_FB%20(1).jpg [Accessed August 2020].

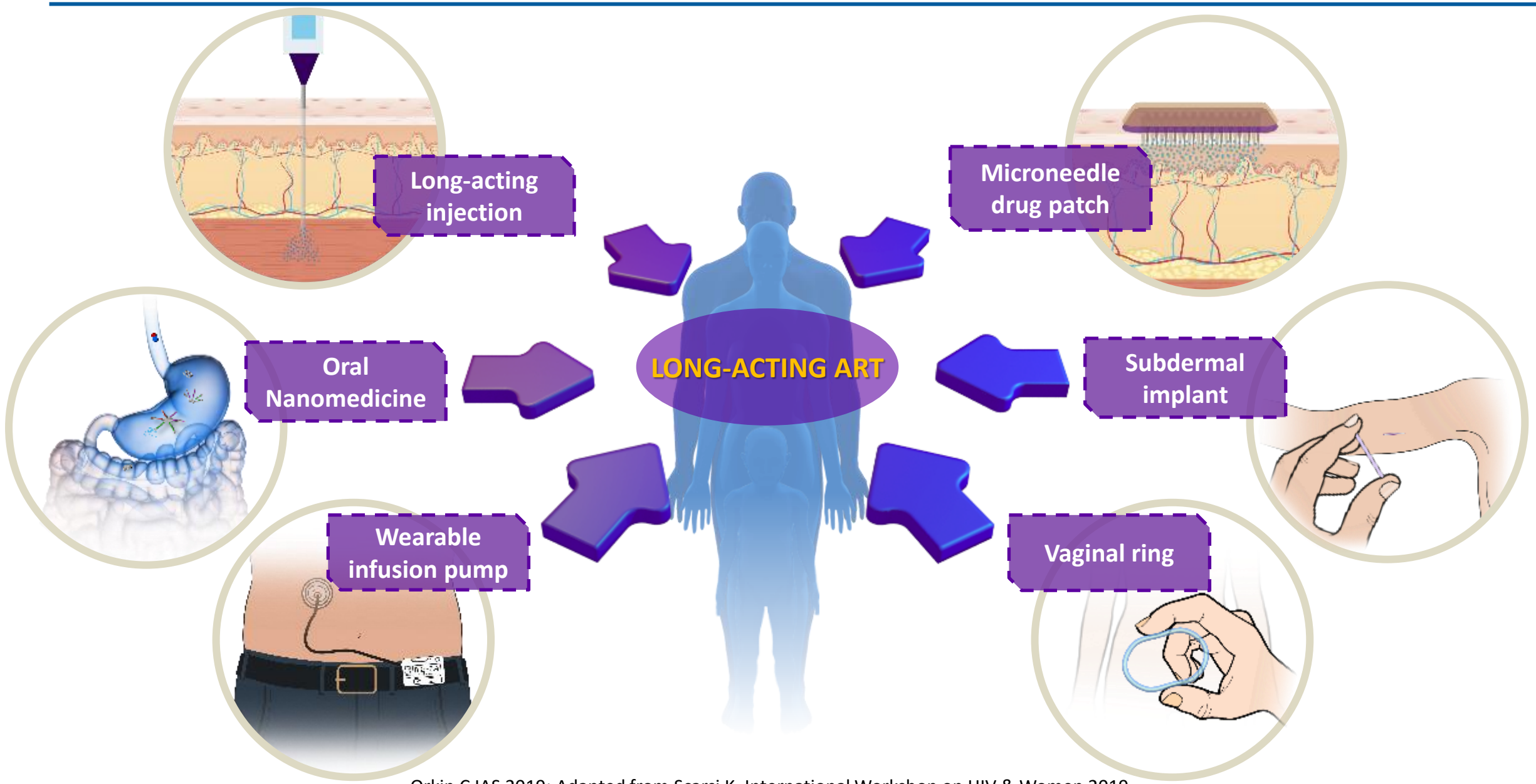
Strategies to Reduce the Drug Burden

- ✓ Reduce # of doses a day
- ✓ Reduce # of pills
- ✓ Reduce the # of drugs
- ✓ Reduce the drug dosage
- ✓ Reduce the # of days on ART
- ✓ Increase the dosing interval

Long Acting

Adapted from: Cahn P. Integrase Forum Belem 2019.

Long Acting Technologies for Drug Delivery



Orkin C IAS 2019; Adapted from Scarsi K, International Workshop on HIV & Women 2019.

Overview

1. Antiretroviral Therapy: Where are we?
2. Antiretroviral Therapy & Gender: PK Differences?
3.

2 Key Questions

1. What do we know?

2. What do we need to know?

Women and Girls and HIV

Source: UNAID Report 2018: Women and girls and HIV
https://www.unaids.org/sites/default/files/media_asset/women_girls_hiv_en.pdf

Global Demographics of PLWH

	Female (%)	Male (%)
White	3	6
Black	42	30
Other	7	12
Total	52	48

Pepperrell T et al J Virus Eradication 2020; 6: 70-73

Women and Girls in ARV Therapy Clinical Trials

ORIGINAL RESEARCH

Journal of Virus Eradication 2020; **6**: 70–73

Phase 3 trials of new antiretrovirals are not representative of the global HIV epidemic

Toby Pepperrell[1], Andrew Hill[2]*, Michelle Moorhouse[3], Polly Clayden[4], Kaitlyn McCann[5], Simiso Sokhela[3], Celicia Serenata[6], Willem Daniel Francois Venter[3]

[1]Faculty of Medicine, Imperial College London, UK
[2]Department of Translational Medicine, Liverpool University, Pharmacology, Liverpool, UK
[3]Ezintsha, Wits Reproductive Health and HIV Institute, Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, South Africa
[4]HIV iBase, London, UK
[5]Imperial College London, UK
[6]Wits Reproductive Health and HIV Institute, Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, South Africa

	DTG Trials (n = 7667)		BIC Trials (n = 2248)		TAF Trials (n = 7750)	
	F (%)	M (%)	F (%)	M (%)	F (%)	M (%)
White	14	53	14	45	16	49
Black	7	15	11	21	7	17
Other	3	8	5	4	4	7
Total	24	76	30	70	27	73

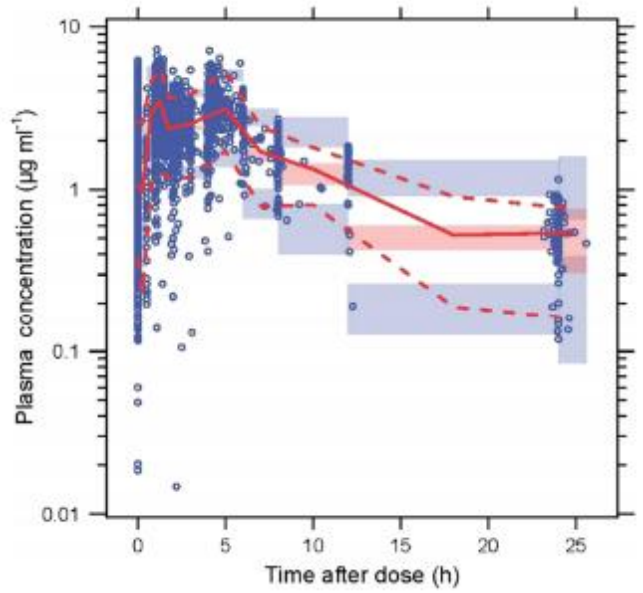
Gender Effect on Pharmacokinetics of Dolutegravir

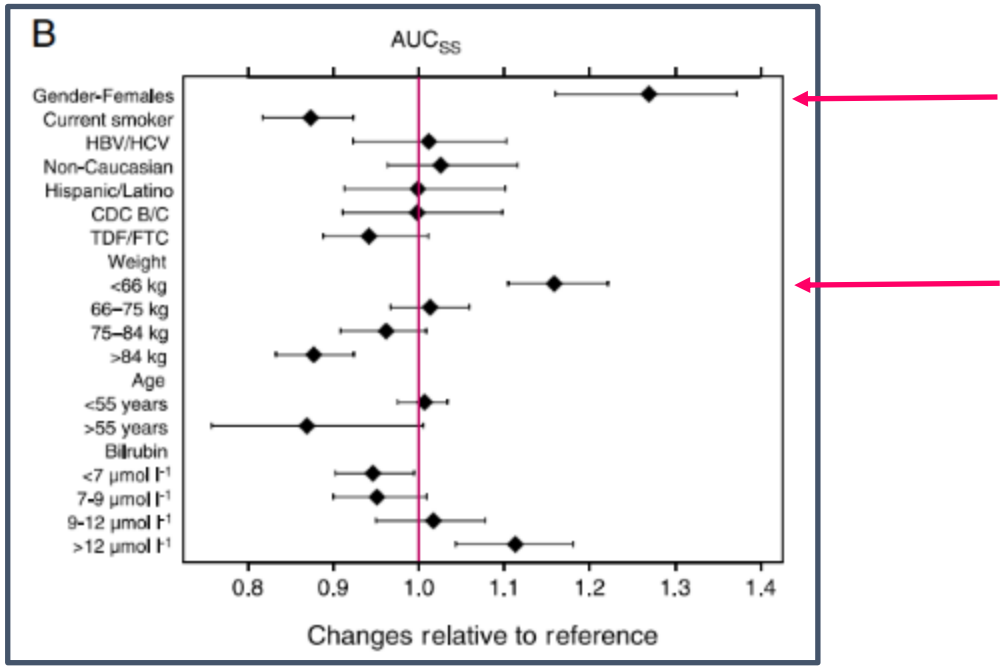
BJCP British Journal of Clinical Pharmacology

Population pharmacokinetics of dolutegravir in HIV-infected treatment-naive patients

Jianping Zhang,[1] Siobhán Hayes,[2] Brian M. Sadler,[2] Ilisse Minto,[3] Julie Brandt,[3] Steve Piscitelli,[1] Sherene Min[3] & Ivy H. Song[1]

- Pop PK analysis of plasma concentrations (n = 3357) of DTG from 563 HIV+ treatment naïve patients (475 M; 82 F; 15% F) in Phase 2/3 Clinical trials.





No DTG dose adjustment by these intrinsic factors is necessary.

Zhang J et al BJCP 2015; 80: 502-514

Gender Effect on Pharmacokinetics of Dolutegravir

The appropriate dose for any population is determined from clinical pharmacology (PK, exposure-response and exposure-safety relationships) + Phase 2 & 3 Efficacy and Safety studies.

No dose adjustment of Dolutegravir for Women - includes women on contraceptives and during the 2nd and 3rd trimester of pregnancy.

Higher rates of neuropsychiatric adverse events leading to dolutegravir discontinuation in women and older patients

C Hoffmann,[1,2] T Welz,[3] M Sabranski,[1] M Kolb,[3,4] E Wolf,[5] H-J Stellbrink[1] and C Wyen[3,4]

[1]ICH Study Center Hamburg, Hamburg, Germany, [2]Department of Medicine II, University of Schleswig-Holstein, Kiel, Germany, [3]Praxis am Ebertplatz, Cologne, Germany, [4]Department I of Internal Medicine, University Hospital Cologne, Cologne, Germany and [5]MUC Research GmbH, Munich, Germany

- ❑ PK related?
- ❑ Much higher rates than in pivotal trials

Adkinson et al 9th Int Workshop on HIV & Women; 2019; Hoffmann C et al HIV Med 2017; 18: 56-63.

Gender Effect on Pharmacokinetics of Darunavir/cobi

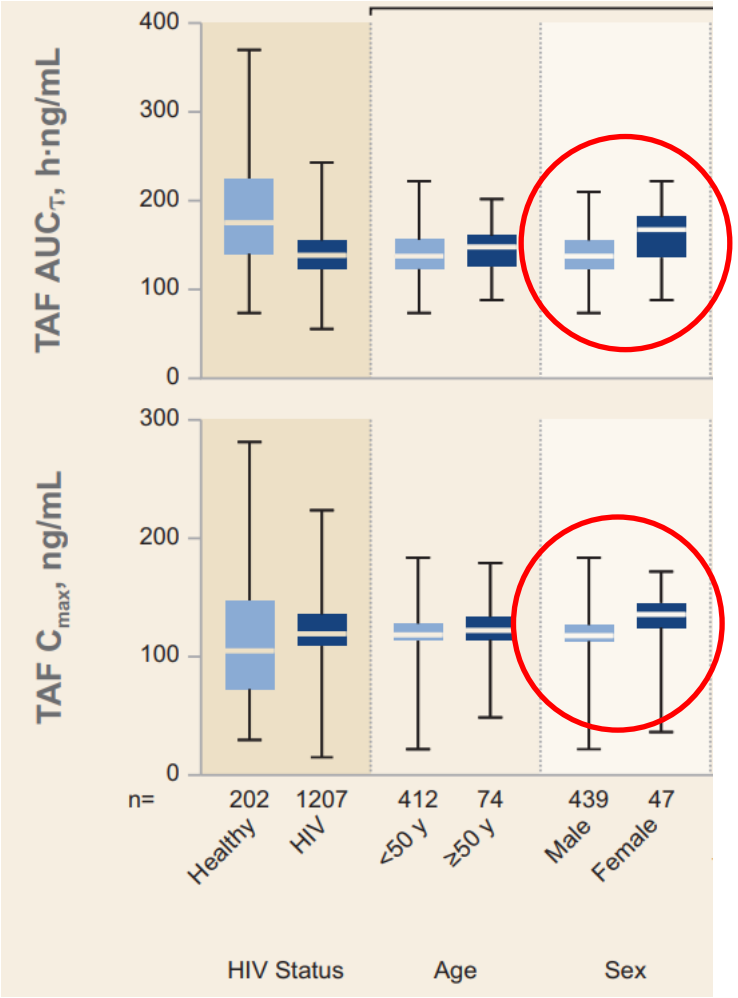
Exploration of Reduced Doses and Short-Cycle Therapy for Darunavir/Cobicistat in Patients with HIV Using Population Pharmacokinetic Modeling and Simulations

Gabriel Stillemans[1,2,5] · Leila Belkhir[2,3] · Bernard Vandercam[3] · Anne Vincent[3] · Vincent Haufroid[2,4] · Laure Elens[1,2]

- A total of 309 sparse samples and 96 rich samples for serum concentrations of DRV from 127 PLWH (85 M; 42 F) were included in the PopPK study.
- Gender was found to be a significant covariate for CL/F (21% decrease in CL in Females) when introduced in a univariate manner in the basic model.
- The BW difference between men and women not discussed!

Stillemans G et al Clin Pharmacokin 2020 (ahead of print)

Gender Effect on Pharmacokinetics of Tenofovir Alafenamide (TAF)

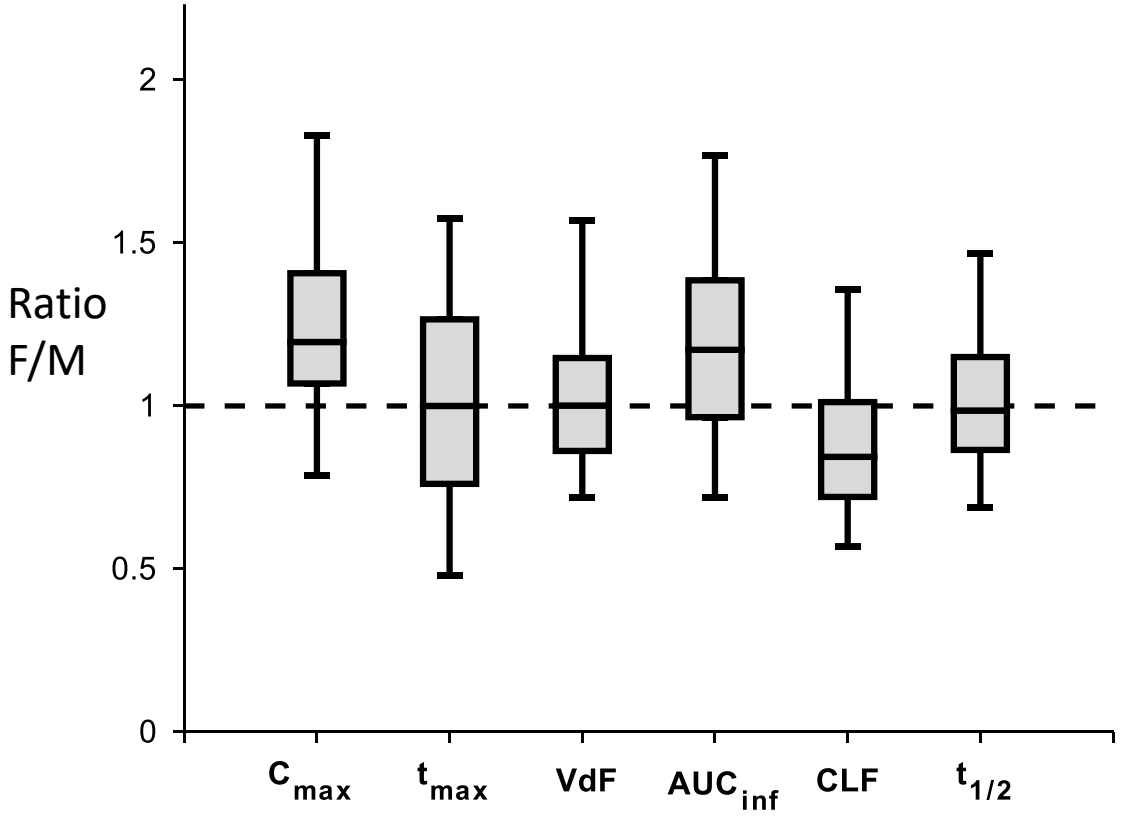


Mean TAF exposures in males (n=439) and females (n=47) differed by 12–15%

Lutz JD et al HIV Glasgow 2018 P262

Gender Effect on Pharmacokinetics of Oral and iv Drugs

Meta analysis of existing studies (n = 64) comparing gender PK



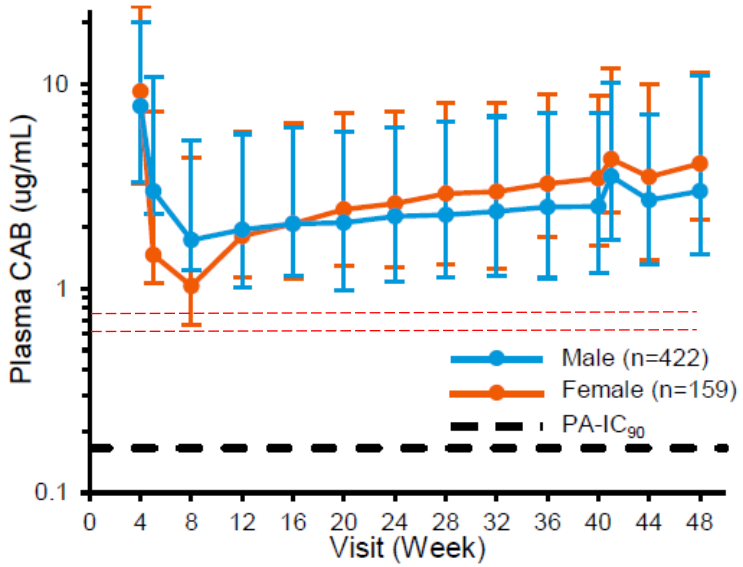
Parameter	Difference F/M
C_{max}	↑ 20%
t_{max}	**0%**
AUC_{inf}	↑ 17%
CLF	↓ 11%
VdF	**0%**
$t_{1/2}$	**-1%**

Explained by differences in body weight and metabolism (reduced first pass effect and hepatic metabolism).
However – within Bioequivalence

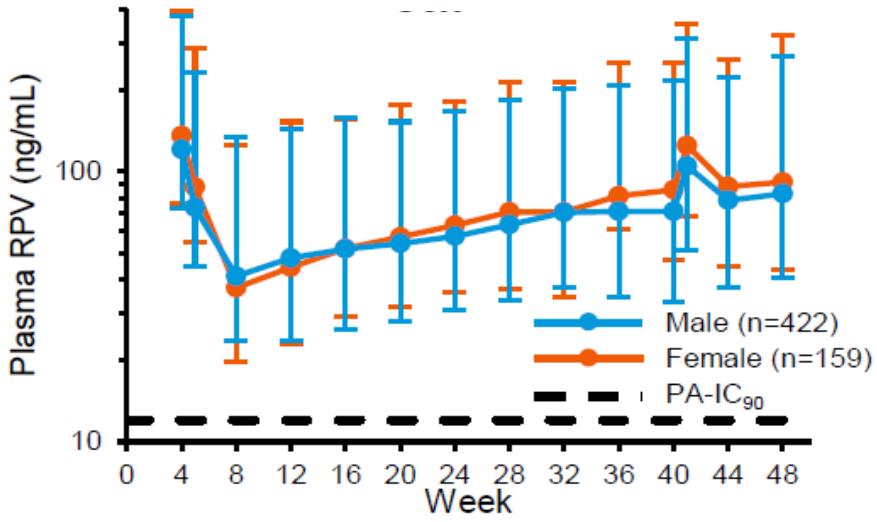
Stader F. EACS Conference 2019

Cabotegravir and Rilpivirine Plasma Levels in Female vs Male

Median (5th and 95th percentile) plasma CAB and RPV trough levels over time – data from the ATLAS and FLAIR Trials



4xPA-IC90*
3xPA-IC90*



4 weeks following the first injection, median cabotegravir levels were 40% lower in female vs male

- In a low dose rectal challenge model, plasma CAB concentrations > 3x PA-IC90 provided 100% protective efficacy, 1-3 x PA-IC90 provided 97% protective efficacy
- In a vaginal challenge model, plasma CAB concentrations > 4x PA-IC90 provided 87% protective efficacy

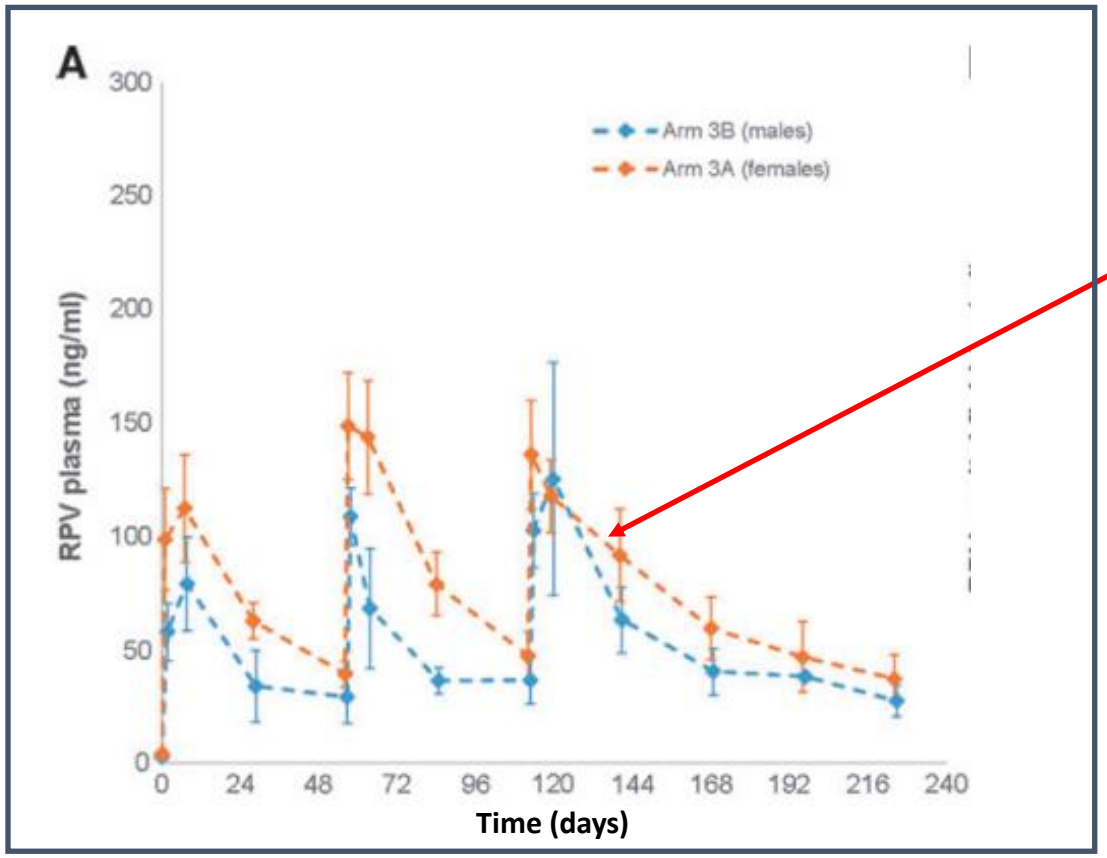
Andrews CD et al. Science 2014

Patel P et al. ID week 2019

Gender Effect on Pharmacokinetics of LA Rilpivirine

A Multiple Dose Phase 1 Assessment of Rilpivirine Long Acting in a Model of Preexposure Prophylaxis Against HIV

Ross D. Cranston,[1] Charlene S. Dezzutti,[1,2,*] Aaron Siegel,[2] Jarret Engstrom,[2] Cory Shetler,[2] Nicola Richardson-Harman,[3] Kaleab Z. Abebe,[1] David Back,[4] Laura Else,[4] Deidre Egan,[4] Saye Khoo,[4] James E. Egan,[5] Ronald Stall,[5] Peter Williams,[6] Rhonda M. Brand,[1] Urvi M. Parikh,[1] and Ian McGowan[7,8]



Cumulative RPV exposure in Females (n=8) higher than Males (n=4; p = 0.042)

But

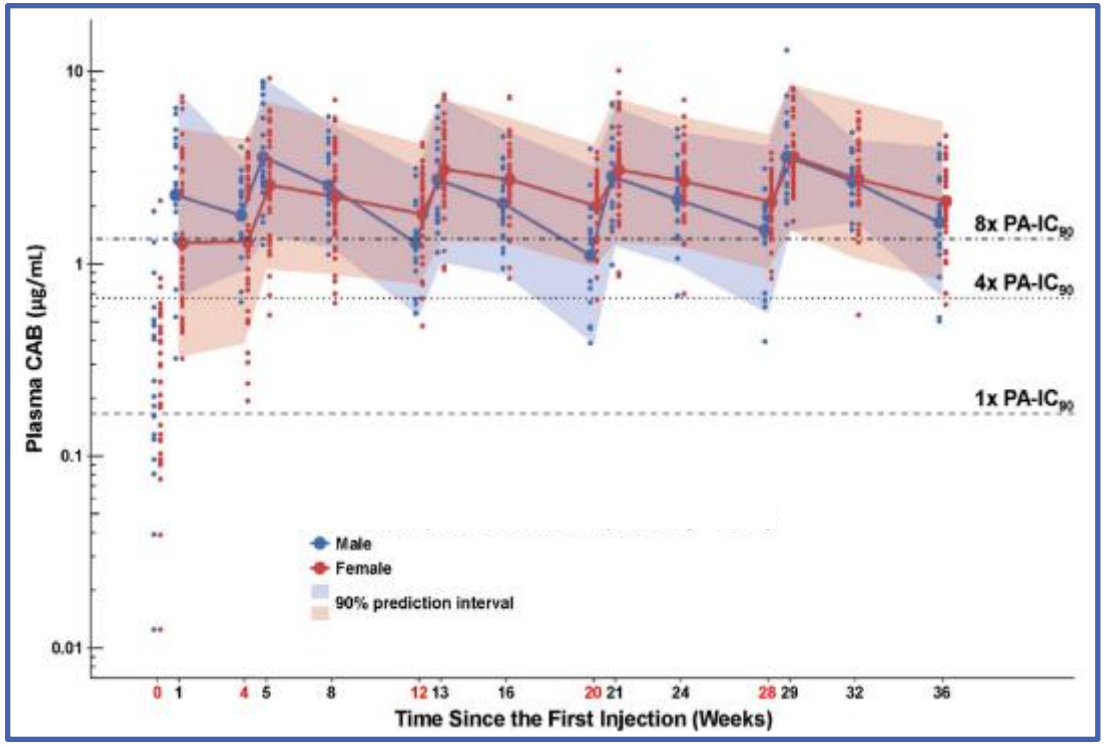
i) Small numbers

ii) Another study did not show this difference (Jackson A et al CPT 2014; 96: 314-323).

Gender Effect on Pharmacokinetics of LA Cabotegravir

Safety, tolerability, and pharmacokinetics of long-acting injectable cabotegravir in low-risk HIV-uninfected individuals: HPTN 077, a phase 2a randomized controlled trial

Raphael J. Landovitz[1]*, Sue Li[2], Beatriz Grinsztejn[3], Halima Dawood[4], Albert Y. Liu[5], Manya Magnus[6], Mina C. Hosseinipour[7], Ravindre Panchia[8], Leslie Cottle[2], Gordon Chau[2], Paul Richardson[9], Mark A. Marzinke[9], Craig W. Hendrix[9], Susan H. Eshleman[9], Yinfeng Zhang[9], Elizabeth Tolley[10], Jeremy Sugarman[9,11], Ryan Kofron[1], Adeola Adeyeye[12], David Burns[12], Alex R. Rinehart[13], David Margolis[13], William R. Spreen[13], Myron S. Cohen[14], Marybeth McCauley[10], Joseph J. Eron[14]



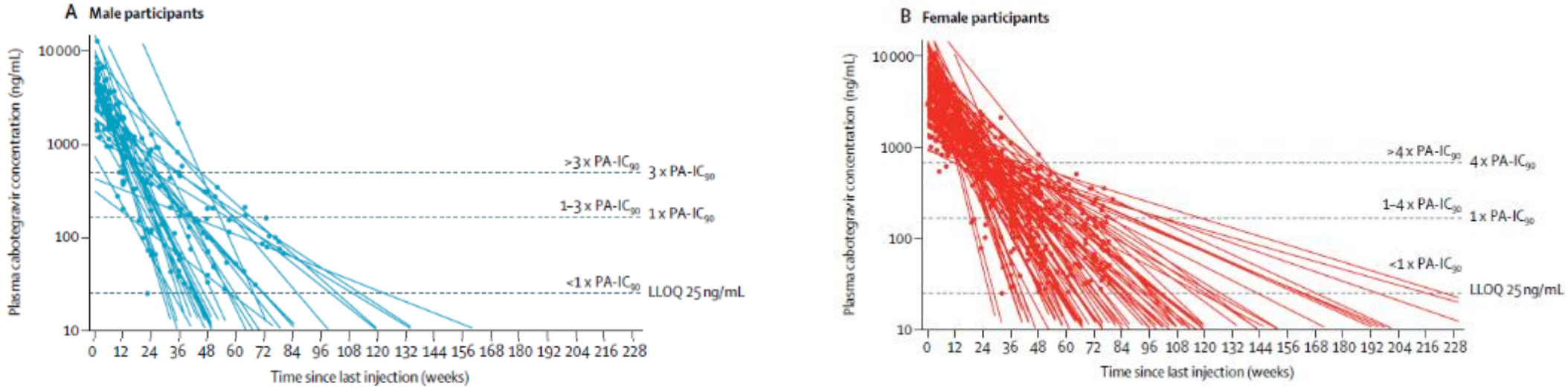
Parameter	Female (n=39)	Male (n= 20)	p value
Injection 2			
C_{max} (µg/ml)	2.96	3.90	0.07
C_{tau} (µg/ml)	1.82	1.29	0.05
Injection 3			
C_{max} (µg/ml)	3.46	2.96	0.325
C_{tau} (µg/ml)	2.04	1.11	<0.001

Landovitz R et al PLOS Med Nov 8 2018;

Gender Effect on Pharmacokinetics of LA Cabotegravir Tail

Tail-phase safety, tolerability, and pharmacokinetics of long-acting injectable cabotegravir in HIV-uninfected adults: a secondary analysis of the HPTN 077 trial

Raphael J Landovitz, Sue Li, Joseph J Eron Jr, Beatriz Grinsztejn, Halima Dawood, Albert Y Liu, Manya Magnus, Mina C Hosseinipour, Ravindre Panchia, Leslie Cottle, Gordon Chau, Paul Richardson, Mark A Marzinke, Susan H Eshleman, Ryan Kofron, Adeola Adeyeye, David Burns, Alex R Rinehart, David Margolis, Myron S Cohen, Marybeth McCauley, Craig W Hendrix



Landowitz RJ et al Lancet 2020; Published online June 1st.

CAB PK Tail: Women Have Detectable Levels Longer Than Men

Tail-phase safety, tolerability, and pharmacokinetics of long-acting injectable cabotegravir in HIV-uninfected adults: a secondary analysis of the HPTN 077 trial

Raphael J Landovitz, Sue Li, Joseph J Eron Jr, Beatriz Grinsztejn, Halima Dawood, Albert Y Liu, Manya Magnus, Mina C Hosseinipour, Ravindre Panchia, Leslie Cottle, Gordon Chau, Paul Richardson, Mark A Marzinke, Susan H Eshleman, Ryan Kofron, Adeola Adeyeye, David Burns, Alex R Rinehart, David Margolis, Myron S Cohen, Marybeth McCauley, Craig W Hendrix

Our observation that detectable or quantifiable concentrations of cabotegravir may persist for years (females > males) after final product injection has implications for the risk of HIV infection**, drug–drug interactions**, and resistance after dosing cessation.

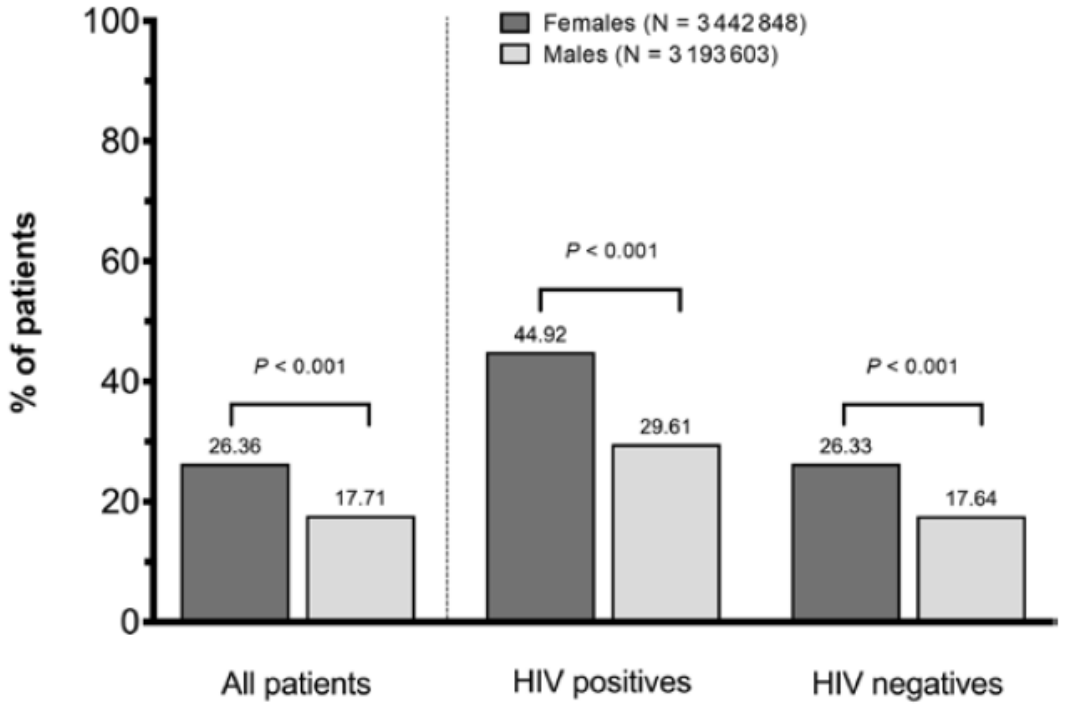
Overview

1. Antiretroviral Therapy: Where are we?
2. Antiretroviral Therapy & Gender: PK differences?
3. Antiretroviral Therapy & Gender: DDI Issues.

Polypharmacy in Men & Women

Polypharmacy and Drug–Drug Interactions in People Living With Human Immunodeficiency Virus in the Region of Madrid, Spain: A Population-Based Study

Beatriz López-Centeno,[1] Carlos Badenes-Olmedo,[2] Ángel Mataix-Sanjuan,[1] Katie McAllister,[3] José M. Bellón,[4,5] Sara Gibbons,[3] Pascual Balsalobre,[4,5] Leire Pérez-Latorre,[4,5] Juana Benedí,[6] Catia Marzolini,[3,7] Ainhoa Aranguren-Oyarzábal,[1] Saye Khoo,[3] María J. Calvo-Alcántara,[1] and Juan Berenguer[4,5]



Prevalence of Polypharmacy (> 5 non-ARVs) by gender

Polypharmacy is more common in Women

- *Consult HCPs more frequently and therefore detect comorbidities and receive medications*

Lopez-Centeno B et al CID 2019;

Polypharmacy in Men & Women

Elderly HIV-positive women: A gender-based analysis from the Multicenter Italian "GEPPO" Cohort

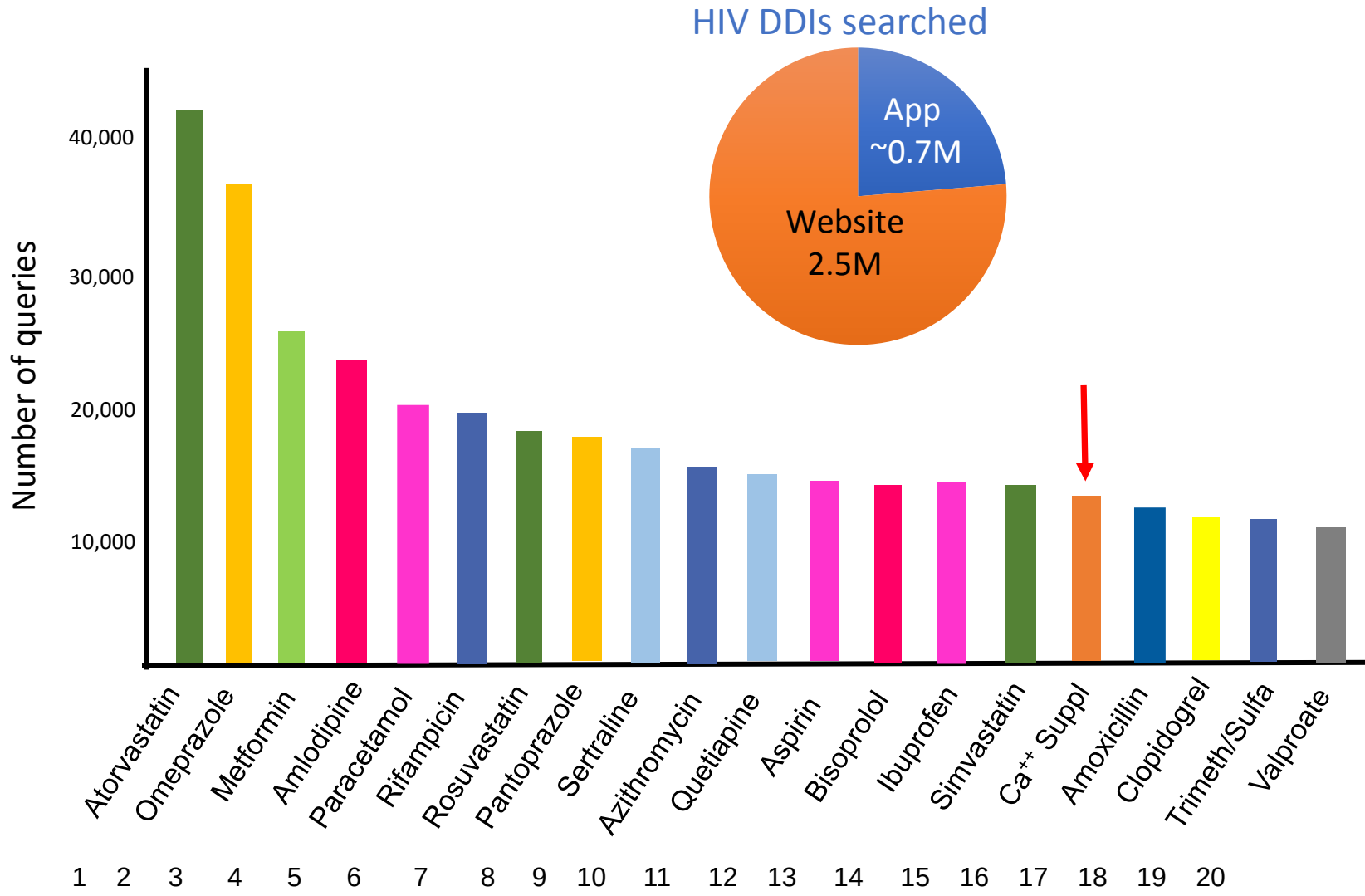
Emanuele Focà[1☯*], Paola Magro[1☯], Giovanni Guaraldi[2], Agostino Riva[3], Anna Maria Cattelan[4], Giuseppe Vittorio De Socio[5], Cecilia Costa[6], Stefania Piconi[7], Benedetto Maurizio Celesia[8], Silvia Nozza[9], Giancarlo Orofino[10], Antonella Castagna[9], Giovanni Di Perri[6], Francesco Castelli[1], Andrea Calcagno[6], on behalf of the GEPPO (GEriatric Patients living with HIV/AIDS: a Prospective Multidimensional cOhort) Study Group[¶]

Polypharmacy the same in men and Women!

Comorbidities	Females (n=210)	Males (n=1027)	Total (n=1237)	P value
CVD	14 (9.5%	154 (22.8%)	168 (20.46%)	<**0.001**
CKD	34 (21.3%)	150 (20.8%)	184 (20.8%)	0.381
Hypertension	113 (65.3%)	456 (64.5%)	569 (64.6%)	0.206
T2DM	38 (24.5%)	201 (29.1%)	239 (28.3%)	0.696
Bone disease	79 (48.8%)	134 (22.9%)	213 (28.5%)	<**0.001**
Hyperlipidemia	134 (75.3%)	497 (70.5%)	631 (71.4%)	0.076
COPD	7 (4.8%)	57 (8.6%)	64 (7.9%)	0.191
Cancer	30 (16%)	147 (22.3%)	177 (20.92%)	0.761
Polypharmacy (≥5 drug excluded cART)	42 (20%)	234 (22.8%)	254 (20.5%)	0.326

Foca E et al PLOS One Oct 17th 2019;

Top 20 Global Co-medication Searches: Jan 2020 to Aug 2020



Co-Medication	Malaysia Search
Atorvastatin	560
Metformin	559
Apixiban	549
Itraconazole	485
Rifampicin	428
Ca^{++} Supplements	391
Simvastatin	384
Sertraline	346
Fluticasone	313
Amlodipine	265

PPI, proton-pump inhibitor.

University of Liverpool. Top 20 Co-medications Generating the Most DDI Queries (MixPanel Analytics) Jan 2020 – Aug 15th 2020. Available at: www.hiv-druginteractions.org.

Co-Medications Frequently Used in Women

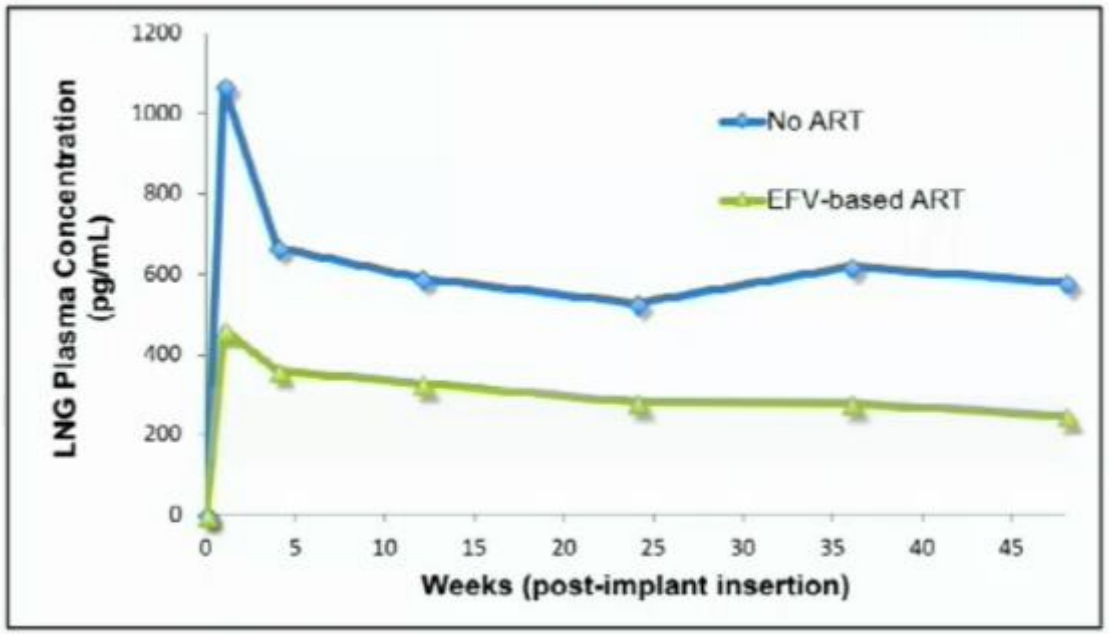
- ❑ Oral or Injectable Contraceptives
- ❑ HRT
- ❑ Supplements
- ❑ Herbal Remedies
- ❑ Anti-depressants
- ❑ Bisphosphonates
- ❑ Tamoxifen

Boffito M. http://www.infectiousdiseasesonline.com/9th-hiv-women-2019-presentations/

There are Important DDIs with Long Acting Contraceptives.

Unintended Pregnancies Observed With Combined Use of the Levonorgestrel Contraceptive Implant and Efavirenz-based Antiretroviral Therapy: A Three-Arm Pharmacokinetic Evaluation Over 48 Weeks[1]

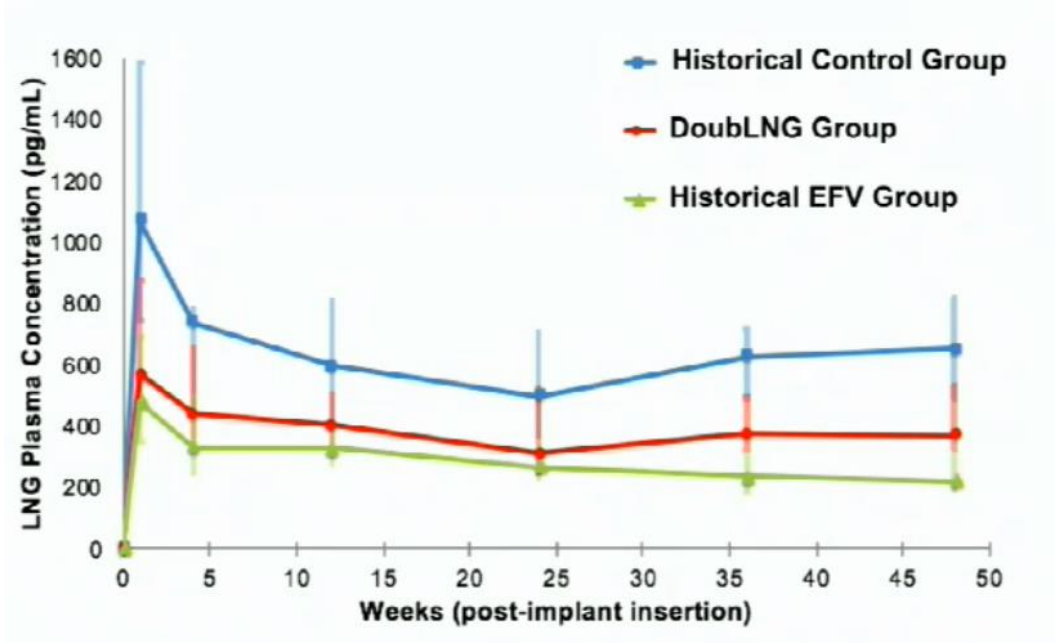
Kimberly K. Scarsi,[1] Kristin M. Darin,[2,3] Shadia Nakalema,[4] David J. Back,[5] Pauline Byakika-Kibwika,[4] Laura J. Else,[5] Sujan Dilly Penchala,[5] Allan Buzibye,[4] Susan E. Cohn,[3] Concepta Merry,[2,4,6] and Mohammed Lamorde[4]



3/20 women had unintended pregnancy in EFV Group

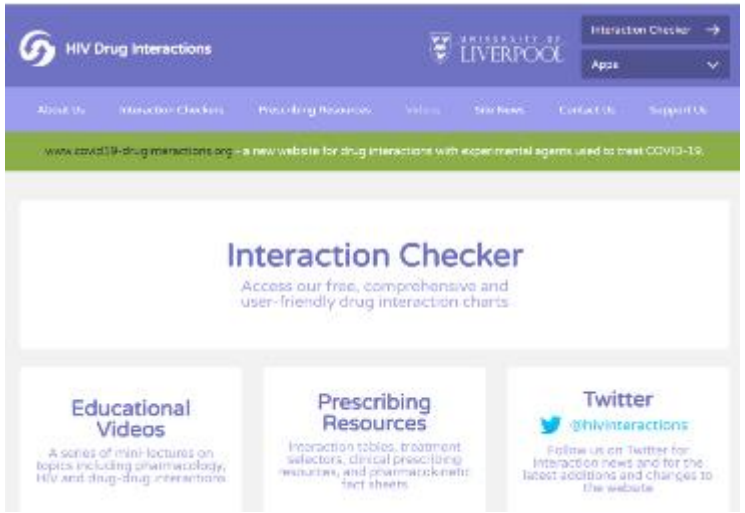
Double dose levonorgestrel implant does not fully overcome interaction with efavirenz.

Scarsi KK, *et al.* CROI 2019 O51



1. Scarsi KK, *et al. Clin Infect Dis* 2016; **62**(6):675–682;

ART Drug Interactions with HRT



www.hiv-druginteractions.org

LIVERPOOL

HRT Treatment Selector

Charts reviewed October 2019. Full information available at www.hiv-druginteractions.org

	ATV/c	ATV/r	DRV/c	DRV/r	LPV/r	DOR	EFV	ETV	NVP	RPV	MVC	BIC/ F/TAF	DTG	EVG/c/ F/TAF	EVG/c/ F/TDF	RAL	ABC	FTC or 3TC	F/TAF	TDF	ZDV
Estrogens																					
Estradiol	↑ [a]	↓ [b]	↑ [a]	↓ [b]	↓ [b]	↔	↓ [b]	↓ [b]	↓ [b]	↔	↔	↔	↔	↑ [a]	↑ [a]	↔	↔	↔	↔	↔	↔
Progestins (HRT)																					
Drospirenone	↑ [a,c]	↑ [a]	↑ [a]	↑ [a]	↑ [a]	↔	↓ [b]	↓ [b]	↓ [b]	↔	↔	↔	↔	↑ [a]	↑ [a]	↔	↔	↔	↔	↔	↔
Dydrogesterone	↑ [a]	↑ [a]	↑ [a]	↑ [a]	↑ [a]	↔	↓ [b]	↓ [b]	↓ [b]	↔	↔	↔	↔	↑ [a]	↑ [a]	↔	↔	↔	↔	↔	↔
Levonorgestrel	↑ [a]	↑ [a]	↑ [a]	↑ [a]	↑ [a]	↔	↓ [b]	↓ [b]	↓ [b]	↔	↔	↔	↔	↑ [a]	↑ [a]	↔	↔	↔	↔	↔	↔
Medroxy-progesterone (oral)	↑ [a]	↑ [a]	↑ [a]	↑ [a]	↑ [a]	↔	↓ [b]	↓ [b]	↓ [b]	↔	↔	↔	↔	↑ [a]	↑ [a]	↔	↔	↔	↔	↔	↔
Norethisterone (Norethindrone)	↑ [a]	↑ [a]	↑ [a]	↑ [a]	↑ [a]	↔	↓ [b]	↓ [b]	↓ [b]	↔	↔	↔	↔	↑ [a]	↑ [a]	↔	↔	↔	↔	↔	↔
Norgestrel	↑ [a]	↑ [a]	↑ [a]	↑ [a]	↑ [a]	↔	↓ [b]	↓ [b]	↓ [b]	↔	↔	↔	↔	↑ [a]	↑ [a]	↔	↔	↔	↔	↔	↔

Colour Legend

- No clinically significant interaction expected.
- These drugs should not be coadministered.
- Potential interaction which may require a dose adjustment or close monitoring.
- Potential interaction predicted to be of weak intensity. No *a priori* dosage adjustment is recommended.

Text Legend

- ↑ Potential increased exposure of the hormone
- ↓ Potential decreased exposure of the hormone
- ↔ No significant effect

Drug Interaction Concerns in Transgender Women

NIH National Institutes of Health
Turning Discovery Into Health

Sea

Health Information | Grants & Funding | News & Events | Research & Training

Home » News & Events » News Releases

NEWS RELEASES

Monday, July 24, 2017

Drug interaction concerns may negatively affect HIV treatment adherence among transgender women

Participants in NIH-supported study apprehensive about combining HIV medications and hormones.

Drug Interactions with Gender-Affirming Hormone Therapy: Focus on Antiretrovirals and Direct Acting Antivirals

Lauren R. Cirrincione , Tessa Senneker , Kimberly K. Scarsi & Alice Tseng

Cirrincione LR et al Ex Opinion Drg Met & Tox 2020 (Online July)

ART DDIs with Hormone Therapy for Gender Affirming

HIV Drug - PERPETRATOR

Estrogen and anti-androgen preparations for use in male to female gender reassignment therapy

		HIV drugs with no predicted effect	HIV drugs predicted to inhibit metabolism	HIV drugs predicted to induce metabolism
Estrogens		DOR, RPV, MVC, BIC, DTG, RAL ABC, ddI, FTC, 3TC, d4T, TAF, TDF, ZDV	ATV alone, ATV/cobi, DRV/cobi, EVG/cobi	ATV/r, DRV/r, FPV/r, IDV/r, LPV/r, SQV/r, TPV/r, EFV, ETV, NVP
Estradiol oral	*Starting dose*	2 mg/day	1 mg/day	Increase estradiol dosage as needed based on clinical effects and monitored hormone levels.
	Average dose	4 mg/day	2 mg/day	
	Maximum dose	8 mg/day	4 mg/day	
Estradiol gel (preferred for >40 y and/or smokers)	*Starting dose*	0.75 mg twice daily	0.5 mg twice daily	Increase estradiol dosage as needed based on clinical effects and monitored hormone levels.
	Average dose	0.75 mg three times daily	0.5 mg three times daily	
	Maximum dose	1.5 mg three times daily	1 mg three times daily	
Estradiol patch (preferred for >40 y and/or smokers)	*Starting dose*	25 µg/day	25 µg/day*	Increase estradiol dosage as needed based on clinical effects and monitored hormone levels.
	Average dose	50-100 µg/day	37.5-75 µg/day	
	Maximum dose	150 µg/day	100 µg/day	
Conjugated estrogen†	*Starting dose*	1.25-2.5 mg/day	0.625-1.25 mg/day	Increase estradiol dosage as needed based on clinical effects and monitored hormone levels.
	Average dose	5 mg/day	2.5 mg/day	
	Maximum dose	10 mg/day	5 mg/day	
Ethinylestradiol	*Starting dose*	No interaction expected, but not recommended due to thrombotic risks	Not recommended	Not recommended
	Average dose			
	Maximum dose			

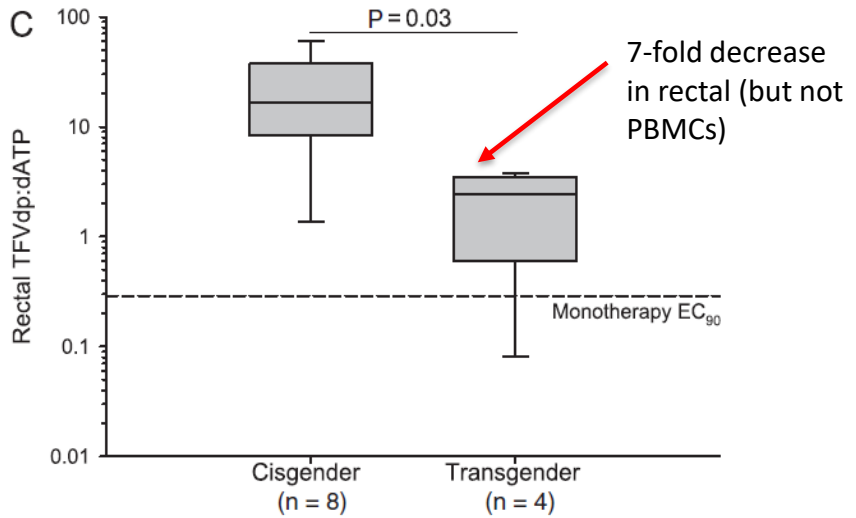
Androgen Blockers		DOR, RPV, MVC, BIC, DTG, RAL ABC, ddI, FTC, 3TC, d4T, TAF, TDF, ZDV	ATV alone, ATV/cobi, ATV/r, DRV/cobi, DRV/r, EVG/cobi, FPV/r, IDV/r, LPV/r, SQV/r, TPV/r	EFV, ETV, NVP
Spironolactone	*Starting dose*	50 mg/day	No interaction expected. No dose adjustment required.	No interaction expected. No dose adjustment required.
	Average dose	150 mg/day		
	Maximum dose	400 mg/day		
Finasteride	*Starting dose*	2.5 mg/day	Finasteride has a large safety margin. No dose adjustment required.	Increase finasteride dosage as needed based on clinical effects and monitored hormone levels.
	Average dose	2.5 mg/day		
	Maximum dose	5 mg day		
Cyproterone acetate	*Starting dose*	50 mg/day	25 mg/day	Increase cyproterone dosage as needed based on clinical effects and monitored hormone levels.
	Average dose	150 mg/day	75 mg/day	
	Maximum dose	150 mg/day	75 mg/day	

ART DDIs with Hormone Therapy for Gender Affirming

HIV Drug - VICTIM

Decreased Tenofovir Diphosphate Concentrations in a Transgender Female Cohort: Implications for Human Immunodeficiency Virus Preexposure Prophylaxis

Mackenzie L. Cottrell,[1] Heather M. A. Prince,[2] Amanda P. Schauer,[1] Craig Sykes,[1] Kaitlyn Maffuid,[1] Amanda Poliseno,[1] Tae-Wook Chun,[3] Erin Huiting,[3] Frank Z. Stanczyk,[4] Anne F. Peery,[5] Evan S. Dellon,[5] Jessica L. Adams,[6,7] Cindy Gay,[2] and Angela D. M. Kashuba[1,2]



7-fold decrease in rectal (but not PBMCs)

Transgender women on oral HIV pre-exposure prophylaxis have significantly lower tenofovir and emtricitabine concentrations when also taking oestrogen when compared to cisgender men

Eugenie Shieh[1], Mark A Marzinke[1,2], Edward J Fuchs[1], Allyson Hamlin[1], Rahul Bakshi[1], Wutyi Aung[1], Jennifer Breakey[1], Tonia Poteat[3], Todd Brown[4], Namandjé N Bumpus[1] and Craig W Hendrix[1,§]

Drug-drug interactions between feminizing hormone therapy and pre-exposure prophylaxis among transgender women: the iFACT study

Akarin Hiransuthikul[1§], Rena Janamnuaysook[1], Kanittha Himmad[1], Stephen J Kerr[2,3], Narukjaporn Thammajaruk[1], Tippawan Pankam[1], Kannapat Phanjaroen[1], Stephen Mills[4], Ravipa Vannakit[5], Praphan Phanuphak[1], Nittaya Phanuphak[1] and on behalf of the iFACT Study Team

These 3 cohort studies provide evidence that Feminizing Hormone Therapy may alter PrEP (TDF/FTC) pharmacology pointing to reduced efficacy or stricter adherence requirements.

Cottrell M et al CID 2019; 69: 2201-2204; Shieh E et al JIAS 2019; 22:e25405; Hiransuthikul A et al JIAS; 69: 22:e25338

Key Messages

- There is evidence of PK differences between Men and Women for orally administered ARVs ie higher drug exposure in women (~20%) *but* body weight is likely a key driver (along with reduced first pass metabolism).

  Difficult to pin point any clinical relevance of gender per se on oral PK.

- There is evidence of PK differences between Men and Women for LA CAB and RPV ie higher drug exposure in women after multiple dose and longer tail.

  Potential relevance for managing the PK tail after last injection

Key Messages

- There is evidence that polypharmacy is more common in women.

  There are 'problematic' co-medications that need monitoring with some ARVs.

- Note the important area of drug interactions with gender-affirming therapies.

  Potential for reduced efficacy of PREP.

Ethnicity: Sorry - that needs to be another discussion!

Grateful Thanks

Liverpool Website Team

David Back
Liverpool

Saye Khoo
Liverpool

Sara Gibbons
Liverpool

Catia Marzolini
Basel

Fiona Mara
Glasgow

representative

David Burger
Nijmegen

Justin Chiong
Liverpool

Katie Hodge
Liverpool

Jasmine Martin
Liverpool

Alison Boyle
Glasgow