HIV Management
Hepatitis Management

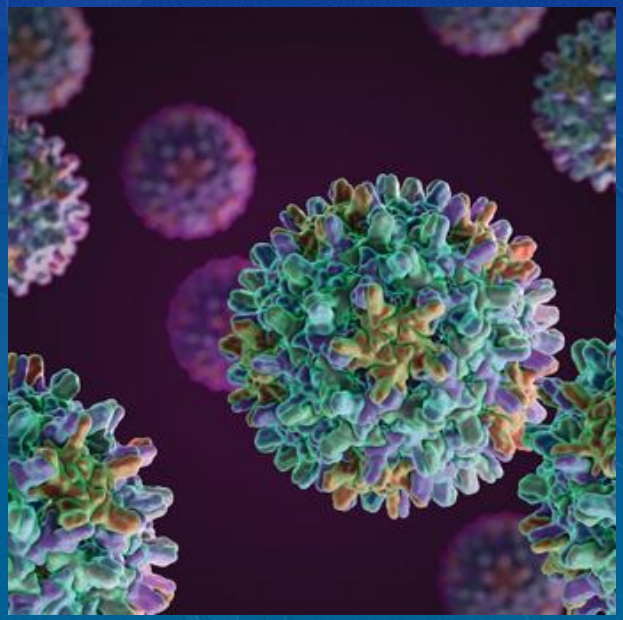
THE NEW YORK COURSE

Drug-Drug Interactions of HBV and HCV Regimens

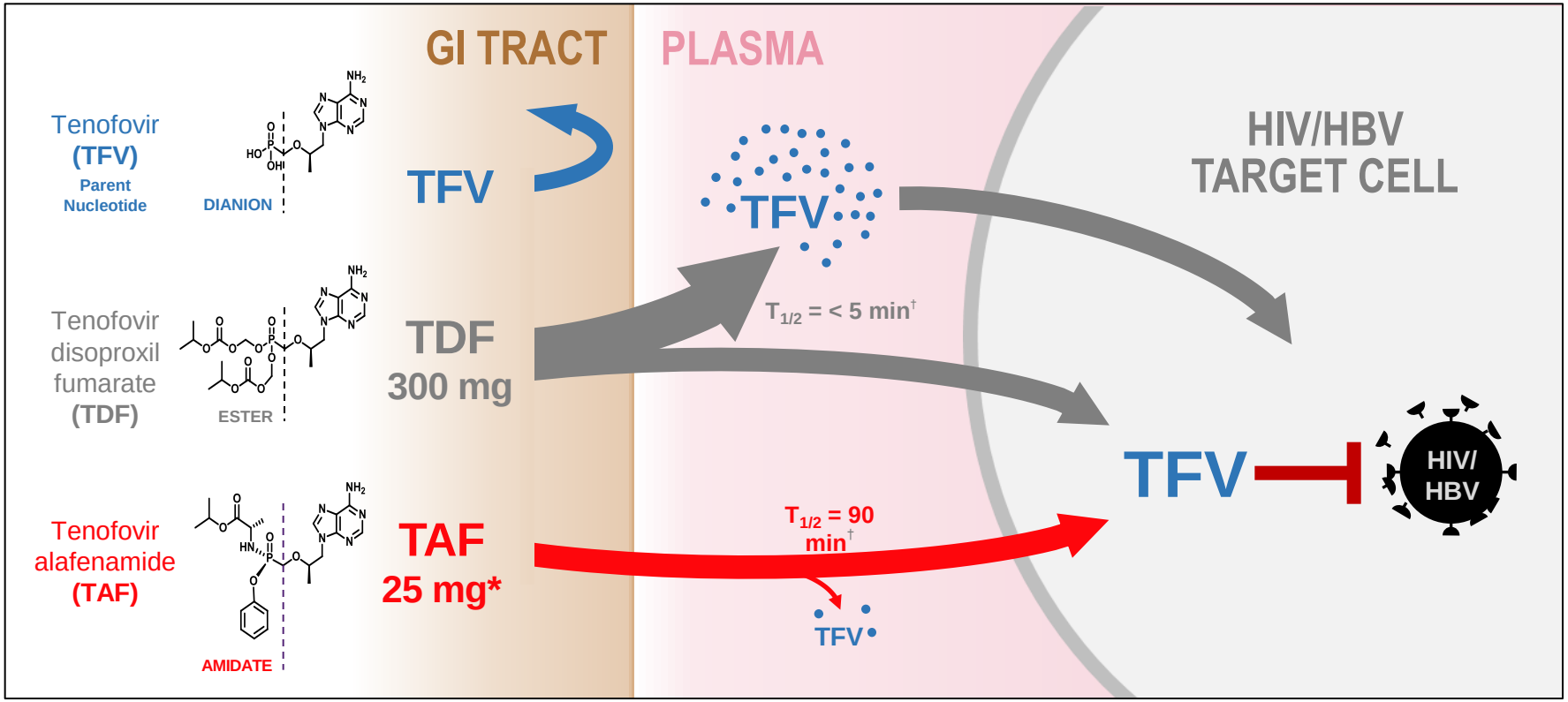
David Back PhD

University of Liverpool
Liverpool, UK.

DDIs of HBV regimens



Absorption of Tenofovir (TFV), Tenofovir Disoproxil Fumarate (TDF) and Tenofovir Alafenamide (TAF)

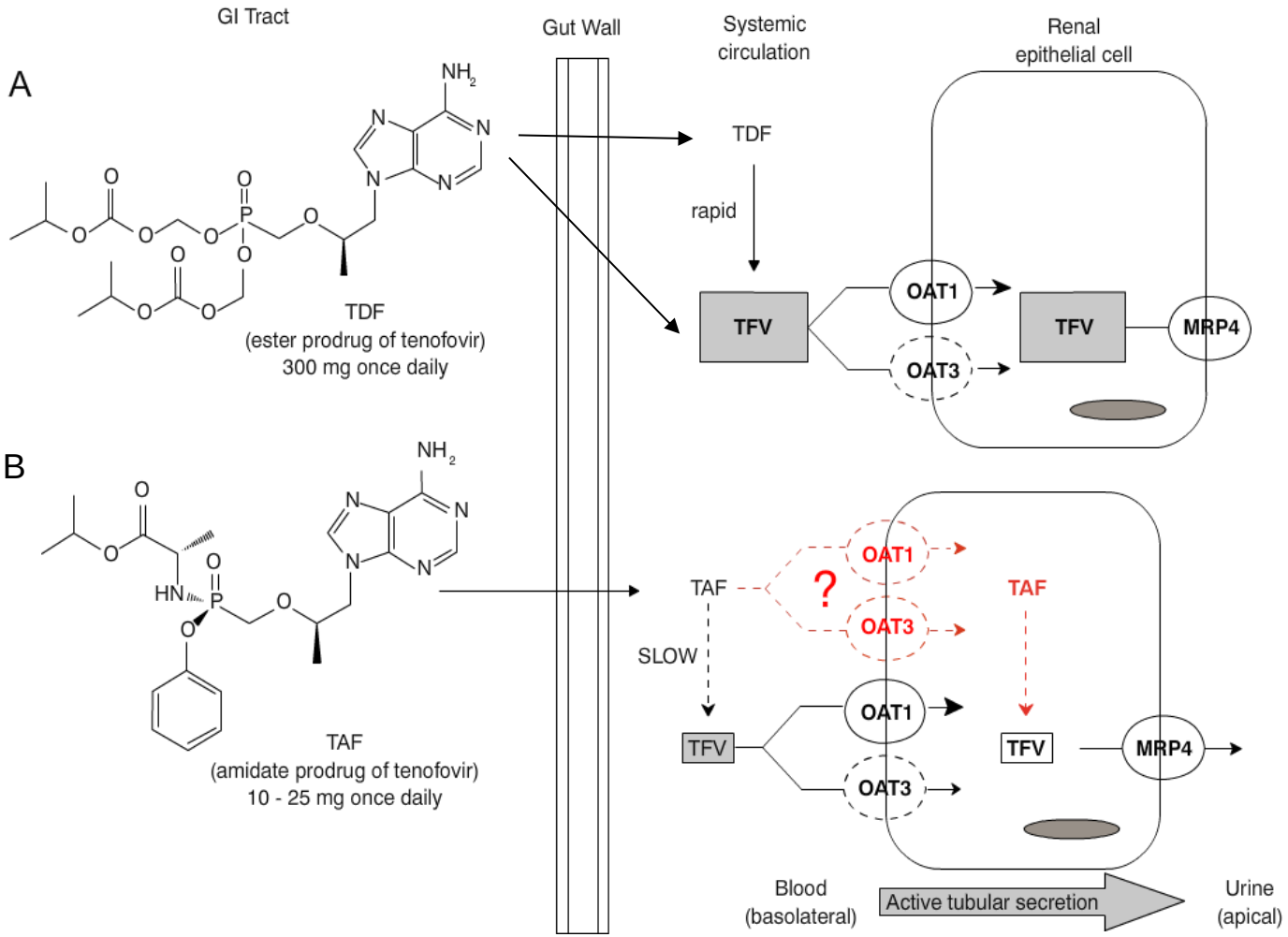


TWO key considerations:

1. The difference in circulating TFV levels after TAF and TDF.
2. The role of P-gp in the absorption process – a site for DDIs

1. Lee W et. *Antimicr Agents Chemo* 2005;49(5):1898-1906. 2. Birkus G et al. *Antimicr Agents Chemo* 2007;51(2):543-550. 3. Babusis D, et al. *Mol Pharm* 2013;10(2):459-66. 4. Ruane P, et al. *J Acquir Immune Defic Syndr* 2013; 63:449-5. 5. Sax P, et al. *JAIDS* 2014. 2014;67(1):52-8. 6. Sax P, et al. *Lancet* 2015;385:2606-15. Gupta SK, et al. IAS 2015. Vancouver, CA; #TUAB0103.

Differential Tenofovir Exposure from TDF and TAF: Effect on Renal Proximal Tubule



Baum RA et al AVT 2014; 19: 687-692

Differences in the DDI Profile of TDF & TAF

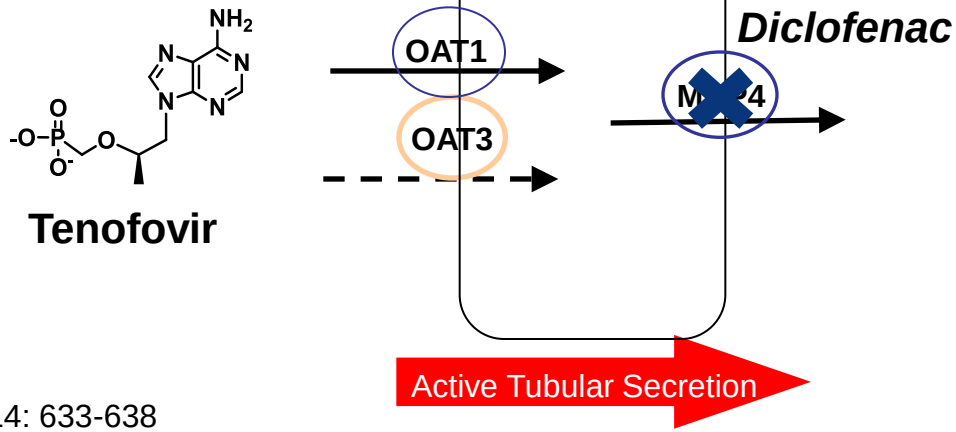
	TDF	TAF	Potential Mechanism
Aspirin			NSAIDS and Renal
Celecoxib			NSAIDS and Renal
Diclofenac			NSAIDS and Renal
Ibuprofen			NSAIDS and Renal
Mefenamic acid			NSAIDS and Renal
Naproxen			NSAIDS and Renal
Nimesulide			NSAIDS and Renal
Acetazolamide			Renal transport
Cefalexin			Renal transport
Dacarbazine			Renal transport
Flucloxacillin			Renal transport
Mycophenolate			Renal transport
Probenecid			Renal transport
Verapamil			P-gp/absorption
Topiramate			Renal toxicity
Oxaliplatin			Renal toxicity
Sirolimus			Renal toxicity
Penicillamine			Renal toxicity
Tacrolimus			Renal dysfunction
Zoledronic acid			Renal dysfunction

Potential interaction. No interaction.

Acute kidney injury caused by tenofovir disoproxil fumarate and diclofenac co-administration

M Bickel,[1] P Khaykin,[1] C Stephan,[1] K Schmidt,[1] M Buettner,[2] K Amann,[2] T Lutz,[3] P Gute,[3] A Haberl,[1] H Geiger,[4] HR Brodt[1] and O Jung[4]

- Retrospective analysis of 89 patients with diclofenac prescriptions
- 68.5% treated with TDF regimen
- 31.5% treated with TDF-sparing regimen
- 13 patients (14.6%) developed AKI after initiating diclofenac. ALL were TDF-treated patients.



NSAID	IC50 MRP4 [uM]
Celecoxib	35
Diclofenac	**0.006**
Ibuprofen	26.3
Indomethacin	6.1
Naproxen	42.3
Piroxicam	216

HIV Med 2013; 14: 633-638

Differences in the DDI Profile of TDF & TAF

ANTICONVULSANTS	
Carbamazepine (titrated from 100 mg to 300 mg twice a day), emtricitabine/tenofovir alafenamide (200 mg/25 mg once daily)[4,5]	Tenofovir alafenamide: AUC: ↓ 55% C_{max}: ↓ 57% Co-administration of carbamazepine, a P-gp inducer, decreases tenofovir alafenamide plasma concentrations, which may result in loss of therapeutic effect and development of resistance.

Fluconazole		Dose according to co-ARV*	Inhibition of P-gp
Itraconazole		Dose 10 mg TAF*	Inhibition of P-gp
Ketoconazole		Dose 10 mg TAF*	Inhibition of P-gp
Cyclosporin		Dose 10 mg TAF*	Inhibition of P-gp
Boceprevir		NR**	Stops intracellular activation
Telaprevir		NR**	Stops intracellular activation

NR = Not Recommended
CA = Consider Alternative
* = SmPC differs from the USPI; ** SmPC

www/hiv-druginteractions.org
Descovy Prescribing Information

Differences in the DDI Profile of TDF & TAF

	TDF	TAF	Potential Mechanism
Rifabutin		NR	Induction of P-gp
Rifampicin		NR	Induction of P-gp
Rifapentine		NR	Induction of P-gp
Carbamazepine		CA	Induction of P-gp
Oxcarbazepine		CA	Induction of P-gp
Phenobarbitone		CA	Induction of P-gp
Phenytoin		CA	Induction of P-gp
St John's Wort		NR	Induction of P-gp
Fluconazole		Dose according to co-ARV*	Inhibition of P-gp
Itraconazole		Dose 10 mg TAF*	Inhibition of P-gp
Ketoconazole		Dose 10 mg TAF*	Inhibition of P-gp
Cyclosporin		Dose 10 mg TAF*	Inhibition of P-gp
Boceprevir		NR**	Stops intracellular activation
Telaprevir		NR**	Stops intracellular activation

NR = Not Recommended
CA = Consider Alternative
* = SmPC differs from the USPI; ** SmPC

www/hiv-druginteractions.org
Descovy Prescribing Information

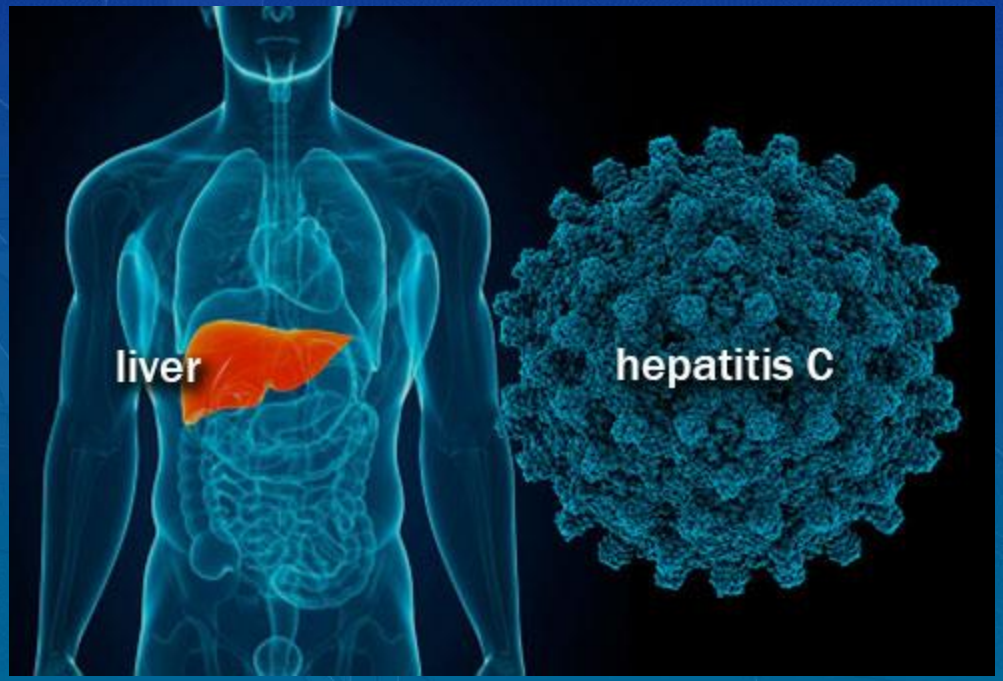
Summary of the DDI Profile of TDF & TAF

1. Overall there are relatively few DDIs with either form of tenofovir.

2. However there are some important differences with the focus on:
   i) TAF absorption and the role of P-gp and
   ii) the difference in circulating TFV

www/hiv-druginteractions.org
Descovy Prescribing Information

DDIs of HCV regimens



HEP iChart app users - please update to the newest version to ensure up-to-date information

HEP Drug Interaction Checker

Access our comprehensive, user-friendly, free drug interaction charts. Providing clinically useful, reliable, up-to date, evidence-based information

Start Now →

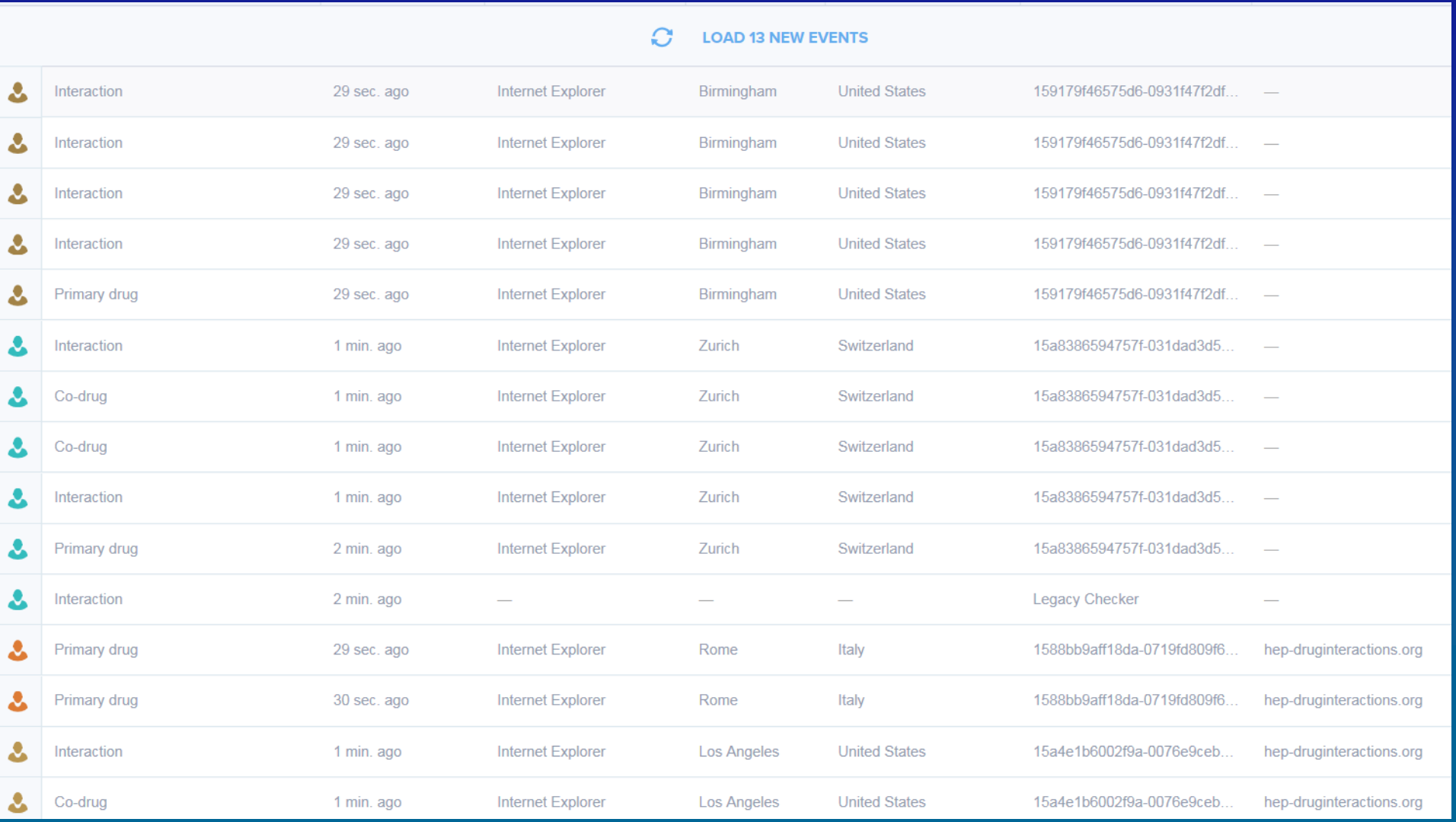
Site News & Twitter Updates

Follow @hepinteractions

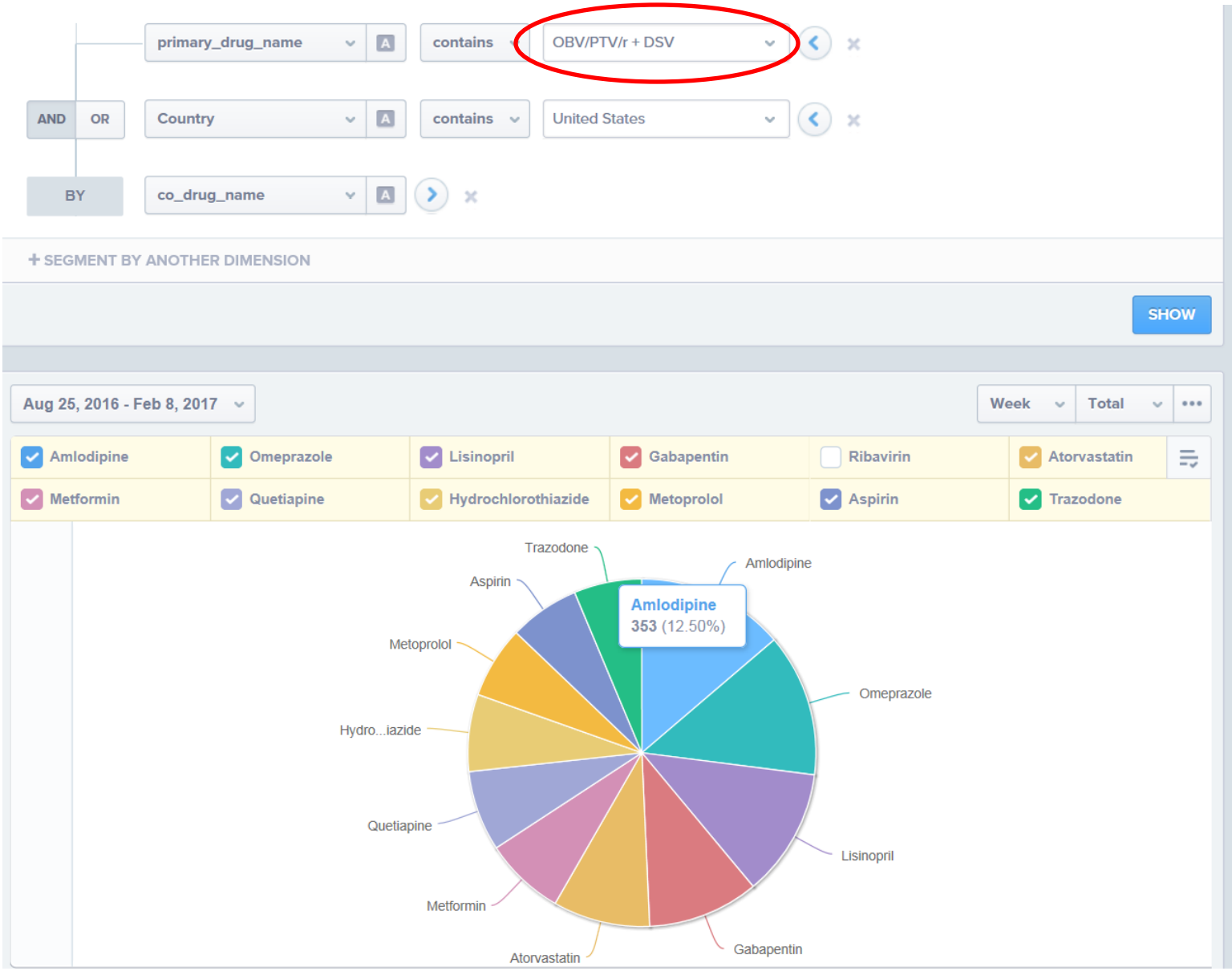
Discover Our HEP Mobile Apps

HEP iChart gives easy access to our drug interaction information on mobile devices. Click the links below for further details and to download the HEP iChart app.

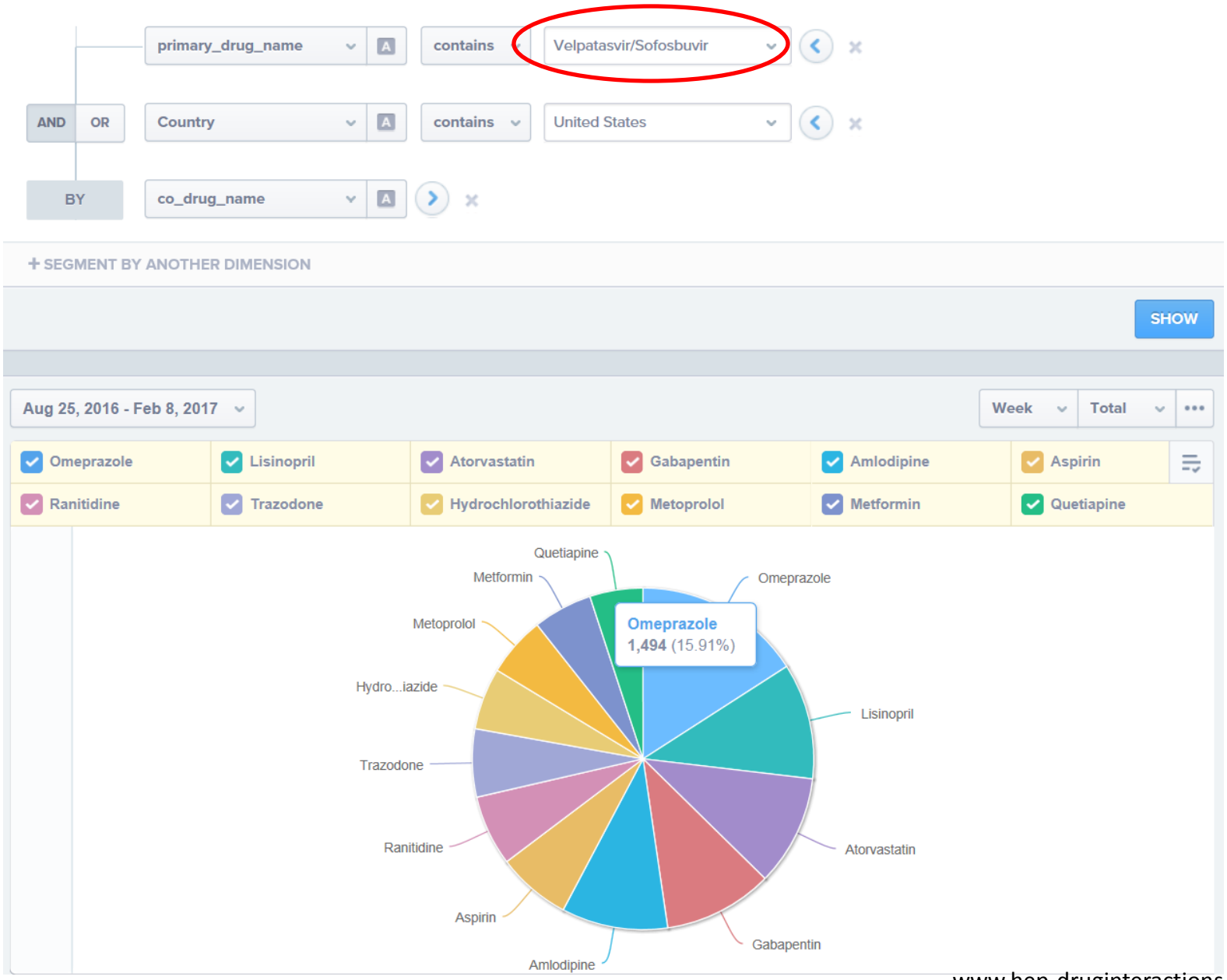
MixPanel Analytics in Real Time



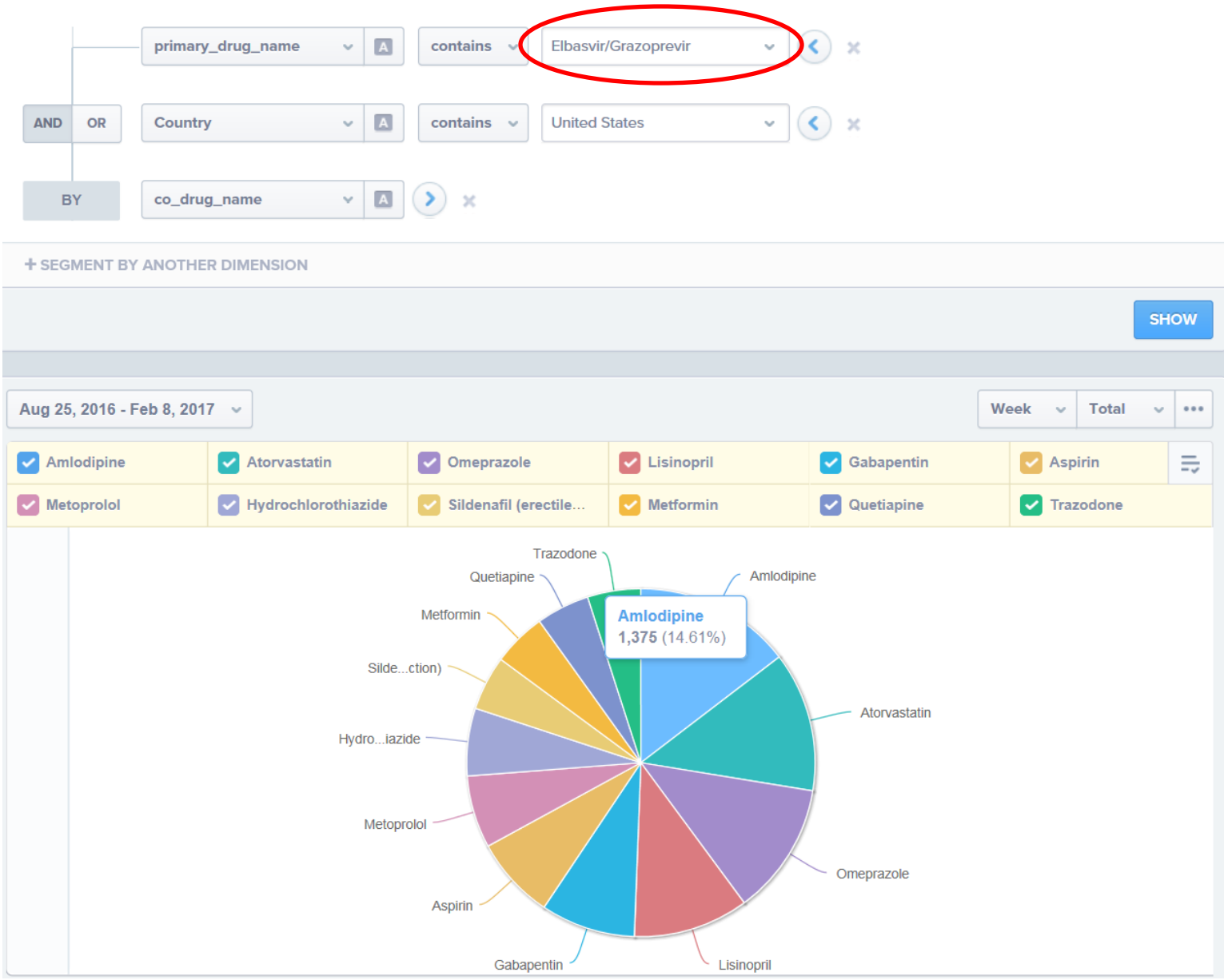
MixPanel – Top Co-med Searches



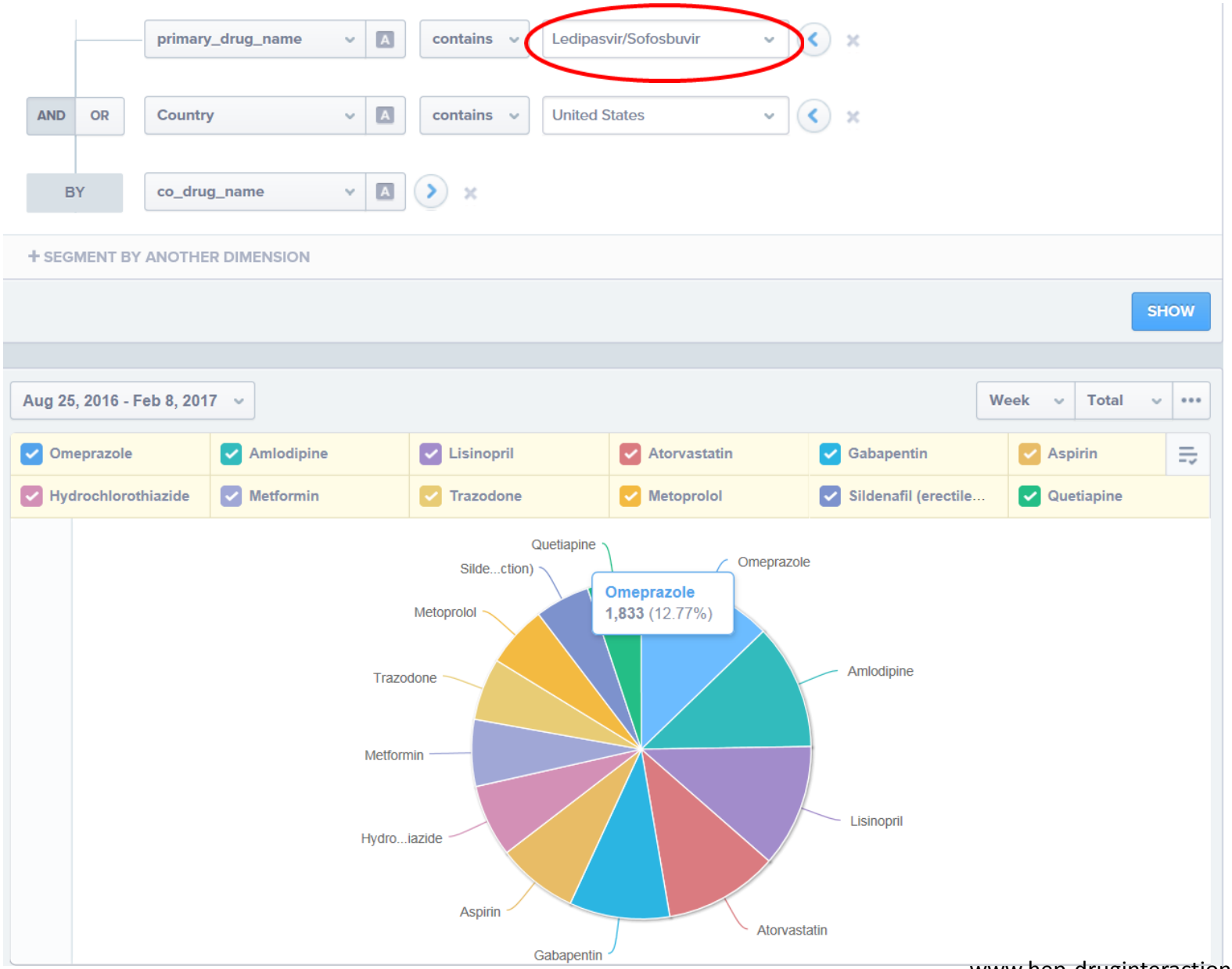
MixPanel – Top Co-med Searches



MixPanel – Top Co-med Searches



MixPanel – Top Co-med Searches



Expansion of the interaction classification to include "yellow".

Tuesday 28 February 2017

We have recently expanded our interaction classification to include a new 'yellow' classification. In contrast to the existing '**amber**' interactions, which are **'potentially clinically significant and likely to require additional monitoring, alteration of drug dosage or timing of administration'**, the new **yellow** classification is for **'potential interactions likely to be of weak intensity where additional action/monitoring or drug dosage adjustment is unlikely to be required**'.

Commonly Searched Interactions: 1. Gastric Acid Modifiers

	Daclatasvir	Elbasvir/Grazoprevir	Ledipasvir/Sofosbuvir	OBV/PTV/r + DSV	Sofosbuvir	Velpatasvir/Sofosbuvir
Aluminium hydroxide	◆	◆	■	◆	■	■
Antacids	◆	◆	■	◆	■	■
Cimetidine	■	◆	■	◆	◆	■
Esomeprazole	◆	◆	■	▲	◆	●
Famotidine	◆	◆	■	◆	◆	■
Lansoprazole	◆	◆	■	▲	◆	●
Omeprazole	◆	◆	■	▲	◆	■
Pantoprazole	◆	◆	■	▲	◆	●
Rabeprazole	◆	◆	■	▲	◆	●

Decrease in LDV exposure with gastric acid modifiers

Decrease in VEL exposure with gastric acid modifiers

Ledipasvir and gastric acid modifiers

- Separate antacids (Mg; Al) by 4 hours
- PPI doses comparable to omeprazole 20 mg can be administered simultaneously with SOF/LDV under fasted conditions *(USPI)*
- H2 blockers should not exceed the equivalent of famotidine 40 mg bd (simultaneously or staggered by 12 h)
- If possible, or doubt best to avoid.

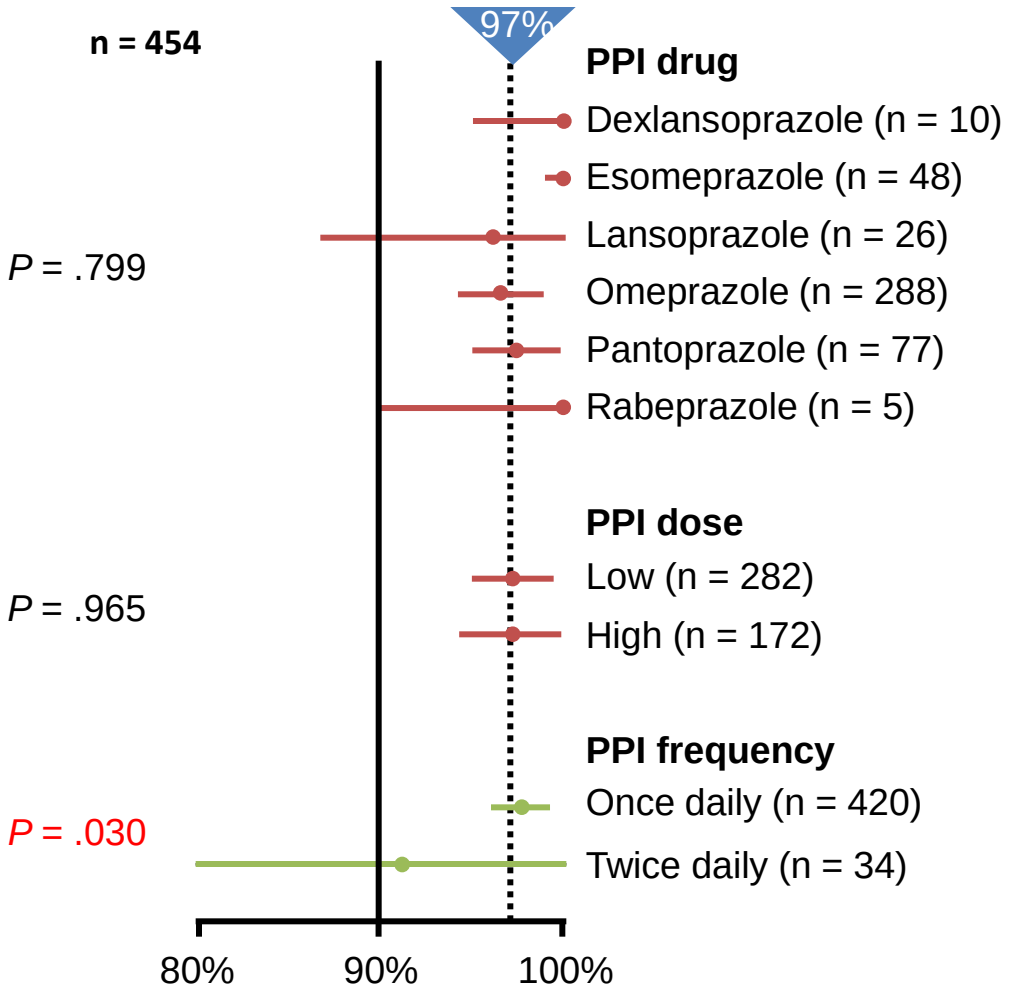
Equivalent PPI doses
Omeprazole 20 mg
Rabeprazole 20 mg
Lansoprazole 30 mg
Pantoprazole 40 mg
Esomeprazole 40 mg

Ledipasvir/Sofosbuvir SMPC (04/16)and US Prescribing Information (02/16)

TRIO Network: Predictors of Response to LDV/SOF by PPI Usage

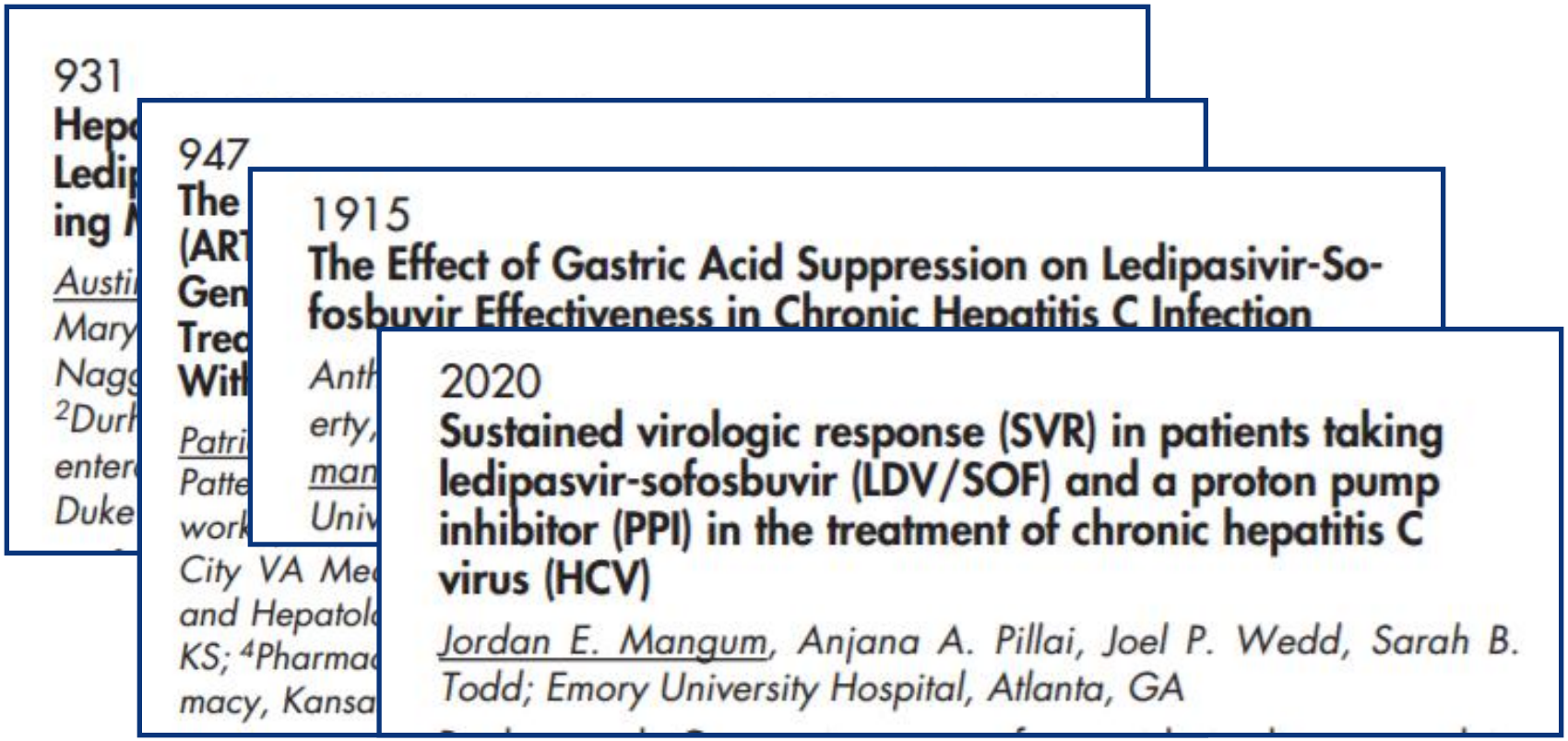
- Per protocol analysis (n = 1979)

"Caution with use of high dose PPIs with LDV/SOF"



Afdhal N, et al. EASL 2016. Abstract LBP519; slide credit clinicaloptions.com.

Real World data: AASLD 2016



931: n=2004 on PPI.	No effect on SVR
947: n=93 on PPI/H2RA.	↓SVR on univariate but no overall effect
1915: n=76/295 on PPI.	Slight ↓ SVR (88.7 v 93.2).
2020: n=102/533 on PPI.	No effect on SVR

1. Who are the patients possibly at risk of PPI Interaction with Ledipasvir/sofosbuvir?

- Those on high dose (or bd) PPI
- Take PPI before the DAA regimen
- HIV co-infected patients

2. Is there a disconnect between PK studies (in healthy) and the 'Real World' data in large HCV cohorts? Importance of PK data in patients.

3. Remember the cost of failure!

Velpatasvir and Gastric Acid Modifiers

- Separate antacids (Mg^{++}; Al^{++}) by 4 hours (*USPI*)

- Coadministration of OMP or other PPIs is **not recommended**. If considered necessary VEL/SOF should be given with food and taken 4 hours before OMP 20 mg. Other PPIs not studied *(USPI)*

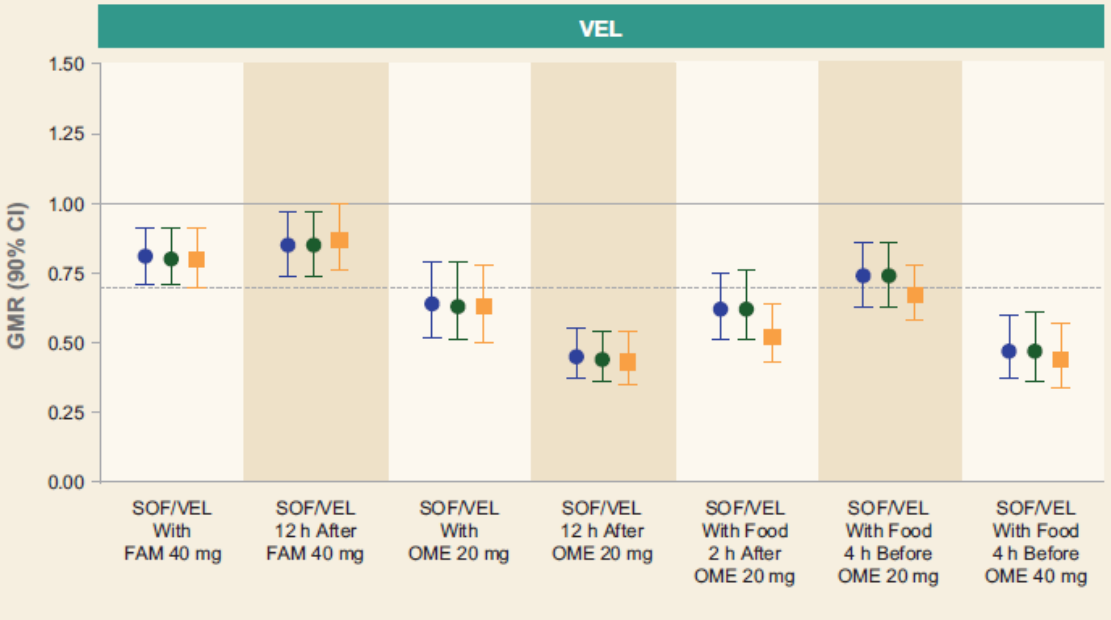
- H2 blockers should not exceed the equivalent of famotidine 40 mg bd (simultaneously or staggered by 12 h).

Equivalent H2R antagonist doses
Famotidine 40 mg bd
Ranitidine 150 mg bd
Cimetidine 400 mg bd

Velpatasvir/sofosbuvir SMPC (04/16)and US Prescribing Information (02/16)

Effect of Food and Acid-Reducing Agents on the Relative Bioavailability and Pharmacokinetics of Sofosbuvir/Velpatasvir Fixed-Dose Combination Tablet

Erik Mogalian, Justin Lutz, Anu Osinusi, Gong Shen, Karim Sajwani, John McNally, John Ling, Anita Mathias
Gilead Sciences, Inc., Foster City, CA



- No significant change in VEL exposure with H_2RA
- Administration of SOF/VEL with food reduced impact of OME 20 mg on VEL (AUC ↓ 26–38% fed vs ↓ 37–56% fasted)
- Higher-dose OME (40 mg) caused 53% lower VEL AUC even with staggered timing and SOF/VEL administration with food

Presented at ASCPT March 2016.

Effect of acid reducing agents on elbasvir exposure

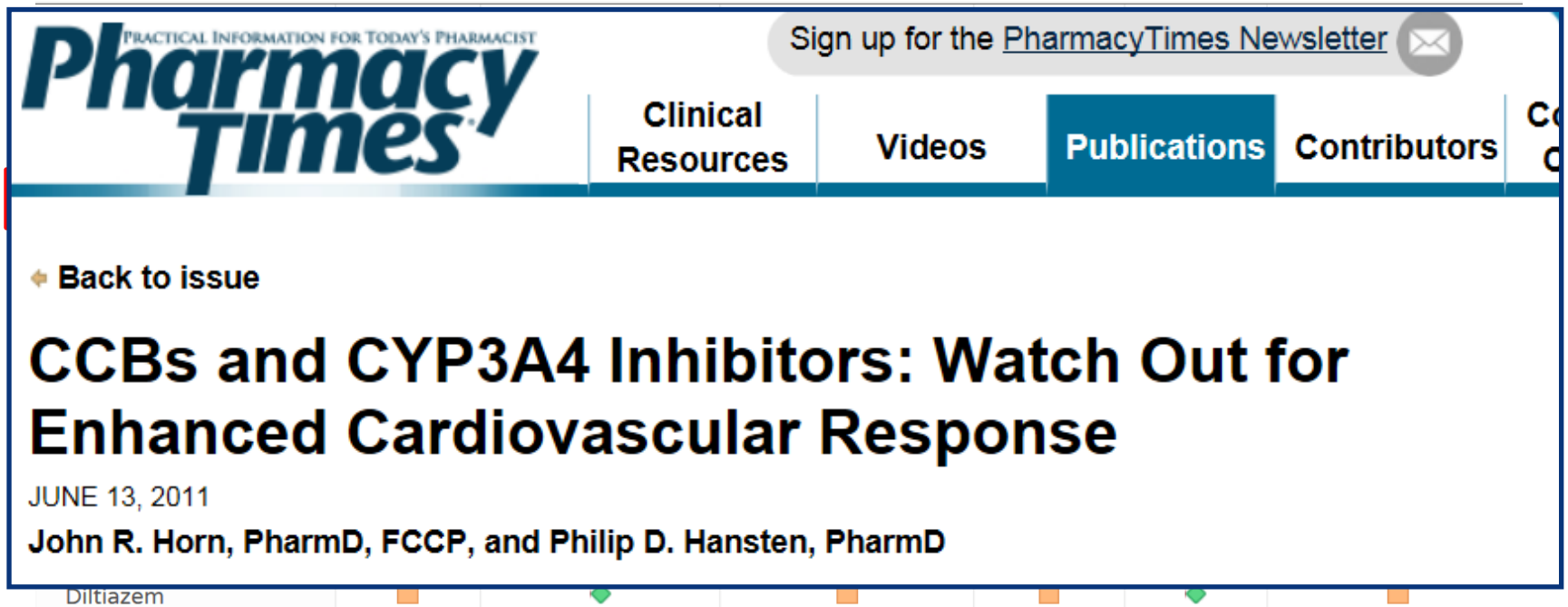
Acid-Reducing Agent							
Famotidine	20 mg single-dose	EBR 50 mg/ GZR 100 mg single-dose	16	EBR	1.05 (0.92, 1.18)	1.11 (0.98, 1.26)	1.03 (0.91, 1.17)
	20 mg single-dose	EBR 50 mg/ GZR 100 mg single-dose	16	GZR	1.10 (0.95, 1.28)	0.89 (0.71, 1.11)	1.12 (0.97, 1.30)
Pantoprazole	40 mg once daily	EBR 50 mg/ GZR 100 mg single-dose	16	EBR	1.05 (0.93, 1.18)	1.02 (0.92, 1.14)	1.03 (0.92, 1.17)
	40 mg once daily	EBR 50 mg/ GZR 100 mg single-dose	16	GZR	1.12 (0.96, 1.30)	1.10 (0.89, 1.37)	1.17 (1.02, 1.34)

Note: EBR/GZR was given 2 hours after Pantoprazole.

The pharmacokinetics of GZR and EBR are not significantly altered by co-administration with famotidine or pantoprazole. Zepatier™ can be co-administered with famotidine, pantoprazole, and other acid reducing agents.

Grazoprevir/elbasvir USPI Feb 2016

Commonly Searched Interactions:
2. Cardiovascular drugs



Pharmacy Times
PRACTICAL INFORMATION FOR TODAY'S PHARMACIST

Sign up for the PharmacyTimes Newsletter

Clinical Resources | Videos | Publications | Contributors

Back to issue

CCBs and CYP3A4 Inhibitors: Watch Out for Enhanced Cardiovascular Response

JUNE 13, 2011

John R. Horn, PharmD, FCCP, and Philip D. Hansten, PharmD

Diltiazem						
Doxazosin						
Enalapril						
Flecainide						
Lisinopril						
Metoprolol						
Nifedipine						
Propranolol						
Ticagrelor						
Vernakalant						
Warfarin						

Exposure-Response Relationship for Ombitasvir and Paritaprevir/Ritonavir in Hepatitis C Virus Subgenotype 1b-Infected Japanese Patients in the Phase 3 Randomized GIFT-1 Study.

Gopalakrishnan S et al Adv Ther 2016; 33: 670-683.

- Data from 321 noncirrhotic and 42 compensated cirrhotic patients analysed (257 on treatment and 106 placebo).
- There were 14 events of peripheral edema (10 grade 1 and 4 grade 2) in patients who received concomitant calcium channel blockers (CCB; 11 amlodipine, 1 nifedipine, 2 benidipine) and OBV/PTV/r; no cases on placebo.
- Incidence of peripheral edema higher in females.
- Not associated with plasma exposure of OBV, PTV or RTV BUT could be related to increased exposure of CCB

Commonly Searched Interactions: 3. Lipid Lowering Drugs

	Daclatasvir	Elbasvir/Grazoprevir	Ledipasvir/Sofosbuvir	OBV/PTV/r + DSV	Sofosbuvir	Velpatasvir/Sofosbuvir
Atorvastatin	■	■	■	●	◆	■
Bezafibrate	◆	◆	◆	◆	◆	◆
Ezetimibe	◆	◆	◆	■	◆	◆
Fenofibrate	◆	◆	◆	◆	◆	◆
Fluvastatin	■	■	■	■	◆	■
Gemfibrozil	◆	■	◆	●	◆	◆
Lovastatin	■	■	■	●	◆	■
Pitavastatin	■	◆	■	■	◆	■
Pravastatin	■	◆	■	■	◆	◆
Rosuvastatin	■	■	●	■	◆	■
Simvastatin	■	■	■	●	◆	■

www.hep-druginteractions.org

Statin Interactions:

	ELB/GZR	LDV/SOF	OBV/PTV/r + DSV	VEL/SOF
Atorvastatin	↑ 94% NTE 20 mg QD	Consider dose reduction	X	Consider dose reduction
Fluvastatin	Use lowest dose NTE 20 mg QD	Consider dose reduction	NR	Use lowest dose
Lovastatin	Use lowest dose	Use lowest dose	X	Consider dose reduction
Pitavastatin	√	Consider dose reduction	NR	Consider dose reduction
Pravastatin	√	Consider dose reduction	↑ 80% NTE 40 mg QD	√
Rosuvastatin	↑ 126% NTE 10 mg QD	X	↑ 2.6-fold NTE 10 mg QD[1] or 5 mg[2]	↑ 170% NTE 10 mg QD
Simvastatin	Use lowest dose NTE 20 mg QD	Use lowest dose	X	Use lowest dose

Is the Statin necessary

NTE, Not to exceed; √, No interaction; X, Do not co-administer; [1] USPI; [2] SMPC. Information from www.hep-druginteractions.org

Commonly Searched Interactions: 4. Gabapentin

	Daclatasvir	Elbasvir/Grazoprevir	Ledipasvir/Sofosbuvir	OBV/PTV/r + DSV	Sofosbuvir	Velpatasvir/Sofosbuvir
Gabapentin	◆	◆	◆	◆	◆	◆

No Interaction Expected

Gabapentin

Summary:

Coadministration has not been studied but based on metabolism and clearance a clinically significant interaction is unlikely. There is no evidence of gabapentin metabolism in humans and it is eliminated unchanged solely by renal excretion with little data on transporters used.

Commonly Searched Interactions: 5. Quetiapine

	Daclatasvir	Elbasvir/Grazoprevir	Ledipasvir/Sofosbuvir	OBV/PTV/r + DSV	Sofosbuvir	Velpatasvir/Sofosbuvir
Quetiapine						

Potential Interaction

Elbasvir/Grazoprevir

Quetiapine

Summary:

Coadministration has not been studied. Concentrations of quetiapine may increase as it is metabolised by CYP3A4 and grazoprevir is a weak inhibitor of CYP3A4 in vitro. As quetiapine has a narrow therapeutic index and unpredictable therapeutic levels, monitor patients closely for signs and symptoms of toxicity. Use with caution and consider therapeutic drug monitoring and/or ECGs during treatment.

Description:

(See Summary)

Viekirax Summary of Product Characteristics, AbbVie Ltd, January 2015.

Clin Pharmacokinet (2016) 55:1471–1494
DOI 10.1007/s40262-016-0407-2

REVIEW ARTICLE

Drug–Drug Interactions Between Direct-Acting Antivirals and Psychoactive Medications

E. J. Smolders[1] · C. T. M. M. de Kanter[2] · R. J. de Knegt[3] · M. van der Valk[4] · J. P. H. Drenth[5] · D. M. Burger[1]

- Grazoprevir is a mild inhibitor of CYP3A4, increasing the exposure of midazolam by ~30%. CYP3A4 substrates are not contraindicated for co-administration with grazoprevir. However, we recommend that prescribers be aware of possible interactions with drugs that are primarily metabolized by CYP3A4 and have a narrow therapeutic range.

Complex Interactions: 1. Anti-Epileptics

- Patient, 57 y male, HCV Genotype 1A
- F4 fibrosis, Child Pugh A, treatment naive.

- Pt treated with lithium for bipolar disorder.
  Lithium led to kidney failure. Patient transplanted and re-transplanted after failure of first kidney graft. Kidney function now normal.

- Lithium stopped, and pt well controlled on oxcarbazepine.

- During treatment for kidney failure, patient infected with HCV but not treated due to concerns of combining treatment with his other medications.

- He then developed epilepsy - controlled by increased doses of oxcarbazepine - **essential** to control both the epilepsy and his bipolar disorder
  - but contra-indicated in combination with all DAAs.

HEP Drug Interactions

UNIVERSITY OF LIVERPOOL

Donate Now

Apps

Interaction Charts | Site Updates | Interaction Query Service | About Us | Pharmacology Resources | Contact Us | Support Us

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

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

Results Key

	Daclatasvir	Elbasvir/Grazoprevir	Ledipasvir/Sofosbuvir	OBV/PTV/r + DSV	Sofosbuvir	Telaprevir	Velpatasvir/Sofosbuvir
Carbamazepine	●	●	●	●	●	●	●
Lacosamide	◆	◆	◆	■	◆	■	◆
Lamotrigine	◆	◆	◆	■	◆	◆	◆
Levetiracetam	◆	◆	◆	◆	◆	◆	◆
Oxcarbazepine	●	●	●	●	●	●	●
Topiramate	◆	◆	◆	◆	◆	◆	◆
Valproate	◆	◆	◆	■	◆	◆	◆
Zonisamide	■	◆	■	◆	◆	■	◆

The impact of carbamazepine on daclatasvir exposure (Hep-NED study)

- 3 patients with severe epilepsy – no switch of carbamazepine possible.
  - Varying genotypes, METAVIR scores, treatment history, treating physicians).
- Varying doses carbamazepine (400 - 1200 mg/day).
- 60mg daclatasvir two times daily or three times daily with normal dose SOF plus intensive PK.
- All subjects obtained SVR.

- Difficult decision, cost implications. Wait for other options?

Smolders E et al EASL April 2017; Early Morning Workshop

Complex Interactions:
2. Recreational Drug User/Chemsex

	Daclatasvir	Elbasvir/Grazoprevir	Ledipasvir/Sofosbuvir	OBV/PTV/r + DSV	Sofosbuvir	Velpatasvir/Sofosbuvir
Cannabis	◆	◆	◆	▲	◆	◆
Cocaine	◆	◆	◆	■	◆	◆
Diamorphine	◆	◆	◆	■	◆	◆
Diazepam	◆	◆	◆	■	◆	◆
Gamma-hydroxybutyrate	◆	◆	◆	■	◆	◆
Ketamine	◆	◆	◆	■	◆	◆
MDMA (Ecstasy)	◆	◆	◆	■	◆	◆
Methamphetamine	◆	◆	◆	■	◆	◆
Phencyclidine	◆	◆	◆	■	◆	◆
Temazepam	◆	◆	◆	◆	◆	◆

■ Potential Interaction ▲ Potential Weak Interaction ◆ No Interaction Expected

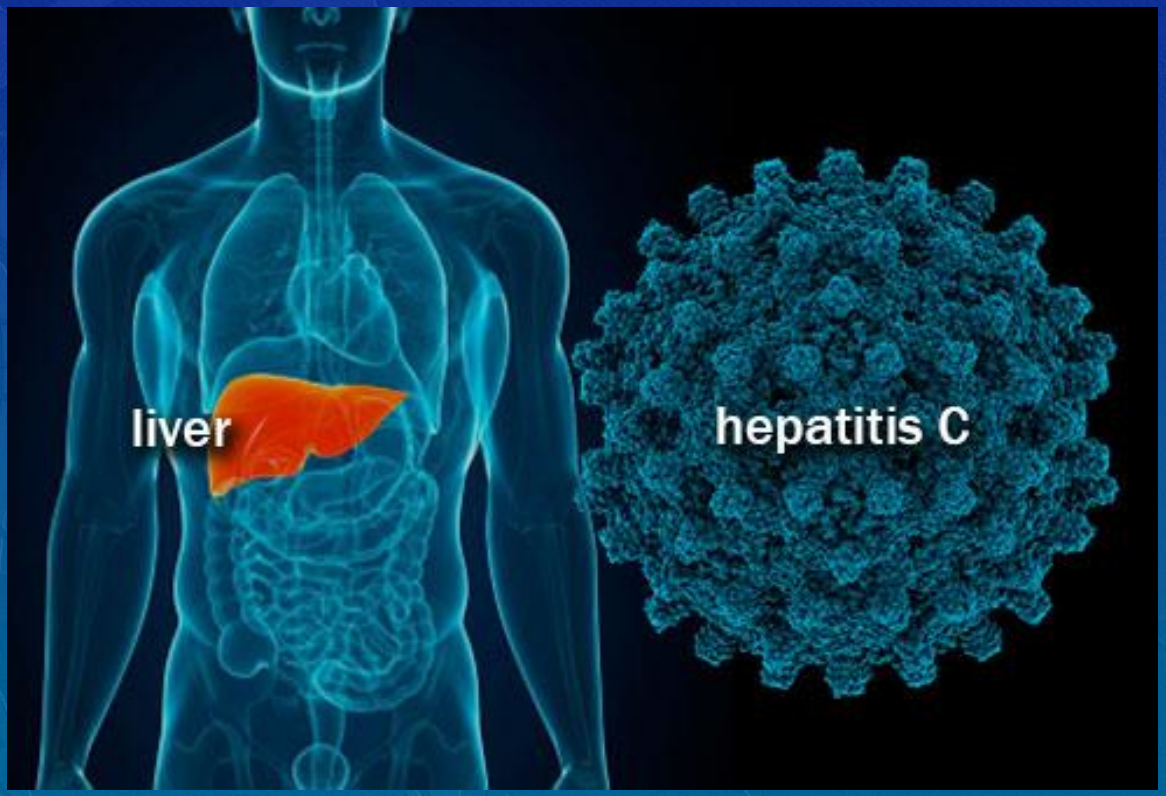
Potential treatment options

Clearly the highest potential for DDIs is with

OBV/PTV/r + DSV

Recreational Drug (AMBERS)	Comment
Cocaine	Some CYP3A4
Diamorphine	Minor CYP3A4 & CYP2D6
Diazepam	STUDY: ↑Cmax ↓AUC
Gamma Hydroxy Butyrate (GHB)	Possible CYP3A4
Ketamine	CYP3A4
MDMA (Ecstasy)	CYP2D6
Methamphetamine	CYP2D6
Phencyclidine	CYP3A4

DDIs of HCV regimens in Development



Glecaprevir/Pibrentasvir

ABT-493*
Pangenotypic NS3/4A protease inhibitor

ABT-530
Pangenotypic NS5A inhibitor

- ❑ Once daily oral dosing
- ❑ Minimal metabolism
- ❑ Primarily eliminated by biliary excretion
- ❑ Negligible renal elimination (< 1%)

Known or potential DDI mechanism		Glecaprevir/Pibrentasvir
Drug Transporter	P-gp, BCRP	Substrate[1], Inhibitor[2]
	OATPs	Substrate[1,3], (Inhibitor)
Drug Metabolising Enzymes	CYP3A4	Weakly inhibits[4,5]
	CYP1A2	Weakly inhibits[4]

1, Kosloski MP, CROI 2017; 2, Kosloski MP, ASCPT 2016; 3, Kosloski MP, AASLD 2015; 4, Kosloski MP, EASL 2016; 5, Kosloski MP, ASCPT 2017.

Glecaprevir/Pibrentasvir

DDI Studied	G/P – the Victim	G/P - Perpetrator
Cyclosporine[1]	G↑37%*; P↑22%*	↔ǂ
Tacrolimus[1]	↔ǂ	↑45% (monitor)
Methadone[2]		↔ǂ
Buprenorphine/Naloxone[2]		↔ǂ
Losartan[3]	↔ǂ	↑56%*
Valsartan[3]	↔ǂ	↑36%*
Felodipine[4]	↔ǂ	↑30%*
Amlodipine[4]	↔ǂ	↑22%*
Midazolam (Cocktail)[5]		↑27%*
Omeprazole (Cocktail)[5]		↓28%*
Rilpivirine[6]	↔ǂ	↑84%*
Raltegravir[6]	↔ǂ	↑47%*
E/C/F/TAF[7]	G↑3-fold*; P↑57%*	EVG↑47%*
DTG/ABC/3TC[7]	G↓21%*; P↓28%*	↔ǂ

1. *Kosloski MP et al; AASLD 2015; 2. Kosloski MP et al; AASLD 2015; 3. Kosloski MP et al AASLD 2016; 4. Kosloski MP et al ASCPT 2017; 5. Kosloski MP et al EASL 2016; 6. Kosloski MP CROI 2016; 7. Kosloski MP et al CROI 2017.*

** Not considered clinically significant; ǂ Change < 20%; CsA effect is dose-dependent.*

G/P in Co-infection

- No dose adjustment is required when the GLE/PIB combination is coadministered with elvitegravir, cobicistat, emtricitabine, TAF, dolutegravir, abacavir or lamivudine.

- Although DRV/r, DRV/cobi and LPV/r (bd) were permitted in patients without cirrhosis in EXPEDITION-2[1] – we await the label data.

[1]Rockstroh J et al EASL 2017 LB-522

Sofosbuvir/Velpatasvir/Voxilaprevir

- Once daily dosing (400/100/100 mg)

Known or Potential DDI Mechanisms of SOF, VEL, and VOX

DDI Mechanism		SOF (nonclinical and clinical)[5*]	VEL (nonclinical and clinical)[6]	VOX (nonclinical)[7,8]
Drug Transporters	P-gp/BCRP	Substrate	Substrate/Inhibitor	Substrate[†]
	OATPs	—	Substrate/Inhibitor[‡]	Substrate/Inhibitor[§]
Drug-Metabolizing Enzymes[‖]	CYP3A4	—	Substrate	Substrate
	CYP2C8	—	Substrate	Substrate
	CYP2B6	—	Substrate	—

Kirby BJ et al 17th IWCPHHT, Washington 2017; Garrison K et al 2017 EASL Abs FRI-187

Sofosbuvir/Velpatasvir/Voxilaprevir

DDI potential

- ❑ SOF/VEL/VOX as **perpetrator** – few interactions.

  Inhibits P-gp, BCRP and OATPs – so eg **rosuvastatin** (BCRP/OATP substrate) is **not recommended;**
  Others - dose adjustment/caution/monitoring (eg **dabigatran**).

- ❑ SOF/VEL/VOX as **victim/object**.

  Strong inducers reduce SOF, VEL and/or VOX (eg **rifampicin**) – **contraindicated**.
  ATV/r (inhibition of VOX) or **efavirenz** (induction of VEL) is **not recommended**
  Increase in VOX with strong OATP inhibitors (eg **CsA**) – **not recommended**

Kirby BJ et al 17th IWCPHHT, Washington 2017; Garrison K et al 2017 EASL Abs FRI-187

Summary

- Patients with HCV have a high burden of comorbidities and concomitant medications
- DDIs between HCV DAAs and co-medications can reduce clinical efficacy and lead to unwanted AEs
- DDIs have to be considered with all HCV DAAs
- Online resources are available to map potential interactions between HCV DAAs and concomitant medications: eg www.hep-druginteractions.org

HIV Management
Hepatitis Management

THE NEW YORK COURSE