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

HBV

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

* Nikolopoulos 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. &

* Lo Re et al Ann Int Med 2014 # Puoti et al AIDS 2004

& Yopp CGH 2012

Interferon based therapies

- In the era of Peg-interferon +ribavirin HIV patients with HCV gt 1 infection had lower SVR rates (29%) than HCV moninfected 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

DAA	Acceptable HAART
Sof/Ledipasvir	TDF/FTC + RPV or EFV or RAL or DTG; DRV/r
Grazo/Elba	TDF/FTC + RPV or RAL or DTG. ABC/3TC

Acceptable HAART with specific HCV DAA's

	Acceptable HAART
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

	HAART CI/not recommended
Sof/Ledipasvir	Maraviroc; TPV; (increased TDF with RTV)
Grazo/Elba	Elvitegravir/cobi; EFV, NVP; no PI's
Daclatasvir/SOF	TPV, NFV
PrOD	Elvitegravir/cobi; RPV; EFV, NVP; LPV, DRV

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**