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AIDS Education and Training Center

May 13-14, 2011
Orlando, FL

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Hepatitis and HIV Coinfection


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- **Speaker – Tibotec, Merck, BIPI, Gilead, BMS**
- **Research Support – ViiV, Tobira Pharmaceuticals, Vertex, Pfizer**
- **Consultant – ViiV, Tibotec, Gilead**

This slide set has been peer-reviewed to ensure that there are no conflicts of interest represented in the presentation.



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**Slide set adapted from
Hepatitis and HIV Coinfection
Presented by: Jeffrey A. Beal, MD
At the 18th Annual Conference of the
Florida/Caribbean AETC**



Session Objectives

- Review treatment options for coinfecting patients including initiation of treatment, selection of treatment regimens, management of complications and follow up of treatment failure patients.
- Discuss novel therapeutic options for treatment.
- Review transplant criteria.



What is true among the statements given below?

1. Entecavir has no activity against HIV
2. Peg-interferon has activity against HCV but not HBV
3. In treating HBV/HIV co infection a liver biopsy will be very useful
4. In treating HCV in coinfection a liver biopsy may be very useful
5. When using direct acting antiviral we can avoid peg-interferon.

Statement	Percentage
1. Entecavir has no activity against HIV	0%
2. Peg-interferon has activity against HCV but not HBV	0%
3. In treating HBV/HIV co infection a liver biopsy will be very useful	0%
4. In treating HCV in coinfection a liver biopsy may be very useful	0%
5. When using direct acting antiviral we can avoid peg-interferon.	100%

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What is true among the statements given below?

1. HCV Genotype one has a poor response to treatment
2. HCV Genotype one has more rapid progression to cirrhosis
3. In HCV/HIV coinfection, if the HCV VL is low the development of cirrhosis is less
4. In HCV/HIV coinfection, the dose of ribarvirin has no relationship to treatment response

Statement	Percentage
1. HCV Genotype one has a poor response to treatment	50%
2. HCV Genotype one has more rapid progression to cirrhosis	17%
3. In HCV/HIV coinfection, if the HCV VL is low the development of cirrhosis is less	25%
4. In HCV/HIV coinfection, the dose of ribarvirin has no relationship to treatment response	8%

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HCV Sources of Infection

- **Blood exposure/perinatal/sexual**
 - HCV 10 X more infectious than HIV 2° blood
 - HCV sexual transmission inefficient
 - Mother to infant in 2-5% of deliveries

MMWR, Vol 58 (early release) March 24, 2009



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Hepatitis C

- In U.S., 4 million HCV+ → 85% chronic
- If chronic → 20% cirrhotic @ 20 years
 - Once cirrhotic → 25% hepatocellular carcinoma (HCC)
(0.5% of total HCV+)
- Alcohol (>20-50 g/d) & HIV worsen prognosis
- Usually no symptoms
 - sometimes fatigue, RUQ ache, difficulty concentrating or isolated ↑ ALT/AST

Guidelines for Prevention and Treatment of Opportunistic Infections in HIV-Infected Adults and Adolescents. MMWR; April 10, 2009, Vol. 58, No. RR-4



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Hepatitis C

- 6 Genotypes
 - Genotypes 1-3 are commonest in US, W. Europe:
 - 75% are 1 (accounts for 90% of AfAm cases)
 - 25% are “Non-1”
 - Most are 2 & 3
 - 4-6 Middle East/Africa/Spain
- African Americans less likely to achieve sustained virologic response (SVR) to treatment
 - 28% AA
 - 52% Cauc

H S Conjeevaram, M W Fried, L J Jeffers, et al. *Gastroenterology*. 131(2): 470-477. August 2006.

SM Martinez, et al. *Clin Microbiol*. 43(10): 5403-5404 October 2005.

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HIV and HCV

- **Meta analysis 37 studies showed prior to HAART, HCV liver disease did not significantly increase mortality.**
- **Post HAART, HCV liver disease increases mortality and has become the most common cause of non-AIDS related death among HIV patients**

Liver related deaths in persons infected with HIV: the D:A:D study. *Archives of Internal Medicine* 166 (15): 1632-1641



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HIV/HCV Co-Infection is Clearly Associated with More Rapid Progression to Cirrhosis

- Soto, et al. J Hepat 1997
 - Compared 547 HIV- with 116 HIV+
 - All with chronic hepatitis C
- Incidence of cirrhosis
 - HIV-
 - 2.6% (mean HCV duration 23.2 years)
 - HIV+
 - 14.9% (mean HCV duration 6.9 years)



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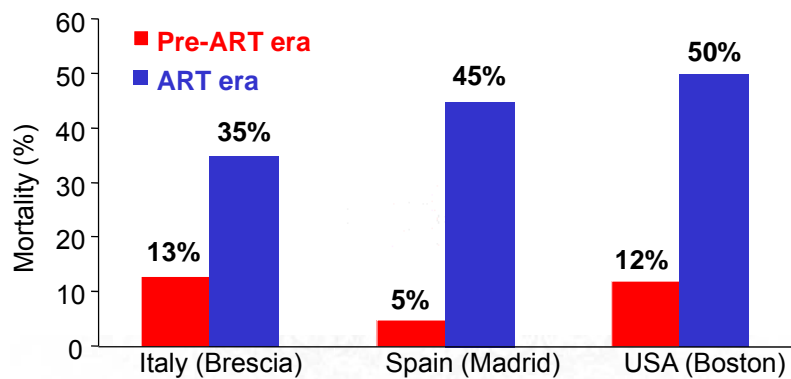
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Liver Disease: A Major Cause of Death

Death from end-stage liver disease (ESLD) as a percentage of all deaths among HIV patients



Bica I et al. *Clin Infect Dis*. 2001;32:492-497.

Puoti M et al. *J Acquir Immune Defic Syndr*. 2000;24:211-217.

Soriano V et al. *Eur J Epidemiol*. 1999;15:1-4. Soriano V et al. *Curr Opin Infect Dis*. 2005 ;18:550-60.

Martin-Carbonero L et al. *AIDS Res Human Retrovirus*. 2001;17:1467-1471.ca



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Other Possible Interactions Between Hepatitis C & HIV

- HCV does not appear to *consistently* affect progression of HIV disease
- Chronic HCV does not appear to *consistently* affect CD4 response to combination ART (cART)
- Cirrhosis suppresses immunity—may affect CD4
- May be associated with changes in psychiatric fxn.,
↓ QOL, ↑ prevalence DM

N Soriano-Sarabia, A Vallejo, S Molina-Pinelo. *AIDS* 21(2): 253-255. January 11, 2007.
 B H McGovern, Y Golan, M Lopez, et al. *Clinical Infectious Diseases* 44(3): 431-437. February 1, 2007.
 Daar ES, et al. 7th Conference on Retroviruses and Opportunistic Infections, 1/30-2/2/00, San Francisco, CA. Abstract 280.
 Guidelines for Prevention and Treatment of Opportunistic Infections in HIV-Infected Adults and Adolescents. *MMWR*; April 10, 2009, Vol. 58, No. RR-4



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Viral Hepatitis in HIV+ Patients

- Acute viral hepatitis may be severe or fatal
- Acute viral hepatitis may add to liver damage already present from other causes
e.g. - Acute hepatitis A on chronic hepatitis C may be deadly
- **Vaccinate if not Immune**
 - Assess response to vaccination
 - Best response when CD4 >350
 - Consider double dose Hep B vaccine

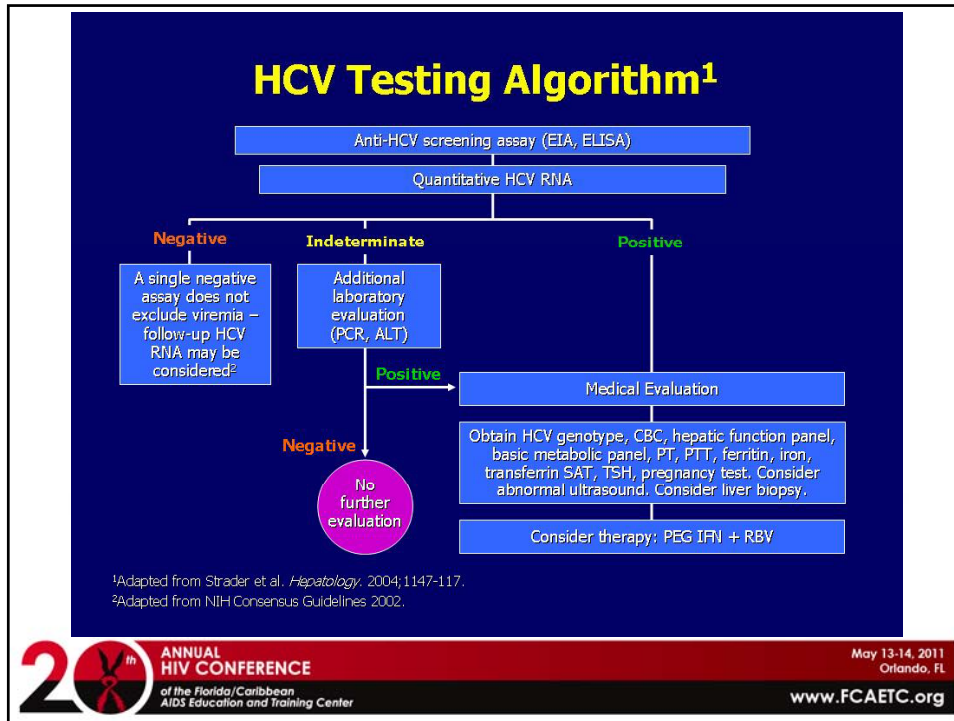
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Evaluating for Treatment

HCV Screening

- Genotyping & Hep C VL are helpful in predicting response to therapy
 - 1 (& 4) is more refractory to treatment
 - If VL <4-500,000 IU/mL Geno 1 easier to treat
 - 2 & 3 are very responsive
- HIV should be controlled and ARV stable
 - Attempt to get CD4>200 with cART\
 - Pts with CD4% >25 are more likely to have SVR
- PHQ-9 Depression Screen – hx of suicidal ideation – MH referral



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HCV Screening

- Preg. test (unless hysterectomy or tubal ligation) & must be willing to use Birth control
- CBC, Platelet – Hgb must be >10.5 g/dL, ANC >1000/ μ L, and Platelets > 50k. Use of hematopoietic growth factor OK.
- LFT, PT, PTT, INR – if coagulopathy, \uparrow bili, encephalopathy, ascites refer to transplant center.
- Cr. Cl. > 50cc/min.



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HCV Screening

- TSH (autoimmune thyroiditis potential complication of therapy)
- Uncontrolled cancer or cardiopulmonary disease is contraindication
- Baseline ECG if hx. pre-existing cardiac ds. or ≥ 50 y/o
- Ophthalmology Exam –IFN retinitis



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Treatment of Disease Benefit > Risk

If no contraindication to Peg-IFN/RBV

- HCV genotype 2 or 3
- HCV genotype 1 with HCV RNA <800,000 IU/ml
- Sig. hepatic fibrosis (bridging or cirrhosis)
- Stable HIV not requiring ART
- Acute HCV (< 6 mo. duration)
- Cryoglobulinemic vasculitis or membranoproliferative glomerulonephritis
- Patient motivated for treatment

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Look for Complications of Chronic Hepatitis

- Alpha-fetoprotein alone not enough to screen out HCC
- Abd. US to r/o mass, lesion, ascites, organomegaly
- Liver biopsy?
 - Gold standard in evaluating hepatitis and cirrhosis—how “close” to cirrhosis is your patient?
- Fibrosure™ & Fibroscan™ not validated in HIV yet, but non-invasive measures of fibrosis
 - Cannot rule out concurrent diseases, over-diagnoses fibrosis
 - Fibrosure™ may be affected by elevated bilirubin due to atazanavir or indinavir

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Comparison of Scoring Systems for Histological Stage

Stage	IASL	Batts-Ludwig	Metavir	Ishak
0	No fibrosis	No Fibrosis	No fibrosis	No fibrosis
1	Mild fibrosis	Fibrous portal expansion	Periportal fibrotic expansion	Fibrous expansion of some portal areas with or without short fibrous septa
2	Moderate fibrosis	Rare bridges or septae	Periportal septae 1 (septum)	Fibrous expansion of most portal areas with or without short fibrous septa
3	Severe fibrosis	Numerous bridges or septae	Porto-central septae	Fibrous expansion of most portal areas with occasional portal to portal bridging
4	Cirrhosis	Cirrhosis	Cirrhosis	Fibrous expansion of most portal areas with marked bridging (portal to portal and portal to central)
5				Marked bridging (portal to portal and portal to central) with occasional nodules (incomplete cirrhosis)
6				Cirrhosis

Ghany et al., Hepatology, vol. 49, no.4, 2009, p. 1339

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Benefits & Goals of Treating Chronic Hepatitis C

- Viral eradication (“sustained viral remission”, SVR)
 - Delay progression of fibrosis
 - Prevent/delay bad clinical outcomes of cirrhosis
 - Liver decompensation
 - Hepatocellular carcinoma
 - Death
- Improve tolerance and *effectiveness* of HAART
 - Allows aggressive antiretroviral drug therapy
 - Enhanced immune reconstitution?
 - Increases survival



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Response Rates to Treatment Chronic Hepatitis C

- In studies, sustained viral remission w/ newer treatments: PEG α IFN + ribavirin
 - Genotype 1 & 4 (~ 30 -70 % SVR)
 - Genotype 2 & 3 (>80% SVR)
- SVR with PEG α IFN + ribavirin reduces cirrhosis, HCC, transplant, death by 9-fold
- HIV disease is *not* affected by α IFN or ribavirin

L Martin-Carbonero, et al. CROI 2008. Abstract 1052.



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Hepatitis C Treatment Toxicities

Pegylated α INF 2a or 2b

- Flu-like symptoms
- Depression/suicidal
- Fatigue, dizziness
- Anorexia, nausea/diarrhea
- Bone marrow suppression
- Serious infections
- Autoimmune disease
- Thyroid, diabetes
- Hair loss, oral ulcers
- Pulmonary fibrosis
- Stevens-Johnson, hypersensitivity
- Retinal hemorrhage, cotton wool spots

Ribavirin

- Anemia/hemolysis
 - dose dependent
 - 2.5-3g \downarrow within 4 weeks
 - Erythropoietin
- Depression
- Embryocidal / Category X
- Teratogenic for up to 6 months after treatment
 - FDA Ribavirin Pregnancy Registry



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Treatment of HCV coinfection

PEG IFN α -2a (fixed 180 mcg) or α -2b (wt-based 1.5 mcg/kg)* subcutaneously every week

+

Ribavirin 1000 mg (wt. <75 kg)-1200mg mg (wt. >75 kg) all genotypes¹.

Duration all genotypes is 48 weeks.²

*Off-label in HIV/HCV. Wgt-based regimens may be more effective in morbidly obese patients.

¹EACS guidelines for the clinical management and treatment of chronic hepatitis B & C coinfection in HIV-infected adults; Rockstroh, et.al.; HIV Medicine (2008), 9, 82-88.

²Guidelines for Prevention and Treatment of Opportunistic Infections in HIV-Infected Adults and Adolescents. MMWR; April 10, 2009, Vol. 58, No. RR-4



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Ribavirin *Interacts* with cART

- ✓ **Didanosine (ddI)** should be replaced before treatment
- ✓ **Zidovudine, stavudine** therapy should be monitored for failure, toxicity
- ✓ **d4T increased risk lactic acidosis**
- Tenofovir- Better HCV treatment response
- Abacavir lower SVR in cohort data? Impairment of RBV phosphorylation by ABC*



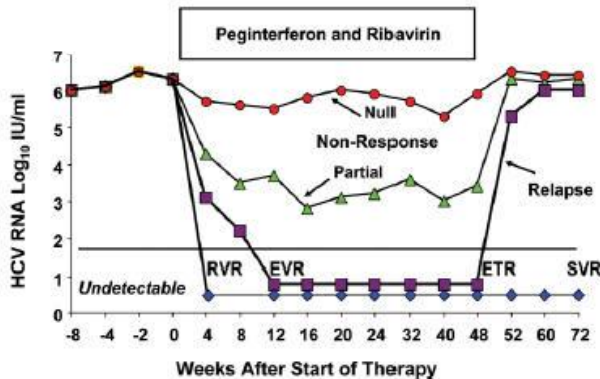
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Peginterferon and Ribavirin



1342 GHANY ET AL.

HEPATOLOGY, April 2009



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Defining Success

RVR = Rapid viral response (undetectable VL) at week 4 predicts SVR

EVR = Early viral response, 12 week viral load is undetectable or decreased by 2 logs.

ETR = End of treatment response, undetectable viral load at end of treatment.

SVR = Sustained viral response, undetectable 6 or more months after therapy.



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Defining Response in HIV/HCV

- Lack of Early Virologic Response ($<2 \log_{10}$ IU/mL ↓ HCV VL from baseline or undetectable) at wk 12 is predicts virologic failure. (<3% chance SVR)
 - Current guideline: discontinue treatment if EVR not seen
- If HCV undetectable @ 12 weeks (EVR) → continue
- If HCV undetectable @ end of tx (ETR) → repeat @ 72 weeks
 - If still undetectable → SVR!!



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Managing Adverse Effects

- Avoid dose reductions where feasible
- Moderate depression
 - ↓ PEG IFN α-2a to 135 mcg and further ↓ to 90 mcg may be needed
 - ↓ PEG IFN α-2b by 50%
 - Supportive counseling/antidepressant medication therapy
- Severe depression or suicidal – D/C Treatment!

HIV and Hepatitis Coinfections, Management & Treatment Guidelines;
Raymond Johnson, M.D., Ph.D; www.hcvadvocate.org



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Managing Adverse Effects

Lab Value ANC	G-CSF	Pegylated Interferon
750-1000	Wt. ≤ 60 Kg. 300 mcg SC q wk given 3 d before PEG IFN Wt. <60 kg. 480 mcg SC q wk given 3 d before PEG IFN	
500-749	↑ to BIW or TIW injection	↓ to 135 mg/wk (↓ Peg-Intron by ½)
<500	↑ to TIW injection	Hold Pegylated IFN

HIV and Hepatitis Coinfections, Management & Treatment Guidelines; Raymond Johnson, M.D., Ph.D; www.hcvadvocate.org



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Managing Adverse Effects

Hemoglobin	Erythropoietin or Darbepoetin	Folic Acid	Ribavirin
≥ 10 – 11 CBC q 2 weeks	10,000 units – 40,000 units SC q wk	25→40→60→100 mcg SC q wk	Add 1 mg po qd if suboptimal response
≥ 8.5 – 9.9 CBC weekly	↑ dose	↑ dose	1 mg folic acid po qd
< 8.5 CBC weekly	↑ dose	↑ dose	1 mg folic acid po qd

HIV and Hepatitis Coinfections, Management & Treatment Guidelines; Raymond Johnson, M.D., Ph.D.; www.hcvadvocate.org



Managing Adverse Effects

- Nausea:
 - Dronabinol (Marinol®) 2.5-10 mg po bid for RBV induced nausea
 - Or**
 - Premedicate with 12.5-25 mg promethazine (Phenergan®) or 5-10 mg prochlorperazine (Compazine®)



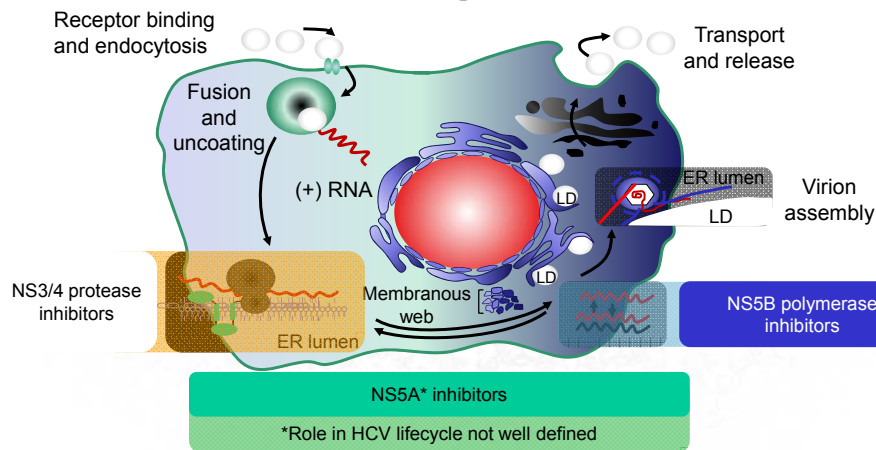
What if ESLD develops?

- Liver transplantation may be a viable option in *selected* HIV+ individuals
- Experimental, outcomes similar to HIV-/HCV+
 - Need good HIV control, adherence
 - HCV recurrence is common in new liver
 - Re-treatment x 3 months after transplant
- 5-year survival is 51% (vs.81% in HIV-/HCV+)

L Castells, J I Esteban, I Bilbao, and others. *Antiviral Therapy* 11(8): 1061-1070. 2006.


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HCV Lifecycle and STAT-C Targets



Adapted from Manns MP, et al. *Nat Rev Drug Discov.* 2007;6:991-1000.


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Multiple Anti-HCV Drugs are in Development

<u>Linear class</u>		<u>Active site</u>	
Telaprevir	BI 201335	RG7128	PSI-7977
Boceprevir		INX-189	IDX184
Narlaprevir			PSI-938

NS3 Protease	NS5A	NS5B Polymerase
Macrocyclic class	BMS-790052	Palm
Danoprevir (RG7227/ ITMN-191)	AZD7295	Thumb
TMC 435350	PPI-461	ABT-333
MK 7009	Cyclophilin	ABT-072
BMS-650032		GS 9190
		ANA598
		Debio 025
		NIM 811
		BI 207127
		Filibuvir
		MK-3281

3/11/2011 FCHH-HCV DrAG 9 Compounds in Ph 1-3 trials (Jan-2010) www.hivforim.org

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New HCV Agents – Boceprevir and Telaprevir

- Boceprevir and Telaprevir, the 2 new oral HCV protease inhibitors has phase 3 data
- Telaprevir (plus peg/rbv) 75% of patients achieved SVR . Telaprevir is taken only for 12 weeks, peg/RBV is taken during the entire 48 weeks
- In mono infection with HCV 68% of patients in studies had undetectable HCV viral load at 4 weeks and 58% at weeks 4 and 12 (212/363).

New HCV Agents Telaprevir,

- Relapse rates were low, 9%. On-treatment virologic failure rates were only 3%. Patients with no, mild or portal fibrosis had a 78% SVR . Patients with cirrhosis with a 62% SVR, and for African A. the SVR was 62%
- Rash 56% with 6% a severe rash, on average hemoglobin went down from 12.3 g/dL approx to 11 by week 8.
- It's expected that FDA will approve this month



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Pharmacokinetic Interactions Between ARVs and Telaprevir

TVR Dose	ARV	TVR AUC	TVR C _{min}	ARV AUC	ARVC _{min}
TVR 750 mg tid	ATV/r	0.80 (0.76-0.98)	0.85 (0.75-0.98)	1.17 (0.97-1.43)	1.85 (1.40-2.44)
	DRV/r	0.65 (0.61-0.69)	0.68 (0.63-0.74)	0.60 (0.57-0.63)	0.58 (0.52-0.63)
	FPV/r	0.68 (0.63-0.72)	0.70 (0.64-0.77)	0.53 (0.49-0.58)	0.44 (0.40-0.50)
	LPV/r	0.46 (0.41-0.52)	0.48 (0.40-0.56)	1.06 (0.96-1.17)	1.14 (0.96-1.36)
TVR 1250 mg tid	EFV			0.82 (0.74-0.90)	0.90 (0.81-1.01)
	TDF	0.82 (0.73-0.92)	0.75 (0.66-0.86)	1.10 (1.03-1.18)	1.17 (1.06-1.28)
TVR 1500 mg bid	EFV			0.85 (0.79-0.91)	0.89 (0.82-0.96)
	TDF	0.80 (0.73-0.88)	0.52 (0.42-0.64)	1.10 (1.03-1.17)	1.06 (0.98-1.15)

Van Heeswijk R, et al. 18th CROI; Boston, MA; February 27-March 2, 2011. Abst. 119.



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New HCV Agents - Boceprevir

- Patients received a 4-week lead in with peg/rbv before starting boceprevir, hence, this will likely be used this way.
- Patients with a 1 log or more decline in viral load after the 4-week lead-in, 82% achieved SVR. Patients with undetectable viral load at week 8, 90% achieved SVR.
- 49% had anemia, 1% discontinued, 13% dose reduced due to anemia, 24% used EPO for treatment of anemia.



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New HCV Agents - Boceprevir

- **RESPOND 2 study** - The SVR were significantly higher in patients randomized to receive boceprevir (56-75%) compared to those who got peginterferon alfa-2b plus ribavirin alone (40 %).
- Week 4 lead-in response predicted SVR: if a patient had 1 log or more decline in viral load at week 4, 73-79% achieved SVR.
- The boceprevir treatment arm, was associated with an incremental risk of significant anemia compared to peginterferon/ribavirin, and epoetin alfa was more frequently used.



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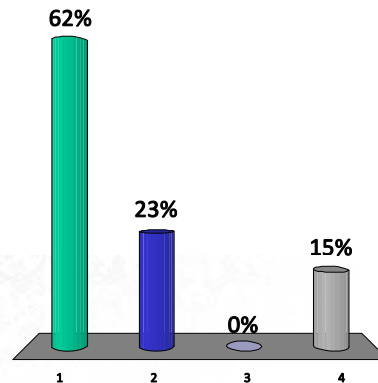
Key Points about HCV/HIV

- ✓ HCV is worse in HIV/HCV
- ✓ Treat based on individual benefits vs. risks
 - If you or patient in doubt, hold off
 - Patient must be committed to birth control
 - Be aware of cART interactions
 - Be alert to & plan for toxicities
 - Continually revisit *contraception!*
- ✓ PEG αIFN + ribavirin x 48 weeks is standard
- ✓ Vaccinate all co-infected patients against HAV and HBV if seronegative



What is true among the statements given below?

1. HCV Genotype one has a poor response to treatment
2. HCV Genotype one has more rapid progression to cirrhosis
3. In HCV/HIV coinfection, if the HCV VL is low the development of cirrhosis is less
4. In HCV/HIV coinfection, the dose of ribarvirin has no relationship to treatment response



Hepatitis B

Hepatitis B

- sex, perinatal, IDU, blood
- 350 million CAH-B worldwide
- 1.25 million CAH-B patients in U.S.
- Carriers increased risk of developing
 - Cirrhosis, hepatic decompensation, and HCC
- 15-40% of carriers will develop serious sequelae in their lifetime

AASLD Practice Guidelines; Hepatology, Vol.50, No. 3, SEP 2009



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Hepatitis B & HIV

- Acute HBV may be more severe
 - *Only 25% symptomatic*: acute jaundice, elevated liver enzymes, fatigue, NVD
 - 10% become chronic → cirrhosis/CA in 20-30 yrs
 - Ethanol, HIV, other hepatitis viruses
- ~10% of HIV⁺ have CAH-B
- HIV/HBV 19x > liver deaths than HBV alone
8x > liver deaths than HIV alone

Thio C, Seaburg E, Skolasky Jr. R, et al. Multicenter Cohort Study [MACS]. Lancet 2002;360:1921-26.



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Hepatitis B & HIV

- 8 genotypes (A→H)
 - Genotype A
 - Most common in HIV/HBV in U.S.– 75%
 - may respond best to pegIFN- α
 - Genotype G
 - Least common in HIV/HBV in U.S. – 25%
 - Marker of rapid fibrosis

K Lacombe and others. *AIDS* 20(3): 419-427, February 14, 2006.



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Hepatitis B & HIV

“Studies of nucleos(t)ide analogue therapies have not shown any relation between HBV genotypes and response”

Additional data needed before HBV genotype determination in clinical practice is recommended.

AASLD Practice Guidelines; *Hepatology*, Vol.50, No. 3, SEP 2009



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Serology of Chronic HBV

HBsAg	HBsAb	HBeAg	HBV DNA
+	-	+/-*	+

*Pre-core protein/core promoter mutation

- Do not express HBeAg
- Lower HBV DNA than eAg+
- Severe inflammation→cirrhosis
- Longer duration of disease→older
- More resistant to therapy
- Non-A genotypes, Asia/Europe



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Hepatitis B & HIV: “Occult” HBV

- Isolated HBcAb IgG

HBsAg	HBsAb	HBcAg	HBV DNA
-	-	-	+

- More common in HIV+ and HCV
- Diagnosed by HBV DNA positive
- If HBV DNA negative, vaccinate

Gandhi RT, Wurcel A, Lee H, et al. J Infect Dis 2005;191:1435-41.
AASLD Practice Guidelines; Hepatology, Vol.50, No. 3, SEP 2009



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Counseling HBsAg Positive

- **Sexual and household contacts need vaccination**
- **Newborn HBIG & HB Vaccine at delivery**
- **Abstinence or limited ETOH**
- **Prevention**
 - Barrier protection
 - Cover cuts and scratches
 - No sharing toothbrushes or razors
 - No donating blood, organs, or sperm
 - Clean blood spills with bleach or detergent

AASLD Practice Guidelines; Hepatology, Vol.50, No. 3, SEP 2009



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Initial Evaluation

- **H&P, FH of liver disease or HCC**
- **CBC, platelet, PT,PTT, CMP**
- Urinalysis – if abnormal 24 hour urine for protein and creatinine
- **HBeAg, HBeAb, HBV DNA**
- **HCV Ab., HDV Ab (if from endemic country or IDU)**
- **Liver US, Liver Biopsy**

AASLD Practice Guidelines; Hepatology, Vol.50, No. 3, SEP 2009



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HDV

- **Mediterranean area, and parts of South Africa**
- **Occurs in two forms:**
 - Coinfection of HBV and HDV resulting in more severe acute hepatitis with higher mortality than acute HBV alone.
 - Superinfection of HDV in a HPV carrier causing severe acute hepatitis and results in chronic infection with both viruses
- **Increases risk of cirrhosis, decompensation, and HCC**

AASLD Practice Guidelines; Hepatology, Vol.50, No. 3, SEP 2009



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Liver Biopsy

- **Most useful in persons not meeting clear cut guidelines to treat**
- **HBV infected with LFT close to ULN (30 U/L for men; 19 U/L for women) especially if > 40 y/o may have abnormal histology and be at increased risk of mortality**

AASLD Practice Guidelines; Hepatology, Vol.50, No. 3, SEP 2009



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Risk Factors for Cirrhosis in CAH-B

- HBV DNA > 10⁴ copies/mL [HR, 2.7) 10⁵ [HR, 8.9-10.7]
- Male [HR, 3.0]
- Advanced age [HR, 3.6-8.3]
- Habitual alcohol consumption [HR, 2.6]
- HBV genotype C
- Coinfection with HCV or HDV or HIV

Clinical Gastroenterology & Hepatology 2008; 6:1315-1341.
AASLD Practice Guidelines; Hepatology, Vol.50, No. 3, SEP 2009



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HCC Screening Recommendations

Asian men > 40, Asian women > 50, persons with cirrhosis, those with FH of HCC, Africans > 20, and any carrier > 40 y/o with persistent or intermittent ALT elevation and/or high HBV DNA >2,000 IU/mL needs US examination every 6-12 months

AFP if US not available

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Risk Factors for HCC in CAH-B

- Cigarette smoking
- Older age
- Reversions from HBeAb⁺ to HBeAg⁺
- Presence of cirrhosis
 - **30-50% HCC occur in absence of cirrhosis**
- HBV genotype C
- Core promoter mutation
- HCV coinfection
- Male gender
- FH of HCC

AASLD Practice Guidelines; Hepatology, Vol.50, No. 3, SEP 2009



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Who to Treat?

- All patients with HBV/HIV need to be treated
- However, in HBV mono infection,-
- Anti-HBV treatment indicated if ↑ ALT and HBV DNA level >
 - 20,000 IU/mL if HBeAg-positive
 - 2,000 IU/mL if HBeAg-negative
- Some experts treat any level of HBV DNA especially if ALT is ↑ or if significant inflammation &/or fibrosis on biopsy



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When to Treat & With What

- (lamivudine or emtricitabine) + tenofovir backbone + ART drug
- Indefinite tx
- FLARES with stopping meds *or onset of YMDD resistance* — USE CAUTION
- 3TC resistant – entecavir or peg-IFN added

Guidelines for Prevention and Treatment of Opportunistic Infections in HIV-Infected Adults and Adolescents. MMWR; April 10, 2009, Vol. 58, No. RR-4


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MEDICATION	DOSING	PILL SIZE	
NUCLEOTIDES			
Adefovir (Hepsera®)	10 mg po qd	10 mg	Can be added to ART
Tenofovir (Viread®)*	300 mg po qd	300 mg	
NUCLEOSIDES			
Lamivudine (Epivir®)	150 mg po bid, or 300mg po qd	150 mg	0.5 for Nuc naive without EPV resistance
Emtricitabine (Emtriva®)	200 mg po qd	200 mg	
Entecavir (Baraclude™)	1 mg po qd	0.5, 1 mg	
Telbivudine (Tyzeka™)	600 mg po qd	600 mg	
INTERFERONS			
Pegylated interferon-α2a (Pegasys®)	180 mcg SC qwk x 1 year	180 mcg prefilled syringes	Contraindicated in cirrhosis 2 HBeAg Pos. 16-24 wk HBeAg Neg. 12 mo. consider 24
Standard interferon-α2b (Intron A®)	5 million IU SC qd, or 10 million IU SC TIW x 16 weeks	Multidose pens for qd or TIW, 10 million IU vials	

* Not FDA approved for HBV therapy

HIV and Hepatitis Coinfections Management & Treatment Guidelines, Raymond Johnson, M.D.; 2007 Hepatitis C Support Project. AASLD Practice Guidelines; Hepatology, Vol.50, No. 3, SEP 2009²


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Monitoring Nucleos(t)ide

- LFT q 3 months
- HBV DNA q 3-6 months
- HBeAg and HBeAb at end of 1 yr treatment and every 3-6 months thereafter

Virologic Breakthrough - Defined as $> 1 \log_{10}$ increase in HBV DNA from nadir during treatment

AASLD Practice Guidelines; Hepatology, Vol.50, No. 3, SEP 2009



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Remember

If altering ARV regimen do not discontinue HBV medications without substituting other HBV therapy unless HBeAg seroconversion has occurred

If stop HBV treatment, monitor closely for relapse

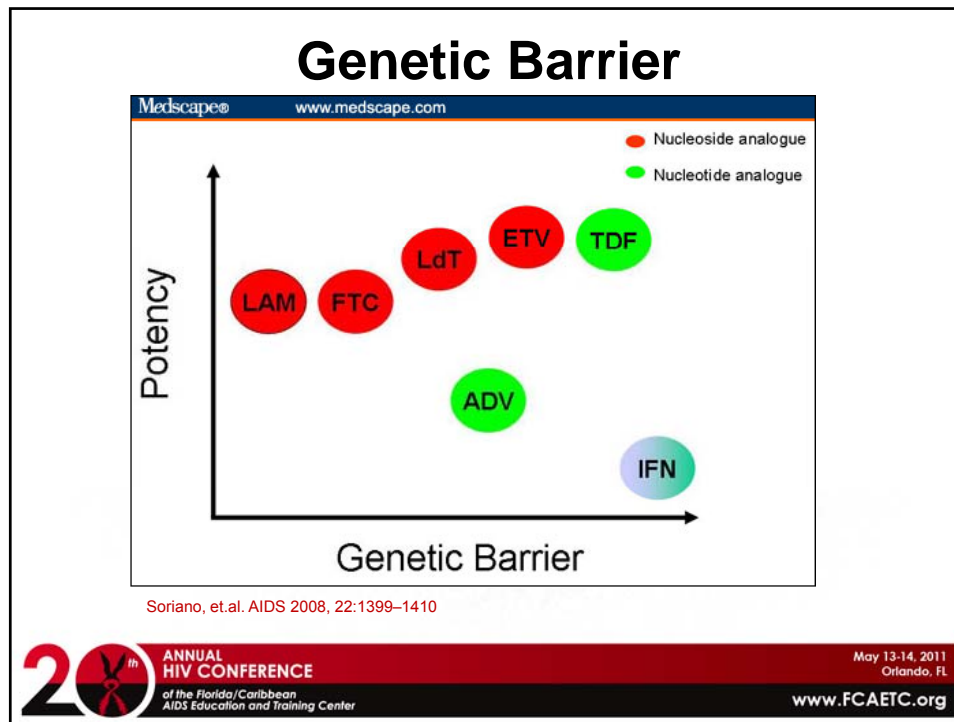
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Defining Treatment Response

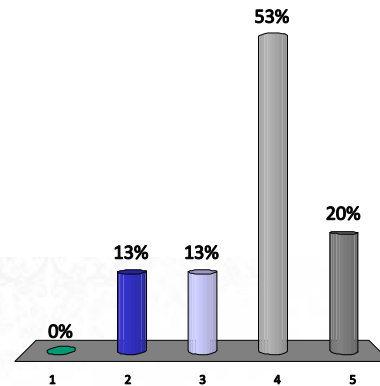
- Virologic response is HBV DNA
 - <2,000 IU/mL at 24 weeks if on IFN
 - Undetectable within 48 weeks on NUC
- Non-response is $< 1 \log_{10}$ IU/mL decrease from baseline at 3 months
- Breakthrough is $> 1 \log_{10}$ IU/mL increase compared to nadir

EASL Clinical Practice Guidelines: Management of chronic hepatitis B; Hepatology 50 (2009) 227-242

Journal of

What is true among the statements given below?

1. Entecavir has no activity against HIV
2. Peg-interferon has activity against HCV but not HBV
3. In treating HBV/HIV co infection a liver biopsy will be very useful
4. In treating HCV in coinfection a liver biopsy may be very useful
5. When using direct acting antiviral we can avoid peg-interferon.



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Key Points about HCV/HIV

- ✓ All patient with HIV and HBV need to be on treatment (using tenofovir / emtricitabine for HIV based on DHHS guidelines irrespective of the CD4 count)
- ✓ When there is resistance to Lamivudine add entecavir but continue lamivudine as there is some activity
- ✓ PEG α IFN is useful in the treatment for HBV is there is resistance to other agents
- ✓ Vaccinate all co-infected patients against HAV



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1. EACS Guidelines for the Clinical Management and Treatment of Chronic Hepatitis coinfection in HIV; 2008 British HIV Association HIV Medicine (2008) 9, 82-88.
2. Clinician's Guide to HIV & Hepatitis, January 2007; MountainPlains AIDS Education and Training Center
3. The Liver Care Clinic at Shands at the University of Florida Clinical Protocol for the Treatment of Chronic Hepatitis C; Version 5.0; March 29, 2007.
4. HIV and Hepatitis Coinfections Management & Treatment Guidelines, Raymond Johnson, M.D.; 2007 Hepatitis C Support Project; www.hcvadvocate.org
5. Guidelines for Prevention and Treatment of Opportunistic Infections in HIV-Infected Adults and Adolescents. MMWR; April 10, 2009, Vol. 58, No. RR-4
6. American Association for the Study of Liver Disease (AASLD) Practice Guideline; Diagnosis, Management and Treatment of Hepatitis C; Strader, et.al., Hepatology, Volume 39, Number 4, 2004. www.aasld.org
7. AASLD Practice Guideline; Chronic Hepatitis B; LOK, et.al., Hepatology Volume 45, February 2007
8. A Treatment Algorithm for the Management of Chronic Hepatitis B Virus Infection in the United States: 2008 Update; Keeffe, et.al.; Clinical Gastroenterology & Hepatology 2008; 6:1315-1341.
9. Hepatitis B Virus and Hepatitis C Virus Drug Resistance ; Vincent Soriano; Medscape HIV/AIDS XV International HIV Drug Resistance Workshop; July 21, 2006
10. EASL Clinical Practice Guidelines: Management of chronic hepatitis B; Journal of Hepatology: 50 (2009) 227-242.
11. Chronic Hepatitis B: Update 2009; AASLD Practice Guidelines; Hepatology, Vol.50, No. 3, SEP 2009



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Thank You

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