HDV HBV co-infection

Prof. Dr. Cihan Yurdaydin
University of Ankara
Dpt. of Gastroenterology

12th Co-infection Workshop
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I have received consultancy and/or lecture fees from AbbVie, BMS, Gilead, Roche, Merck, Boehringer Ingelheim, Janssen, and Novartis, and has received grants from BMS and Roche.
Hepatitis D virus
A cause of liver disease

Immunofluorescence detection of new antigen-antibody system (δ/anti-δ) associated to hepatitis B virus in liver and in serum of HBsAg carriers

M. Rizzetto, M. G. Canese, S. Aricò, O. Crivelli, C. Trepo, F. Bonino, and G. Verme

From the Department of Gastroenterology, Ospedale Mauriziano Umberto I, Turin, Italy, the Electron Microscopy Centre of the Faculty of Medicine, University of Turin, Italy, and INSERM U45, and Laboratory of Hygiene, University Claude Bernard, Lyon, France

δ agent: Association of δ antigen with hepatitis B surface antigen and RNA in serum of δ-infected chimpanzees

(Mario Rizzetto*, Bill Hoyer*, Maria C. Canese*, J. Wai-Kuo Shih*, Robert H. Purcell†, and John L. Geffin‡)

*Division of Molecular Virology and Immunology, Department of Microbiology, Georgetown University School of Medicine and Dentistry, Washington, DC 20057, and †Laboratory of Infectious Diseases, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, Maryland 20892

Communicated by Robert M. Chanock, June 9, 1980
Simultaneous Co-Infection

- Acute HBV
- Acute HDV

95% recovery
More frequent fulminant

HDV Super-Infection

- Acute HDV
- Chronic Hepatitis B

90% chronic
More severe disease
Delta Hepatitis

Early chimpanzee experiments disclosed:

Supression of HBV infection
- Decline or disappearance of HBcAg in liver tissue
- Decrease in HBsAg

Typical patient with delta hepatitis:
- HBeAg-negative, HBeAb-positive
- HBV DNA low
- High HDV RNA
HBeAg-positive chronic delta hepatitis
534 patients; 71/534 (13%) HBeAg (+)

Heidrich et al, Liver Int 2012

HDV RNA levels similar in HBeAg vs. HBeAg-negative CDH
HBcAg IHC in CDH

Nuclear localization

No correlation with liver injury, even in HBV-HDV co-dominant cases

Kabaçam et al, Liver Int 2013
HDAg IHC in CDH

HDAg display (+) correlation with ALT and HBsAg levels

Kabaçam et al, Liver Int 2013
Global overall estimated HDV prevalence: ~5% (4.7-5.3%) of patients with active HBV (240 million HBV cases worldwide—WHO)

HDV is not evenly distributed.
-- low prevalence regions driven primarily by high risk groups
e.g. US (orphan designation 11/25/13), EU, Japan
-- regions of higher prevalence—endemic
e.g. Mongolia, parts of Pakistan, Brasil, Africa, Turkey, etc.
## EEA HDV Prevalence

### Heavily impacted by Immigration and IVDU* Populations

<table>
<thead>
<tr>
<th></th>
<th>High Risk Group Proportion in HDV Population</th>
<th>IVDU HBsAg (+) Population¹</th>
<th>Immigrant HBsAg (+) Population²</th>
<th>High Risk HBsAg (+) Population</th>
<th>% HDV Prevalence³</th>
<th>HDV subjects in High Risk Population</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spain</td>
<td>96%</td>
<td>1,686</td>
<td>155,459</td>
<td>157,145</td>
<td>6-9</td>
<td>11,786</td>
</tr>
<tr>
<td>Sweden</td>
<td>84%</td>
<td>4,466</td>
<td>50,593</td>
<td>55,059</td>
<td>2-5</td>
<td>1,927</td>
</tr>
<tr>
<td>France</td>
<td>83%</td>
<td>50,562</td>
<td>112,704</td>
<td>163,266</td>
<td>6-9</td>
<td>12,245</td>
</tr>
<tr>
<td>UK</td>
<td>74%</td>
<td>29,367</td>
<td>192,128</td>
<td>221,495</td>
<td>6-9</td>
<td>16,612</td>
</tr>
<tr>
<td>Germany</td>
<td>72%</td>
<td>9,394</td>
<td>282,256</td>
<td>291,650</td>
<td>10-12</td>
<td>32,082</td>
</tr>
<tr>
<td>Italy</td>
<td>56%</td>
<td>36,940</td>
<td>202,648</td>
<td>239,588</td>
<td>6-9</td>
<td>17,969</td>
</tr>
</tbody>
</table>

¹ IVDU population figures taken from EMCDDA (European Monitoring Center for Drugs and Drug Addiction)
² Immigrant population figures taken from Eurostat
³ HDV prevalence from post-2006 country specific literature reports

- High risk group proportion in HDV population is 56-96%
  → For Spain, Sweden, France, UK, Germany, and Italy, HDV proportion of high risk groups are 96%, 84%, 83%, 74%, 72%, 56%, respectively (mean = 78%).

- **Total HDV Population** = HDV High Risk Group + HDV Low Risk Group
- **HDV High Risk Group** = [High risk group HBsAg(+) pop] x [% HDV Prevalence]
  → HBsAg(+) High Risk Group = HBsAg(+) Immigrant Pop + HBsAg(+) IVDU Pop

Orphan Disease

• Threshold is less than 5 per 10 000
• EEA: 28 EU states + Iceland + Norway + Liechtenstein
• Total population: 510 064 934
• Orphan Designation Threshold: 255 032
## EEA HDV Prevalence Calculation

<table>
<thead>
<tr>
<th></th>
<th>Total Population (2013)</th>
<th>Total HBsAg (+) Population</th>
<th>High Risk HBsAg (+) Population</th>
<th>% HDV Prevalence</th>
<th>HDV Subjects in High Risk Population (78% HDV Population)</th>
<th>HDV Subjects in Low Risk Population (22% HDV Population)</th>
<th>Total HDV Population</th>
<th>HDV Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>EEA</strong></td>
<td>510,064,934</td>
<td>5,492,518</td>
<td>1,596,264</td>
<td>Country specific prevalence</td>
<td>117,265</td>
<td>34,045</td>
<td>151,310</td>
<td>2.97 in 10,000</td>
</tr>
</tbody>
</table>

**HDV an orphan disease in Europe**
Female patient living in Sweden, migrated from Uzbekistan

- ALT: 78, AST 66
- GGT and Alkalen Phosphatase: normal
- HBsAg (+), HBeAg negatif
- Anti HCV & HIV: negative
- HBV DNA 480 IU/mL
- Hb, WBC normal, platelets: 176 000
- Height: 1.63m; weight: 92 kg
- BMI: 34.6
Diagnosis:

Inactive HBsAg carrier + NASH

Recommendation:
Diet + exercise; No need to treat HBV

Control visit every 3 months

3 x control visits, she loses some weight
Enzymes not much affected
The patient is a physician (gynecologist).

She decides to read, especially hepatitis B.

On her next visit, she asks for an anti HDV test.

Anti HDV (+)

HDV RNA is positive.
RESUME

Order anti HDV test in every HBsAg (+) pt.

Even in Sweden

AT THE VERY LEAST: Order anti HDV test if HBsAg (+), ALT high, HBV DNA low even if she/he looks very “NASHy”

ALT high, HBV DNA high, ALT continues to high despite apparently successful NA tx
HEPATOLOGY

Coinfection with hepatitis B and D: Epidemiology, prevalence and disease in patients in Northern California

Robert G Gish,*† Debbie Hana Yi,†† Steve Kane,§ Margaret Clark,§ Michael Mangahas,§ Sumbella Baqai,§ Mark A Winters,** James Proudfoot‡ and Jeffrey S Glenn**

Results: Of 1191 CHB patients, 499 had been tested for HDV, with 42 (8%) determined to be coinfeected; half of these were also hepatitis C virus-infected. Cirrhosis was present in 73% of the coinfeected, 80% of the tri-infected, but only 22% of the monoinfected.
DELTA HEPATITIS- DIAGNOSIS

- Anti HDV IgM
- Anti HDV (IgG)
- HDV RNA (qualitative, quantitative PCR)
- HDV Ag (immunohistochemistry)
- Quantitative HBsAg,
- HDV & HBV genotype determination
Anti HDV IgM titre correlate with ALT and histologic activity

Wranke et al, PlosOne 2014
Effect of semi-quantitative anti HDV IgM Levels on prognosis

Cumulative event free survival

IgM status
- negative
- negative
- medium
- high
- positive

Number at risk
<table>
<thead>
<tr>
<th>IgM negative</th>
<th>11</th>
<th>8</th>
<th>6</th>
<th>5</th>
<th>3</th>
<th>2</th>
</tr>
</thead>
<tbody>
<tr>
<td>IgM positive</td>
<td>67</td>
<td>48</td>
<td>37</td>
<td>27</td>
<td>19</td>
<td>13</td>
</tr>
</tbody>
</table>

Wranke et al, PlosOne 2014
Anti HDV IgM

- Suggestive of acute infection or chronic active infection
- Not standardized
- HDV RNA more sensitive
Anti HDV (or anti HDV IgG)

- First test to be used for searching for HDV
- Not a neutralizing Ab, depicts encounter with HDV
- HDV RNA testing necessary to establish active HDV infection
- Remains positive for years after successful tx including HBsAg clearance
HDV RNA

• Qualitative or quantitative
• Surrogate marker of tx efficacy
• Standardization was important Now there is a WHO standard (Paul Ehrlich Institute); Labs should get it
HBsAg decline in CDH

Keskin et al, Clin Gastroenterol Hepatol 2015
# HDV and HBV Genotypes

<table>
<thead>
<tr>
<th>Region</th>
<th>HDV genotype</th>
<th>HBV genotype</th>
</tr>
</thead>
<tbody>
<tr>
<td>Europe</td>
<td>1</td>
<td>D / A</td>
</tr>
<tr>
<td>Brazil</td>
<td>1 / 3</td>
<td>F / A / D</td>
</tr>
<tr>
<td>China, Taiwan, Japan</td>
<td>1 / 2 / 4</td>
<td>B / C</td>
</tr>
<tr>
<td>Turkey, Romania, Albania, Iran, Pakistan, India</td>
<td>1</td>
<td>D</td>
</tr>
<tr>
<td>Western Pacific</td>
<td>1 / 2</td>
<td>B / C / D</td>
</tr>
<tr>
<td>Africa</td>
<td>1, 5-8</td>
<td>D / A / E</td>
</tr>
</tbody>
</table>
Different HDV Genotypes Are Associated With Different Clinical Outcomes

![Image of survival curve showing different HDV genotypes with follow-up years and patients at risk]

- **HDV genotype I:**
  - Patients at risk: 46
  - Follow-up years: 29, 25, 10

- **HDV genotype II:**
  - Patients at risk: 72
  - Follow-up years: 55, 49, 27

*P = 0.0105*
Hepatitis Delta co-infection in humanized mice leads to pronounced induction of innate immune responses in comparison to HBV mono-infection

Katja Giersch¹, Lena Allweiss¹, Tassilo Volz¹, Martina Helbig¹, Jeanette Bierwolf², Ansgar W. Lohse¹,³, Joerg M. Pollok², Joerg Petersen⁴, Maura Dandri¹,³,*†, Marc Lütgehetmann¹,⁵,†

E  hOAS1  F  hISG15  G  hHLA-E  H  hSTAT1

J Hepatol 2015; 63:346-53
TREATMENT OF CHRONIC DELTA HEPATITIS

* Evidence based successful treatment: interferon

* High dose, long treatment period (one year)

* Sustained virologic response LOW
Treatment of Hepatitis Delta With PEG-IFNα 2a: ~25% Sustained HDV RNA Clearance

**Figure 1.** Virologic Response to Treatment as Determined by Serum Level of HDV RNA, According to Treatment Group.

PEG-IFNα 2a – Adefovir Combination Resulted in a More Pronounced HBsAg Suppression

HDV RNA Response Until Week 120
Intent-to-Treat Analysis

Patients HDV RNA negative (%)

PEG-IFNα 2a + Tenofovir
PEG-IFNα 2a + Placebo

Relapse 11/25 (44%)
Relapse 8/20 (40%)

HDV RNA Clearance after Therapy
Neg post Tx, 1 patient
Neg post Tx, 3 patients

Wedemeyer, Yurdaydin, et al. EASL 2014.
 Patients with HBsAg decline
>0.5 log_{10} U/mL (%)

- PEG-IFNα 2a + Tenofovir
- PEG-IFNα 2a + Placebo

<table>
<thead>
<tr>
<th>Treatment</th>
<th>FU</th>
</tr>
</thead>
<tbody>
<tr>
<td>HBsAg loss: 4/59 patients (6.7%)</td>
<td></td>
</tr>
<tr>
<td>HBsAg loss: 3/61 patients (4.9%)</td>
<td></td>
</tr>
</tbody>
</table>

Mean HBsAg levels [log_{10} IU/mL]

Wedemeyer, Yurdaydin, et al. EASL 2014.
No Progress in HDV Treatment, why?

- Progress in HBV tx did not contribute
  - HBV Tx acts on HBV DNA Polymerase
  - Very efficient
  - The only fn of HBV needed by HDV is HBsAg synthesis
  - NA tx in HBV has no effect on HBsAg synthesis

- RNA Polymerase is a cell enzyme and cannot be targeted for tx

- HDV is considered an ‘orphan disease’ and the potential financial reward is likely to be insufficient for the BMI to invest in CDH
Well, nobody's perfect.
# Studies with pegylated interferons in CDH

<table>
<thead>
<tr>
<th>Author</th>
<th>Treatment schedule</th>
<th>N</th>
<th>EOT VR</th>
<th>EOFU VR</th>
</tr>
</thead>
</table>
| Niro et al\textsuperscript{41} | Peg-IFNα-2b, 1.5µg/kg, qw x18 mo.  
Peg-IFNα-2b, 1.5µg/kg, qw x18 mo.  
+ Ribavirin, 1-1.2g, qd x 12 mo. | 16 | 19%    | 25%    |
|                 |                                                                                    | 22 | 9%     | 18%    |
| Castelnau et al\textsuperscript{42} | Peg-IFNα-2b, 1.5µg/kg, qw x12 mo.                                               | 14 | 57%    | 43%*   |
| Erhardt et al\textsuperscript{43} | Peg-IFNα-2b, 1.5µg/kg, qw x12 mo.                                               | 12 | 17%    | 17%    |
| Wedemeyer et al\textsuperscript{44} | Peg-IFNα-2a, 180μg, qw x12 mo.  
Peg-IFNα-2b, 180μg, qw x12 mo.  
+ Adefovir, 10 mg, qd | 29 | 24%    | 26%    |
|                 |                                                                                    | 31 | 23%    | 31%    |
| Gheorge et al\textsuperscript{45} | Peg-IFNα-2b, 1.5µg/kg, qw x12 mo.                                               | 48 | 33%    | 25%    |
| Örmeci et al\textsuperscript{46}  | Peg-IFNα-2b, 1.5µg/kg, qw x24 mo.                                               | 9  | 56%    | 44%    |
|                 |                                                                                    | 7  | 57%    | 100%   |
| Abbas et al\textsuperscript{47} | Peg-IFNα-2a, 180μg, qw x12 mo.                                                   | 104| 42%    | 23%    |
| Karaca et al\textsuperscript{48} | Peg-IFNα-2a, 180μg, or Peg-IFNα 2b, 1.5ug/kg, qw x24 mo. | 32 | 50%    | 47%**  |
| Wedemeyer et al\textsuperscript{49} | Peg-IFNα-2a, 180μg, qw x24 mo.  
Peg-IFNα-2a, 180μg, qw x24 mo.  
+ Tenofovir, 300mg, qd | 61 | 33%    | 21%    |
|                 |                                                                                    | 59 | 48%    | 29%    |
HDV RNA and HBsAg kinetics in CDH during peg-IFN therapy

HDV RNA declines in a biphasic manner:
Fast 1st phase decline followed by a slow 2nd phase decline (or plateau)

HBsAg kinetics parallel kinetics of HDV RNA

There is a long delay before Peg-IFN shows an effect

Guedj J et al, Hepatology 2014
IFN treatment: Problems

• How can treatment efficacy be assessed?
• How consistent and reliable is a sustained virologic response?
• The impact of therapy in the high proportion of patients with cirrhosis
• What is the response of treatment-naïve vs treatment experienced patients?
• What is the optimal duration of treatment?
• Can response to treatment be predicted?
• Or can NRs be predicted?
• Are better markers of treatment efficacy needed?
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• Or can NRs be predicted?
• Are better markers of treatment efficacy needed?
IFN treatment: Problems

• How can treatment efficacy be assessed?
  
  Best: HBsAg clearance
  Realistic: Posttreatment HDV RNA negative

• How consistent and reliable is a sustained virologic response?
  
  Not reliable
Is 6 months treatment-free follow-up a reliable surrogate marker of tx efficacy?

Heidrich et al, Hepatology 2014
IFN treatment: Problems

• How can treatment efficacy be assessed?
• How consistent and reliable is a sustained virologic response?
• The impact of therapy in the high proportion of patients with cirrhosis
• What is the response of treatment-naïve vs treatment experienced patients?
• What is the optimal duration of treatment?
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• Or can NRs be predicted?
• Are better markers of treatment efficacy needed?
Figure 2A: Flow chart of maintained viral response and treatment duration

Keskin et al, AASLD 2015
Figure 2B: Cumulative probability of a maintained viral response in patients treated with interferons
Keskin et al, AASLD 2015
“Maintained Virologic Response” Associated With Improved Outcome

Keskin et al, AASLD 2015
High rate of HBsAg clearance in pts with “Maintained Virologic Response”

Keskin et al, AASLD 2015
IFN treatment: Problems

• How can treatment efficacy be assessed?
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• What is the response of treatment-naïve vs treatment experienced patients?
• What is the optimal duration of treatment?
• Can response to treatment be predicted?
• Or can NRs be predicted?
• Are better markers of treatment efficacy needed?
HDV RNA levels in INF early responders

Yurdaydin et al, J Viral Hepat 2008
Multivariate logistic regression analysis for predicting end of treatment and post- treatment week 24 virologic response

### End of treatment response:

<table>
<thead>
<tr>
<th></th>
<th>OR</th>
<th>95% CI</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>HDV RNA week 24</td>
<td>1.627</td>
<td>1.070 – 2.474</td>
<td>0.023</td>
</tr>
<tr>
<td>Baseline HAI</td>
<td>0.586</td>
<td>0.366 – 0.937</td>
<td>0.026</td>
</tr>
</tbody>
</table>

### Post-treatment week 24 response:

<table>
<thead>
<tr>
<th></th>
<th>OR</th>
<th>95% CI</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>HDV RNA week 24</td>
<td>2.538</td>
<td>1.347 – 4.782</td>
<td>0.004</td>
</tr>
</tbody>
</table>

Figure 2: Predictive value of on-treatment week 24 undetectable HDV RNA for post-treatment week 24 virologic response

Week 24 HDV RNA decline

- > 1 log decline, N = 27
- < 1 log decline, N = 12

Week 24 HBsAg decline

- Yes, 21
- No, 6

Week 48 “null” response

- 2/21 9.5%
- 2/6 33%
- 3/6 50%
- 5/6 83%

NPV 90.5%

PPV 83%

Figure 2D: Predictive value of on-treatment week 24 HDV RNA and HBsAg levels for EOT virologic “null response” (<1 log decline of HDV RNA at EOT)

Chronic hepatitis B, anti delta (+) patient

Treatment with IFNα 2a or 2b, 9 or 10 MU, tid or peg-IFNα 2a, 180μg, qw for 1 year

HDV RNA(+)
ALT N

HDV RNA(-)
ALT N

HDV RNA(+)
ALT ↑

Check ALT, HDV RNA, Q 3 mo.

Repead, if same
FU q6 mo. with US

Treat if ALT ↑, HDV RNA(+)

Check ALT, HDV RNA, Q 3 mo.

Partial response:
HDV RNA ↓ >2log
ALT ↑ or N

Consider tx continuation
for an additional year. If tx
continued consider this algorithm
also at end of 2nd year

If ALT↑↑, HDV RNA(+)
Consider restarting tx

If ALT N, HDV RNA(-)
Check ALT, HDV RNA
q3-6 mo., HB serology
q 6 mo.

If HDV RNA(+), ALT N
Check HDV RNA, ALT q3 mo.
Consider restarting tx if ALT↑

Response:
HDV RNA(-)
ALT N

Dc tx, follow-up q2 mo
for 6 mo.

No response:
HDV RNA no change or
decline < 2log, ALT ↑ or N

Consider experimental tx

Yurdaydin, Sem Liver Dis 2012
Targets in HDV Treatment

- TLR Agonists
- Entry Inhibitors
- Nucleic Acid Polymers
- Prenylation Inhibitors
Effect of the hepatocyte entry inhibitor, Myrcludex in CDH

8 pts receive Myrcludex, 2mg/kg for 6 months
8 pts receive Myrcludex, 2mg/kg + Peg IFN for 6 months
Daily sc injections

Urban S et al, AASLD 2014, LB 20
• 6 of 7 patients experienced HDV RNA decline $>1 \log_{10}$ at week 24 during Myr B monotherapy
• 7 of 7 patients experienced HDV RNA decline $>1 \log_{10}$ at week 24 during Myr B/PEG-IFNα combination therapy
• HDV RNA became negative in 2 patients during Myr B monotherapy and in 5 patients in combination with PEG-IFNα
Heparin sulfate glycoproteins as HBV-HDV rec’s

Glypican 5
Treatment of CDH with Lonafarnib

Mean (SD) Change in HDV RNA Per Week

-3 -2 -1 0 1 2
HDV RNA Log IU/mL

Therapy Post-Therapy Follow-up
Time in Weeks Time in Months

Placebo
Lonafarnib 100mg BID
Lonafarnib 200mg BID

Koh C et al, Lancet Infect Dis 2015
Week 4 Reduction in HDV RNA with Lonafarnib

National Institutes of Health
NIH POC (Lancet Infect. Dis. 2015)

- Placebo
- Lonafarnib 100 mg BID
- Lonafarnib 200 mg BID

Ankara University
LOWR-1 (EASL 2015)

- Lonafarnib 100 mg BID
- Lonafarnib 100 mg TID
- Lonafarnib 200 mg BID
- Lonafarnib 300 mg BID
- Lonafarnib 100 mg BID + Ritonavir 100 mg QD
- Lonafarnib 100 mg BID + PEG IFN-α 2a 180 mcg QW

Mean ∆
- 0.2 Log
- 0.74 Log
- 1.6 Log
- 1.2 Log
- 1.6 Log
- 2.0 Log
- 2.4 Log
- 1.8 Log

N = 4
N = 6
N = 6
N = 3
N = 3
N = 3
N = 3
N = 3

Mean Change in Log HDV RNA
Side effects Improved with LNF Combos

- Mainly GI side effects

<table>
<thead>
<tr>
<th></th>
<th>N=3</th>
<th>N=3</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>LNF 200 mg BID</td>
<td>LNF 300 mg BID</td>
<td>LNF 100 mg BID RTN 100 mg QD</td>
<td>LNF 100 mg BID PEG IFN 180 mcg QW</td>
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<tr>
<td>Grade</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Nausea</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Diarrhea</td>
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<td>Fatigue</td>
<td>✓</td>
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</tr>
<tr>
<td>Wt Loss</td>
<td>✓</td>
<td>✓</td>
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<td>✓</td>
</tr>
<tr>
<td>Anorexia</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
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</tr>
</tbody>
</table>

- Graded according to Common Terminology Criteria for Adverse Events

- Lonafarnib chronically dosed in Progeria for 2 years (PNAS, 2012, 16666)
Serum Concentration and Viral Load
Statistically Significant Linear Relationship

Effect of ARC-520, a siRNA based tx as single injection on HBsAg levels in HBeAg (-) CHB

Yuen MF et al, AASLD 2014, LB 21
Nucleic acid polymers (NAPs) are oligonucleotides whose biochemical function is strictly dependent on the polymer chemistry of oligonucleotides.

They bind with high affinity to amphipathic protein structures.

These amphipathic protein structures are very rare in normal human biology (already complexed with each other inside proteins where they help stabilize the protein structure).

However amphipathic targets are required for various stages of viral replication. NAPs effectively block the functions of these proteins, providing an effective, broad-spectrum antiviral activity.
Nucleic Acid Polymers (NAPS) for HBV/HDV Coinfection

- 12 HDV pts in Moldova
- Anti-HDV/RNA +
- HBsAg >1000
- Non-cirrhotic

Results: (1) HBsAg

500mg REP 2139-Ca qW

250 mg REP 2139-Ca qW
180 ug Pegasys® qW

Follow-up 4, 12 and 24 wks

(2) HDV RNA

500mg REP 2139-Ca qW

250 mg REP 2139-Ca qW
180 ug Pegasys® qW

Vaillant A, et al. EASL 2015, Vienna. #LO2
Summary and Conclusion - 1

The only effective treatment is with interferons.

Treatment beyond 1 year needed in a sizeable proportion of patients.

Post-treatment week 24 ≠ SVR in CDH.

HDV RNA standard now available.
Summary and Conclusion - 2

The future:
There is now hope:
Hepatocyte entry inhibitors
Prenylation inhibitors
Nucleic acid polymers
siRNAs

Stay tuned
DANKE SEHR
REPLICATION OF THE DELTA VIRUS