### COMPETING INTEREST OF FINANCIAL VALUE > £1,000:

<table>
<thead>
<tr>
<th>Speaker Name</th>
<th>Statement</th>
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<tbody>
<tr>
<td>Dr Andrew Ustianowski</td>
<td>acts in a consultancy capacity for Abbvie, Gilead, Janssen, MSD, and ViiV; and as a speaker at company-sponsored events for BMS, Gilead, Janssen, and ViiV. He has also received personal grants for attending conferences from Gilead and Janssen.</td>
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<tr>
<td>Date</td>
<td>October 2014</td>
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HEPATITIS B AND HIV

Andy Ustianowski
Regional Infectious Diseases Unit
North Manchester General Hospital
Chair: British Viral Hepatitis Group
I am doing a clinic....

• **First Patient:**
  - Recent diagnosis of HIV
    - Not on ART
  - CD4 355
  - VL 150,000

• Hep B non-immune:
  - sAg negative
  - cAb negative
  - sAb 0
What would you do in terms of his Hep B immunity?

Would you:

1. Provide standard (20mcg) x3 vaccination regimen
   - 6%

2. Provide double dose (40mcg) x3 vaccination regimen
   - 18%

3. Provide double dose (40mcg) x4 vaccination regimen
   - 63%

4. Get his HIV under control first and CD4 higher and then try vaccinating
   - 12%

5. Something else....
   - 1%
High Dose (40mcg) x4 vaccination…

• Go straight for high dose vaccine at 0, 1, 2 & 6 months
  • And then check immunity afterwards…

• Evidence:
  • Meta-analyses have shown a better serological response to high dose vaccine (OR 1.96; 95% CI: 1.47, 2.61)
  • Studies have shown a better response to 4 doses

You try this.....

- But sAb < 10
- In meantime starts Atripla
- After 9 months you try vaccinating him again
- Still no good…
  - sAb < 10

- What should you do?
HIV treatment and HBV transmission: Dutch cohort

Dutch HIV cohort of 2,942 patients

Kaplan-Meier: HBV free-survival (MSM)

- 871 'HBV-susceptible', 35 HBV infected during follow-up
- In MSM, the lowest incidence rate was found in persons using HBV active cART containing TDF (0.14 per 100 PYFU; IRR 0.05), compared with persons without HBV-active cART (incident rate 2.85)
- Chance of HBV infection in patients receiving HBV-active cART with tenofovir (logrank P<0.001)

HBV-active cART protects against primary HBV infection (≈ HBV PrEP)

Heuft M et al. AIDS 2014.
HIV treatment and HBV transmission: Japan cohort

354 HIV+ patients, Tokyo, Japan

<table>
<thead>
<tr>
<th>ART</th>
<th>Observation Period (Person-Years)</th>
<th>Incident Infection</th>
<th>Hazard Ratio (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>No ART</td>
<td>446</td>
<td>30</td>
<td>1</td>
<td>. . .</td>
</tr>
<tr>
<td>Other-ART</td>
<td>114</td>
<td>6</td>
<td>.924 (.381–2.239)</td>
<td>.861</td>
</tr>
<tr>
<td>ART containing at least 1 of LAM, TDF, and FTC(^a)</td>
<td>1047</td>
<td>7</td>
<td>.113 (.049–.261)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>LAM-ART</td>
<td>814</td>
<td>7</td>
<td></td>
<td></td>
</tr>
<tr>
<td>TDF-ART</td>
<td>233</td>
<td>0</td>
<td></td>
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</table>

- The rate of incident infections was lower during LAM- or TDF-containing ART (0.669 incident infections in 100 person-years) than during no ART period (6.726 incident infections in 100 person-years) and other ART (5.263 incident infections in 100 person-years) (P < .001).
Same clinic…

- **Second patient:**
  - CD4 450
    - Not on ART
    - Well
  - HBV sAg+
    - HBV viral load 1000 iu/ml
    - ALT 29
    - US normal
    - Fibroscan – 5.5kPa (probably normal)
Start ART or not?
Would you:

1. Hold off on ART and monitor his liver  
   9%
2. Start ART containing 3TC or FTC  
   4%
3. Start ART containing 3TC or FTC and TDF  
   87%
4. Something else…  
   1%
CD4 < 500, regardless of whether HBV needs Rx: Start TDF & FTC/3TC-based ART
What if...

- **Second patient:**
  - CD4 450 - 800
  - Not on ART
  - Well
- **HBV sAg+**
  - HBV viral load 1000 iu/ml
  - ALT 29
  - US normal
  - Fibroscan – 5.5kPa (probably normal)

Neither the HIV nor the HBV necessarily need treatment...
BHIVA Guidelines....

British HIV Association Guidelines for the Management of Hepatitis Viruses in Adults Infected with HIV 2013

British HIV Association guidelines for the treatment of HIV-1-positive adults with antiretroviral therapy 2012

(Updated November 2013. All changed text is cast in yellow highlight.)

CD4 > 500 and HBV not needing Rx: Consider ART (including TDF & FTC) (2C)
What if...

• Second patient:
  • CD4 450–800
    • Not on ART
    • Well
  • HBV sAg+
    • HBV viral load 4000–60,000 iu/ml
    • ALT 29–47 (persistently elevated)
    • US normal
    • Fibroscan – 5.5–7.8 kPa (fibrotic)

Normal ALT when considering HBV are:
  • <19 for women
  • <30 for men
Needs treatment for his HBV…
Would you:

1. Start 3TC or FTC or TDF monotherapy  
   - 1%
2. Start 3TC or FTC and TDF dual therapy  
   - 7%
3. Start Entecavir  
   - 3%
4. Start Peg-interferon  
   - 1%
5. Start Adefovir  
   - 1%
6. Start full ART as in earlier patients  
   - 87%
Entecavir and HIV...

The HBV Drug Entecavir — Effects on HIV-1 Replication and Resistance

Moira A. McMahon, B.S., Benjamin L. Jilek, B.S., Timothy P. Brennan, M.S., Lin Shen, M.D., Yan Zhou, Ph.D., Megan Wind-Rotolo, Ph.D., Sifei Xing, B.S., Shridhar Bhat, Ph.D., Braden Hale, M.D., Robert Hegarty, M.S.N., Curtis R. Chong, M.Phil., Jun O. Liu, Ph.D., Robert F. Siliciano, M.D., Ph.D., and Chloe L. Thio, M.D.

McMahon et al., NEJM 2007; 356: 2614-21
# Summary of BHIVA Guidance

<table>
<thead>
<tr>
<th>CD4 &lt; 500</th>
<th>HBV not requiring treatment</th>
<th>HBV requiring treatment</th>
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<tbody>
<tr>
<td></td>
<td>Start ART (1B)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(Include TDF and FTC)</td>
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</tbody>
</table>

| CD4 > 500 | Consider ART (2C)           | Start ART (1C)          |
|           | (Include TDF and FTC*)      | (Include TDF and FTC*)  |

* BHIVA Hepatitis Guidelines state TDF/FTC or TDF/3TC

Back to clinic...

• **Third patient:**
  • Known HIV and HBV
  • Has been on Atripla for past 12 months
    • HBV and HIV undetectable

• **Now:**
  • Creatinine increased
  • Normoglycaemic glycouria
  • Proteinuria
  • Low phosphate

• Need to discontinue the TDF....
What about his ART? Would you:

1. Switch out the TDF (e.g. to Abacavir) and continue his FTC and EFV?  
   - 17%

2. Stop his TDF and FTC and give him nucleoside-sparing therapy  
   - 1%

3. Switch out the TDF (e.g. to Abacavir), continue the rest of his ART, and add Entecavir  
   - 76%

4. Switch out the TDF and give Peg-Interferon  
   - 3%

5. Something else....  
   - 3%
He is intolerant of Entecavir....

- Has bad GI upset which persists on Entecavir...

- Difficult situation....

- You could try low dose TDF (with separate fully-active ART regimen)
  - Either alternate day
  - Or lower dose daily
- Or possibly Adefovir (and watch closely)
Back to clinic…

- **Fourth patient:**
  - HBV undetectable on Eviplera
  - However failing HIV control
    - VL 125,000
    - Resistance testing – M184V, K65R, some NNRTI too….

- You want to switch her ART
  - You choose a boosted PI and Raltegravir

- But what about her HBV??

- Continue the TDF (on top of her PI/r & Ral)
For all these patients…

• What should I do about hepatocellular carcinoma (HCC) screening?

• If cirrhotic:
  • Definitely need 6 monthly ultrasounds
  • Also do alpha-fetoprotein

• If not cirrhotic:
  • Still *recommended* to do 6 monthly ultrasounds…
  • Also do alpha-fetoprotein
  • ???
Other good practice....

- *No* need to check baseline HBV resistance (or genotypye) *unless* been exposed to nucleosides/nucleotides previously

- If at 1-2 years the HBV VL is still detectable??
  - If going down still don’t panic...
  - Check compliance
    - TDF resistance v.v. unusual
Good practice - monitoring

• Monitoring:
  • If not being treated:
    • i.e. HBV always under 2000, ALT always normal, Fibroscan <6.0 (or otherwise know that not fibrotic)
    • 6 monthly HBV VL and ALT
    • Annual Fibrosis estimation
  • If being treated:
    • Watch HBV VL 6 monthly
  • If undetectable on treatment:
    • Check serology each year (lose HBeAg or HBsAg?)
Summary

- Actually – HIV/HBV is easier than HBV mono-therapy

- Consider HBV-active ART in all patients
  - Recommended if CD4 < 500, consider if CD4 > 500

- Avoid 3TC or FTC monotherapy, or Entecavir monotherapy

- If cannot use TDF: add Entecavir onto fully active ART regimen
  - If cannot use TDF or Entecavir….get specialist help…. 