Viral hepatitis in patients living with HIV: can we still speak of “special population”? 

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YES for HBV

• Excluded by most clinical trials
• Natural history HBV is different
• Higher risk of delta coinfection
• Risk of HBV flares in HIV patients
• Therapy for HBV commonly initiated in this group
YES for HCV

• Excluded by most clinical trials
• More severe clinical course
• Drug interactions for HCV infected patients
• Acute HCV in MSM is more frequent
New clinical trials

• Liver steatosis is as frequent in HIV patients as in patients without HIV
• HCV studies with DAA’s
• HBV studies with anti-core molecules

HIV patients routinely excluded
Guidelines based on evidence

- NIH: A Strong; B Moderate; C Optional
  Based on I (RCT); II (other trials); III (Expert opinion)

- AASLD: GRADE approach (Grades of recommendations, assessment, development and evaluation)
  - Strength of evidence
  - Strength of recommendation (Recommends vs. suggests)
Guidelines in HIV patients

• Both HBV and HCV tested in all patients (A III)
• If either HIV OR HBV need to be treated, then TDF-FTC (or 3TC) should be the backbone (A I)
• Patients on TDF need to be evaluated for Creatinine and Phosphorus, also U/A at least annually
• ETV cannot be used as monotherapy (A II)

NIH HIV Guidelines rev 2016
Natural History HBV

• Patients with HIV/HBV had 8-fold greater liver mortality (vs. HBV alone)
• This decreased to 2-fold after 1996 #
• Recent meta-analysis suggests improved overall mortality in HIV/HBV co-infected patients after HAART *
• preHAART all cause mortality 1.60 (1.07-2.4)
• After HAART 1.28 (1.03-1.60)

# Thio et al Lancet 2002
* Nikolopoulous et al CID 2009
Delta hepatitis

• Associated with more advanced liver disease
• Associated with IDU

• VA study: prevalence of Delta Ab in HIV+ (5.2%) vs HIV –ve (3.5%) @
• European data suggest ~15% Delta Ab vs. worldwide estimates ~ 5% * &

@ Kushner J Hepatol 2015
* Soriano AIDS 2011 & Rizzetto Sem Liv Dis 2012
HBV flares

- Abrupt elevation of ALT > 5 x ULN in a patient who is HBsAg positive
- Usually associated with elevated HBV DNA
- After therapy: due to HBV DNA rebound
- During N(t)A therapy:
  - Early: IRD vs non compliance
  - Late: Resistance vs. non compliance

Chang and Liaw J Hepatol 2014
HBV flares

- During Lam 4% flare *
- During PEG-IFN 5-6% *
- During TDF 6% #

- During Lam in HIV+ 38% flare &
- During TDF in HIV+ 13% flare &

* Lau GKK NEJM 2005
# Chang and Liaw J Hepatol 2014 & Crane JID 2009
HCV
Guidelines for HCV in HIV

- If CD4 > 500 and untreated; may consider first treat HCV to avoid DDI (C III)
- If CD4 < 500; should tackle HIV first and start anti-HCV therapy when stable (B II)
- HCV associated with DILI, thus recommendation to test ALT, week 2, 8, then q 3-6 months after starting ARV

NIH HIV guidelines rev. 2016
Natural History HCV

• HIV/HCV co-infected patients with HIV >500 copies have 50% higher chance of liver decompensation compared to HCV monoinfected *

• Coinfected patients have more advanced stages of HCC in Europe #, but not in the U.S. &

Interferon based therapies

- In the era of Peg-interferon + ribavirin HIV patients with HCV gt 1 infection had lower SVR rates (29%) than HCV monoinfected patients (41% with 800 mg RBV; 53% with wt based dosing)

Pegasys PI updated 2014
Main DDI in HIV patients

• Daclatasvir dose needs to be adjusted with EFV (90 mg/day) or boosted ATV (30 mg/d)

• LDV (part of Harvoni) inhibits p-GP, thus enhances TDF bioavailability

• Paritaprevir: OK with RAL or ATV (w/o boosting)

• Tipranavir induces p-GP, thus reduces bioavailability of several HCV antivirals
## Acceptable HAART with specific HCV DAA’s

<table>
<thead>
<tr>
<th>DAA</th>
<th>Acceptable HAART</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sof/Ledipasvir</td>
<td>TDF/FTC + RPV or EFV or RAL or DTG; DRV/r</td>
</tr>
<tr>
<td>Grazo/Elba</td>
<td>TDF/FTC + RPV or RAL or DTG. ABC/3TC</td>
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## Acceptable HAART with specific HCV DAA’s

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</table>
| Daclatasvir/SOF | TDF/FTC + RPV or EFV or RAL or DTG; DRV/r  
High dose if EFV  
Low dose for boosted PI’s |
| PrOD    | TDF/FTC + ATV w/o RTV;  
Integrase inhib OK; 3TC/ABC                                                     |
## HAART contraindications

<table>
<thead>
<tr>
<th>HAART CI/not recommended</th>
</tr>
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<tbody>
<tr>
<td><strong>Sof/Ledipasvir</strong></td>
</tr>
<tr>
<td>Maraviroc; TPV; (increased TDF with RTV)</td>
</tr>
<tr>
<td><strong>Gazo/Elba</strong></td>
</tr>
<tr>
<td>Elvitegravir/cobi; EFV, NVP; no PI’s</td>
</tr>
<tr>
<td><strong>Daclatasvir/SOF</strong></td>
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<tr>
<td>TPV, NFV</td>
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<tr>
<td><strong>PrOD</strong></td>
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<tr>
<td>Elvitegravir/cobi; RPV; EFV, NVP; LPV, DRV</td>
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</table>
Acute HCV infection

• Definition: HCV diagnosed within 6 months of exposure
• Monthly HCV RNA testing advised to be able to diagnose a spontaneous cure
• Do all acute patients need therapy?
Acute HCV infection

• In MSM the annual incidence increased from 0.8% (1995) to 2-3% (2005) *

• In all risk groups combined (USA data) 0.02% #

* Soriano AIDS Rev 2013    # CDC data 2013
Tenets of HCV management in HIV patients

• Work closely with HIV provider *
• Try not to change a successful ART *
• Prevention acute HCV infection
• Vaccination HAV and HBV

* HCV guidance AASLD/IDSA Feb 2016
Conclusions

• Patients living with HIV may respond to HBV and HCV antivirals in a manner similar to patients without HIV
• In terms of natural history, HBV and HCV patients with HIV may well have worse hepatic outcomes
• Because of higher risk of delta coinfection and higher risk of flares with HBV
• Because of major DDI’s and higher rates of acute HCV
• Patients with HIV and either HBV or HCV remain a special population