Hepatitis C Virus: Pharmacologic Considerations
Disclosures for Cody Chastain, MD

- No financial disclosures
Objectives

At the end of this session, the learner will be able to:

- Review pharmacokinetic properties of currently utilized HCV medications
- Identify common drug interactions that impact HCV medications
- Discuss practical management of drug interactions and drug elimination
Pharmacokinetics

- “Movement of drugs”

- Study of the relationship between dose, amount of drug in the body and therapeutic or toxic effects of a drug

- Pharmacokinetic data helps us understand:
  - Dose and schedule
  - Dose adjustments due to drug interactions and other issues
Pharmacokinetics: Steps

- **Absorption**
  - Drug enters the blood

- **Distribution**
  - Drug travels in the blood
  - Drug disbursement in the body

- **Metabolism**
  - Body changes the drug
  - Usually in intestine or liver

- **Excretion**
  - Kidneys through urine
  - Liver through stool
Schematic representation of drug-metabolizing enzymes and drug transporters demonstrated to be affected by the 3D regimen as perpetrators (A) and important pathways involved in the disposition and elimination of the 3D regimen as victims (B).

Mohamad Shebley et al. Drug Metab Dispos 2017;45:755-764

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## Pharmacokinetics: CYP3A4

### CYP 3A4 Inhibitors
- Azole antifungals
- Protease inhibitors
- Ritonavir
- Calcium Channel Blockers (CCBs)
- Clarithromycin
- Nefazodone
- Telithromycin

### CYP3A4 Inducers
- Anticonvulsants
- Rifamycins
- St Johns Wort
- Non-Nucleoside Reverse Transcriptase Inhibitors
- Modafinil
- Dexamethasone
- Bosentan
- Nafcillin
Pharmacokinetics: Final Review

- Drug Transporters
  - Move drug across membranes
  - Affect absorption, excretion, movement into organs
  - Efflux (e.g. P-gp)
  - Uptake (e.g. OATP)

- P-gp Inhibitors: azoles, CCBs, PIs, amiodarone
- P-gp Inducers: carbamazepine, rifampin, phenytoin, St John’s Wort
- P-gp Substrates: digoxin, loperamide

- OATP1B1 and BCRP substrate: rosuvastatin
HEP Drug Interactions

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Start Now →
COMMON THINGS BEING COMMON…
## Acid Suppressing Agents

<table>
<thead>
<tr>
<th>Impacted</th>
<th>Not Impacted</th>
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<tbody>
<tr>
<td>Ledipasvir</td>
<td>Elbasvir/Grazoprevir</td>
</tr>
<tr>
<td>Velpatasvir</td>
<td>Daclatasvir</td>
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<tr>
<td>Glecaprevir</td>
<td>Sofosbuvir</td>
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<td></td>
<td>Ombitasvir/Dasabuvir/pibrentasvir/ritonavir</td>
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<tr>
<td></td>
<td>Voxilaprevir</td>
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<tr>
<td></td>
<td>Pibrentasvir</td>
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</table>
H2 Antagonists/Antacids

- **H2 Antagonist:**
  - Administration: Simultaneously or 12 hours apart
  - Maximum equivalent to famotidine 40mg twice daily

- **Antacids:** Separate by 4 hours
Proton Pump Inhibitors

- **Ledipasvir/sofosbuvir**:  
  - Administer *simultaneously*  
  - Maximum equivalent to pantoprazole 40mg

- **Sofosbuvir/velpatasvir**:  
  - Administer with food *4 hours before PPI*  
  - Maximum equivalent to omeprazole 20mg. No other PPIs have been studied.

- **Glecaprevir/pibrentasvir**  
  - Administer simultaneously  
  - Limit does to omeprazole 20mg or equivalent if possible
<table>
<thead>
<tr>
<th></th>
<th>Rosuvastatin</th>
<th>Atorvastatin</th>
<th>Pravastatin</th>
<th>Lovastatin</th>
<th>Simvastatin</th>
<th>Pitavastatin</th>
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<td>↑ atorva-</td>
<td>↑ prava-</td>
<td>↑ lova-</td>
<td>↑ simva-</td>
<td>↑ pitava-</td>
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<td>Lowest dose, Monitor</td>
<td>Monitor</td>
<td>Lowest dose, Monitor</td>
<td>Monitor</td>
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<td>↑ atorva-</td>
<td>OK</td>
<td>↑ lova-</td>
<td>↑ simva-</td>
<td>↑ pitava-</td>
</tr>
<tr>
<td></td>
<td>Max 10mg</td>
<td>Lowest dose, Monitor</td>
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<td>Monitor</td>
<td>Lowest dose, Monitor</td>
<td>Monitor</td>
</tr>
<tr>
<td><strong>Pibrentasvir/glecaprevir</strong></td>
<td>↑ rosuva-</td>
<td>↑ atorva-</td>
<td>↑ prava-</td>
<td>↑ lova-</td>
<td>↑ simva-</td>
<td>↑ pitava-</td>
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<td>Max 20mg</td>
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<td>Monitor</td>
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<td>Reduce 50%</td>
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<td>↑ atorva-</td>
<td>OK</td>
<td>↑ lova-</td>
<td>↑ simva-</td>
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<tr>
<td><strong>Velpatasvir/Voxilaprevir/Sofosbuvir</strong></td>
<td>↑ rosuva-</td>
<td>↑ atorva-</td>
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<td>↑ lova-</td>
<td>↑ simva-</td>
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</table>
HCV Medication Interactions

HEP Drug Interactions

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Summary

- Due to pharmacokinetic properties of HCV meds, drug interactions are common
- Patients should be screened closely prior to and during treatment for interactions
- Complicated patients (i.e. HIV coinfected, cirrhotic patients, severe renal impairment) require additional considerations