Treatment of HIV/HCV co-infection with direct acting antiviral (DAAs)

Mehri Nikbin, MD
Infectious Diseases and Tropical Medicine specialist
Iran Hepatitis Network (IHN)
Middle East Liver Disease (MELD)
Email: nikbin_mehri@yahoo.com

1

Background

HIV / HCV co-infection is double trouble

Compared to HIV-negative individuals, those with HIV suffer:

- Accelerated rate of fibrosis, higher rates of cirrhosis
- Higher rates of decompensation & higher liver-related mortality
- Unfortunately these patients have decrease access to liver transplantation compare with mono infected patients

To reduce the burden of HIV/HCV co-infection we must screen, test, and treat!

2

Background

- ❖Treatment of HCV in this patients population should have a high priority
- ❖All HIV infected patients should be screened for HCV

3

Background

Treatment

- HIV/HCV coinfected patients should be treated and retreated the same as patients without HIV
- After recognizing and managing interactions with antiretroviral medications and direct acting antivirals (DAAs)
- Antiretroviral drug switches ,when needed , should be done with goal of maintaining HIV suppression without compromising future options
- (prior treatment history – response to antiretroviral therapy – resistance profiles – drug tolerance)

4

Antiviral HCV Treatments

(FDA-approved as of February 12), 2016

Monotherapies

IFN-2a

IFN-2b

PEG-IFN 2a

PEG-IFN 2b

IFN-2a + Ribavirin

IFN-2b + Ribavirin

PEG-IFN 2a + Ribavirin*

PEG-IFN 2b + Ribavirin

PEG-IFN + ribavirin plus either:

Boceprevir (GT1)

Telaprevir (GT1)

Simeprevir (GT1)

In combination with other agents:

Sofosbuvir

Daclatasvir + Sofosbuvir (GT1,3)*

Elbasvir + Grazoprevir (FDC) GT1,4

Sofosbuvir +velpatasvir All GT

Ledipasvir + Sofosbuvir (FDC) (FDC, GT1,4,5,6*

Paritaprevir / ritonavir / ombitasvir (FDC) + dasabuvir (GT1)

Paritaprevir / ritonavir / ombitasvir (FDC) (GT4

Simeprevir + Sofosbuvir (GT1)

5

Regimens not recommended for Patients with HIV/HCV

- Antiretroviral treatment interruption to allow HCV therapy is not recommended
- Ribavirin should not be used with Didanosine/Stavudine or Zidovudine
- Sofosbuvir-based regimen should not be used with Tipranavir
- Should not be used treatment shorter than 12 weeks

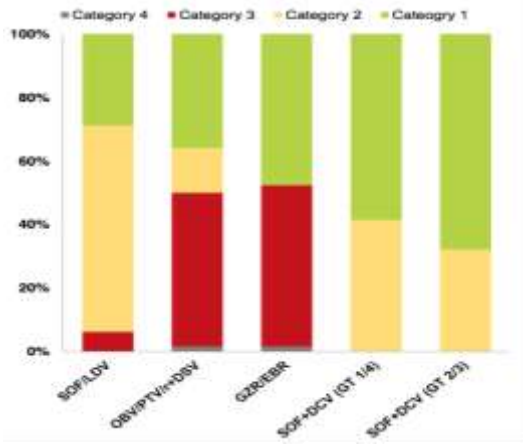
6

Drug – Drug interaction

- Contraindication :
- Simeprevir
- Elbasvir / Grazoprevir
- No problem :
- Sofosbuvir / Ledipasvir
- Sofosbuvir
- Interaction:
- Sofosbuvir / Velpatasvir with EFV / NVP / ETV

Treatment of HCV/HIV co-infection, July 2016

Drug-Drug Interactions Remain Important for:



CAT 1 = no DDI
CAT 2 = potential, may require dose reduction or monitoring
CAT 3 = contraindicated
CAT 4 = unknown interaction

Martinello et al, CROI 2016, Abstract 451

8

Treatment Guidelines:

- ✓ 2017 HCV/HIV treatment EASL guidelines :
- ✓ Sofosbuvir ®+Dacatasvir®
- ✓ Sofosbuvir®+Ledipasvir®
- ✓ Sofosbuvir +velpatasvir

In genotype 1a,1b,3a,4,5,6

- ➢ Treatment duration is more systematically extended to 6 months in case of compensated cirrhosis depending upon to genotype

9

Treatment of HCV/HIV co-infection, July 2016

Study Design and Methodology

10

Study Design and Methodology

- Prospective longitudinal study
- 122 patients with chronic HCV coinfected with HIV,undertreat ART and 38 previously treated for HCV (Peginterferon® +Ribavirin®) and no SVR
- All patients CD4 > 127
- HCVRNA viral load :was assessed by Cobas Tagman assey with the low detection of 6 IU/ml
- HCVRNA viral load : was assessed 4 weeks of therapy , and4 weeks and 12 weeks after end of therapy

Age (year)	38
Men	104 (86%) of 104 case
HCV RNA (copy/mL)	540-11000000
HCV genotype	
1a	51 (42%)
1b	7 (5%)
3a	63(52%)
1a, 3a	1 (0.8)
Fibroscan	
F0-F3	88(72%)
F4	34(28%)
HBS Ag (Positive)	7 (6%)
Treatment Experienced (Pegi-RBV)	38(31%)
AST(prior treatment)	46 -315
ALT(prior treatment)	39 -288

RESULTS

Results

- SVR (cutoff HCV RNA :6 IU/ml) 3 months or 12 weeks after end of treatment: 98%
- RVR : all 122 patients had RVR
- One patient died ,in which had no connection with treated
- Another patient left the treatment
- Non- Response : NONE
- Although Tenfovir® was included ART : no rising of BUN –Cr
- The most common adverse effects :headache , fatigue , weakness, anorexia nausea, insomnia ,diarrhea ,

CONCLUSIONS

Conclusions

- Ledipasvir 90 mg/day and Sofosbuvir® 400 mg/day for 12 weeks provided +Ribaverin (based on cirrhosis) sustained virological response near (100%) in Iranian patients coinfected with HIV-1 and HCV genotype 1a-1b with compensated cirrhosis.

- HIV / HCV genotype 3 treated with Daclatasvir (with adjusted dose) + Sofosbuvir + Ribaverin 12- 24 weeks(based on cirrhosis) also well tolerated and provided sustained virological response near 100%

- N Engl J Med. 2015 Aug 20;373(8):714-25. doi: 10.1056/NEJMoa1503153. Epub 2015 Jul 21.
- **Daclatasvir plus Sofosbuvir for HCV in Patients Coinfected with HIV**

- Wyles DL[1], Ruane PJ, Sulkowski MS, Dieterich D, Luetkemeyer A, Morgan TR, Sherman KE, Dretler R, Fishbein D, Gathe JC Jr, Henn S, Hinestrosa F, Huynh C, McDonald C, Mills A, Overton ET, Ramgopal M
- **Author information**

- **CONCLUSIONS:**

- Among previously untreated HIV-HCV coinfected patients receiving daclatasvir plus sofosbuvir for HCV infection, the rate of sustained virologic response across all genotypes was 97.0% after 12 weeks of treatment and 76.0% after 8 weeks

AASLD IDSA **Patients With HIV/HCV Coinfection**
From www.HCVGuidance.org on October 10, 2018

The combination of daclatasvir and sofosbuvir once daily for 12 weeks achieved SVR12 in 97% of HIV/HCV-coinfected patients with genotype 1, 2, 3, or 4 infection, and was safe and well tolerated. Ninety-seven percent of treatment-naive patients and 98% of treatment-experienced patients achieved SVR. However, among patients who received 8 weeks of therapy, only 76% of patients achieved SVR. Factors associated with relapse in this patient group included high baseline HCV RNA level (>2 million IU/mL; 69%), concomitant use of a boosted darunavir-based antiretroviral regimen with 30 mg of daclatasvir (67%), and the presence of compensated cirrhosis (60%).

- Discovery of new classes of (DAAs) agents that target the HCV replication cycle .
- Recently approved DAAs are used with or without RBV have :
  - higher SVR
  - fewer side effect
  - shorten duration of therapy

Treatment of HCV/HIV co-infection, July 2016

Recommendation

- HCV treatment in patients with HIV coinfection. **AASLD/IDSA Guidance** "The guidance from the American Association for the Study of Liver Diseases (AASLD) and the Infectious Diseases Society of Am (IDSA)".
- ARV should be consider for most patients with HIV/HCV coinfection regardless of their CD4 count .
- In naïve patients with CD4>500 ART could be deferred until after treatment of HCV.
- In patients with lower CD4 counts (eg, <200 cells/mm3), ART should be initiated promptly **(AI)** and HCV therapy may be delayed until
- the patient is stable on HIV treatment **(CIII)**.

20

- Sofosbuvir/ velpatasvir can be used with most antiretrovirals ,but not Efavirenz , Etravirine or Nevirapine .
- becuse Velpatasvir has the potential to increase Tenofovir level , avoided in those with an GFR<60 ml/min .
- Sometimes TAF (tenofovir alafenamid) may be an alternative .