

# **SEVERE LIVER DISEASES & HIV INFECTION**

# **SEVERE LIVER DISEASES AND HIV INFECTION**

**Liver diseases ranks as a serious cause of morbidity and mortality in HIV – infected persons, whose HIV disease is effectively controlled with HAART.**

**HCV and HBV represent the most significant causes of liver disease in HIV – infected persons**

**The shared routes of transmission for HIV, HCV, HBV help to explain the phenomenon.**

**Even more the elevated transaminases in HIV-infected patients in the absence of chronic viral hepatitis suggest other causes of ongoing liver injury.**

# SEVERE LIVER DISEASE AND HIV INFECTION

## POTENTIAL OTHER CAUSES OF LD

- Alcoholic hepatitis
- Alcoholic cirrhosis
- Non alcoholic fatty liver disease
- Drug induced liver injury
- Autoimmune hepatitis
- PBC , PSC
- Haemochromatosis
- Wilson disease
- A1 antithrypsin deficiency

# **SEVERE LIVER DISEASE AND HIV INFECTION**

**HIV persons are at high risk for life-threatening complications of cirrhosis, such as**

- Liver failure**
- Ascites**
- Variceal bleeding**
- Encephalopathy**
- HCC ( 3-6 fold), faster in HIV/HCV patients**

# **CASE 1**

- **Male, born in 1967**
- **Hemophiliac (Hemophilia A severe)**
- **First transfusion in early childhood**
- **Smoker ~20 cigarettes/day (started in 1984)**
- **Social drinker (not alcoholic)**
- **HIV positive (first positive sample 1985)**
- **HCV positive (f. p. s. 1992)**
- **HBsAg positive (unknown origin) 1979**

# ***ART HISTORY***

- **Patient of the 2<sup>nd</sup> Hemophilia Center, 'Laiko' Hospital – Athens Greece**
- **1993: started ART with Zidovudine**
- **1995: added Didanosine**
- **1996: stopped DDI and added Lamivudine**
- **1997: added Saquinavir**
- **1998: Stavudine+ Lamivudine+ Indinavir**
- **2004: LAM+TDF+Efavirenz**
- **2008: Truvada+Lopinavir/r**

## 1996

- Liver biopsy: grade 8, stage 2
- ALT/AST:  $\geq 1.5-2$  X<sub>ULN</sub>

## 2001

- HCV RNA positive, GT 4a/4c/4d
- CD4 374/mm<sup>3</sup>, TSH normal
- Therapy for HCV: pegylated IFN a-2b 100 µg/wk and ribavirin 1000 mg every day, divided in 2 doses
- Treatment duration 48 weeks
- No treatment details

## 2003-2008

- HCV RNA positive
- Abnormal transaminases,  
PLT  
200,000 → 110,000/mm<sup>3</sup>

## 2009

- CT: small nodule in liver segment VII.
- MRI: nodule  $\leq 2$ cm, hypervascularized in the arterial phase and not seen in the second phase. Diffuse chronic hepatocellular disease. Splenomegaly.



# Differential Diagnosis

➤ HCC?

➤ Dysplastic nodule?

➤ Hematoma?

➤ AFP=10.8 ng/ml

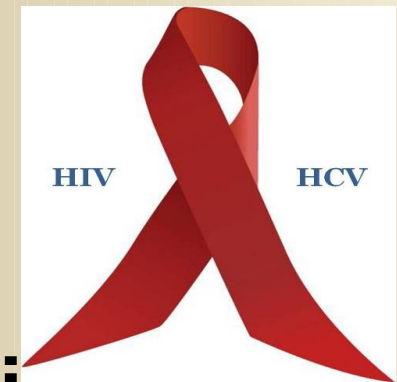


## 2009-2011

- No action taken
- Every 6 months U/S and MRI
- No difference

## Feb 2011

- Fibroscan: 36.3 kPa
- Gastroscopy: HP-positive gastritis
- HCV RNA  $1.8 \times 10^6$  IU/ml
- HBV DNA  $<45$  IU/ml
- HIV RNA  $<50$  cp/ml, CD4  $340/\text{mm}^3$



***New  
therapy***



- **Response to IFNa? Compliance?**

- **July 2011**

- **Started Peg-IFNa-2a 180 µg/week & Riba 1000 mg every day, divided in 2 doses.**
    - **12 weeks (10/2011): HCV RNA <20 IU/ml**
    - **24 weeks (01/2012): HCV RNA not detectable**
    - **48 weeks (06/2012): HCV RNA not detectable**
    - **MRI: no nodule; nodular, focal severe fibrosis in segment VIII**

- **01/2013 – Detectable HCV RNA (relapse)**
- **Hemophiliac patient, male, 46 years old**
- **On HAART for 20 years**
- **Now on Kaletra (lopinavir/ritonavir) + Truvada (tenofovir/emtricitabine)**
- **Fibroscan 46.4 kPa**
- **Treatment did not help? Other causes?**

# Metabolic profile

- **Glucose normal**
- **Cholesterol levels normal**

**HDL <40 mg/dl**

**LDL normal**

**Triglycerides 180 mg/dl**

- **Waiting for new drugs**

**2012-2014**

- **Telaprevir/Boceprevir? (GT1)**

**04/2014**

- **Gastroscopy: 2 small esophageal varices – esophagitis**
- **Start propranolol 20 mg x2, Lansoprazole 30 mg x1**

# **NEW DAAS - 2014**

- ✓ **SOFOSBUVIR (NS5B polymerase inhibitor)**
- ✓ **SIMEPREVIR (Protease inhibitor)**
- ✓ **DACLATASVIR (NS5A inhibitor)**



# Treatment options for GT4 - 2014

## With IFNa

- Sofosbuvir (SOF) + Peg-IFNa + RBV (x12 weeks)
- Simeprevir (SMV) + Peg-IFNa + RBV (x48 weeks)
- Daclatasvir (DCV) + Peg-IFNa + RBV (x48 weeks)

## Without IFNa

- SOF + RBV (x24 weeks)
- SOF + SMV ± RBV (x12 or 24 weeks,



# HCV & HIV coinfection



**Sofosbuvir**

**Simeprevir**

**Daclatasvir**

**Drug-Drug interactions with HIV drugs**

**None**

**Not with cobicistat\*, efavirenz, delavirdine, etravirine, nevirapine, ritonavir & any HIV protease inhibitor**

**Not with darunavir, **lopinavir**, etravirine ή nevirapine - DCV 30 mg with atazanavir/r, DCV 90 mg with efavirenz.**

\*cobicistat: elvitegravir + cobicistat + emtricitabine + tenofovir

# 2015

- **HCV RNA 8.02 x10<sup>5</sup> IU/ml**
- **AFP 15.5 ng/ml**
- **ALT/AST 98/94 IU/L**
- **ALP 204 U/L (ULN: 130), GGT 86 U/L**
- **Alb 3.6 g/dl**
- **PLT 85,000/mm<sup>3</sup>**
- **WBC, Hb, PT normal**
- **Fibroscan 35.3 kPa**

# NEW DAAS - 2015

- ✓ **LEDIPASVIR/SOFOSBUVIR (LDV/SOF)**  
(NS5A inhibitor/ NS5B polymerase inhibitor)
- ✓ **PARITAPREVIR/ritonavir/OMBITASVIR (PRV/r/OMV)** (Protease inhibitor/NS5A inhibitor)
- ✓ **DASABUVIR (DSV)** (Non-nuc polymerase inhibitor)

# Treatment options for GT4 - 2015

## Without IFNa

- LDV/SOF  $\pm$  RBV (x12 or 24 weeks)
- PRV/r/OMV  $\pm$  RBV (x12 or 24 weeks)



# HCV & HIV coinfection

Sofosbuvir

Simeprevir

Daclatasvir

Sofosbuvir/Ledipasvir

Paritaprevir/r/Ombitasvir ±  
Dasabuvir

Drug-Drug interactions with HIV  
drugs

None

Not with cobicistat, efavirenz,  
delavirdine, etravirine, nevirapine,  
**ritonavir & any HIV protease inhibitor**

Not with darunavir, lopinavir,  
etravirine or nevirapine - DCV 30 mg  
with atazanavir/r,  
DCV 90 mg with efavirenz

Not with cobicistat, tripanavir/r

Not with efavirenz, rilpivirine or  
**lopinavir**



## July 2015

- **Harvoni (1 tablet/day)**  
**(ledipasvir  
90mg + sofosbuvir 400mg)**
- **EASL Recommendation: A1**