READYING HIV/HCV COINFECTED PATIENTS FOR HCV TREATMENT: OCCURRENCE AND MANAGEMENT OF ANTIVIRAL INTERACTIONS

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PREVIOUS CHALLENGES FOR TREATMENT OF HIV/HCV COINFECTION

- Safety & Tolerability
- Efficacy
- Dosing Complexity
- Payer Sources
- Drug-Drug Interactions
OBJECTIVE

To assess the frequency and degree of potential drug-drug interactions between antiretroviral agents and DAA drug in HIV/HCV co-infected patients receiving care at an academic medical center.
METHODS

- Retrospective review of HIV/HCV Coinfected patients in care at University of Colorado Hospital Infectious Disease Group Practice Clinic
  - All patients 18 years of age or older
  - Chronic HCV Infection
  - Active HIV antiviral prescription within last year
- Analysis of possible drug-drug interactions between baseline HIV antivirals and different HCV regimens
- Categories of drug-drug interactions
  - **Severe Interaction:** Unsafe, the medications should not be coadministered
  - **Moderate Interaction:** Requires additional monitoring and/or dose adjustments
  - **No Significant Interaction:** Safe, no adjustments required
### ASSESSMENT OF DRUG-DRUG INTERACTIONS

<table>
<thead>
<tr>
<th></th>
<th>Simeprevir¹</th>
<th>Sofosbuvir²</th>
<th>Ledipasvir³⁻⁵</th>
<th>Daclatasvir⁶⁻⁷</th>
<th>AbbVie 3D⁸⁻¹⁰</th>
</tr>
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<tbody>
<tr>
<td><strong>ATV/r</strong></td>
<td>No data</td>
<td>No data</td>
<td>↑ LDV, ↑ ATVᵃ</td>
<td>DCV ↑ᵇ</td>
<td>ABT450 ↑; ATV ↑</td>
</tr>
<tr>
<td><strong>DRV/r</strong></td>
<td>SIM ↑; DRV ↔</td>
<td>SOF ↑; DRV ↔</td>
<td>↑ LDV, ↔ DRVᵃ</td>
<td>DCV ↑</td>
<td>3D ↓/↑; DRV ↓</td>
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<tr>
<td><strong>LPV/r</strong></td>
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<td>No data</td>
<td>No data</td>
<td>DCV ↑</td>
<td>ABT450 ↑; LPV ↳</td>
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<tr>
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<td>No data</td>
<td>No data</td>
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<tr>
<td><strong>EFV</strong></td>
<td>SIM ↓; EFV ↔</td>
<td>SOF ↔; EFV ↔</td>
<td>LDV ↓; EFV ↓ᵃ</td>
<td>DCV ↓ᵇ</td>
<td>No PK dataᶜ</td>
</tr>
<tr>
<td><strong>RPV</strong></td>
<td>SIM ↔; RPV ↔</td>
<td>SOF ↔; RPV ↔</td>
<td>LDV ↔; RPV ↔</td>
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<td>ABT450 ↑; RPV ↑</td>
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<tr>
<td><strong>ETR</strong></td>
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<tr>
<td><strong>RAL</strong></td>
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<td>SOF ↔; RAL ↔</td>
<td>LDV ↔; RAL ↔</td>
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<td>3D ↔; ↑ RAL</td>
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<tr>
<td><strong>EVG/cobi</strong></td>
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<td>SOF ↑; ELV/cobi ↑</td>
<td>LDV ↑; ELV/cobi ↑</td>
<td>No data</td>
<td>No data</td>
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<tr>
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<tr>
<td><strong>MVC</strong></td>
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<td>No data</td>
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<td><strong>TDF</strong></td>
<td>SIM ↔; TFV ↔</td>
<td>SOF ↔; TFV ↔</td>
<td>LDV ↔; ↑ TFV</td>
<td>DCV ↔; TFV ↔</td>
<td>3D ↔; TFV ↔</td>
</tr>
</tbody>
</table>

ᵃWatch renal function, TFV levels increased, ᵃᵇDecrease DCV dose to 30mg QD with ATV, increase DCV dose to 90mg QD with EFV, ᵇ3D + EFV led to premature study discontinuation due to toxicities

ASSESSMENT OF 4 POSSIBLE REGIMENS

<table>
<thead>
<tr>
<th></th>
<th>NS3/4A</th>
<th>NS5A</th>
<th>NS5B</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Function</td>
<td>Component of HCV Replication Complex</td>
<td>RNA-dependent RNA polymerase</td>
</tr>
<tr>
<td></td>
<td>Serine Protease</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Drugs</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>Simeprevir</td>
<td>Ledipasvir</td>
<td>Nucleoside analogs</td>
</tr>
<tr>
<td>2.5</td>
<td>Paritaprevir/rit</td>
<td>Daclatasvir</td>
<td>Sofosbuvir</td>
</tr>
<tr>
<td>3</td>
<td></td>
<td>Ombitasvir</td>
<td>Non-nucleoside</td>
</tr>
<tr>
<td>4</td>
<td></td>
<td></td>
<td>Dasabuvir</td>
</tr>
</tbody>
</table>

1. SIM/SOF  2. SOF/LDV  3. SOF/DCV  4. 3D
RESULTS

- 125 patients identified and analyzed
- Contained the below medications

- **Tenofovir**: 81% (101/125)
- **Raltegravir**: 35% (44/125)
- **Efavirenz**: 16% (20/125)
- **Protease Inhibitor**: 40% (50/125)

*2 patients (1.6%) were not taking HIV medications at time of analysis*
Percentage of HIV Regimens with Moderate or Severe Interactions

- SIM/SOF: 70%
- SOF/LDV: 64%
- SOF/DCV: 46.6%
- 3D: 61%
SEVERE INTERACTIONS

Percentage of HIV Regimens with Severe Interactions

- SIM/SOF: 64%
- SOF/LDV: 9.6%
- SOF/DCV: 0%
- 3-D: 40.8%
MODERATE INTERACTION

Percentage of HIV Regimens with Moderate Interactions

- SIM/SOF: 7%
- SOF/LDV: 54%
- SOF/DCV: 46.6%
- 3D: 20%
NO SIGNIFICANT INTERACTION

Percentage of HIV Regimens with No Significant Interactions

- SIM/SOF: 29%
- SOF/LDV: 34%
- SOF/DCV: 52%
- 3D: 38%
Percentage of patients’ HIV Antiviral Interactions with SOF/LDV

- Severe: 5.7%
- Moderate: 48.6%
- No Significant: 45.7%

SUBSET:
35 OF 125 PTS PRESCRIBED SOF/LDV
17 (48.6%) patients with moderate interactions

- 10 patients switched their HIV regimen
- 7 patients did not switch their HIV regimen
  - 2 on salvage regimens
  - 3 had adherence issues and low viremia
  - 2 preferred to stay on their regimen
Resistance:
- Analyzed the resistance profile of all 35 patients
  - All available HIV Genotypes, Phenotypes, and/or Phenosense
- 7 (20%) of the 35 patients would not be eligible to change their HIV regimen due to resistance
- 5 did not have significant drug interactions, but 2 had moderate interactions and switching their regimen was not an option

Patient Adherence Challenges
- Switch from once daily regimen to BID (raltegravir)

Regimen Specific Requirements
- Food, time of day
Potential moderate or severe interactions with at least one of the four HCV regimens were identified in 70.4% (88/125) patients.

- Did not assess any concomitant medications

This analysis shows that drug-drug interactions between HIV and HCV medications are common.

Illustrates the need for expertise in management of drug-drug interactions in this population and that many patients will require a change to antiretroviral therapy or increased monitoring.