milano

15 MAGGIO 2018

BASE B Fondazione the Bridge

IL DIRITTO ALLA SALUTE è DIRITTO di TUTTI

IL DOPPIO BINARIO

TRANSGENDER HIV e MALATTIE INFETTIVE

ENTE PROMOTORE

Fondazione theBRIDGE SCIENZA TRA CLINICA E SOCIETÀ

Interazioni farmacologiche tra ARV e ormoni

Marta Boffito

HIV and Transgender People

- TW high incidence of HIV acquisition

- Centers for Disease Control and Prevention 2013 meta-analysis estimated:
  - 22% of TW living with HIV in 5 high-income countries, including USA

www.cdc.gov/hiv

Braun et al. LGBT Health. 2017

- Study supported by NIH and Gilead among TW in LA
- >50% concerned that taking cART and feminizing hormone therapy (FHT) may be associated with harmful drug interactions
- Little is clinically understood
- Reason for not taking cART, FHT, or both

Demographics and self-reported treatment regimens of TW (n = 87) LA, CA, USA 2016

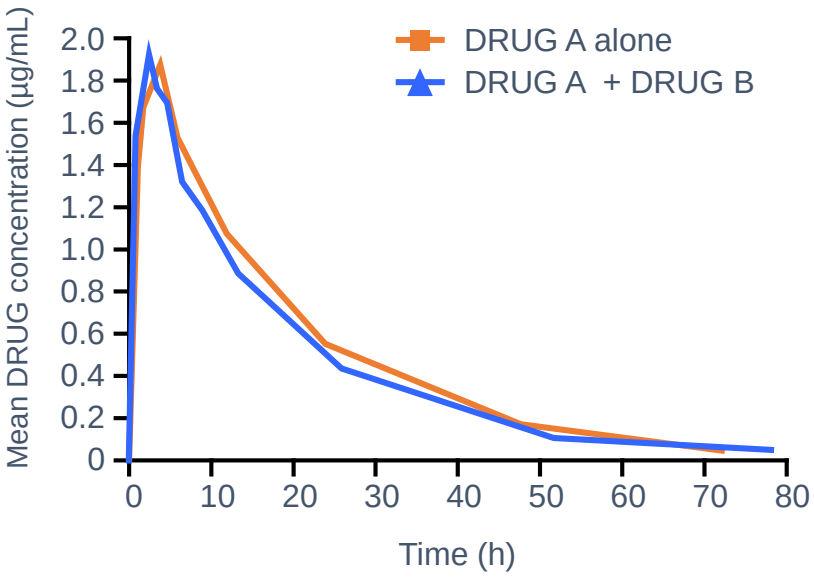
	HIV serostatus		
	All (n = 87)	*Not living with HIV (n = 40)*	*Living with HIV (n = 47)*
Age (years)*	45.3 (SD 10.8)	42.6 (SD 11.6)	47.5 (SD 9.7)
Living with HIV	47 (54%)	N/A	N/A
Race/ethnicity			
Hispanic	54 (62%)	26 (65%)	28 (60%)
Black/African American	15 (17%)	5 (13%)	10 (21%)
Multiracial	11 (13%)	3 (8%)	8 (17%)
Asian, Alaskan Native/American Indian, White, other	7 (8%)	6 (15%)	1 (2%)
Health insurance coverage			
Medi-Cal (California's Medicaid Program)	39 (45%)	14 (35%)	25 (53%)
Medicare	5 (6%)	4 (10%)	1 (2%)
Dual Medi-Cal–Medicare coverage or private plan	20 (23%)	9 (23%)	11 (23%)
No healthcare insurance	23 (26%)	13 (33%)	10 (21%)
Feminizing HT use			
Current use	56 (64%)	25 (63%)	31 (66%)
HT acquisition outside of medical system ($n = 55$; $n = 23$ HIV− and $n = 32$ HIV+)	14 (25%)	3 (13%)	11 (34%)
Planning future use	17 (20%)	10 (25%)	7 (15%)
No current or planned use	14 (16%)	5 (13%)	9 (19%)
Substance use (last 90 days)*	32 (37%)	10 (25%)	22 (47%)
Alcohol use (last 90 days)	43 (49%)	19 (48%)	24 (51%)
Current tobacco use	31 (36%)	12 (30%)	19 (40%)
Past tobacco use	14 (16%)	9 (23%)	5 (11%)
Unsupervised injections for body modification ($n = 81$; $n = 38$ HIV− and $n = 43$ HIV+)	11 (14%)	5 (13%)	6 (14%)
Antiretroviral therapy			
NRTI	—	1 (2.5%) [PrEP]	46 (98%)
Tenofovir[a]	—	1 (2.5%)	37 (79%)
Abacavir[a]	—	—	11 (23%)
NNRTI	—	—	13 (28%)
PI	—	—	15 (32%)
INSTI	—	—	19 (40%)
Current $CD4^+$ T lymphocyte count (cells/μL, median [IQR], $n = 44$)	—	—	555 (320–763)
HT and/or ART taken differently than prescribed due to DDI concern ($n = 43$)	—	—	17 (40%)
ART (only) taken differently than prescribed due to DDI concern	—	—	5 (12%)
HT (only) taken differently than prescribed due to DDI concern	—	—	5 (12%)
Both HT and ART taken differently than prescribed due to DDI concern			7 (16%)

Mean (standard deviation) or number (percent), unless specified. Percentages may not total 100 due to rounding.

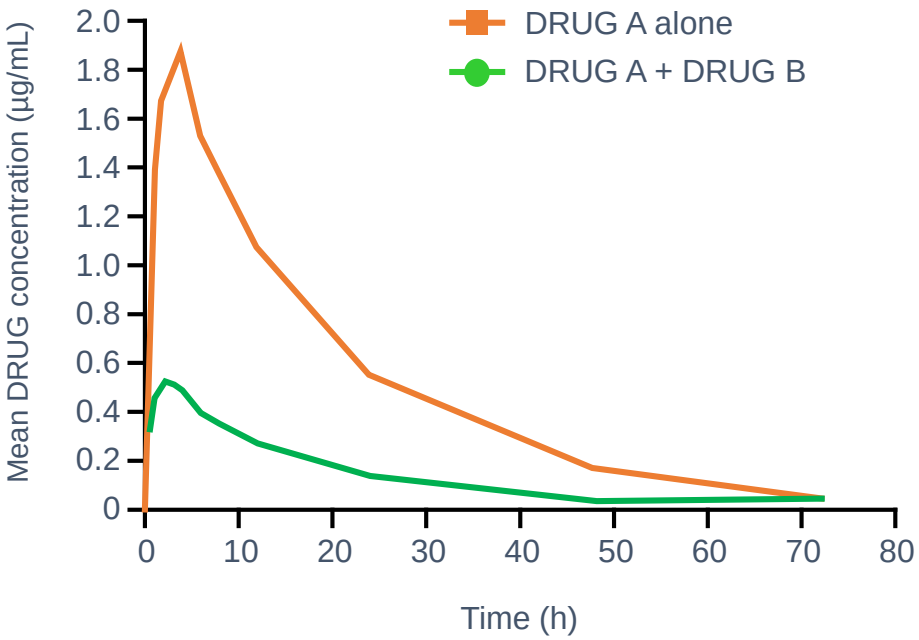
*$P < 0.05$ for transgender women living with HIV compared with transgender women not living with HIV.
[a]Participants were able to report therapy with both tenofovir and abacavir.

ART, antiretroviral therapy; DDI, drug–drug interactions; HT, hormone therapy; INSTI, integrase inhibitor; N/A, not applicable; NNRTI, non-nucleoside reverse transcriptase inhibitor; NRTI, nucleoside reverse transcriptase inhibitor; PI, protease inhibitor; PrEP, preexposure prophylaxis.

DDI


Mean DRUG concentration (µg/mL)
2.0
1.8
1.6
1.4
1.2
1.0
0.8
0.6
0.4
0.2
0
0
10
20
30
40
50
60
70
80
Time (h)
DRUG A alone
DRUG A + DRUG B

NO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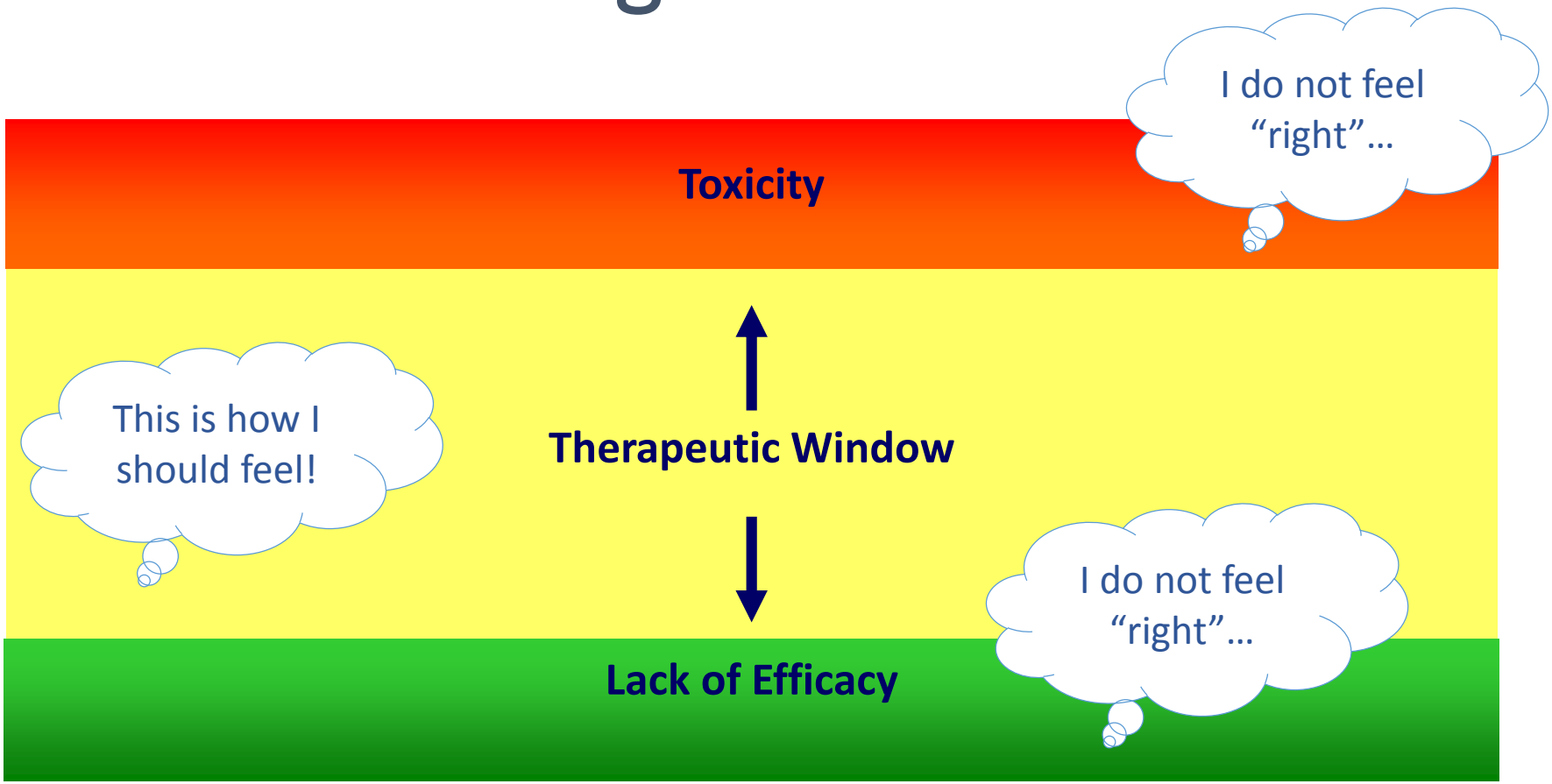
60
70
80
Time (h)
DRUG A alone
DRUG A + DRUG B

YES

Hormones and cART

- Drug interactions between FHT and cART have not been tested
- Data with oral contraceptives (OC)-containing ethinyl estradiol used as a guide
- FHT for TW (tablets, patches, injections) require a much higher dose of estrogen than that used in OC

Clinical significance of DDI



www.hiv-druginteractions.org

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Hormone Therapy for Gender Transitioning

Revised September 2017 *Page 1 of 2*

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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		RPV, MVC, DTG, RAL, NRTIs (ABC, ddI, FTC, 3TC, d4T, TAF, TDF, ZDV)	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		RPV, MVC, DTG, RAL, NRTIs (ABC, ddI, FTC, 3TC, d4T, TAF, TDF, ZDV)	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	
Goserelin	*Starting dose*	3.6 mg/month	No interaction expected. No dose adjustment required.	No interaction expected. No dose adjustment required.
	Average dose	3.6 mg/month		
	Maximum dose	3.6 mg/month		
Leuprorelin acetate	*Starting dose*	3.75 mg/month	No interaction expected. No dose adjustment required.	No interaction expected. No dose adjustment required.
	Average dose	3.75 mg/month		
	Maximum dose	3.75 mg/month		
Triptorelin	*Starting dose*	3.75 mg/month	No interaction expected. No dose adjustment required.	No interaction expected. No dose adjustment required.
	Average dose	3.75 mg/month		
	Maximum dose	3.75 mg/month		

† Conjugated estrogen is associated with high thromboembolic risk and therefore should be avoided.

* Matrix type transdermal patch can be cut in order to reduce the amount of hormone delivered/day.

Colour Legend

- No clinically significant interaction expected.
- Potential interaction which may require dosage adjustment and/or close monitoring.
- Coadministration is not recommended.

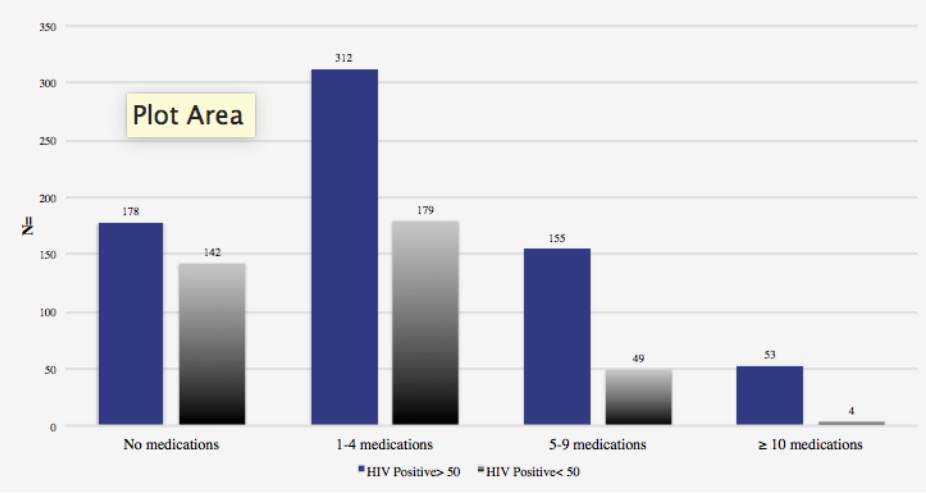
Estrogens		ATV/r, DRV/r, FPV/r, IDV/r, LPV/r, SQV/r, TPV/r, EFV, ETV, NVP
Estradiol oral	*Starting dose*	Increase estradiol dosage as needed based on clinical effects and monitored hormone levels.
	Average dose	
	Maximum dose	
Estradiol gel (preferred for >40 y and/or smokers)	*Starting dose*	Increase estradiol dosage as needed based on clinical effects and monitored hormone levels.
	Average dose	
	Maximum dose	
Estradiol patch (preferred for >40 y and/or smokers)	*Starting dose*	Increase estradiol dosage as needed based on clinical effects and monitored hormone levels.
	Average dose	
	Maximum dose	
Conjugated estrogen†	*Starting dose*	Increase estradiol dosage as needed based on clinical effects and monitored hormone levels.
	Average dose	
	Maximum dose	

POPPY
Pharmacokinetic and clinical observations in people over 50

Polypharmacy and potential drug-drug interactions in older and younger people living with HIV: The POPPY Study

M. O Halloran[1], C. Boyle[1], B. Kehoe[1], E. Bagkeris[2], P. Mallon[3], D. Babalis[4], J. Vera[5], A. Winston[4], C. Sabin[2], M. Boffito[4], for the POPPY Study
1Mater Misericordiae University Hospital, Pharmacy Department, Dublin, Ireland, 2University College London, London, United Kingdom, 3University College Dublin, Dublin, Ireland, 4Imperial College London, London, United Kingdom, 5Brighton and Sussex University Hospitals NHS Trust, Brighton, United Kingdom

Number of medications excluding ARVs in PLWH



CONCLUSIONS

- Older PLWH were more likely to have polypharmacy than HIV-negative controls or younger PLWH, even when ARVs were excluded.
- Older people were more likely to be at risk o Plot Area nvolving non-ARV/ARV drugs compared to younger PLWH.
- Older PLWH were more likely to be at risk of a PDDI involving non-ARV drugs than HIV-negative controls or younger PLWH.
- These results highlight the need for increased awareness and additional research around polypharmacy and all PDDI.

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Estradiol oral	*Starting dose*	2 mg/day	1 mg/day	Increase estradiol dosage as needed
	Average dose	4 mg/day		
	Maximum dose	8 mg/day		
Estradiol gel (preferred for >40 y and/or smokers)	*Starting dose*	0.75 mg twice daily		
	Average dose	0.75 mg three times daily		
	Maximum dose	1.5 mg three times daily		
Estradiol patch (preferred for >40 y and/or smokers)	*Starting dose*	25 µg/day		
	Average dose	50-100 µg/day		
	Maximum dose	150 µg/day		
Conjugated estrogen†	*Starting dose*	1.25-2.5 mg/day		
	Average dose	5 mg/day		
	Maximum dose	10 mg/day		
Ethinylestradiol	*Starting dose*	No interaction expected, but not recommended due to thrombotic risks		
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	Maximum dose			
Androgen Blockers		RPV, MVC, DTG, RAL, NRTIs (ABC, ddI, FTC, 3TC, d4T, TAF, TDF, ZDV)	EVG	
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Finasteride	*Starting dose*	2.5 mg/day	Fi	
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	Maximum dose	5 mg day		
Cyproterone acetate	*Starting dose*	50 mg/day		
	Average dose	150 mg/day		
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Goserelin	*Starting dose*	3.6 mg/month	No dose adjustment required.	No dose adjustment required.
	Average dose	3.6 mg/month		
	Maximum dose	3.6 mg/month		
Leuprorelin acetate	*Starting dose*	3.75 mg/month	No interaction expected. No dose adjustment required.	No interaction expected. No dose adjustment required.
	Average dose	3.75 mg/month		
	Maximum dose	3.75 mg/month		
Triptorelin	*Starting dose*	3.75 mg/month	No interaction expected. No dose adjustment required.	No interaction expected. No dose adjustment required.
	Average dose	3.75 mg/month		
	Maximum dose	3.75 mg/month		

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Colour Legend

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- Potential interaction which may require dosage adjustment and/or close monitoring.
- Coadministration is not recommended.

PrEP?

Conclusions

- Lack of knowledge of DDI is not an excuse not to manage DDI
- Individualized care
- Listen to how people feel rather than measure drug concentrations
- Need of data from EU

The TIME study: Trans people living with HIV throughout Europe