CHAP HIV101 Series

Antiretroviral drug-drug interactions
(or: I wish someone would explain drug interactions to me!)

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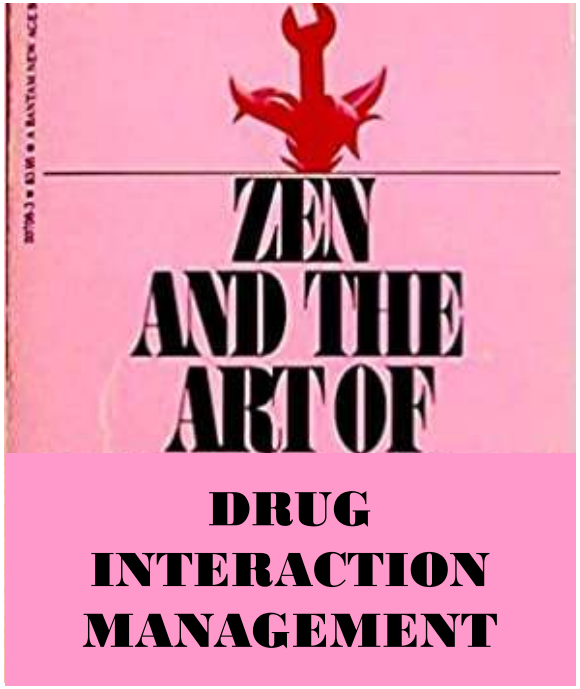
2026

Learning Objectives



- By the end of this three part-session, participants will be able to:

- Describe key mechanisms driving clinically significant DDIs with modern antiretrovirals.
- Identify high-risk ARVs and comedications.
- Apply a practical, structured framework to assess, prevent, and manage DDIs using reliable interaction resources.

Land Acknowledgement

Michener Gitigan, UHN Indigenous healing garden

Disclosures/Acknowledgements

- Consulting/advisory boards: Gilead, Merck, ViiV
- Research grants/coinvestigator: Gilead, Merck, ViiV

CHAP HIV101 Series

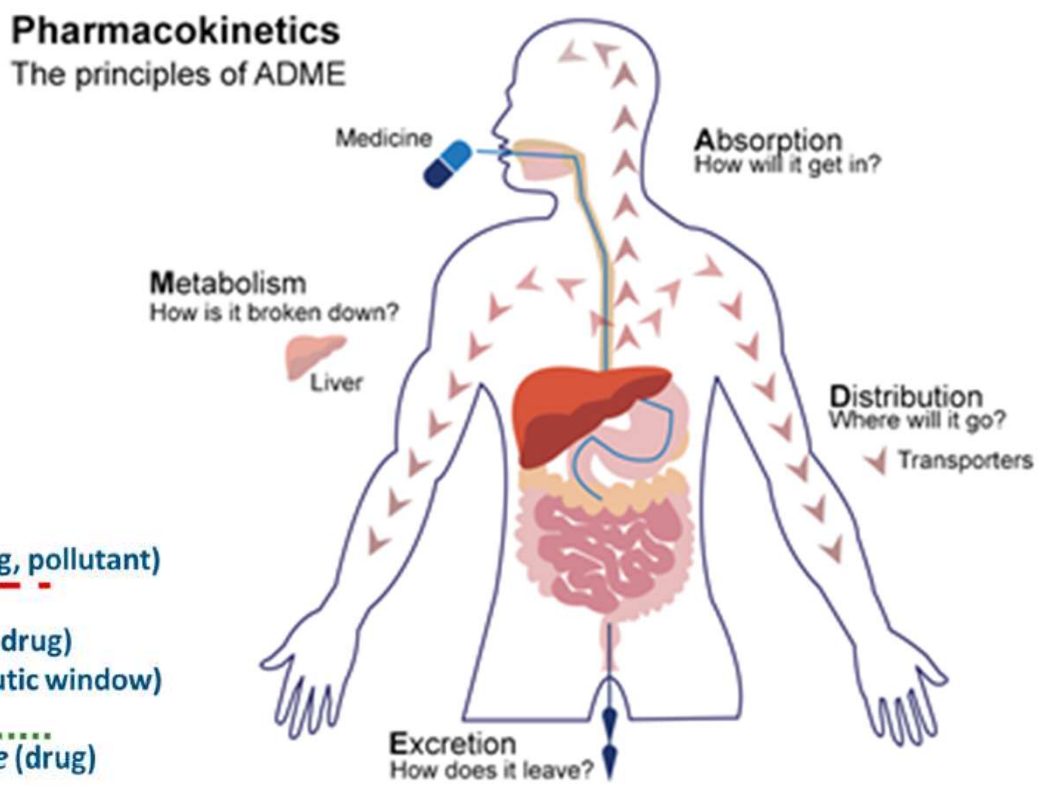
Drug-Drug Interactions: Part 1

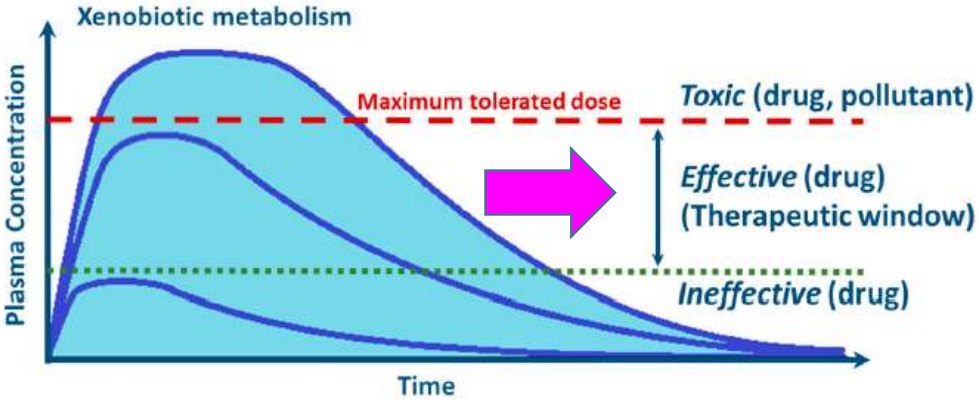
- Basics (terminology, mechanisms)
- DDI risks with older vs modern ART
- Inhibition interactions

DDI Primer

Acronym	Definition
DDI	Drug-drug interaction (also = didanosine, but not in this context) 
PK	***Pharmacokinetic*** interaction: • change in the <u>amount</u> of drug in body • absorption, distribution, metabolism, elimination can be impacted
PD	***Pharmacodynamic*** interaction: • change in the pharmacological <u>effect</u> of a drug • additive, synergistic, or antagonistic
Booster, PK enhancer	Agent which interferes with breakdown of another drug e.g., ritonavir, cobicistat • Allows drug to remain in body for longer at higher concentration • No effective anti-HIV activity

Pharmacokinetics : a drug's journey through the body





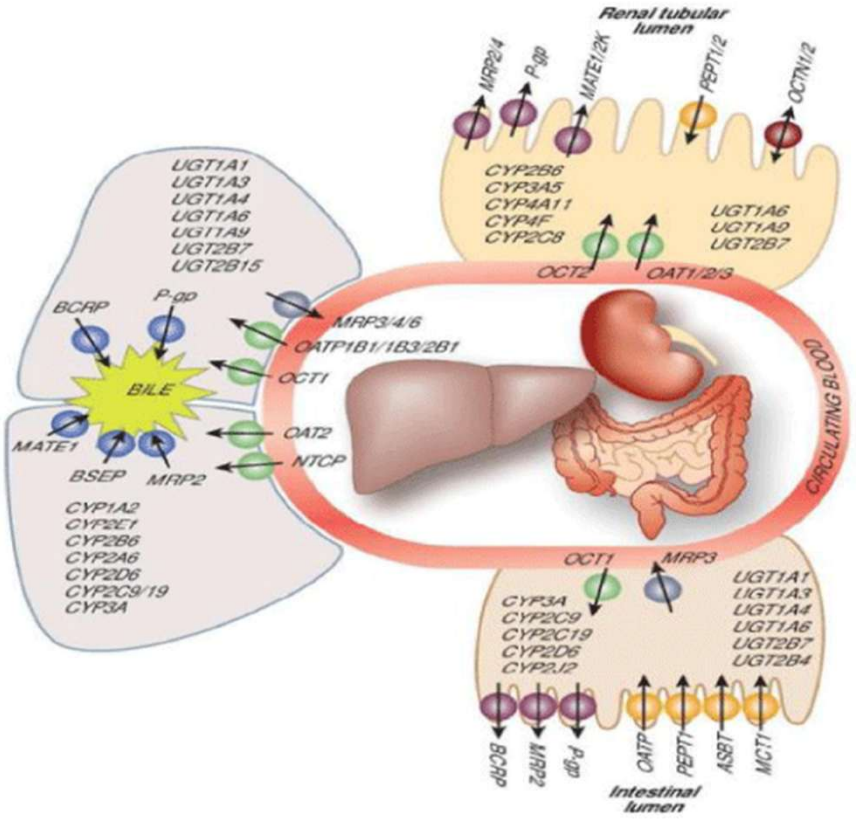
https://www.genomind.com/360/an-introduction-to-pharmacokinetics-four-steps-of-pharmacokinetics

Esteves et al. J Xenobiotics 2021;11:94-114.

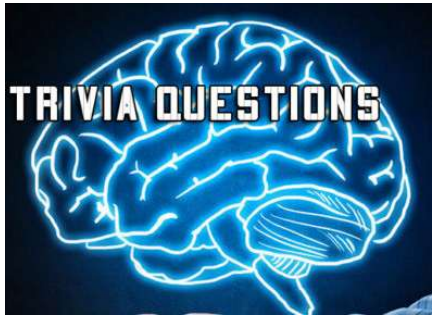
Drug metabolism: how the body breaks down drugs

- **Drug metabolizing enzymes:**
  - Cytochrome P450 (CYP); ***CYP3A4***
    - *also 2B6, 2C9, 2C19, 2D6, 1A2….*
  - UDP glucuronyl transferases (UGT); ***UGT1A1***

- **Drug transporters:**
  - mediate cellular uptake & efflux of xenobiotics
  - ***P-gp, BCRP, OATP1B1/3***
  - *OCT2, MATE1*



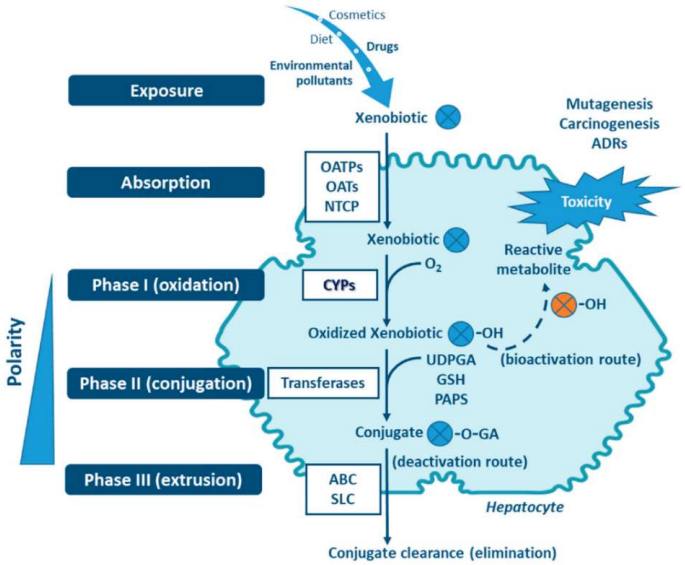
Bonus Question:
What does CYP450 stand for?



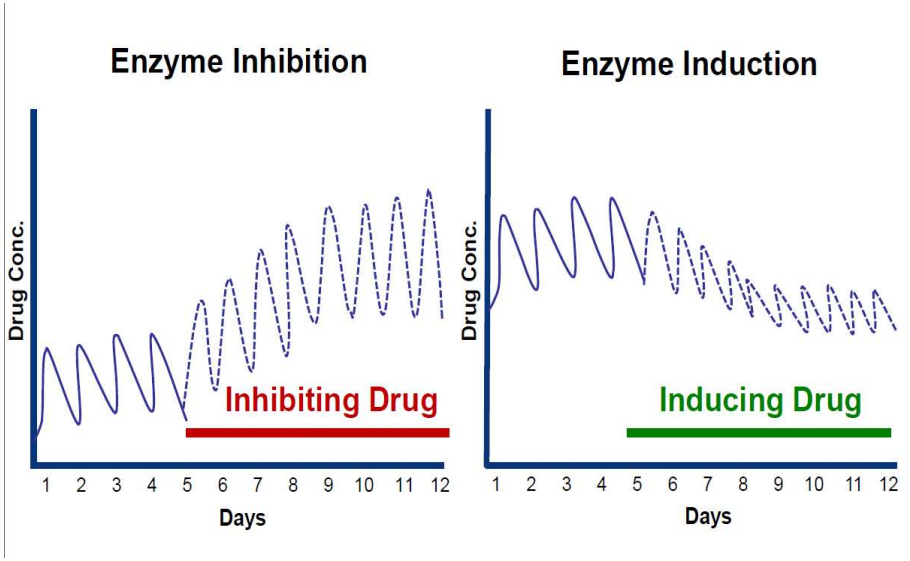
- CYP450 derived from:
  - initial beliefs that these enzymes were thought to be similar to mitochondrial **cytochromes**
  - they are red in colour (***p***igment)
  - they maximally absorb light at ***450*** nm wavelength under certain conditions

DDI Primer: Terminology

- Substrate ("victim")
  - Metabolized via CYP450 enzymes and/or taken up by transporters



- Inhibitors/Inducers ("perpetrators")
  - Impact rate of drug (substrate) clearance

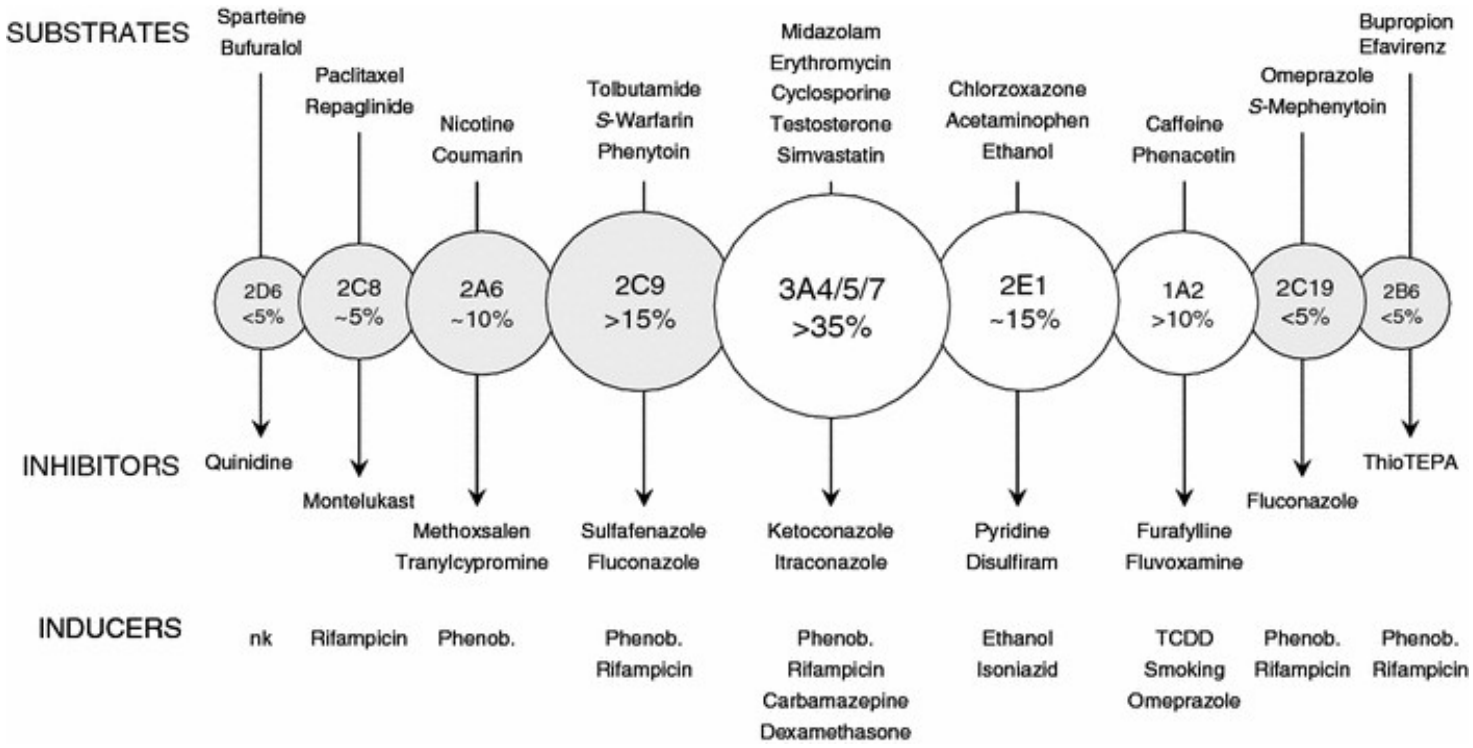


- Risk of drug toxicity
- Risk of decreased drug efficacy

Esteves F et al. J Xenobiotics 2021;11:94-114.

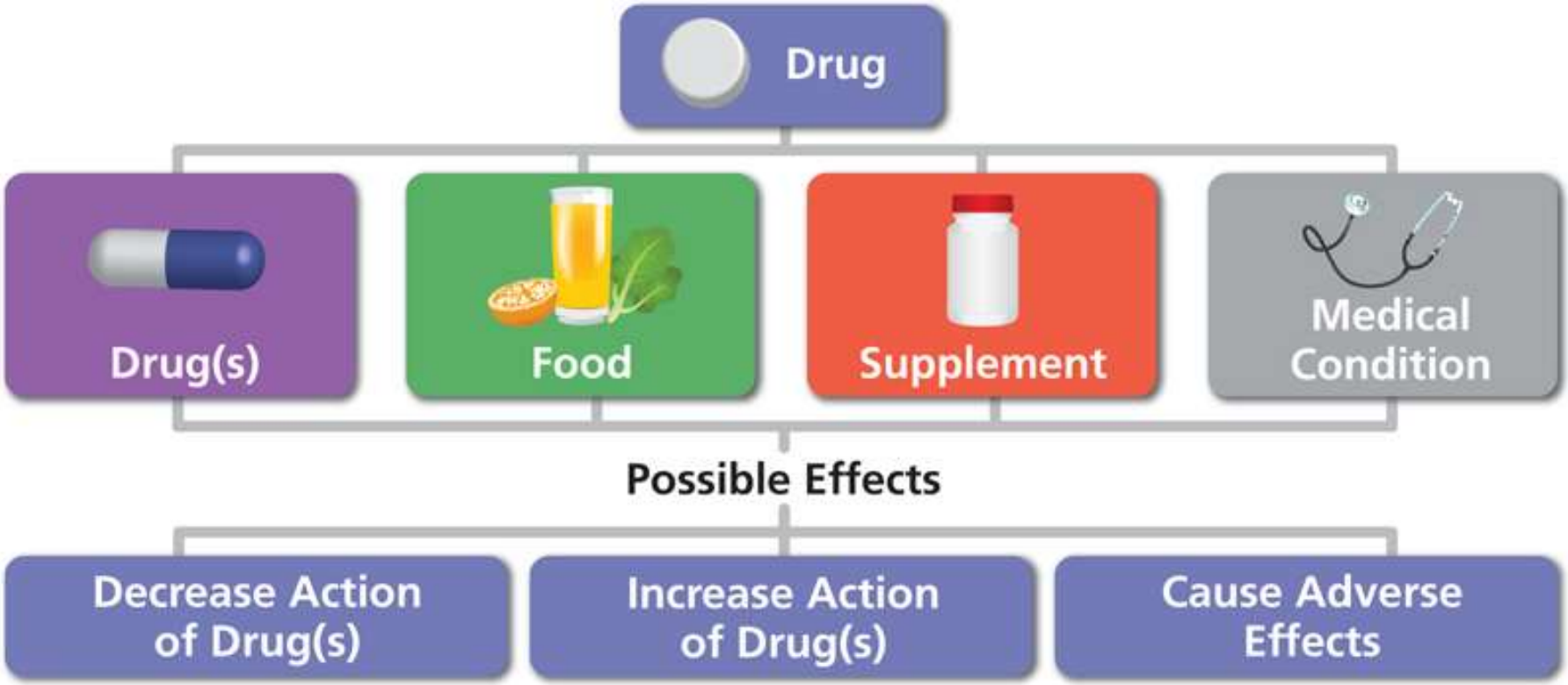
slide courtesy of Prof. D. Back

CYP enzymes: relative abundance in liver and examples of substrates, inhibitors & inducers



Pelkonen et al. Arch Toxicol 2008;82:667-715.

Drug Interaction



Interactions can be multi-directional

Rhabdomyolysis in a Prostate Cancer Patient Taking Ketoconazole and Simvastatin: Case Report and Review of the Literature

Jack L Watkins, Bradley J Atkinson, and Lance C Pagliaro

Ann Pharmacother 2011;45:e9.

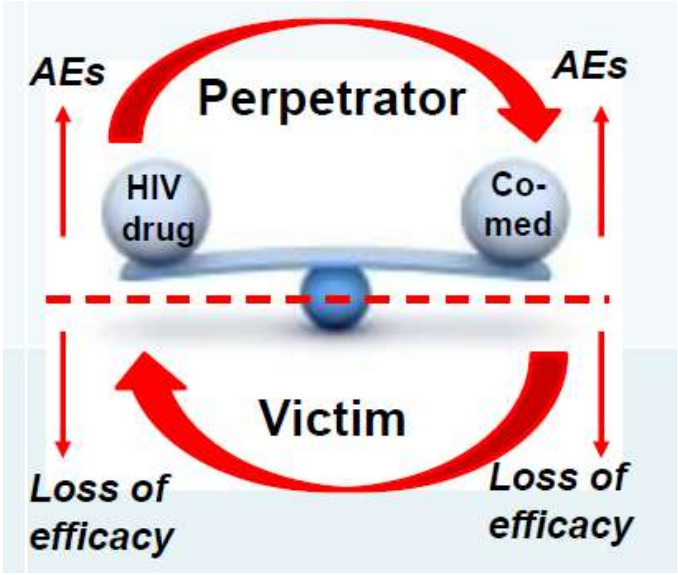


Figure courtesy of Prof. David Back

Coadministration of Lopinavir/Ritonavir and Phenytoin Results in Two-Way Drug Interaction Through Cytochrome P-450 Induction

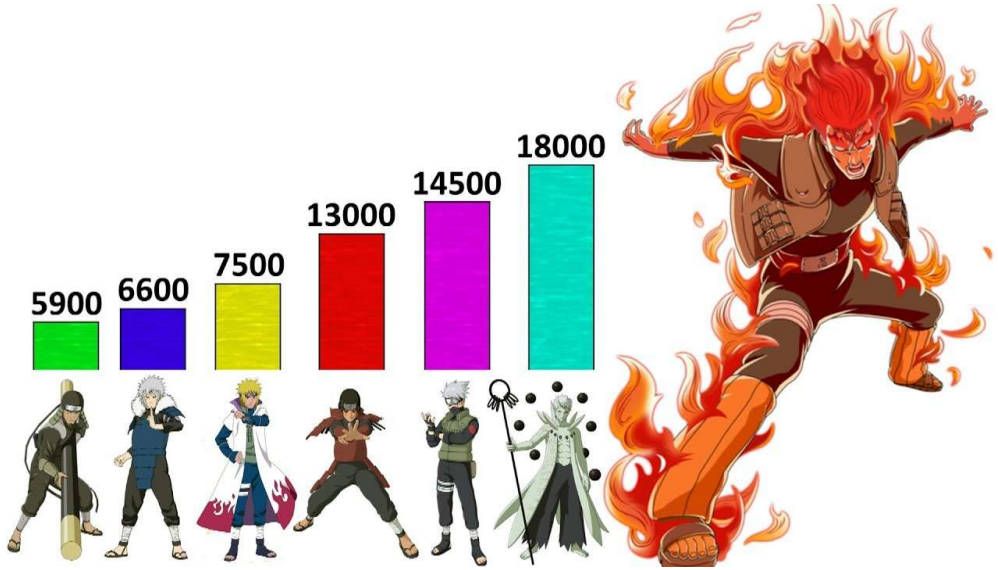
(*J Acquir Immune Defic Syndr* 2004;36:1034–1040)

Pharmacokinetics of a Three-Way Drug Interaction Between Danoprevir, Ritonavir and the Organic Anion Transporting Polypeptide (OATP) Inhibitor Ciclosporin

Clin Pharmacokinet (2013) 52:805–813

Drug interaction potential of antiretrovirals:

Assess:	Consider:
Can it be a victim?	Is absorption affected by anything?
	How is it metabolized or cleared?
Can it act as a perpetrator?	Does it inhibit or induce enzymes or transporters?

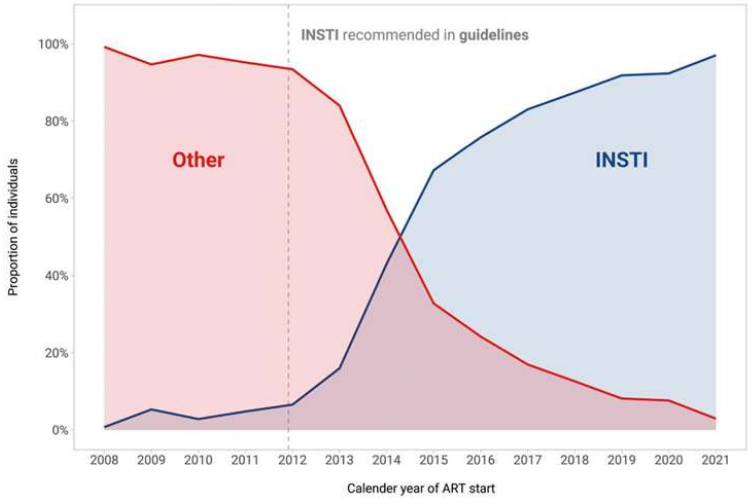


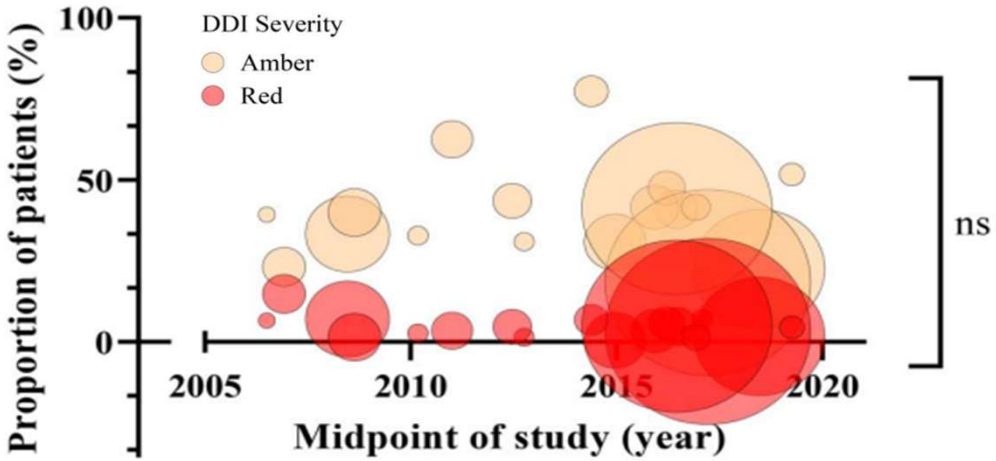
Perpetrator	RTIs, NNRTIs (newer) < INSTIs < LEN, FOS < NNRTIs (older) < PIs
Victim	INSTIs, LEN, NNRTIs, FOS, TAF, PIs

Do drug interactions even matter with modern antiretroviral therapies?

Higher Rates of DDIs in Older People With HIV

- Despite shift to INSTI use, prevalence of amber & red DDIs have remained stable
- Positive correlation between red DDIs & age





Surial et al. Clin Infect Dis 2023;77:729-37. Hodge et al. JAIDS 2023;92:97-105.

Drug Interactions with Modern ART

Evolving factors:

- *Antiretroviral therapy choices*
  - Shift from PIs, NNRTIs to INSTIs
  - 3DR to 2DR treatment
  - Long-acting regimens

- *Patient population*
  - Aging, polypharmacy
  - Multi-resistant virus
  - Pharmacology of newer ARVs

What type of DDIs are important with modern antiretrovirals?

- Absorption
- Metabolism (inhibition/induction)

Gastric pH Interactions

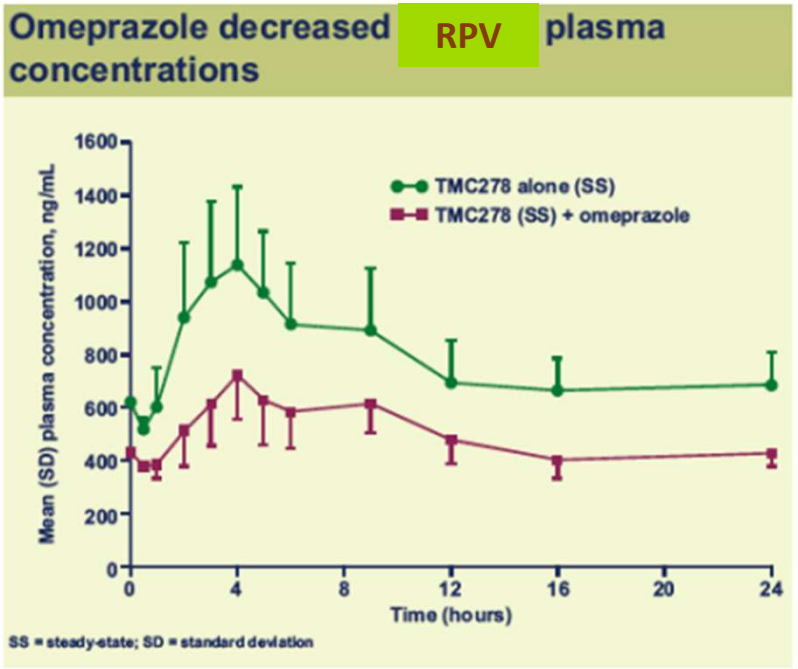
NNRTI	**Rilpivirine (Odefsey, Complera, Edurant, Juluca, Cabenuva*)** *during oral lead-in period
PI	**Atazanavir (Reyataz, Evotaz)**

+

- Acid suppressing drugs:
  - PPIs, H2RAs, antacids

Management:

- PPIs contraindicated
- H2RAs, antacids: space apart dosing
- Or consider alternate ARV
  - Rilpivirine → doravirine
  - Atazanavir → darunavir
  - Different ARV class



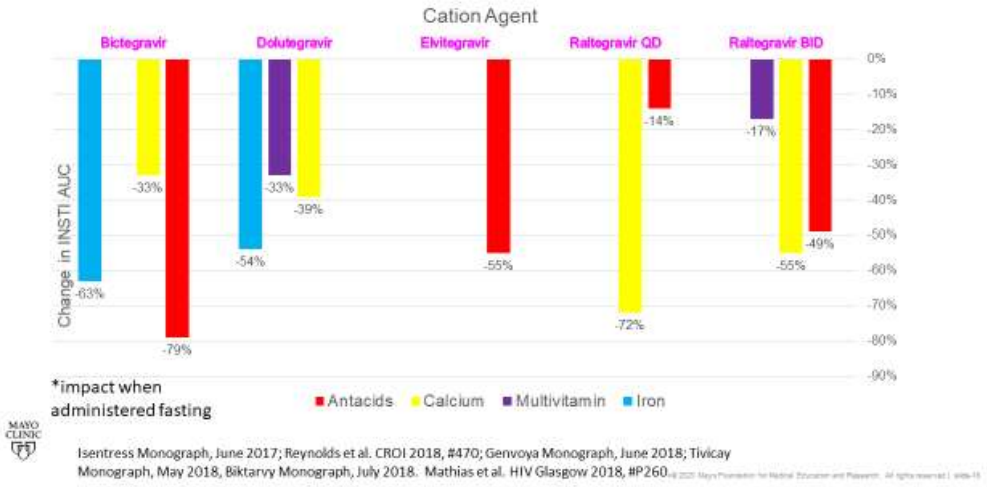
Chelation Interactions

INSTI	**ALL:** **Bictegravir, cabotegravir*, dolutegravir, elvitegravir, raltegravir** *during oral lead-in period

+

- Cation-containing agents
  - Antacids, supplements

Impact of Cation-Containing Agents on INSTI Absorption



Isentress Monograph, June 2017; Reynolds et al. CROI 2018, #470; Genvoya Monograph, June 2018; Tivicay Monograph, May 2018, Biktarvy Monograph, July 2018. Mathias et al. HIV Glasgow 2018, #P260.

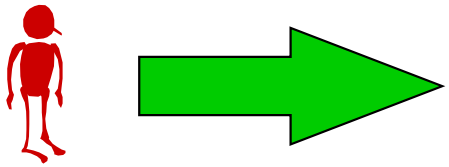
- Use of polyvalent cations while on INSTI associated with ↑ risk of virologic failure

Reminder	
Management	Space apart dosing or give together with food.
	*Specific recommendations vary according to individual INSTI
	Many polyvalent cation products can be purchased without Rx (OTC, CAM)

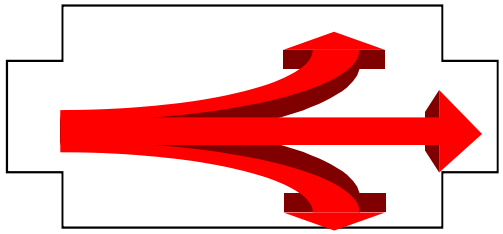
James et al. AIDS 2020;34:487-9. Peng et al. AIDS 2021;35:2054-7.

Understanding Drug Interactions: CYP450 & Transporters "Revolving Door" analogy

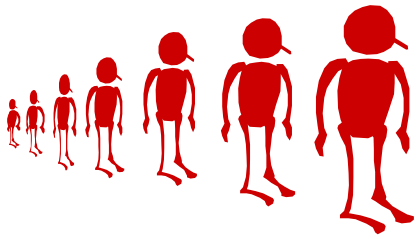
Entrance



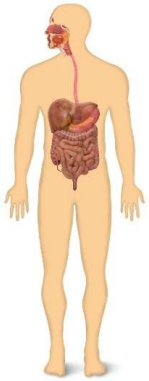
Inside Building



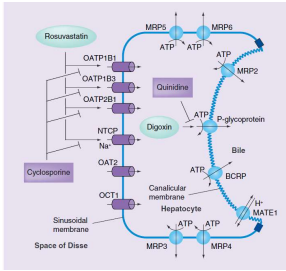
Exit



Drug (Substrate)

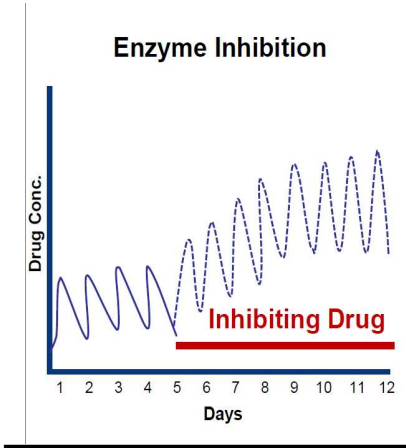


Body



Enzyme/ transporters

Inhibition Interactions

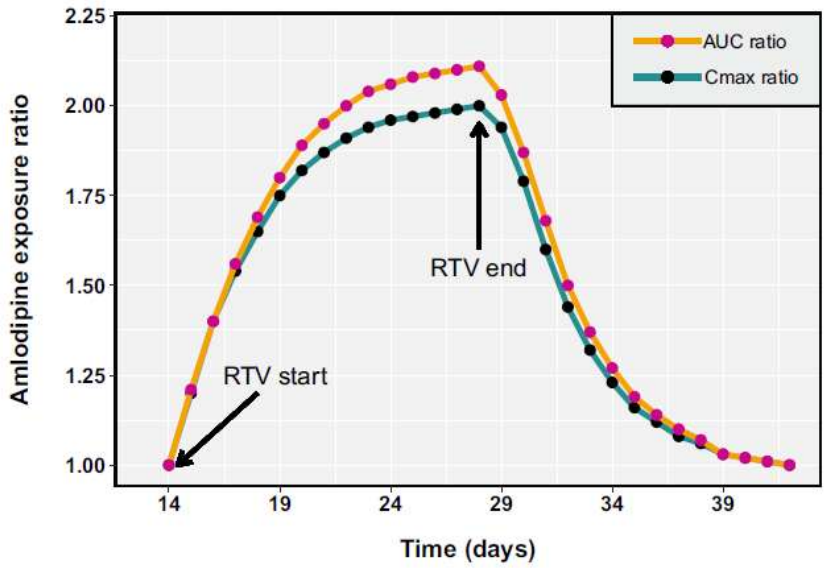


- Inhibitor competes with another drug for binding/uptake at enzymatic or transporter site
- ↓ clearance of substrate = ↑ drug concentration

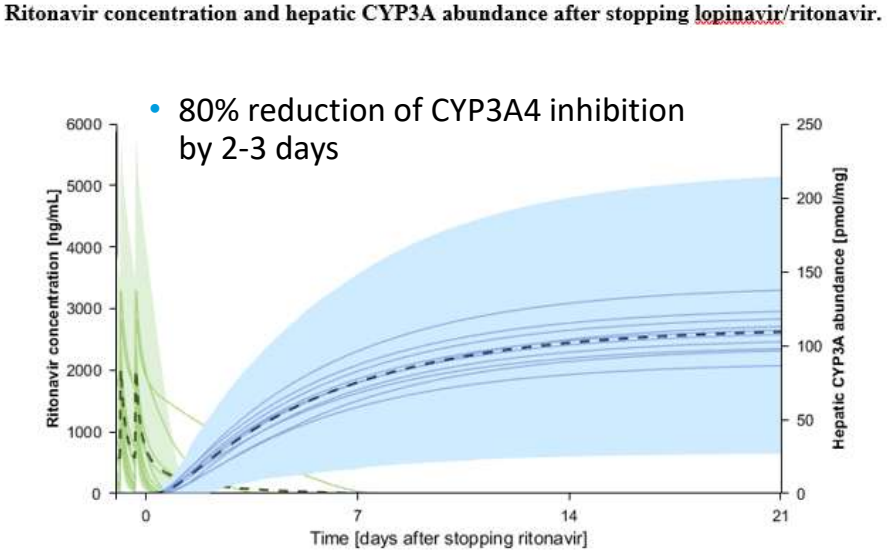
PIs	**All (with ritonavir or cobicistat)**	**CYP3A4, transporters**
INSTIs	**Elvitegravir/cobicistat**	**CYP3A4, transporters**
	Dolutegravir > bictegravir	OCT2, MATE1
NNRTI	Etravirine	2C19
Capsid	Lenacapavir	CYP3A4
AI	Fostemsavir	transporters
Co-meds	**Azoles, macrolides**	**3A4, P-gp**

Time Course of Inhibition Interactions

- Usually a competitive and reversible process (quick onset & offset)



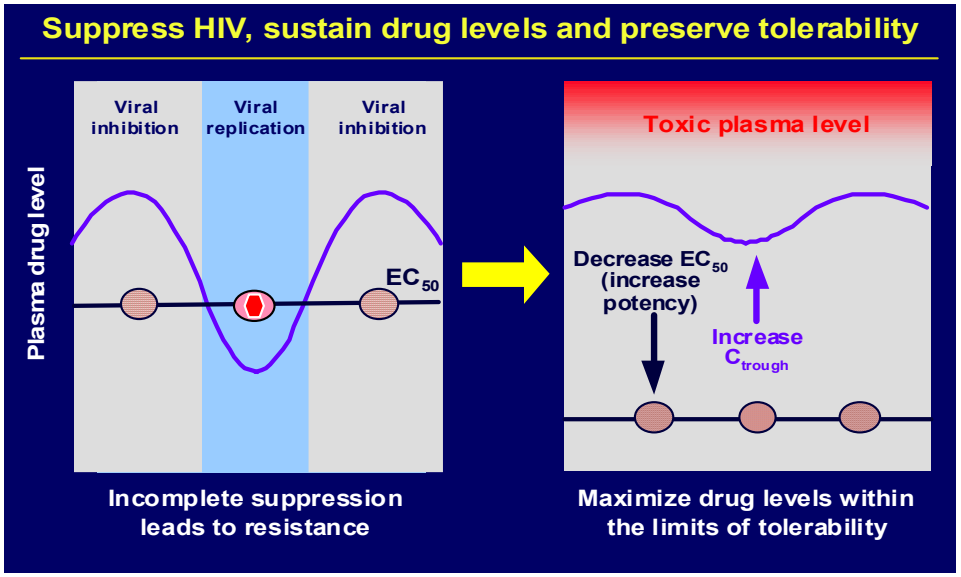
Mukherjee et al. J Pharmacokinet Pharmacodynamics 2018;45:443-56.



Stader et al. JAC 2020;75:3084-6.

Inhibition Interactions: The Good, The Bad & the Ugly

- PK boosters:
  - PIs (darunavir, lopinavir, atazanavir)
  - Elvitegravir/cobicistat (Stribild, Genvoya)
  - HCV DAA: Paritaprevir/ritonavir (Holkira Pak)
  - COVID antiviral: nirmatrelvir/ritonavir (Paxlovid)



Severe rhabdomyolysis-induced acute kidney injury following concomitant use of Genvoya® (EVG/COBI/FTC/TAF) and simvastatin; a case report

Rita Godinho, Serge Bugnon, Terezija Gracin and James Tataw

Godinho *et al. BMC Nephrology* (2019) 20:69

Fatal interaction between ritonavir and MDMA

J A Henry, I R Hill

THE LANCET • Vol 352 • November 28, 1998

ISMP Canada Safety Bulletin

Drug Interaction Incident with HIV Post-exposure Prophylaxis

and serum drug levels, the cause of death was determined to be fentanyl toxicity due to an interaction with Kaletra.

Case

- 60 yo male, HIV+ 1987, extensive ARV Hx and resistance
  - Virally suppressed >10 years on tenofovir/FTC/efavirenz, abacavir, darunavir/ritonavir BID, VL<50

- Recent diagnosis diffuse large B cell lymphoma of stomach & small bowel (stage 2Ae)
- Started CHOP x 6 cycles
  - ritonavir d/c by oncologist because of interaction concern with cyclophosphamide
  - continued with darunavir, abacavir, tenofovir/FTC/efavirenz

Darunavir Dosing (Prezista mongraph)

- Effect of ritonavir on darunavir:
  - ↑ darunavir AUC 14-fold with ritonavir

- PREZISTA must be administered with low-dose ritonavir to ensure its therapeutic effect.
- Failure to correctly co-administer PREZISTA with ritonavir will result in reduced plasma levels of PREZISTA that may be insufficient to achieve the desired antiviral effect.

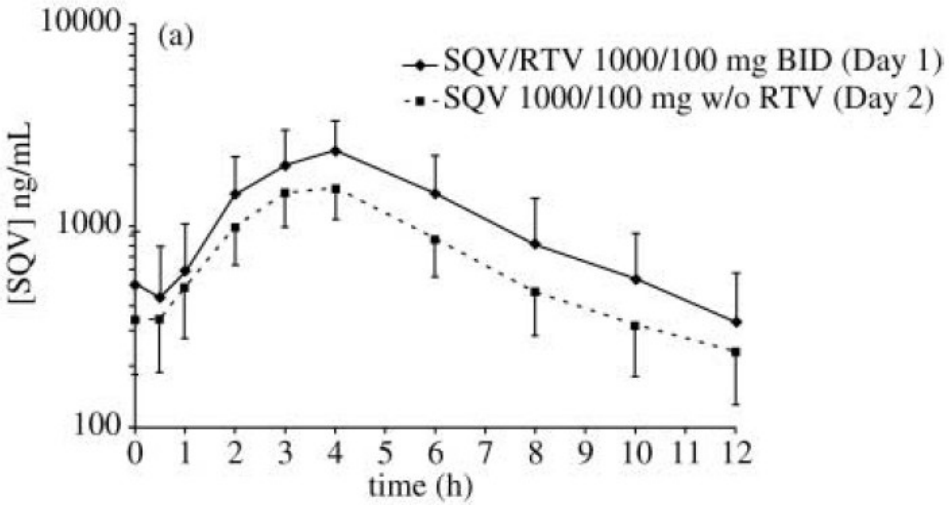
Case: follow-up

- Three months later: CD4 203, VL 2,459 copies/mL
- TDM: Subtherapeutic concentrations of darunavir
  - no ritonavir booster, inducing effect of efavirenz
  - already had 4 darunavir RAMS

- Restarted ritonavir but unable to completely resuppress VL
- Added INSTI → VL<50, CD4 244

Inhibition Interactions: Practical Considerations

Boosted Antiretrovirals	
Management	Take booster at same time as partner ARV



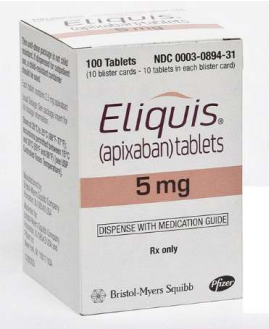
- RTV 100 mg once daily does not adequately boost BID SQV

	Comedication Interactions
Onset	Rapid
Management	Dose reduction of substrate drug
Monitoring	Counsel patients to monitor for adverse effects within first few days
After stopping inhibitor	Can resume original dose once inhibitor is cleared (2-3 days)

- May also consider:
  - replacing drug with something less likely to interact (ARV or comed)
  - Temporarily discontinuing comedication
  - Additional monitoring (incl. labwork, TDM)

Boffito et al. JAC 2005;55:542-5.

Recommendations Can Differ According to DDI Resource



CA	Contraindicated
EU	Not recommended
US	Reduce apixaban dose

Case report

INTERNATIONAL JOURNAL OF STD & AIDS

Ritonavir- or cobicistat-boosted antiretroviral therapy and direct oral anticoagulants: A case for apixaban

International Journal of STD & AIDS
2019, Vol. 30(7) 718–722

DOI: 10.1177/0956462419832099
journals.sagepub.com/home/std
SAGE

Sarah A Nisly[1] and Brooke N Stevens[2]

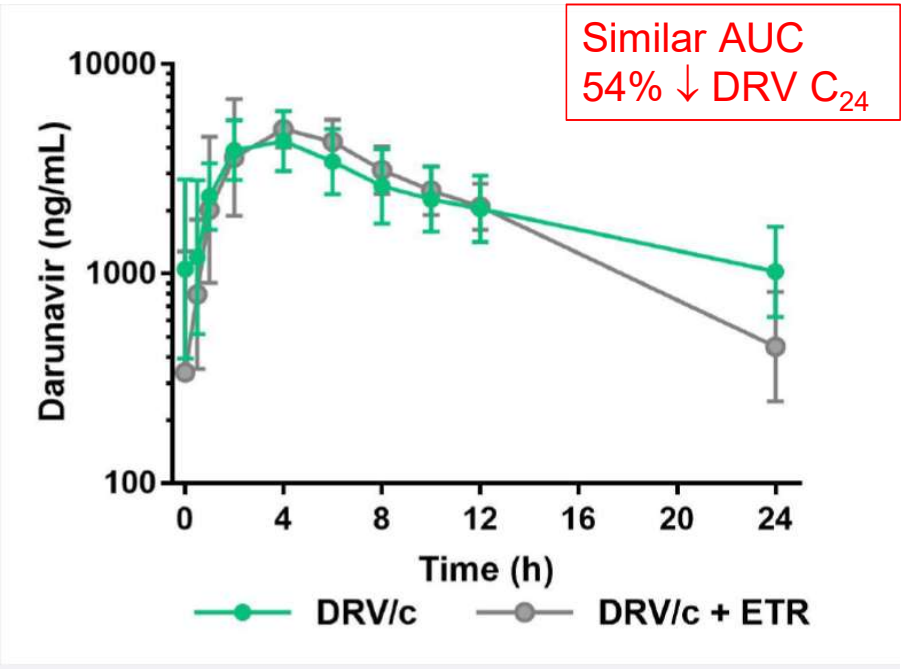
DDI information	
	Monographs, DDI resources often country specific Case series/reports can be informative

Not all boosters are the same

- Generally, cobicistat 150 mg provides equivalent boosting to ritonavir 100 mg (but some exceptions)

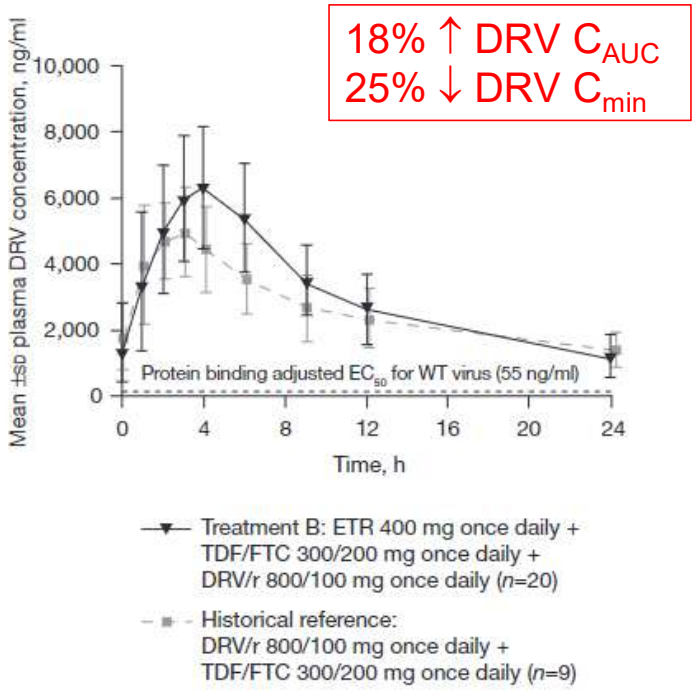
Sometimes ritonavir is a more potent inhibitor than cobicistat

- Darunavir/c + Etravirine



- Molto et al. HIV PK 2017.

- Darunavir/r + Etravirine



DeJesus et al. Antiviral Ther 2010;15:711-20.

Sometimes cobicistat is a more potent inhibitor than ritonavir

A Curious Tale: Quetiapine Toxicity with Cobicistat but not with Ritonavir in a Person Living with HIV

Duncan A[1], Syme T[2], Mackie K[1], Grannell L[1], Lewin S[3,4]

[1]Alfred Health Pharmacy Department, [2] Alfred Health Department of psychiatry, [3] The Doherty Institute, [4]Alfred Health Department of Infectious Diseases

- 58 yo male, stable on quetiapine 1000 mg daily plus 3TC, TAF, DTG, DRV/r BID
- DRV/r BID → DRV/cobi, no other changes
- +++ sedation; continued despite ↓ quetiapine to 700 mg
- Changed back to DRV/r, increased quetiapine to 1000 mg with no adverse effects

Pharmacokinetic Interaction Between Single and Multiple Doses of Darunavir, in Combination With Cobicistat or Ritonavir, and Single-dose Dabigatran Etexilate in Healthy Adults

Sandy Van Hemelryck,[1]* Erika Van Landuyt,[1] Jay Ariyawansa,[1] Martyn Palmer,[1] Martine J.C. Kothe,[2] Caroline Polleflet[2]

[1]Janssen Pharmaceutica NV, Beerse, Belgium; [2]Clinical Pharmacology Unit, Janssen Research & Development, Merksem, Belgium

	Darunavir/c	Darunavir/r
Multiple doses:		
Dabigatran AUC	1.88-fold ↑	1.18-fold ↑
Dabigatran Cmax	1.99-fold ↑	1.22-fold ↑

- ↑ dabigatran & thrombin time concentrations with COBI but not ritonavir
- Case reports of therapeutic dabigatran concentrations with DRV/r, ATV/r, LPV/r suggest standard dosing is safe in normal renal function

Posters 197, HIV Glasgow 2022. Van Hemelryck et al. AAPS Open 2024;10:10.
Kumar et al. AAC 2017;61:e01201-17. Kakadiya et al. AAC 2018;28:e02275-17.

Case

- 70 yo male, HIV+ since 1990, MDR-HIV. Virally suppressed since 2001; on dolutegravir and darunavir/cobicistat

- Comorbidities:
  - stroke, depression, diabetes, hypertension, renal insufficiency (eGFR 40)

- Comedications:
  - citalopram 20 mg
  - diltiazem 180 mg
  - loxapine 10 mg
  - methylphenidate 10 mg BID
  - pantoprazole 40 mg
  - rosuvastatin 20 mg
  - benztropine 1 mg BID
  - ferrous fumarate 300 mg
  - KCl 8 mmol

Case – con't

- Recent admission for falls/upper GI bleed. DOAC changed from edoxaban to apixaban 2.5 mg BID due to renal function.

- Significant interaction between darunavir/cobicistat and apixiban
  - Contraindicated in Canadian monograph
  - US monograph states ok to reduce apixiban by 50% to 2.5 mg BID in normal renal function; avoid if already taking low dose apixaban

- Switched to fostemsavir 600 mg BID plus dolutegravir 50 mg daily

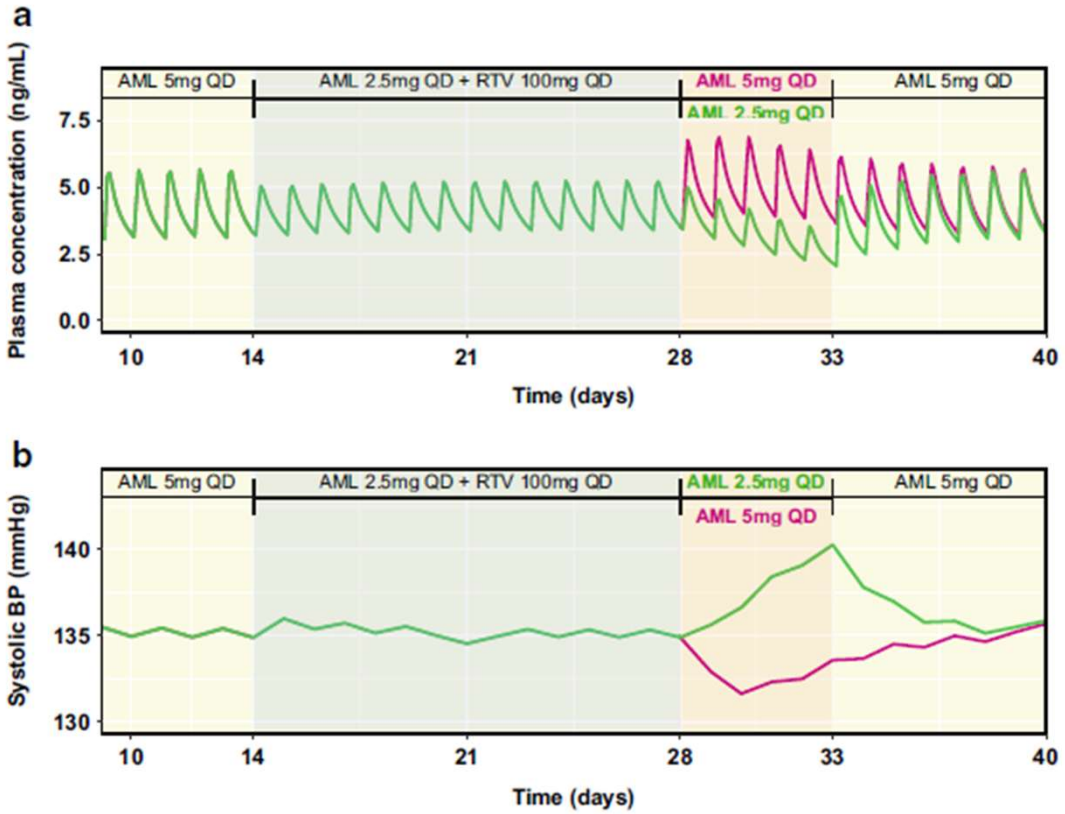
Case – con't

- Two months later, elevated BP (in 200s) noted at nephrology follow-up
- Nephrologist felt it was due to fostemsavir, recommended going back to darunavir/cobicistat

- Hypertension not mentioned in fostemsavir monograph
- Removal of darunavir/cobicistat likely led to a reduction in diltiazem

After discontinuing ritonavir, amlodipine concentrations drop and blood pressure increases

- Modelling study on dose adjustment of calcium channel blocker (amlodipine) with/without ritonavir



Mukherjee et al. J Pharmacokinet Pharmacodynamics 2018;45:443-56.

Case – con't

- → explained mechanism of interaction with nephrologist, agreed to go back to fostemsavir
- Titrate diltiazem from 180 mg to 240 mg daily, then 360 mg if needed

- Lesson: it's not just what you start, but what you stop!

Stopping Antiretroviral Inhibitors

- Concentrations of comedications which are currently being boosted may decrease once the inhibitor is stopped
- Review all comedications and identify drugs which may require follow-up/dose adjustment after ART switch

	Comedication Interactions
Onset	Rapid (2-3 days after stopping inhibitor)
Management	Dose increase of substrate drug
Monitoring	Counsel patients to monitor for therapeutic effect within first few days/weeks; TDM or other lab parameters as appropriate
After stopping inhibitor	Can titrate to standard dose to maintain efficacy

Part 1: Key Takeaways

Modern HIV Drug–Drug Interactions: Key Points for Clinicians

1. Key Concepts

- **PK vs. PD:**
  Substrates ("Victims") vs. Inhibitors/Inducers ("Perpetrators")

- **Critical Pathways:**
  CYP3A4,
  UGT1A1,
  P-gp, BCRP, OATP

2. Major DDI Mechanisms

Absorption

- ***Gastric pH:***
  RPV, ATV, vs. PPIs/H2RAs

- ***Chelation:***
  INSTIs + Cations
  ↓ Exposure

Metabolism

- ***Inhibition:***
  Fast, ▲ Drug Levels

3. Boosters Are Not Equivalent

- **Ritonavir** = Inhibitor + Inducer
- **Cobicistat** = Inhibitor Only

Consider effect on co-medications when:

- **Stopping** boosters
- **Switching** boosters

CHAP HIV101 Series

Antiretroviral drug-drug interactions
(or: I wish someone would explain drug interactions to me!)

Alice Tseng, Pharm.D., FCSHP, AAHIVP

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Immunodeficiency Clinic, University Health Network

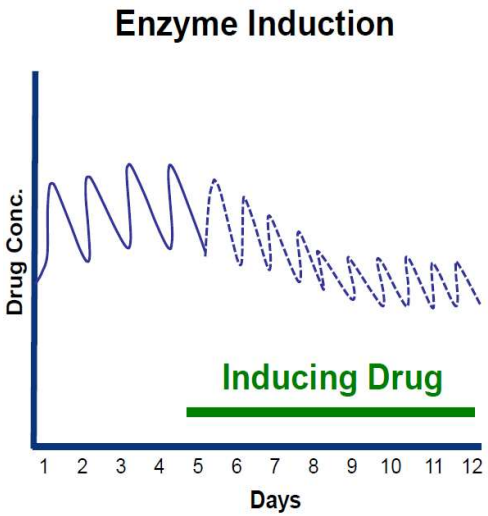
2026

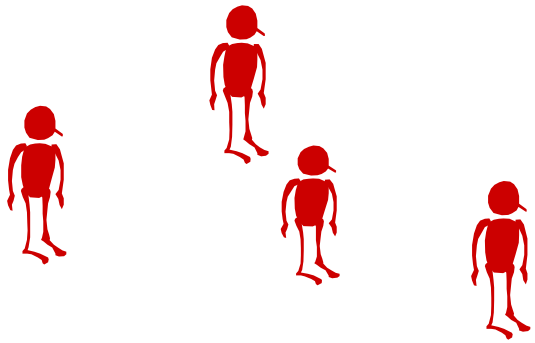
CHAP HIV101 Series

Drug-Drug Interactions: Part 2

- Induction DDIs
- DDIs with non-oral medications
- DDIs with LA-ART

Induction Interactions

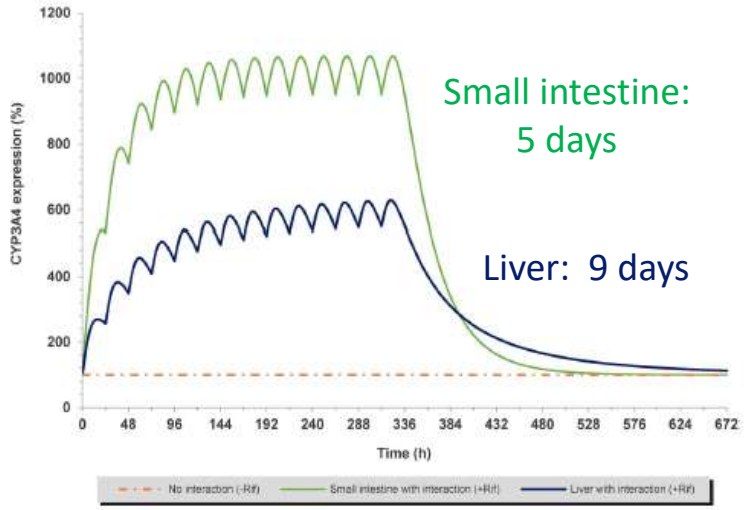




- Inducer stimulates production of additional metabolic enzymes/transporters
- ↑ clearance of substrate = ↓ drug concentrations
  - Risk of ↓ efficacy, development of resistance

Time Course of Induction Interactions

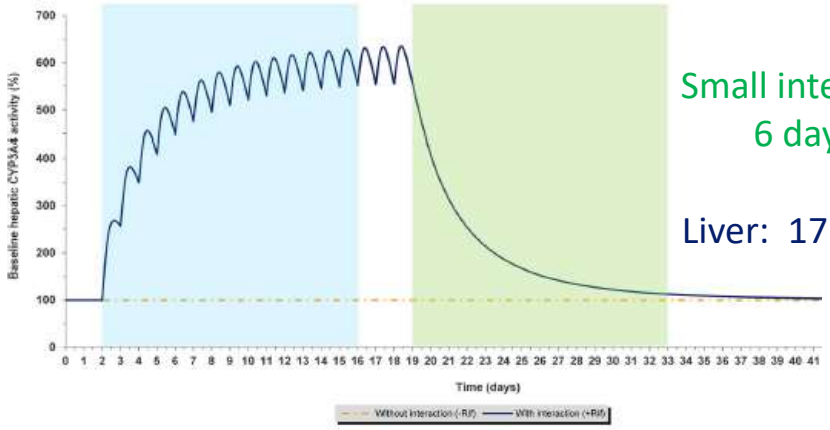
Onset of Induction: 5-9 days (RIF)



Small intestine: 5 days

Liver: 9 days

Enzyme De-Induction: 6-17 days (RIF)



Small intestine: 6 days

Liver: 17 days

Kapetas et al. AAPS Journal 2019;21:78.

Case

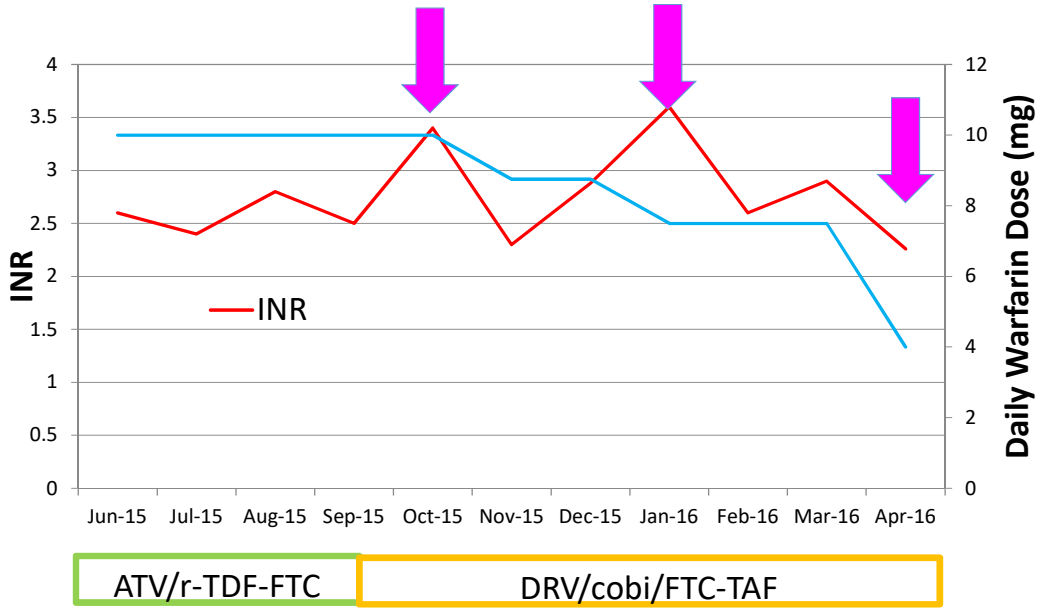
- 72 yo male on atazanavir/ritonavir +2 NRTIs with suppressed VL, CD4 437 cells/mm3
  - Past MI, CABG, atrial flutter, COPD/emphysema, neuropathy

- Switched to darunavir/cobicistat/emtricitabine/TAF STR
  - Concomitant meds: acyclovir, pravastatin, EC ASA, metoprolol, warfarin, Advair, salbutamol, pregabalin
- Had been on stable warfarin dose of 10 mg daily for over the past year with a recent INR of 2.5 prior to antiretroviral switch

INR increase after switching from atazanavir/r to darunavir/cobicistat

Time after ART switch	Daily Warfarin Dose	INR
Baseline	10 mg	2.5
1 month	↓ to 8.75 mg	3.4
5 months	↓ to 7.5 mg	3.6
8 months	↓ to 4 mg	2.5

- A 60% ↓ in warfarin dose was required



Tseng et al. AIDS 2017;31:176-6.

Cobicistat Versus Ritonavir: Similar Pharmacokinetic Enhancers But Some Important Differences

Annals of Pharmacotherapy
2017, Vol. 51(11) 1008–1022

DOI: 10.1177/1060028017717018
journals.sagepub.com/home/aop
SAGE

- Both inhibit CYP3A4 and transporters
- Ritonavir induces various metabolic enzymes and pathways
- Cobicistat has no inducing effects

	Ritonavir	Cobicistat
CYP3A4	inhibit	inhibit
P-gp, BCRP, OATP1B1/3, MATE1	inhibit	inhibit
CYP1A2, 2B6, 2C9/2C19	*induce*	-
UGT	*induce*	-

Tips:

- Be mindful when switching from one booster to another

Tseng A et al. Ann Pharmacother 2017;5:1008-22.

Inducing Agents

NNRTIs	Efavirenz, etravirine, nevirapine	CYP3A4, 2B6
PIs	Ritonavir (*but not cobicistat!)	CYP1A2, 2B6, 2C9/19, UGT
INSTIs	Elvitegravir/cobicistat	2C9
Co-meds	rifamycins, anticonvulsants, St. John's Wort, dexamethasone	3A4, P-gp 

Starting/Stopping Inducers

	Interaction Considerations
Onset	Delayed
Management	Dose increase of substrate drug
Monitoring	Counsel patients to monitor for therapeutic effect within first 1-2 weeks
After stopping inducer	Can titrate to original dose after de-induction period (~2-4 weeks)
Switching boosters	Ritonavir → cobicistat: • May need to ↓ substrate dose Cobicistat → ritonavir: • May need to ↑ substrate dose

- Doravirine monograph:

Co-administration is contraindicated with these anticonvulsants.

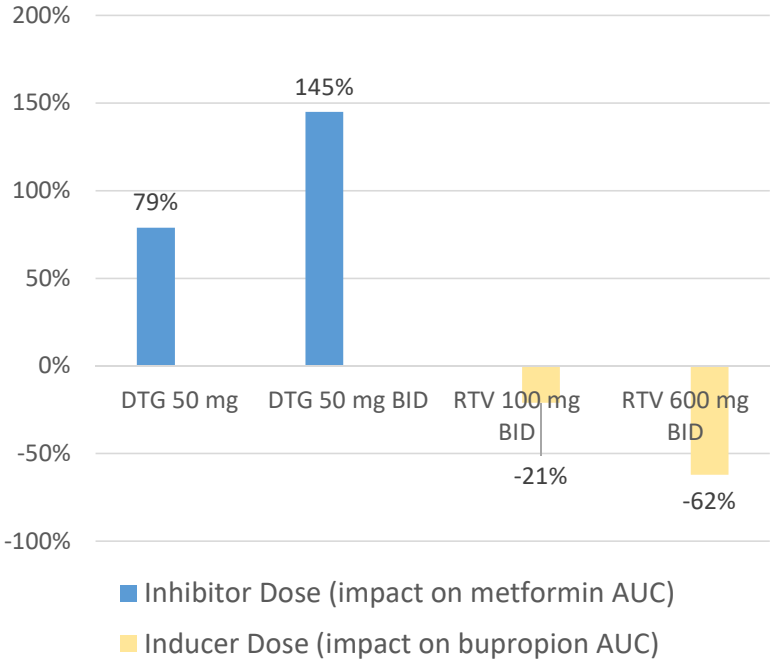
At least a 4-week cessation period is recommended prior to initiation of PIFELTRO.

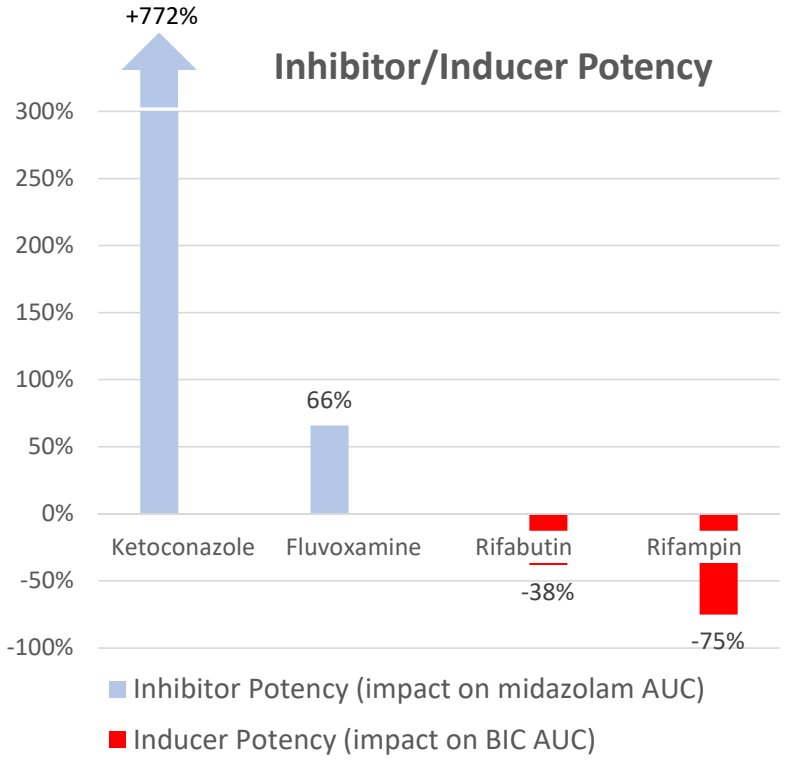
With Drug Interactions, Size Matters!

- Dose

- Potency (inducing or inhibiting effect)

Enzyme Inhibition & Induction: Dose and Potency





Song et al. JAIDS 2016;72:400-7. Lam et al. J Clin Pharmacol 2003;43:1274-82. Biktarvy monograph, 2018. Dooley et al. JAIDS 2013;62:21-7.

Case

- 57 yo male, HIV+ >30 years, extensive HIV resistance
- Virally suppressed since 2007 on darunavir/ritonavir, etravirine and raltegravir BID, and tenofovir DF/emtricitabine
- Diagnosed with prostate cancer; progressed on 1st line treatments; oncologist recommended enzalutamide

- However, limited ARV treatment alternatives
  - Susceptible only to darunavir/r, etravirine, INSTIs

Enzalutamide is a potent inducer (≅ rifampin)

Induction effects	Data	Potential ARVs impacted
CYP3A4 (strong)	86% ↓ midazolam AUC	PIs, NNRTIs, INSTIs (BIC>DTG), fostemsavir, lenacapavir
CYP2C19 (moderate)	70% ↓ omeprazole AUC	Etravirine (minor)
CYP2C19 (moderate)	56% ↓ s-warfarin AUC	Etravirine, rilpivirine (minor)
CYP2B6 (possible)	In vitro effects	Efavirenz, nevirapine (minor)
UGT1A1 (possible)	In vitro effects	INSTIs (RAL, CAB, DTG>BIC), lenacapavir

- Long t1/2: effects on enzymes may persist for ≥1 month or longer after stopping

Enzalutamide can significantly decrease ARVs

Merative **Micromedex**®

Drugs:	Severity:	Documentation:	Summary:
ENZALUTAMIDE -- RITONAVIR	Contraindicated	Fair	Concurrent use of ENZALUTAMIDE and RITONAVIR may result in reduced ritonavir exposure, potential for loss of virologic response and possible resistance, increased enzalutamide exposure and an increased risk of enzalutamide-related toxicity.
ENZALUTAMIDE -- ETRAVIRINE	Major	Fair	Concurrent use of ENZALUTAMIDE and ETRAVIRINE may result in decreased enzalutamide plasma concentrations; decreased etravirine plasma concentrations.

Lexicomp®

Drug-Drug Interactions

- X Enzalutamide (CYP3A4 Inducers (Strong)) – Etravirine
- X Enzalutamide (CYP3A4 Inducers (Strong)) – Ritonavir
- C Darunavir – Enzalutamide (CYP3A4 Inducers (Strong))
- C Darunavir (CYP3A4 Inhibitors (Strong)) – Enzalutamide

- All recommend to avoid coadministration
- But what if you can't????

HIV Drug Interactions

Do Not Coadminister | Potential Interaction | Potential Weak Interaction | No Interaction Expected

	DRV/r	ETR	RAL
Enzalutamide	●	●	■

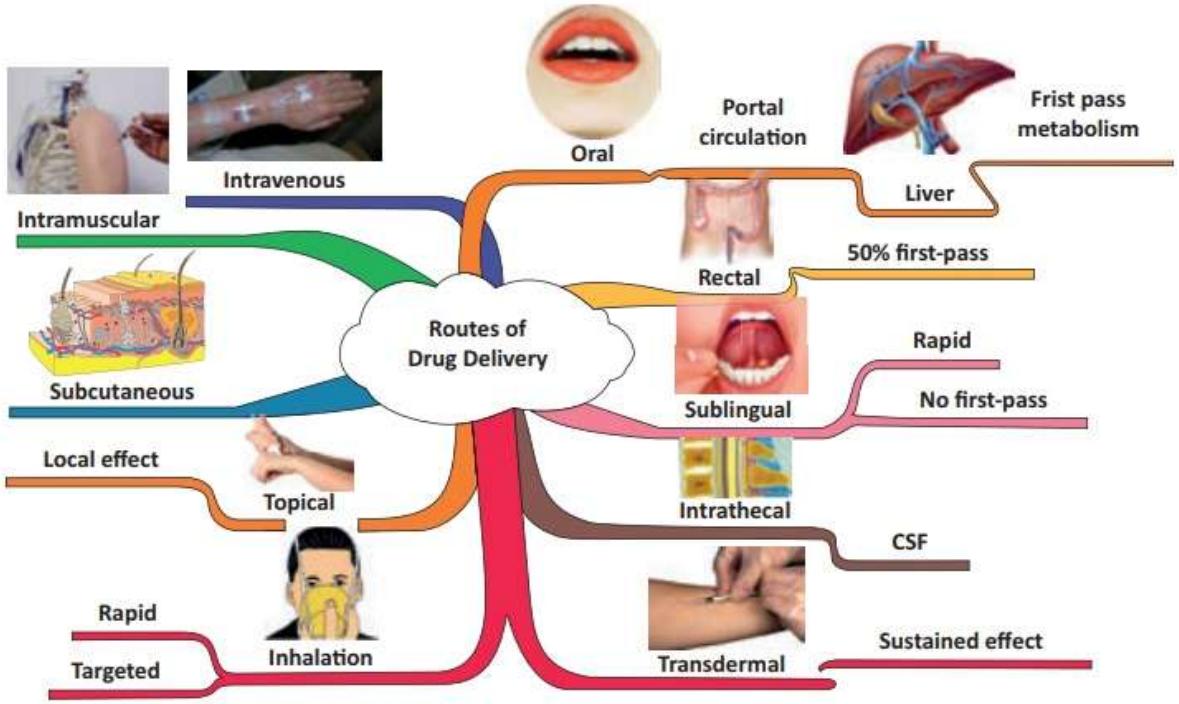
Modified Antiretroviral Dosing To Compensate for Enzalutamide Induction

Cancer Drug	Antiretroviral	Potential Interaction	Modification
Enzalutamide	Darunavir (CYP3A)	possible ↓↓↓ antiretroviral concentrations	Increase ritonavir to 200 mg BID
	Etravirine (CYP3A4, 2C9, 2C19)		Maintain current dose, monitor
	Raltegravir (UGT1A1)		Switch to dolutegravir (CYP3A4, UGT), higher genetic barrier to resistance, give 50 mg BID

- 1 month before: switch RAL to DTG to insure tolerability
- 1 week after starting ENZ, increase ritonavir to 200 mg BID
- TDM at baseline, 2, 4, 8 weeks after starting enzalutamide: therapeutic ARV
- After 2.5 years, viral load remains suppressed and PSA is low

Nhean et al. AIDS 2018;32:2640-2.

Routes of Drug Administration

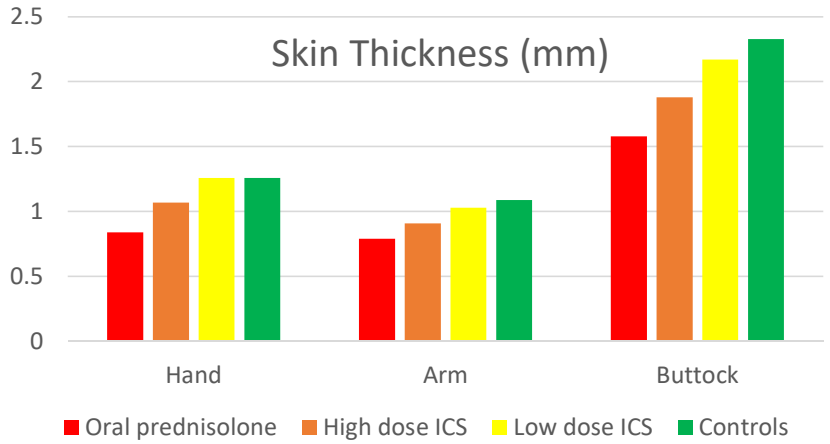


Case

- 60 yo male, HIV+ in 2021, started on TDF/FTC, DRVr, VL<40
- Asthma since age 4, COPD, osteoporosis
  - rosuvastatin, tadalafil, Symbicort (budesonide/ formoterol), Bricanyl (terbutaline) inh
- Reported extreme thinning of the skin/bleeding, bruising; “90% worse” since starting ART

Purpura and dermal thinning associated with high dose inhaled corticosteroids

- Cross sectional study of patients (n=68) at an outpatient chest clinic to assess the effect of high dose inhaled corticosteroids on skin



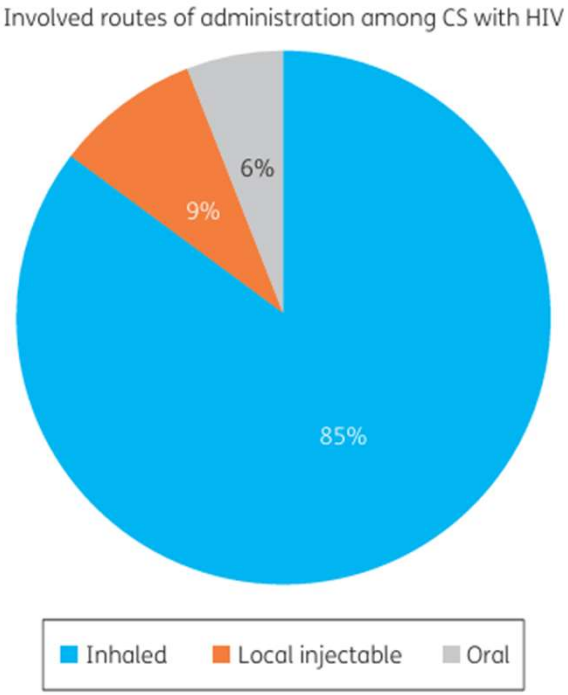
	Purpura	Pt aware of bruising/ fragility	Striae
Oral prednisolone (n=15)	12	13	2
High dose ICS (n=21)	10	8	4
Low dose ICS (n=15)	5	8	5
Controls (n=17)	2	3	6

- Patients on oral prednisolone and high dose ICS had significantly thinner skin at all three sites vs controls
- Purpura significantly greater in patients receiving oral prednisolone and high dose inhaled corticosteroids than in controls ($p<0.01$)

Capewell et al. BMJ. 1990 June 16; 300(6739): 1548–1551.

Cushing's Syndrome due to DDI between ritonavir or cobicistat and corticosteroids

- Retrospective case-control study of Cushing's Syndrome (CS) cases recorded in French Pharmacovigilance Database
- 34/35 cases of CS (86% severe) in people with HIV had DDIs with ritonavir or cobicistat
- Main steroid involved was inhaled fluticasone (n=28, 80%), intra-articular triamcinolone (n=3), and oral budesonide (n=2)
- Mean duration of DDI exposure was 9 months (14 days-3 years)



Peyro-Saint-Paul et al. JAC 2019;74:3291-4.

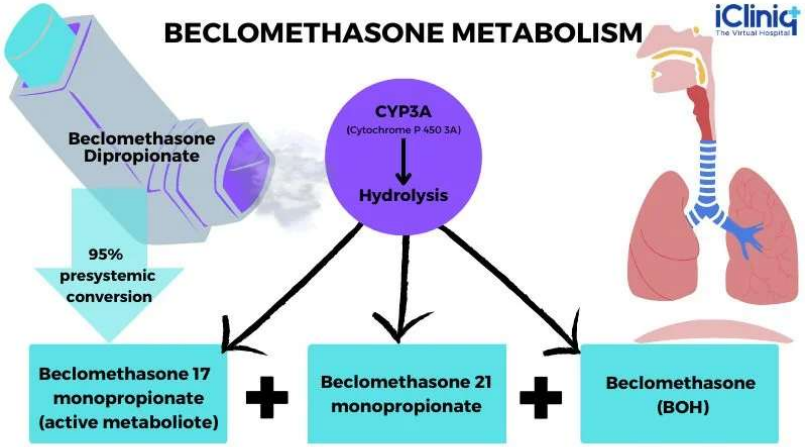
Significant Interactions Between Ritonavir and Topical Corticosteroids

- Topical cream:
  - 41 yo male on ritonavir-boosted ART developed new onset diabetes & cushingoid features over a 4 week period after starting triamcinolone 0.1% BID

- Corticosteroid eye drops:
  - 51 yo HIV+ woman on ATV/r presented with Cushingoid features, avascular necrosis of the hip and adrenal axis suppression with low ACTH. On dexamethasone 0.1% eye drops 6x/d and betamethasone 0.1% eye ointment qhs for >8 months
  - 17 yo male on DRV/r developed Cushing's syndrome 2 weeks after starting dexamethasone 0.1% eye drops hourly for vernal keratoconjunctivitis

Purser et al. AACE Clin Case Rep 2020;6:e346-8. Molloy et al. AIDS 2011;25:1337–9. Rainsbury et al. Ped Infect Dis J 2017;36:502-3.

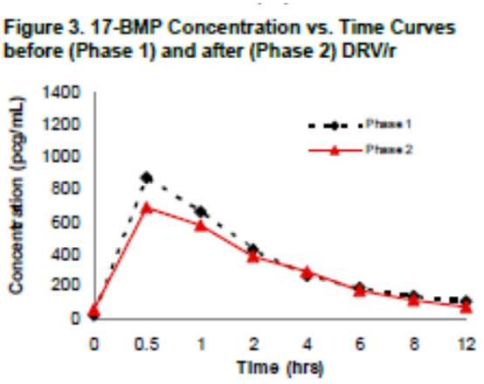
Beclomethasone is Preferred Inhaled/Intranasal Steroid with Boosted Regimens

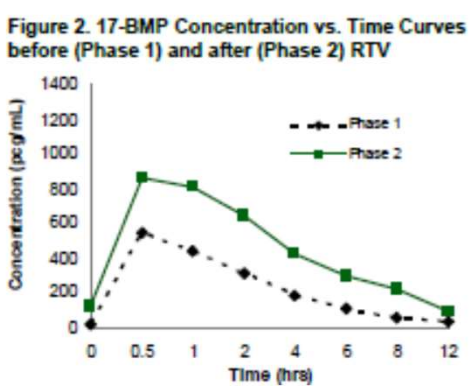


- Beclomethasone is a pro-drug
- Hydrolyzed via esterase enzymes to active metabolite, 17-BMP which is then metabolized by CYP3A4/5

https://www.icliniq.com/articles/drug-and-supplements/beclomethasone

Boyd S et al. J Acq Immune Def Syndr 2013;63(3):355-61.





- 17-BMP exposures:
  - not impacted by darunavir/ritonavir BID
  - 108% ↑ by ritonavir 100 mg BID (clinically insignificant)
  - No adrenal suppression with coadministration for 28 days

Interactions can occur with non-oral medications

- Systemic absorption of drugs administered via non-oral route
- Toxicity reported when boosted regimens given with corticosteroids:
  - Inhaled
  - Intranasal
  - Topical (incl. eye drops)
  - Intra-articular injection

Medication History	
Medication history 	Ask about inhalers, eye drops, creams, injections, etc. (*may be intermittent or temporary use)
Steroid use	Minimize duration of use Consider beclomethasone
ART	Switch to non-boosted ART regimen if possible

Cureus 2020;12:e9644. Rajoli et al. JID 2019;219:1735-42.

Long-Acting Antiretroviral Regimens

Are DDIs a concern?

Interactions with Long-Acting Antiretroviral Therapy (LA-ART)

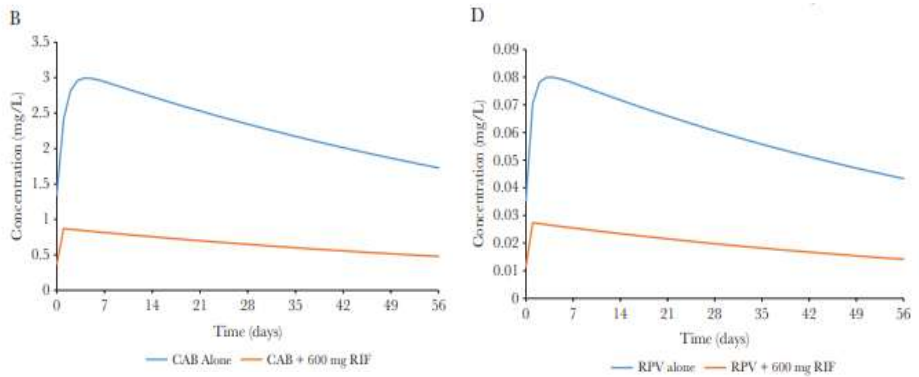
- Some interactions with oral ART are not relevant with LA-ART
  - E.g., absorption DDIs

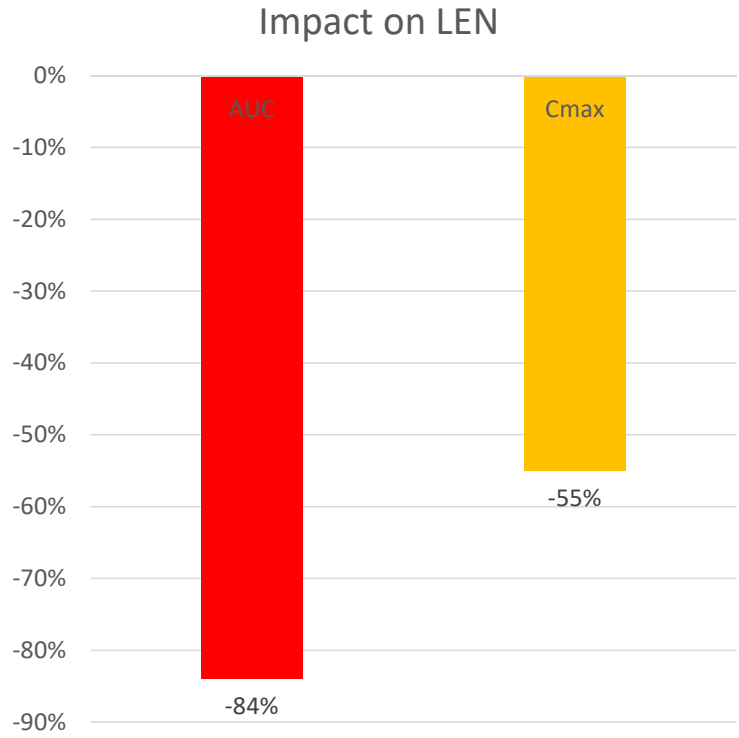
- LA-ART provide systemic exposures of therapy and are susceptible to interactions with enzyme inducers

	Oral ARV	LA-ART
Acid-reducing agents	Rilpivirine – contraindicated	OK
Cations	INSTIs - space	OK
Enzyme inducers	Contraindicated	Contraindicated

Rifampin Effects on Long-Acting Antiretroviral Therapy

- 45% ↓ CAB AUC
- 82% ↓ RPV AUC





Cureus 2020;12:e9644. Rajoli et al. JID 2019;219:1735-42. Sunlenca monograph, 2025.

Lenacapavir can act as DDI perpetrator

Cabotegravir/rilpivirine:

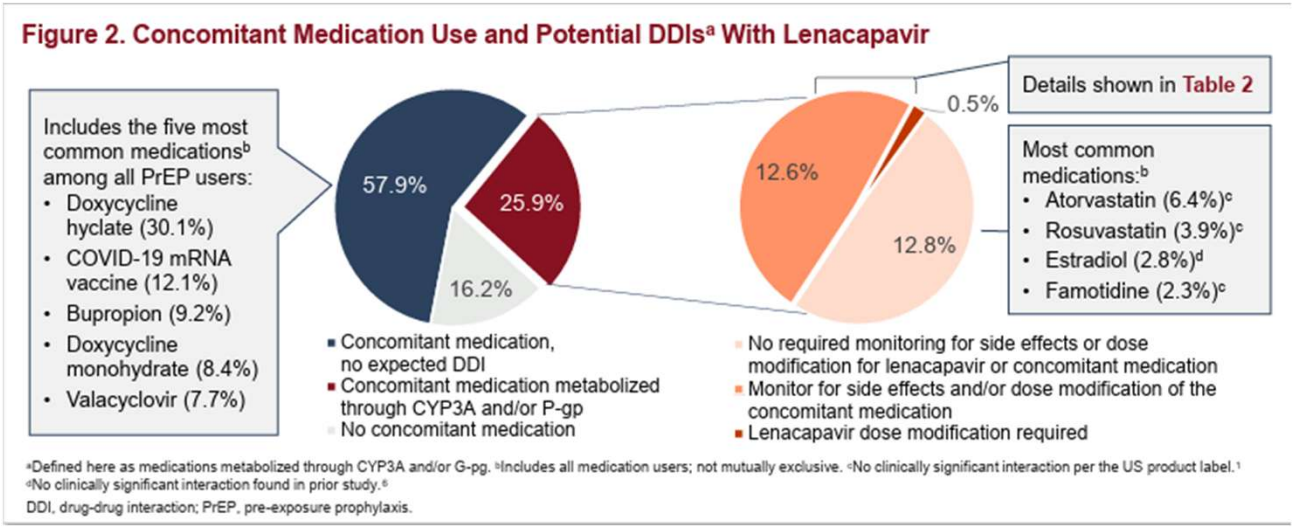
- Considered “neutral”
- No significant inhibiting or inducing properties

- Lenacapavir is a moderate CYP3A4 inhibitor and P-gp inhibitor
  - caution with narrow therapeutic index CYP3A4 drugs (e.g., digoxin, DOACs, corticosteroids, ergotamines, sedatives, statins, PDE5 inhibitors)
- Persistence of LEN concentrations:
  - may affect the exposures of other drugs (ie, sensitive CYP3A substrates) that are initiated within 9 months after the last subcutaneous dose of LEN

Sunlenca monograph, 2025.

Real World Medication Use and Potential DDIs with LEN for PrEP

- N=457,402 people with ≥1 dispensed oral/injectable PrEP Rx in US in 2024
  - Median 38 yo, 90.9% male
- 83.8% on concomitant medications
- 25.9% with a CYP3A4/P-gp comedication



If LEN used in place of current PrEP:	Most commonly implicated comeds:
0.5% would require LEN dose modification	oxcarbazepine (0.3% of all PrEP users), carbamazepine (0.1%) and rifampin (<0.1%)
12.6% would require monitoring/potential dose modification	PDE5 inhibitors for ED (10.7%) or PAH (1.04%), simvastatin (0.53%), dexamethasone (0.45%), rivaroxaban (0.3%)

Tao et al. CROI 2026, #1062.

Case

- 55 year old male, HIV+ 2003, VL suppressed on abacavir/3TC and nevirapine since 2005
- Diabetes, bipolar disorder, hyperlipidemia:
  - Bupropion, aripiprazole, loxapine, pregabalin, pantoprazole, gliclazide, sitagliptin/metformin, empagliflozin, liraglutide, rosuvastatin, ezetimibe, fenofibrate, valacylovir, tadalafil
- Wants to switch to CAB/RPV IM

Interactions?

- Currently reduced by nevirapine:
  - Bupropion (2B6)
  - Aripiprazole (3A4, 2D6, P-gp)
  - Loxapine (3A4, 1A2, 2D6)
  - Sitagliptin (P-gp, 3A4)
  - Tadalafil (3A4)
- Contraindicated with oral rilpivirine:
  - pantoprazole

Case: follow-up

- Liaised with psychiatrist re: potential dose adjustments
  - Decreased bupropion to 300 mg daily 2 weeks after stopping nevirapine
  - Monitor response of other co-medications, titrate as necessary
- Patient d/c pantoprazole cold turkey
- Switched to CAB/RPV IM
- Continues with maintenance injections, remains virally suppressed

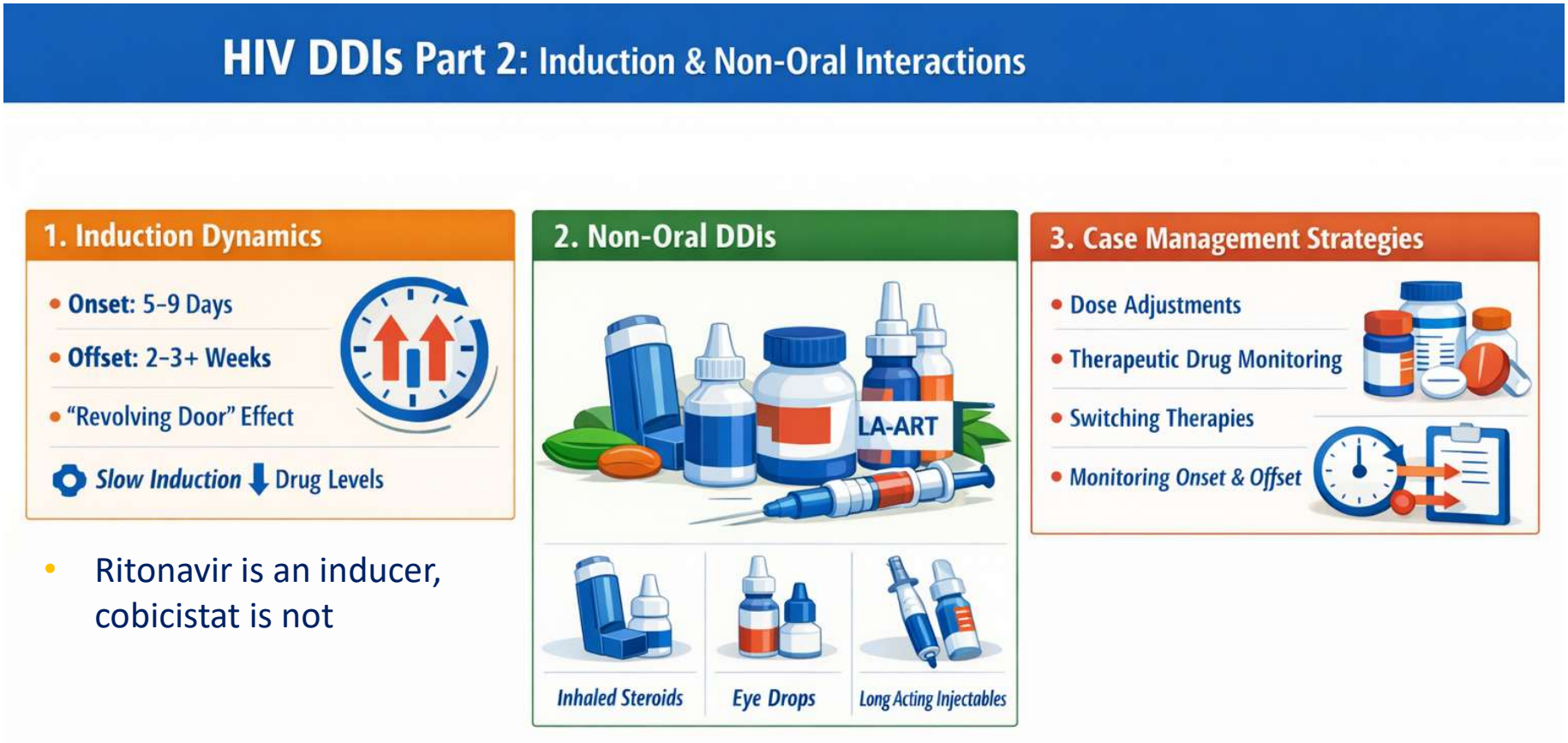
Interactions with LA-ART

- Absorption DDIs not relevant for LA-ART
- Enzyme inducers are generally contraindicated regardless of route of ART administration
- LEN can act as a perpetrator of DDIs

	LA-ART considerations
Acid-reducing agents, cations	OK
Enzyme inducers	AVOID
Injection schedule	Assess for DDI risk if ≤9 months since last LEN injection
Medication history	Remember OTC, non-orally administered agents (e.g., puffers), identify narrow therapeutic index drugs

Cureus 2020;12:e9644. Rajoli et al. JID 2019;219:1735-42.

Part 2: Key Takeaways



- Ritonavir is an inducer, cobicistat is not

CHAP HIV101 Series

Antiretroviral drug-drug interactions
(or: I wish someone would explain drug interactions to me!)

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Immunodeficiency Clinic, University Health Network

2026

CHAP HIV101 Series

Drug-Drug Interactions: Part 3

- DDIs with NHPs
- DDI concerns with polypharmacy
- DDI resources
- DDI management strategy

Just because it's natural doesn't mean it's always safe

St. John's Wort

- Commonly used herbal for treating depression
- However, can interact with many HIV and hepatitis C medications
  - cause significant ↓ in drug concentrations; risk of virologic failure, resistance
- St. John's wort is contraindicated with all antiretrovirals and hepatitis C antiviral agents

Ginko Biloba

- Thought to have positive effects on cognitive function
- Ginko biloba can reduce levels of certain drugs
  - Two case reports of HIV-positive males on efavirenz who developed low efavirenz concentrations, virologic failure and resistance after starting ginko biloba

Naccarato et al. JIAPAC 2012;11:98-100.
Wiegman et al. AIDS 2009;23:1184-5.

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The most authoritative resource on supplements, natural medicines, and integrative therapies.

Results Summary (Click for Details)

Interactions found!

Click on any interaction below for more information.

Biktarvy <<interacts with>> ST. JOHN'S WORT contained in "St. John's Wort" View Details
Interaction Rating = Major Do not take this combination.

Biktarvy <<interacts with>> GINKGO contained in "Gingko Biloba 500 mg by Greenbrier International" View Details
Interaction Rating = Moderate Be cautious with this combination.

Disclaimer: Currently this does not check for drug-drug interactions. This is not an all-inclusive comprehensive list of potential interactions and is for informational purposes only. Not all interactions are known or well reported in the scientific literature, and new interactions are continually being reported. Input is needed from a qualified healthcare

Case

- 43 yo female, HIV+ since 2002
  - Ongoing viral replication (non-adherence, GI Sx); CD4 <50, VL~10,000

		VL Copies/mL	**CD4** Cells/mm3	**T bilirubin** umol/L	**ATV TDM**
Sep/2009	Started TDF/FTC, atazanavir/r	11,139	23	4	
Nov/2009	"	<50		36	
Feb/2010	"	<50	100	36	therapeutic

After being virally suppressed for 9 months…

		VL Copies/mL	**CD4** Cells/mm3	**T bilirubin** umol/L	**ATV TDM**
Sep/2009	Started TDF/FTC, atazanavir/r	11,139	23	4	
Nov/2009	"	<50		36	
Feb/2010	"	<50	100	36	therapeutic
Jul/2010	"	46,848	33	5	0
Aug/2010	"		5		0

- Patient insists she is adherent

Sampling date	*Drug*	*Dose*	*Concentration*
150710	atazanavir	300 mg qd	0 *mg/l*
Sampling date	ritonavir	100 mg qd	0 *mg/l*
110810			

Oh, you mean THOSE other drugs

- October 2010:
  - Discovered that patient had been taking activated charcoal to manage GI symptoms

Activated Charcoal

- Adsorbent/gastrointestinal agent/nutraceutical
- A 50 g dose of activated charcoal has a surface area ~ 10 football fields

- Binds drugs in the gastrointestinal tract:
  - Carbamazepine: 90% ↓ AUC
  - Digoxin: 96-98% ↓ absorption
- Administer medication at least 2 hours before or 4-6 hours after activated charcoal

Case: Stopped taking activated charcoal in August

		VL copies/mL	**CD4** cells/mm3	**T bilirubin** umol/L	**ATV TDM**
Jul/2010	"	46,848	33	5	0
Aug/2010	"		5		0
Oct/2010	"	226	62	43	therapeutic
Dec/2010	"	694	49	24	
Mar/2011	" genotype: K65R, 184V (new), L90M	14,553	70	44	therapeutic

- Switched to TDF/FTC, darunavir/r → viral suppression

Drug Interaction Probability Scale (DIPS)

The Drug Interaction Probability Scale (DIPS) is designed to assess the probability of a causal relationship between a potential drug interaction and an event. It is patterned after the Naranjo ADR Probability Scale (Clin Pharmacol Ther 1981;30:239-45).

Directions:

- ☐ Circle the appropriate answer for each question, and add up the total score.
- ☐ Object drug = Drug affected by the interaction.
  Precipitant drug = Drug that causes the interaction.
- ☐ Use the Unknown (Unk) or Not Applicable (NA) category if (a) you do not have the information or (b) the question is not applicable (eg, no dechallenge; dose not changed, etc.).

Questions	Yes	No	Unk or NA
1. Are there previous *credible* reports of this interaction in humans?	+1	**−1**	0
2. Is the observed interaction consistent with the known interactive properties of precipitant drug?	**+1**	−1	0
3. Is the observed interaction consistent with the known interactive properties of object drug?	**+1**	−1	0
4. Is the event consistent with the known or reasonable time course of the interaction (onset and/or offset)?	**+1**	−1	0
5. Did the interaction remit upon dechallenge of the *precipitant* drug with no change in the object drug? (if no dechallenge, use Unknown or NA and skip Question 6)	**+1**	−2	0
6. Did the interaction reappear when the precipitant drug was readministered in the presence of continued use of object drug?	+2	−1	**0**
7. Are there reasonable alternative causes for the event?[a]	−1	**+1**	0
8. Was the object drug detected in the blood or other fluids in concentrations consistent with the proposed interaction?	**+1**	0	0
9. Was the drug interaction confirmed by any objective evidence consistent with the effects on the object drug (other than drug concentrations from question 8)?	**+1**	0	0
10. Was the interaction greater when the precipitant drug dose was increased or less when the precipitant drug dose was decreased?	+1	−1	**0**

[a]Consider clinical conditions, other interacting drugs, lack of adherence, risk factors (eg, age, inappropriate doses of object drug). A NO answer presumes that enough information was presented so that one would expect any alternative causes to be mentioned. When in doubt, use Unknown or NA designation.

Total Score ___

Highly Probable:	>8
Probable:	5–8
Possible:	2–4
Doubtful:	<2

Total Score: 6 (probable)

Horn et al. Ann Pharmacother 2007;41:674-80.

Antiviral Therapy 2013;18(5):735-8.

Case report

Significant interaction between activated charcoal and antiretroviral therapy leading to subtherapeutic drug concentrations, virological breakthrough and development of resistance

Alice L Tseng[1,2], Charles la Porte[3,4], Irving E Salit[1,5]*

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A 42-year-old, treatment-experienced woman, virologically suppressed on tenofovir/emtricitabine and boosted atazanavir, experienced virological breakthrough, drop in CD4+ T-cell count and undetectable drug concentrations. Adherence to treatment was confirmed, but repeat testing yielded similar results. After 2 months, the patient stated that she had been taking activated charcoal to manage gastrointestinal symptoms associated with her combination antiretroviral therapy, but she had recently discontinued the charcoal. Atazanavir concentrations were therapeutic but the patient's viral load rebounded and genotype testing revealed new reverse transcriptase mutations. The patient was changed to zidovudine, lamivudine, and boosted darunavir and achieved viral suppression. At 1 year follow-up, her viral load remained <40 copies/ml. According to the drug interaction probability scale, our patient experienced a probable drug interaction between activated charcoal and atazanavir/ritonavir leading to virological breakthrough and development of resistance.

Antiviral Therapy 2013; **18:**649–650 (doi: 10.3851/IMP2688)

Commentary

Drug–drug interactions in HIV therapy: is it all clear?

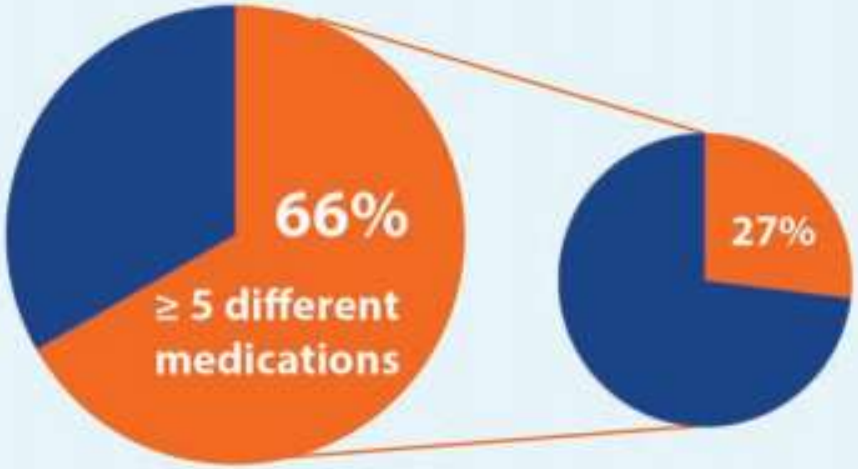
David Burger[1]*, *David Back*[2]

Drug–drug interactions in HIV therapy have been known to the clinic from earliest days of HIV treatment. Hundreds of well-designed pharmacokinetic studies have been performed in either HIV-infected patients or, mostly, in healthy volunteers. Case reports generally are graded lower in terms of evidence-based medicine but sometimes provide valuable information. In this issue of *Antiviral Therapy* a case of virological failure on an atazanavir-containing regimen was explained by an interaction with charcoal that was used as self-medication for diarrhoea. Clinicians are invited to continue submitting well-documented case reports to increase knowledge on drug–drug interactions in HIV therapy even further.

How many prescription medications are Canadian seniors taking?

2 out of 3 Canadians over the age of 65 take **at least 5** different prescription medications.

1 out of 4 Canadians over the age of 65 take **at least 10** different prescription medications.



Seniors taking ≥10 medications

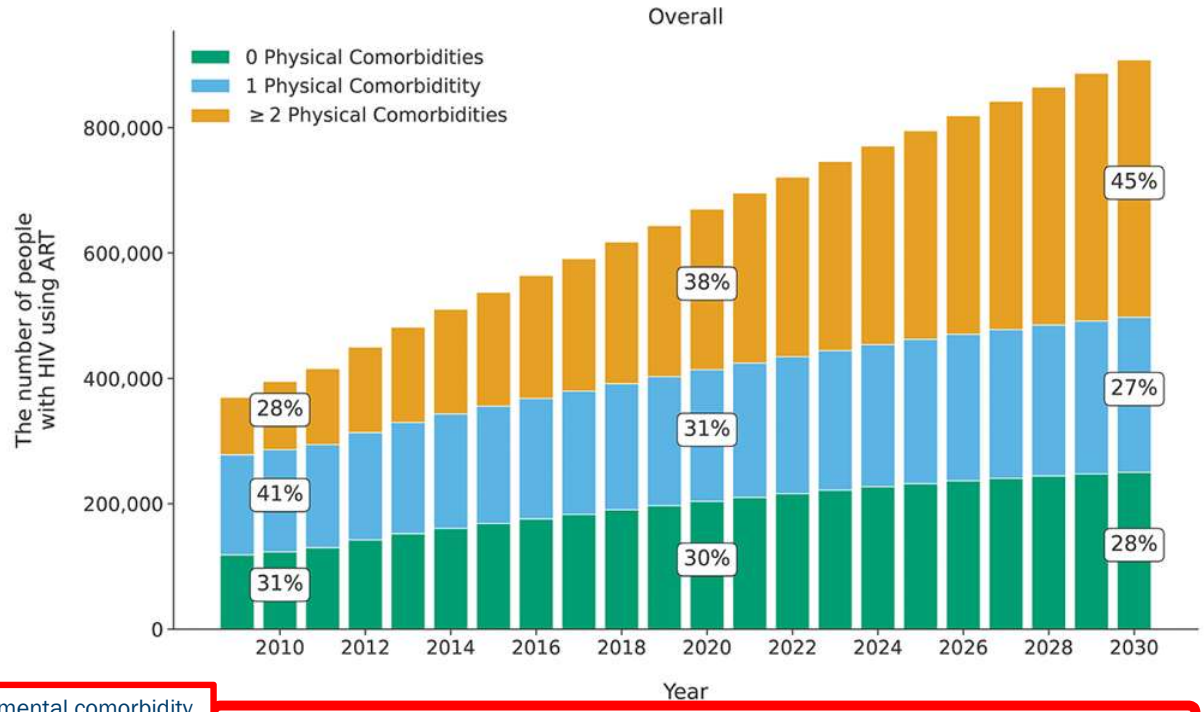
20% of seniors age 65 to 74

32% of seniors age 75 to 84

39% of seniors age 85+

(CIHI 2014)

Forecasted Prevalence of Comorbidities and Multimorbidity in People With HIV in US to 2030



- Increase in prevalence of most comorbidities
  - Dyslipidemia, diabetes, CKD, MI
  - Depression, anxiety
- Multi-morbidity (physical + mental) projected to increase from 63% in 2020 to 70% in 2030

CKD = chronic kidney disease; MI = myocardial infarction

Althoff et al. PLoS Med 2024;21(1):e1004325.

Polypharmacy and Inappropriate Medication use in Older Adults with HIV (CHANGE-Rx)

N=440 PARTICIPANTS

Median age 69 years (65–89)

♂ 91.6% male

♀ 75.8% white

92.6% HIV RNA <50 copies/mL

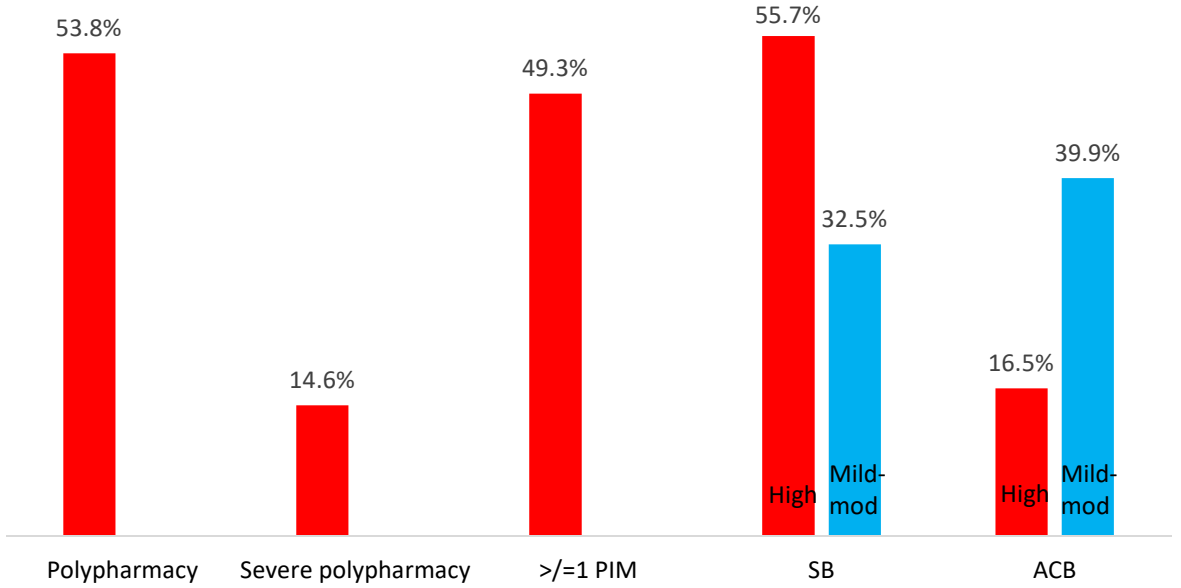
Median 26 years since HIV diagnosis:
Dyslipiddemia (50.3%),
Hypertension (43.7%),
Cancer (29.1%)

Median 5 comedications and 2 OTC/NHPs per person

16% frail

63% pre-frail

20% fall in past 6 months, 8% recurrent falls



Polypharmacy= ≥5 non ARVs; severe polypharmacy = ≥10 non ARVs; PIM=potential inappropriate medication; SB=sedative burden; ACB = anticholinergic burden

- Total 2349 non-ARV medications in cohort

Hopwood-Raja et al. AIDS 2025;39:1898-1906.

Case

- 74-year-old male, started ARVs in 1990 (incl. mono/dual RTIs, unboosted/boosted PIs, NNRTIs, enfuvirtide, INSTIs)
- Viral load undetectable since 2011

- His physician has requested a medication review because “he’s on a lot of drugs”

- Past medical history/ comorbidities:
  - Lipodystrophy --> cheek implants
  - Dyslipidemia
  - Hypertension
  - Chronic obstructive pulmonary disease
  - Peripheral neuropathy
  - History of falls
  - Hip fracture (2022)
  - Parkinson's with mild cognitive impairment

ARVs = antiretrovirals; INSTIs = integrase strand transfer inhibitors; NNRTIs = non-nucleoside reverse transcriptase inhibitors; PIs = protease inhibitors; NRTIs = nucleoside reverse transcriptase inhibitors

Co-Medications

- 26 pills/day
- 2 inhalers
- 2 liquids
- 1 rectal

- Abacavir/lamivudine 600/300 mg daily
- Dolutegravir 50 mg daily
- Darunavir 800 mg daily
- Ritonavir 100 mg daily
- Diltiazem 180 mg daily
- Pravastatin 20 mg daily
- Alendronate 10 mg daily
- Umeclidinium bromide/vilanterol trifenatate (Anoro Ellipta) inhaler daily
- Salmeterol inhaler q4h PRN
- Omeprazole 20 mg daily
- Levodopa 100 mg/carbidopa 25 mg 1.5 tabs QID
- Calcium 500 mg daily
- Lactulose 15 mL BID PRN
- Senna 2 tabs daily
- Bisacodyl 10 mg daily PRN
- PEG 17 g daily and PRN
- Sodium phosphate fleet q3d and PRN
- Trazodone 50 mg qhs PRN
- Triazolam 0.25 mg qhs PRN
- Melatonin 3 mg qhs
- Vitamin D 2000 IU daily
- Acetaminophen 300 mg/codeine 15 mg q6h

How many potentially significant drug-drug interactions does this patient's regimen contain?

A. 7
B. 12
C. 19
D. 29

Red: Serious; do not coadminister.

Amber: Potential; use with caution, additional monitoring or dose adjustment.

Green: No significant drug interaction.

Answer: It Depends On Where You Look!

	HIV (Liverpool)	General (Lexidrug)
Red [X]	1: darunavir/r + triazolam	1: darunavir/r + triazolam
Amber [C/D]	11: • darunavir/r + codeine, diltiazem, levodopa, melatonin, PEG, pravastatin, trazodone, umeclidinium, vilanterol • Dolutegravir + calcium	8 • darunavir/r + codeine, diltiazem, omeprazole, pravastatin, trazodone, vilanterol, vitamin D • Dolutegravir + calcium
TOTAL:	12	9

- May be poor concordance between drug interaction databases[1]
- HIV DDI resource identified more potential ARV interactions
- General DDI resource included some DDIs which are not clinically relevant/contained less current information

1. Lopez-Iniguez et al. IAS 2025, TUPEB020.

Answer: It Depends On Where You Look!

	HIV (Liverpool)	General (Lexidrug)	
Red [X]	1: darunavir/r + triazolam	1: darunavir/r + triazolam	
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TOTAL:	**12 ARV + 17 co-medications = 29 DDIs**		

- General DDI databases also check for interactions between co-medications
- Use both HIV-specific & general DDI checkers for completeness

ACCURATE-DDI Study: ChatGPT Shows Limited Accuracy in Identifying Serious ARV DDIs

	Correct	Incorrect	Composite Score*
No DDI	29%	71%	2.7 (34%)
Potential DDI	91%	9%	4.2 (53%)
Serious DDI	0%	100%	4.3 (54%)

*Domains: severity, mechanism, clinical effects, management; total maximum score 8

- Compared to HIV-specific DDI resources (Liverpool, HIV/HCV Drug Therapy Guide), ChatGPT correctly classified 40.4% (38/94) of DDI pairs

- ChatGPT responses often combined correct and incorrect information
- Underreported serious/contraindicated DDIs; management strategies often incorrect
- Frequently issued warnings about non-existent/not clinically significant DDIs
- ChatGPT failed to identify non-CYP3A4 ritonavir interactions and pharmacodynamic interactions

Ready et al. AIDS in press

DDI Resources

- Use more than 1 resource when checking for drug interactions!

Use >1 DDI resource	
ARV-comed DDI	HIV-specific DDI websites may be more comprehensive, up to date
Comed-comed DDI	General resources (Lexicomp, Micromedex)
Product monographs	May be country-specific differences
AI platforms	May not always be reliable

Managing HIV DDIs: Survival tips

1. Obtain a complete (best possible) medication history at each visit

Type of Drugs	Examples
Drugs not taken by mouth	Creams, eye drops, injections
Temporary or once in a while drugs	Puffers for allergy season, antibiotics, antacids, etc.
You mean *those* are drugs?	Vitamins, herbal products, supplements, complementary medicine
"Do I really need to tell you" drugs	Recreational agents, PDE5 inhibitors, steroids

- *including new drugs, new dose, drugs stopped
- Encourage patients to have all Rx filled at one pharmacy, and to ASK before starting anything new

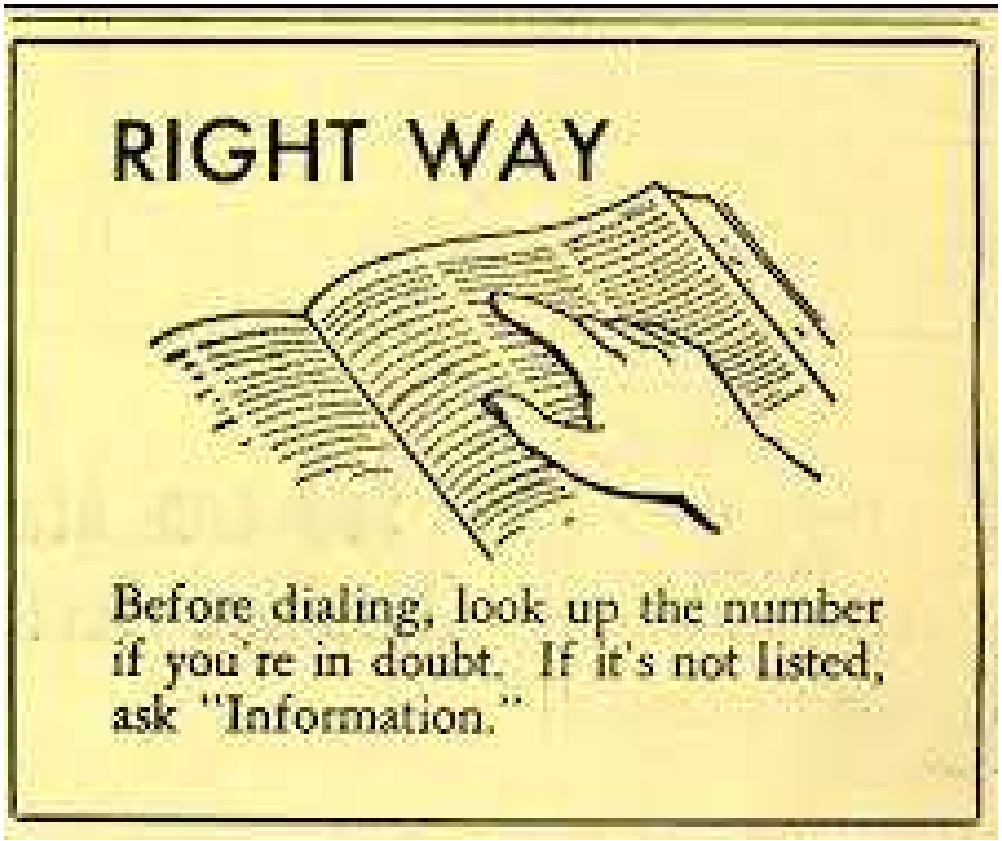
2. Think about interactions

- High-index drugs (perpetrators, victims)
  - Inhibitors: PK boosters, LEN
  - Inducers: older NNRTIs
  - Acid/chelation: INSTIs, rilpivirine

Top Red Flag Drug Classes in People with HIV
Corticosteroids (topical, inhaled)
Anticoagulants, antiplatelets
Cardiovascular drugs
Cations (supplements)
Statins
Proton pump inhibitors
Psychotropic agents

Lepik et al. AIDS 2022;36:1105-15. Hodge et al. JAIDS 2023;92:97-105. Lopez Delhoulle et al. Front Pharmacol 2025;16:1632108.

If in doubt, look it up!



3. Use Multiple DDI Resources

HIV//HCV DRUG THERAPY GUIDE

- https://hivclinic.ca/app/

HIV Drug Interactions — UNIVERSITY OF LIVERPOOL

HEP Drug Interactions — UNIVERSITY OF LIVERPOOL

COVID-19 Drug Interactions — UNIVERSITY OF LIVERPOOL

- https://www.hiv-druginteractions.org/
- https://www.hep-druginteractions.org
- https://www.covid19-druginteractions.org/

Drugs.com Interaction Checker
Solid offering that is made nearly unusable by ads interspersed with interactio
drugs.com

Epocrates Interaction Checker
Unfortunately behind a free registration wall.
epocrates.com - Registration Required

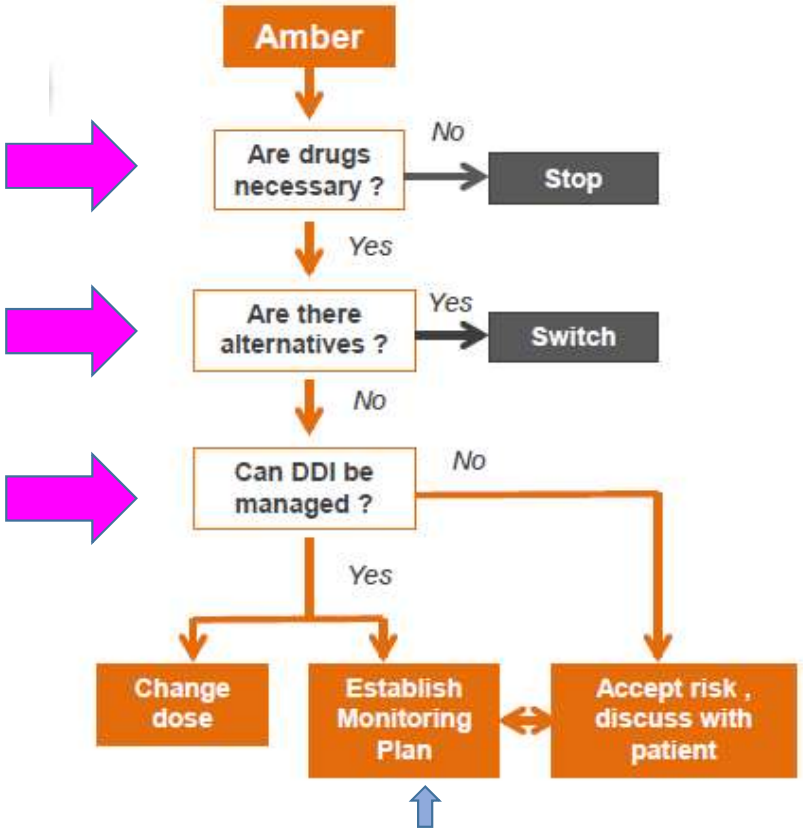
Subscription Services

Lexi-Interact
Leading provider of interaction data for healthcare professionals.
lexi.com - Subscription

Micromedex Drug Interactions
Drug interaction lookup service from IBM/Truven. Institutional access only.
ibm.com - Subscription

NatMed — a trchealthcare brand
The most authoritative resource on supplements, natural medicines, and integrative therapies.

4. Use a step-wise, pragmatic approach



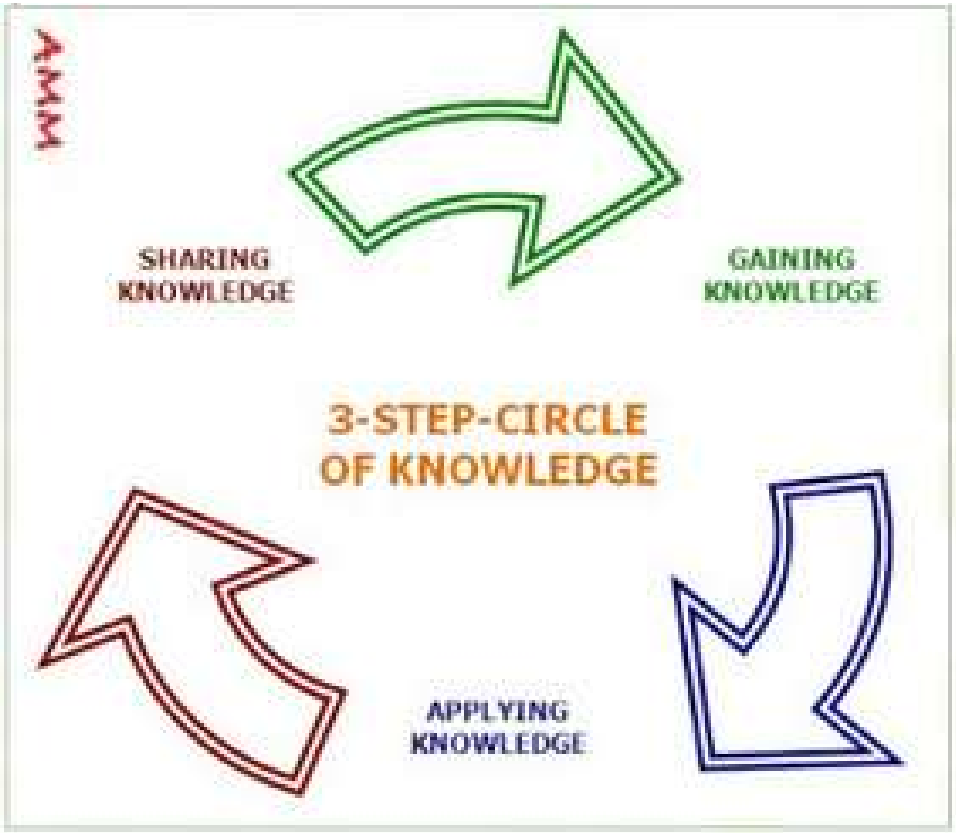
Based on time frame of DDI onset/offset

- Ensure communication with other HCP

Back DJ. HIV-HCV Coinfection Workshop, Paris, June 2014

5. Share new DDI information

- DDI information:
  - Include causality assessment Drug Interaction Probability Scale (DIPS) [Horn et al. Ann Pharmacother 2007]
- Publish:
  - clinicalcasesDDIs.com
  - Case report/series
- Contribute to DDI knowledge base



Part 3: Key Takeaways

HIV DDIs Part 3: NHPs, Polypharmacy & DDI Management

1. NHP Considerations

- St. John's Wort
- Garlic Supplements
- Cannabis (CBD, THC)
- Other Herbal Products

2. Polypharmacy Challenges

- Aging Patients
- Multiple Medications
- Adherence Issues

3. DDI Management Strategies

- Interaction Resources
- Stepwise Approach
- Patient Education
- Team Communication

Dr. Strangelove:

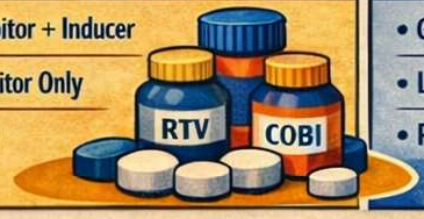
or How I Learned to Stop Worrying and Love DDIs

1. Know the Perpetrators

- Inhibitors & Inducers
- "Revolving Door" Theory

2. Assess Your Arsenal

- Ritonavir - Inhibitor + Inducer
- Cobicistat - Inhibitor Only
- INSTIs = Neutral



3. Protect the Victims

- Gastric pH, Chelation Threats
- Long-acting, non-oral ARVs
- Polypharmacy

4. The DDI War Room

- Interaction Checkers
- Multidisciplinary Team

5. Timed Explosions / Risk Neutralization

- Slow Burn Induction
- Rapid Withdrawal Risks
- Dose adjustments & monitoring

★★ Ladies and Gentlemen: You Have to Manage the DDIs! ★★


Zen and the Art of
DRUG INTERACTION MAINTENANCE
Observe & Assess
Balance the Risks
Adjust & Harmonize
MINDFUL MONITORING FOR MEDICATION MASTERY