Hepatitis and HIV Coinfection

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Disclosure of Financial Relationships

This speaker has no significant financial relationships with commercial entities to disclose.

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

- Damage to liver cells caused by inflammation or cell death
- Can be caused by infections, drug toxicity, poisoning, biliary tract obstruction
- If persists, can lead to progressive scarring of the liver (cirrhosis) and end-stage liver dysfunction
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


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. Facilitated by HIV co-infection

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


Compared to HCV Mono-infection, HIV/HCV→:

• More rapid progression to
  – Cirrhosis
  – Decompensated liver disease
  – HCC
  – Death

Liver Disease: A Major Cause of Death

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

<table>
<thead>
<tr>
<th>Location</th>
<th>Pre-ART era</th>
<th>ART era</th>
</tr>
</thead>
<tbody>
<tr>
<td>Italy (Brescia)</td>
<td>13%</td>
<td>35%</td>
</tr>
<tr>
<td>Spain (Madrid)</td>
<td>5%</td>
<td>45%</td>
</tr>
<tr>
<td>USA (Boston)</td>
<td>12%</td>
<td>50%</td>
</tr>
</tbody>
</table>


Diagnosing HCV in HIV

- Do not rely on transaminases! There is no correlation between transaminase levels and disease severity.

1. HCV ELISA antibody (low-threshold, sensitive)
   - If + (or advanced HIV) → HCV RNA quantitative PCR.

2. If HCV ELISA or RNA PCR —, no further intervention.

3. If HCV RNA PCR + → active hepatitis is present...

Council Early and Often

- STOP ALL ETHANOL
- Consider methadone, naltrexone, or buprenorphine to reduce illicit drug use and its complications
- Assure vaccinated or immune Hepatitis A & B
- Counsel on condoms and safer sex
- Introduce risks vs. benefits of treatment
- Begin encouraging good support system in anticipation of Hepatitis C therapy

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

Guidelines for Prevention and Treatment of Opportunistic Infections among HIV-Exposed and HIV-Infected Children June 20, 2008
Hepatitis C 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
- **Attempt to get CD4>200 with cART**
  - Pts with CD4% >25 are more likely to have SVR
- **Preg. test unless hysterectomy or tubal ligation**
- **CBC, Platelet, CMP/Lipid, PT, PTT, INR**
- **TSH (autoimmune thyroiditis potential complication of therapy)**

Hepatitis C Screening

- **Rule out other causes of liver disease if liver enzymes are abnormal**
  - Autoimmune hepatitis (ANA, AMA, ASMA)
  - Biliary disease (ultrasound of liver)
  - Hemochromatosis (Ferritin, Iron, TIBC, %Sat)
- **Insulin level**
  - HOMA IR score at http://www.dtu.ox.ac.uk/homa
  - Insulin resistance reported as neg. predictor to achieve SVR
- **Baseline ECG if hx. pre-existing cardiac ds. or ≥ 50 y/o**
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

Talking to Your Patient: Benefits & Goals of Treating Chronic Hepatitis C

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

Hepatitis C Treatment Toxicities

**Pegylated αINF 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

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

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**Risk > Benefit**

- Pregnancy /unwilling to use birth control
- Advanced HIV – uncontrolled on cART
- Hepatic decompensation – coagulopathy, ↑bili, encephalopathy, ascites
- Uncontrolled comorbid conditions (CA or cardiopulmonary disease)
- Severe depression with suicidal ideation
- Hgb <10.5 g/dL, ANC<1000/µL, platelet < 50,000/ µL, CrCl <50cc/min

- Sarcoidosis or RA or SLE

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Talking to Your Patient: Best Odds and Best Reasons to Treat

- **Stable HIV disease with intact immune function**
  (to eradicate virus, delay cirrhosis/CA)

- **Advanced hepatic fibrosis**
  (to delay cirrhosis/CA)

- **Starting cART**
  (to limit cART interruptions by hepatotoxicity)

Sułkowski MS, 8th Conf on Retrov and OI, 2000, Abstract S11

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Talking with Your Patient: Which to Treat First? HIV or HCV?

- **CD₄ < 350 → treat HIV**
  - Higher risk of HIV morbidity/mortality

- **CD₄ > 350 → treat HCV**
  - HCV response is better @ higher CD₄s
  - Lower pressure to start cART
  - Possibly avoid cART interruptions due to hepatotoxicity
Ribavirin *Interacts with cART*

- Didanosine (ddI) should be **replaced** before treatment
  - Ribavirin will markedly increase ddI
  - Increased lactic acidosis, mitochondrial toxicity, peripheral neuropathy & pancreatitis
- Zidovudine, stavudine therapy should be monitored for failure, toxicity
  - RBV inhibits phosphorylation of pyrimidine nucleoside analogs and raises ZDV levels
  - Bone marrow suppression by ZDV + RBV may be additive
- d4T increased risk lactic acidosis

**Other cART Considerations with Hepatitis C**

- NNRTIs (efavirenz, nevirapine, etravirine)
  - Increased severe hepatotoxicity is ~1% w/ NNRTIs
  - NNRTIs need not be withheld in HCV/HIV
- Tenofovir- Better HCV treatment response
- Abacavir lower SVR in cohort data? Impairment of RBV phosphorylation by ABC*

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*Sulkowski, et al, 8th COROI, #618 Dieterich et al, 2002
* Rockstroh, et.al.; HIV Medicine (2008), 9, 82-88*
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 (wt. >75 kg) all genotypes¹.
Duration all genotypes is 48 weeks.²

*Off label in HIV/HCV. Wt-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.

Peginterferon and Ribavirin

[Graph showing viral load over time with definitions of RVR, EVR, ETR, SVR, and HCV RNA Log10 IU/ml as undetectable, Null, Non-Response, Partial, and Relapse]
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!!

Prescreening

Prescreening tests:
- HCV VL & genotype
- Serum or urine β HCG
- Serum TSH
- Serum ANA, AMA, ASMA
- Iron, ferritin, TIBC, %Sat
- HAV & HBV serology
- CBC & differential
- PT, PTT, platelet count
- Fasting CMP/lipid/ <insulin>

- Ophthalmology
- ECG &/or exercise tolerance test
- Liver US & biopsy (later not requirement of treatment)
- Depression screen
- Antidepressant therapy
Monitoring During Treatment

Monitoring:

- **Monthly**
  - CBC & diff (& @ 2 weeks of start)
  - lytes, FBS, creatinine, liver enzymes
  - serum or urine β HCG

- **@ 4, 12, 24, 48, & 72 weeks**
  - HCV RNA PCR

- **Every 12 weeks**
  - β HCG

- **@ 2, 6, 12, 24, and 48 week**
  - Ophthalmology exam

- Routine HIV monitoring lab as indicated

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_
### Managing Adverse Effects

<table>
<thead>
<tr>
<th>Lab Value ANC</th>
<th>G-CSF</th>
<th>Pegylated Interferon</th>
</tr>
</thead>
<tbody>
<tr>
<td>750-1000</td>
<td>Wt. ≤ 60 Kg, 300 mcg SC q wk given 3 d before PEG IFN</td>
<td>Wt. &lt; 60 Kg. 480 mcg SC q wk given 3 d before PEG IFN</td>
</tr>
<tr>
<td>500-749</td>
<td>↑ to BIW or TIW injection</td>
<td>↓ to 135 mg/wk (↓ Peg-Intron by ½)</td>
</tr>
<tr>
<td>&lt;500</td>
<td>↑ to TIW injection</td>
<td>Hold Pegylated IFN</td>
</tr>
</tbody>
</table>

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

### Managing Adverse Effects

<table>
<thead>
<tr>
<th>Hemoglobin</th>
<th>Erythropoetin or Darbepoetin</th>
<th>Folic Acid</th>
<th>Ribavirin</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥ 10 – 11</td>
<td>10,000 units – 40,000 units SC q wk</td>
<td>Add 1 mg po qd if suboptimal response</td>
<td></td>
</tr>
<tr>
<td>CBC q 2 weeks</td>
<td>25–40–60–100 mcg SC q wk</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥ 8.5 – 9.9</td>
<td>↑ dose</td>
<td>↑ dose</td>
<td>1 mg folic acid po qd</td>
</tr>
<tr>
<td>CBC weekly</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 8.5</td>
<td>↑ dose</td>
<td>↑ dose</td>
<td>1 mg folic acid po qd</td>
</tr>
<tr>
<td>CBC weekly</td>
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_HIV and Hepatitis Coinfections, Management & Treatment Guidelines; Raymond Johnson, M.D., Ph.D; www.hcvadvocate.org_
### Managing Adverse Effects

<table>
<thead>
<tr>
<th>Lab Value Platelet</th>
<th>Pegylated IFN</th>
<th>CBC</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 70,000</td>
<td>135 mcg/week (↓ Peg-Intron by 1/2)</td>
<td>Every 2 weeks</td>
</tr>
<tr>
<td>25,000 to 49,999</td>
<td></td>
<td>Weekly</td>
</tr>
<tr>
<td>&lt; 25,000</td>
<td>Hold until Platelets &gt; 70,000, then restart at 90 mcg/wk</td>
<td>Weekly</td>
</tr>
</tbody>
</table>

**Eltrombopag**

*Note: RBV D/C if Cr.Cl. < 50 mL/min.*
Managing Adverse Effects

• ↑ALT above baseline – dose reduce IFN as in depression dose adjustment. If progressive ↑, stop tx.

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
The Future of HIV/HCV?

- Non-invasive fibrosis markers?
- Eltrombopag for thrombocytopenia?
- HCV protease & polymerase inhibitors?
- Liver transplantation?...

H Al-Mohri, T Murphy, Y Lu, and others. JAIDS. January 4, 2007

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HCV Drug Pipeline

<table>
<thead>
<tr>
<th>Modified Interferons</th>
<th>Polymerase Inhibitors</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Nucleoside analogs</td>
</tr>
<tr>
<td>Albuferon</td>
<td>NIV-233</td>
</tr>
<tr>
<td>Consensus interferon</td>
<td>R126</td>
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<tr>
<td></td>
<td>MK-0608</td>
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CHRONIC ACTIVE HEPATITIS B
CAH-B

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*
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


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

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

Serology of Chronic HBV

<table>
<thead>
<tr>
<th>HBsAg</th>
<th>HBsAb</th>
<th>HBeAg</th>
<th>HBV DNA</th>
</tr>
</thead>
<tbody>
<tr>
<td>+</td>
<td>-</td>
<td>+/-</td>
<td>+</td>
</tr>
</tbody>
</table>

*Pre-core protein/core promoter mutation*

– Do not express HBeAg
– Lower HVB DNA than eAg+
– Severe inflammation→cirrhosis
– Longer duration of disease→older
– More resistant to therapy
– Non-A genotypes, Asia/Europe
Hepatitis B & HIV: “Occult” HBV

– Isolated HBcAb IgG

<table>
<thead>
<tr>
<th>HBsAg</th>
<th>HBsAb</th>
<th>HBcAg</th>
<th>HBV DNA</th>
</tr>
</thead>
<tbody>
<tr>
<td>-</td>
<td>-</td>
<td>-</td>
<td>+</td>
</tr>
</tbody>
</table>

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

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

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
Who to Treat?

- Patient needs cART – treat the Hepatitis B regardless of Hep B VL level.
- If ART not required, then treatment indication is same as for HBV monoinfected patients

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
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

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
A  Management of Chronic HBV Infection*

HBsAg +

HBeAg

Positive

ALT < 1 X ULN
- Q 3-6 mo ALT
- Q 6-12 mo HBeAg

ALT 1-2 X ULN
- Q 3 mo ALT
- Q 6 mo HBeAg
Consider biopsy if persistent or age > 40,
Rx as needed

ALT > 2 X ULN
- Q 1-3 mo ALT, HBeAg
Treat if persistent
Liver bx optional
Immediate Rx if jaundice or decompensated

* HCC surveillance if indicated

B  Management of Chronic HBV Infection*

HBsAg +

HBeAg

Negative

ALT ≥ 2X ULN
HBV DNA ≥ 20,000 IU/mL
Treat if persistent,
Liver biopsy optional

ALT 1-2X ULN
HBV DNA 2,000-20,000 IU/mL
Q 3 mo ALT & HBV DNA
Consider biopsy if persistent
Rx as needed

ALT < 1X ULN
HBV DNA < 2,000 IU/mL
Q 3 mo ALT X 3,
Then Q 6-12 mo
if ALT still <1x ULN

* HCC surveillance if indicated
Indications for Treatment

• Anti-HBV treatment indicated if \( \uparrow \) 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 \( \uparrow \) or if significant inflammation &/or fibrosis on biopsy

Remember

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

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

HBeAg-positive CAH B

- Until 6 months treatment after detection of HBeAb-positive and HBeAg-negative and undetectable HBV DNA
- Monitor closely for relapse

HBeAg-negative CAH B

- Until achieve HBsAg clearance

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

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<table>
<thead>
<tr>
<th>MEDICATION</th>
<th>DOSING</th>
<th>PILL SIZE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adefovir (Hepserz®)</td>
<td>10 mg po qd</td>
<td>10 mg</td>
</tr>
<tr>
<td>Tenofovir (Viread®)</td>
<td>300 mg po qd</td>
<td>300 mg</td>
</tr>
<tr>
<td>Lamivudine (Epivir®)</td>
<td>150 mg po bid, or 300 mg po qd</td>
<td>150 mg</td>
</tr>
<tr>
<td>Emtricitabine (Emtriva®)</td>
<td>200 mg po qd</td>
<td>200 mg</td>
</tr>
<tr>
<td>Entecavir (Baraclude®)</td>
<td>1 mg po qd</td>
<td>0.5, 1 mg</td>
</tr>
<tr>
<td>Telbivudine (Tyzeka®)</td>
<td>600 mg po qd</td>
<td>600 mg</td>
</tr>
</tbody>
</table>

INTERFERONS

- Pegylated interferon-α2a (Pegasys®) 180 mcg SC qwk x 1 year 180 mcg prefilled syringes
- Standard interferon-α2b (Intron A®) 5 million IU SC qd, or 10 million IU SC TIW x 18 weeks Multidose pens for qd or TIW, 10 million IU vials

* Not FDA approved for HBV therapy

Can be added to ART

0.5 for Nuc naïve without EPV resistance

2 HBeAg Pos. 16-24 wk
HBeAg Neg. 12 mo. consider 24

INF, Adefovir anf Tenofovir

- Adefovir and interferon are preferred for HIV/HBV coinfected patients who do not require ART

- INF alfa 2a: 180 mcg sq Qweek X 48 wks (first medicine approved for treating CHB)

- Adefovir (10 mg daily) associated with lower rates of resistance mutations than Lamivudine. Higher dose-toxic

- Tenofovir (300 mg daily): only be used in the context of multidrug ART regimen due to its ability to select

Entecavir

- Inhibits HBV replication at three different steps (priming, reverse transcriptase and positive strand synthesis).

- More potent in suppressing serum HBV-DNA than LAM and ADV

- Effective against wild type (0.5 mg/day) and LAM-resistant and ADV-resistant HBV (1 mg/day)

- McMahon M et al in 2007 published in NEJM: ETV can reduce plasma HIV-RNA and select M184V in HIV.

- Use in combination with active HAART

Potential interactions of ETV with some
Telbivudine

- Greater anti-HBV efficacy than either LAM or ADV and low rates of resistance mutations
- Telbivudine cannot be used following LAM failure, and vice versa. Interestingly, there is no evidence of cross-resistance between LdT and ADV

Lamivudine-resistant HBV:

- If fully suppressed HIV: consider the addition of adefovir or pegIFN to lamivudine, or exchange tenofovir for one of the other nucleoside agents in the ART regimen

- Either lamivudine or emtricitabine should be continued because this may ↓ development of mutations to other anti-HBV drugs
### When to Treat & With What

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

**Not ready for cART?**
- **Consider PEG αINF 2a x 48 weeks**
  - advanced fibrosis
  - HIV/HBV/HCV
  - improves fibrosis
  - may clear virus
- **Adefovir X 48 weeks**
- **Consider earlier HAART w/ HBV-active agent**

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### Pairs to Avoid

- emtricitabine + lamivudine
- adefovir + tenofovir (closely related with similar resistance profiles)
- emtricitabine or lamivudine + telbivudine (Inferior for all parameters of response as compared to telbivudine alone)


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

• Tx. not on cART/HBeAg+/and become HBeAg – and eAB +, tx 6-12 mos beyond eAg seroconversion.

• All pts on cART when HBV treated need to continue on HBV tx even if seroconverted to anti-HBe (Exception = pegIFN tx. Only 48 weeks)


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 log₁₀ IU/mL decrease from baseline at 3 months

• Breakthrough is > 1 log₁₀ IU/mL increase compared to nadir

Last words: Hepatitis A, B, C & HIV

Prevention is KEY

– Screen & vaccinate early

  • Lower CD4s will lower antibody response
    – CD4 < 200 ~15-40% antibody
    – CD4 >500 ~ 90% antibody
  
  • ?Re-vaccinate w/ double-dose (50.7% response in previous non-responders in Dutch prospective open-label study)

– Counsel about risk factors

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
7. AASLD Practice Guideline; Chronic Hepatitis B; LOK, et.al., Hepatology Volume 45, February 2007