Non-alcoholic fatty liver: a practical approach

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Division of Digestive Diseases
Imperial College
42% of abnormal ALT was attributable to coinfection with HBV or HCV. 28% of those scanned had fatty liver. 16% had bridging fibrosis or cirrhosis.
NAFLD is the most important cause of abnormal LFTs with normal serology

<table>
<thead>
<tr>
<th>Final Diagnosis</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>NASH</td>
<td>34</td>
</tr>
<tr>
<td>Steatosis</td>
<td>32</td>
</tr>
<tr>
<td>Cryptogenic hepatitis</td>
<td>9</td>
</tr>
<tr>
<td>DILI</td>
<td>7.6</td>
</tr>
<tr>
<td>Normal</td>
<td>5.9</td>
</tr>
<tr>
<td>Autoimmune</td>
<td>1.9</td>
</tr>
<tr>
<td>Granulomas/Sarcoid</td>
<td>1.7</td>
</tr>
<tr>
<td>PBC</td>
<td>1.4</td>
</tr>
<tr>
<td>PSC</td>
<td>1.1</td>
</tr>
</tbody>
</table>

Skelly J.Hep 2001
Causes of HIV-NAFLD

- HIV mediated toxicity in hepatocytes / adipocytes
- Drug toxicity
- Gut translocation of bacterial products
- Metabolic syndrome
HIV and Metabolic Syndrome
A Comparison With the General Population

Paolo Bonfanti, MD,* Cristina Giannattasio, MD,† Elena Ricci, ScD,* Rita Facchetti, ScD,†
Elena Rosella, MD,‡ Marzia Franzetti, MD,§ Laura Cordier, MD,* Luigi Passerla, MD,†
Michele Bombelli, MD,‡ Roberto Sega, MD,† Tiziana Quarino, MD,§ and Giuseppe Mancia, MD†

**Figure 1.**

**Prevalence of MS Components in HIV Patients and Controls**

- **BP**
  - Controls: 35.9%
  - HIV Patients: 46.9%
- **HDL-C**
  - Controls: 23.3%
  - HIV Patients: 48.4%
- **TG**
  - Controls: 33.7%
  - HIV Patients: 6.7%
- **Glycemia**
  - Controls: 17.8%
  - HIV Patients: 14.2%

*P < 0.0001

Bofanti, P et al. JAIDS, 2007
HIV infected individuals are getting older and fatter

Crum-Cianflone, N et al. PlosOne, 2010
Gut Translocation Exacerbates NAFLD
Risk factors for NAFLD in HIV

Maurice et al. Unpublished
Diagnosis

• Is it NAFLD?
  – Evidence of steatosis
  – Exclusion of other causes of liver disease
  – Exclusion of secondary steatohepatitis

• What is the stage of disease
  – Simple steatosis vs Steatohepatitis
Diagnosing Steatosis

- Ultrasound
- MRI
- CT
- Fibroscan CAP score
Secondary Hepatic Steatosis

• Macrovesicular
  – Alcohol
  – Hepatitis C (Gt3)
  – Wilson’s disease
  – Lipodystrophy
  – Starvation
  – Parenteral nutrition
  – Abetalipoproteinaemia
  – Drugs
    • Amiodarone, methotrexate, tamoxifen, corticosteroids

• Microvesicular
  – Reye’s syndrome
  – Drugs
    • Valproate, ART
  – Acute fatty liver of pregnancy
  – Genetic disorders (eg Lysosomal acid lipase deficiency)
NORMAL

12-20%

STEATOSIS

5-15%

NASH

0-12%

CIRRHOSIS

DISEASE PROGRESSION

BMI
DM-II
Waist circumference
Sedentary lifestyle

Inflammation on histology

PNPLA3 & TM6SF2 genotypes

(Day, Liver Int., 2006)
NASH Progression

Caldwell. Dig Dis Sci 2010
IS A BIOPSY ALWAYS NECESSARY?

• Not always necessary but may be helpful.
  – Exclude alternative/secondary pathology
  – Stratify disease progression risk
Non-Invasive Diagnosis of NASH

• Steatohepatitis
  – CK18 fragments Feldstein 2009
  – Methacetin breath test
  – Ferritin

• Fibrosis Markers
  – PIIINP
  – ELF
  – Fibrotest
  – Fibroscan
NAFLD Fibrosis Score

- NAFLD Fibrosis Score =
  - 1.675
  - 0.037 x Age (years)
  - 0.094 x BMI (kg/m²)
  - 1.13 x IFG/diabetes (yes = 1, no = 0)
  - 0.99 x AST/ALT ratio
  - 0.013 x platelet (x10⁹/l)
  - 0.66 x Albumin (g/dl).

- A score of less than -1.455 excludes fibrosis (NPV 88-93%).
- A score of greater than 0.676 predicts fibrosis (PPV 82-90%).

Angulo et al, Hepatology, 2007
European Liver Fibrosis Panel (ELF)

- TIMP1, Hyaluronic acid, Procollagen III peptide

Guha. Hepatology 2008
FIBROSCAN
Elastography Diagnostic Performance

A

AUROC
SSI - 0.86
FS - 0.82
ARFI - 0.77

B

AUROC
SSI - 0.89
FS - 0.86
ARFI - 0.84

C

AUROC
SSI - 0.88
FS - 0.84
ARFI - 0.87

Cassinotto Hepatology 2016
THERAPEUTIC TARGETS

1. Weight loss

2. Control metabolic syndrome & optimise management of components
   - Hypertension
   - Dyslipidaemia
   - Insulin resistance/Type 2 Diabetes mellitus

3. Prevent progression of fibrosing steatohepatitis
Effect of Weight Loss on ALT

Suzuki et al. J. Hepatol 2005
LIFESTYLE MODIFICATION

• **Weight Loss**
  – Dietary modification
    • Dietician in clinic
  – Exercise
    • Pedometers
    • Subsidised gym in hospital for group ‘get fit’ sessions

• **Behavioural Therapy**
  – Clear Targets
  – Positive Feedback
Regular Exercise

Exercising improves

- Insulin resistance
- Steatosis
- Independently from the weight loss

Fatty Liver assessment by spectrometry

- Placebo
- Exercise

n = 7
n = 12

Johnson, Hepatology 2009
Helmerhost, Diabetes 2009
Exercise & Visceral Fat

Keating J. Hep 2015
TREATING OBESITY

• Central appetite suppressants
  – Rimonabant (Acomplia)
    • Cannaboid receptor antagonist
    • No longer available

• Slowing absorption
  – Orlistat (Xenical)
    • Lipase inhibitor
    • Reduces dietary fat absorption
    • BMI >30 or >28 plus Metabolic Syndrome
    • May cause steatorrhoea

• Bariatric Surgery
Bariatric Surgery and NAFLD

Lassailly. Gastro 2015
THERAPEUTIC TARGETS

1. Weight loss

2. Control metabolic syndrome & optimise management of components
   - Hypertension
   - Dyslipidaemia
   - Insulin resistance/Type 2 Diabetes mellitus

3. Prevent progression of fibrosing steatohepatitis
NAFLD, the hepatic manifestation of the Metabolic Syndrome

<table>
<thead>
<tr>
<th>Central obesity</th>
<th>Abdominal circumference:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Europeans ≥ 94 cm (M) or ≥ 80 cm (F)</td>
</tr>
<tr>
<td></td>
<td>Americans: ≥ 102 (M) ≥ 88 cm (F)</td>
</tr>
<tr>
<td></td>
<td>Asians: ≥ ≥ 90 cm (M) ≥ 80 cm (F)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>High Blood Pressure</th>
<th>BP ≥ 130 mmHg and/or ≥ 85 mmHg or treated Hypertension</th>
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</thead>
</table>

<table>
<thead>
<tr>
<th>Low cholesterol HDL</th>
<th>&lt; 0,4 g/L (1 mmol/L) (M) or &lt; 0,5 g/L (1,3 mmol/L) (F) or treated Chol</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>High blood triglycerides</th>
<th>≥ 1,5 g/L (1,7 mmol/L) or treated hyperTG</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>High Blood glucose</th>
<th>Glucose ≥ 1 g/L (5,6 mmol/L) or antidiabetic treatement</th>
</tr>
</thead>
</table>

Alberti, circulation 2009
Statins and LFTs

- Statins do cause LFTs
- Statins do not cause liver failure
- Statins are not contraindicated in patients with
  - LFTs
  - Cirrhosis
  - NASH
- Statins are contraindicated in decompensated liver disease

- Check LFTs before starting statin therapy
- Do not monitor LFTs
  - Do as patients to report jaundice, fatigue, malaise

- An Assessment of Statin Safety by Hepatologists. Am.J. Cardiol 2006:
THERPEUTIC TARGETS

1. Weight loss

2. Control metabolic syndrome & optimise management of components
   - Hypertension
   - Dyslipidaemia
   - Insulin resistance/Type 2 Diabetes mellitus

3. Prevent progression of fibrosing steatohepatitis
DRUG THERAPY

Available Now

• Insulin sensitising agents
  – Metformin
  – Glitazones (PPARg agonists)

• Anti-oxidant therapy
  – Vitamin E

• Bile Acid Metabolism
  • Ursodeoxycholic acid

In Development

• Insulin sensitising agents
  – PPAR α/δ agonists
  – GLP-1 agonists

• Bile Acid Metabolism
  • FXR agonists

• Anti-inflammatory
  • CCR2/CCR5 Inhibition

• Anti-fibrotics
  • Lysyl Oxidase antibody
# Metformin & Liver Cancer

## Study Results

<table>
<thead>
<tr>
<th>Study</th>
<th>Treatment n/N</th>
<th>Control n/N</th>
<th>Liver Cancer</th>
<th>OR (95%CI)</th>
<th>P</th>
</tr>
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<tbody>
<tr>
<td><strong>Observational Study</strong></td>
<td></td>
<td></td>
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<td></td>
<td></td>
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<tr>
<td>Hassan, 2010</td>
<td>44/98</td>
<td>78/110</td>
<td></td>
<td>0.30</td>
<td>(0.20 to 0.60)</td>
</tr>
<tr>
<td>Kavaguchi, 2009</td>
<td>4/9</td>
<td>134/232</td>
<td></td>
<td>0.59</td>
<td>(0.15 to 2.24)</td>
</tr>
<tr>
<td>Lee, 2011^3</td>
<td>45/11236</td>
<td>28/4215</td>
<td></td>
<td>0.06</td>
<td>(0.02 to 0.16)</td>
</tr>
<tr>
<td>Oliveira, 2008</td>
<td>./.</td>
<td>./.</td>
<td></td>
<td>0.73</td>
<td>(0.34 to 1.56)</td>
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<tr>
<td>Donadon, 2010</td>
<td>18/71</td>
<td>172/334</td>
<td></td>
<td>0.15</td>
<td>(0.04 to 0.50)</td>
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<tr>
<td>Nkontchou, 2011</td>
<td>2/26</td>
<td>37/74</td>
<td></td>
<td>0.19</td>
<td>(0.04 to 0.79)</td>
</tr>
<tr>
<td>Lai, 2012^1</td>
<td>158/16282</td>
<td>66/3067</td>
<td></td>
<td>0.49</td>
<td>(0.37 to 0.66)</td>
</tr>
<tr>
<td>Ruiter, 2012</td>
<td>16/52698</td>
<td>15/32591</td>
<td></td>
<td>0.67</td>
<td>(0.53 to 0.86)</td>
</tr>
<tr>
<td><strong>OVERALL</strong></td>
<td></td>
<td></td>
<td></td>
<td>0.34</td>
<td>(0.19 to 0.60)</td>
</tr>
</tbody>
</table>

With in-group heterogeneity test \( \chi^2 = 31.00, P = 0.0001 \); \( (I^2 = 77\%) \)

## RCT

<table>
<thead>
<tr>
<th>Study</th>
<th>Treatment n/N</th>
<th>Control n/N</th>
<th>Liver Cancer</th>
<th>OR (95%CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Home, 2010^4C</td>
<td>2/1122</td>
<td>0/1103</td>
<td></td>
<td>4.92</td>
<td>(0.24 to 102.68)</td>
</tr>
</tbody>
</table>

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Franciosi et al. PLOS One 2014
Pioglitazone, Vitamin E, or Placebo for Nonalcoholic Steatohepatitis

Arun J. Sanyal, M.D., Naga Chalasani, M.B., B.S., Kris V. Kowdley, M.D.,
Arthur McCullough, M.D., Anna Mae Diehl, M.D., Nathan M. Bass, M.D., Ph.D.,
Brent A. Neuschwander-Tetri, M.D., Joel E. Lavine, M.D., Ph.D.,
James Tonascia, Ph.D., Aynur Unalp, M.D., Ph.D., Mark Van Natta, M.H.S.,
Jeanne Clark, M.D., M.P.H., Elizabeth M. Brunt, M.D.,
David E. Kleiner, M.D., Ph.D., Jay H. Hoofnagle, M.D.,
and Patricia R. Robuck, Ph.D., M.P.H., for the NASH CRN*
PIVENS: ALT, AST, Insulin Resistance, and Weight, According to Study Group.

# PIVENS: Histological Outcomes.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Placebo</th>
<th>Vitamin E</th>
<th>Pioglitazone</th>
<th>P Value*</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Primary outcome</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No. of subjects randomly assigned</td>
<td>83</td>
<td>84</td>
<td>80</td>
<td></td>
</tr>
<tr>
<td>Subjects with improvement (%)</td>
<td>19</td>
<td>43</td>
<td>34</td>
<td>0.001</td>
</tr>
<tr>
<td>Changes from baseline in histologic features</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No. of subjects with biopsy specimens at baseline and 96 wk</td>
<td>72</td>
<td>80</td>
<td>70</td>
<td></td>
</tr>
<tr>
<td>Steatosis</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Subjects with improvement (%)</td>
<td>31</td>
<td>54</td>
<td>69</td>
<td>0.005</td>
</tr>
<tr>
<td>Mean change in score</td>
<td>-0.1</td>
<td>-0.7</td>
<td>-0.8</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Lobular inflammation</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Subjects with improvement (%)</td>
<td>35</td>
<td>54</td>
<td>60</td>
<td>0.02</td>
</tr>
<tr>
<td>Mean change in score</td>
<td>-0.2</td>
<td>-0.6</td>
<td>-0.7</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Hepatocellular ballooning</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Subjects with improvement (%)</td>
<td>29</td>
<td>50</td>
<td>44</td>
<td>0.01</td>
</tr>
<tr>
<td>Mean change in score</td>
<td>-0.2</td>
<td>-0.5</td>
<td>-0.4</td>
<td>0.03</td>
</tr>
<tr>
<td>Total NAFLD activity score (mean change)</td>
<td>-0.5</td>
<td>-1.9</td>
<td>-1.9</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Fibrosis</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Subjects with improvement (%)</td>
<td>31</td>
<td>41</td>
<td>44</td>
<td>0.24</td>
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<tr>
<td>Mean change in score</td>
<td>-0.1</td>
<td>-0.3</td>
<td>-0.4</td>
<td>0.19</td>
</tr>
<tr>
<td>Resolution of definite nonalcoholic steatohepatitis (% of subjects)</td>
<td>21</td>
<td>36</td>
<td>47</td>
<td>0.05</td>
</tr>
</tbody>
</table>

*P values calculated using the Chi-squared test for categorical variables and the t-test for continuous variables.

Why not Pioglitazone/Vitamin E for All NAFLD Patients?

Neither drug tested in diabetics
No data on efficacy/safety in cirrhotics

Vitamin E
• Increased risk of haemorrhagic stroke
• Increased risk of urinary tract cancer
• Increased overall mortality

Pioglitazone
• Increased weight
• Long term safety questions
**FXR Agonist in NASH – Flint trial**

<table>
<thead>
<tr>
<th></th>
<th>Obeticholic acid</th>
<th>Placebo</th>
<th>Relative risks or mean changes from baseline* (95% CI) (obeticholic acid vs placebo)</th>
<th>p value*</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Primary outcome†</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number of patients at risk‡</td>
<td>110</td>
<td>109</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patients with improvement</td>
<td>50 (45%)</td>
<td>23 (21%)</td>
<td>2.2 (1.4 to 3.3)</td>
<td>0.0002</td>
</tr>
<tr>
<td><strong>Changes from baseline in histological features</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number of patients with biopsy specimens at baseline and 72 weeks</td>
<td>102</td>
<td>98</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Resolution§ of definite non-alcoholic steatohepatitis</td>
<td>22 (22%)</td>
<td>13 (13%)</td>
<td>1.7 (0.9 to 3.2)</td>
<td>0.08</td>
</tr>
<tr>
<td>Fibrosis¶</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patients with improvement</td>
<td>36 (35%)</td>
<td>19 (19%)</td>
<td>2.0 (1.2 to 3.4)</td>
<td>0.004</td>
</tr>
<tr>
<td>Change in score</td>
<td>-0.2 (1.0)</td>
<td>0.1 (0.9)</td>
<td>-0.3 (-0.6 to -0.1)</td>
<td>0.01</td>
</tr>
<tr>
<td>Total NAFLD activity score</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Change in score</td>
<td>-1.7 (1.8)</td>
<td>-0.7 (1.8)</td>
<td>-0.9 (-1.3 to -0.5)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Hepatocellular ballooning</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patients with improvement</td>
<td>47 (45%)</td>
<td>30 (31%)</td>
<td>1.5 (1.0 to 2.1)</td>
<td>0.03</td>
</tr>
<tr>
<td>Change in score</td>
<td>-0.5 (0.9)</td>
<td>-0.2 (0.9)</td>
<td>-0.2 (-0.5 to 0.0)</td>
<td>0.03</td>
</tr>
<tr>
<td>Steatosis</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patients with improvement</td>
<td>62 (61%)</td>
<td>37 (38%)</td>
<td>1.6 (1.2 to 2.2)</td>
<td>0.001</td>
</tr>
<tr>
<td>Change in score</td>
<td>-0.8 (1.0)</td>
<td>-0.4 (0.8)</td>
<td>-0.4 (-0.6 to -0.2)</td>
<td>0.0004</td>
</tr>
<tr>
<td>Lobular inflammation</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patients with improvement</td>
<td>54 (53%)</td>
<td>34 (35%)</td>
<td>1.6 (1.1 to 2.2)</td>
<td>0.006</td>
</tr>
<tr>
<td>Change in score</td>
<td>-0.5 (0.8)</td>
<td>-0.2 (0.9)</td>
<td>-0.3 (-0.5 to -0.1)</td>
<td>0.0006</td>
</tr>
</tbody>
</table>

*Neuschwander-Tetri*  
*Lancet 2015*
FXR Agonist in NASH – Flint trial

Key side effects
- Pruritus
- Increased LDL cholesterol
PPAR$\alpha/\delta$ Agonist

Elafibrinor
Elafibranor in NASH

<table>
<thead>
<tr>
<th>NAS</th>
<th>n</th>
<th>Placebo, n (%)</th>
<th>Elafibranor 80 mg, n (%)</th>
<th>Elafibranor 120 mg, n (%)</th>
<th>OR (95% CI)</th>
<th>P value</th>
<th>P value</th>
</tr>
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<tbody>
<tr>
<td>Protocol-defined primary</td>
<td></td>
<td></td>
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<tr>
<td>outcome</td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>274</td>
<td>92 (17)</td>
<td>93 (23)</td>
<td>89 (21)</td>
<td>1.53 (0.70–3.34)</td>
<td>.280</td>
<td></td>
</tr>
<tr>
<td>NAS ≥ 4 (moderate and</td>
<td>234</td>
<td>76 (11)</td>
<td>83 (20)</td>
<td>75 (20)</td>
<td>3.16 (1.22–8.13)</td>
<td>.018</td>
<td></td>
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<tr>
<td>severe)</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>NAS 3 (mild)</td>
<td>40</td>
<td>16 (50)</td>
<td>10 (40)</td>
<td>14 (29)</td>
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<td>Modified definition of</td>
<td></td>
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<td>Total</td>
<td>274</td>
<td>92 (12)</td>
<td>93 (13)</td>
<td>89 (19)</td>
<td>2.31 (1.02–5.24)</td>
<td>.045</td>
<td></td>
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<tr>
<td>NAS ≥ 4 (moderate and</td>
<td>234</td>
<td>76 (9)</td>
<td>83 (13)</td>
<td>75 (19)</td>
<td>3.52 (1.32–9.40)</td>
<td>.013</td>
<td></td>
</tr>
<tr>
<td>severe)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>NAS 3 (mild)</td>
<td>40</td>
<td>16 (25)</td>
<td>10 (10)</td>
<td>14 (21)</td>
<td></td>
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</tr>
</tbody>
</table>

*Elafibranor 120 mg vs placebo, direct treatment effect.
Actions of glucagon-like peptide 1

<table>
<thead>
<tr>
<th></th>
<th>Liraglutide</th>
<th>Placebo</th>
<th>Relative risks or mean changes (95% CI) from baseline to 48 weeks (liraglutide vs placebo)</th>
<th>p value*</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Primary outcome</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number of patients with paired liver biopsies</td>
<td>23</td>
<td>22</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>Patients with resolution of non-alcoholic steatohepatitis</td>
<td>9 (39%)</td>
<td>2 (9%)</td>
<td>4.3 (1.0 to 17.7)</td>
<td>0.019</td>
</tr>
<tr>
<td><strong>Changes from baseline in histopathological parameters</strong></td>
<td></td>
<td></td>
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<tr>
<td>Total NAFLD activity score</td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Change in score</td>
<td>-1.3 (1.6)</td>
<td>-0.8 (1.2)</td>
<td>-0.5 (-1.3 to 0.3)</td>
<td>0.24</td>
</tr>
<tr>
<td>Patients with improvement</td>
<td>17 (74%)</td>
<td>14 (64%)</td>
<td>1.2 (0.8 to 1.7)</td>
<td>0.46</td>
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<tr>
<td>Hepatocyte ballooning score</td>
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<tr>
<td>Mean change</td>
<td>-0.5 (0.7)</td>
<td>-0.2 (0.6)</td>
<td>-0.3 (-0.7 to 0.1)</td>
<td>0.15</td>
</tr>
<tr>
<td>Patients with improvement</td>
<td>14 (61%)</td>
<td>7 (32%)</td>
<td>1.9 (1.0 to 3.8)</td>
<td>0.05</td>
</tr>
<tr>
<td>Steatosis</td>
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<tr>
<td>Change in score</td>
<td>-0.7 (0.8)</td>
<td>-0.4 (0.8)</td>
<td>-0.2 (-0.6 to 0.2)</td>
<td>0.32</td>
</tr>
<tr>
<td>Patients with improvement</td>
<td>19 (83%)</td>
<td>10 (45%)</td>
<td>1.8 (1.1 to 3.0)</td>
<td>0.009</td>
</tr>
<tr>
<td>Lobular inflammation</td>
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<tr>
<td>Change in score</td>
<td>-0.2 (0.6)</td>
<td>-0.2 (0.5)</td>
<td>-0.01 (-0.3 to 0.3)</td>
<td>0.97</td>
</tr>
<tr>
<td>Patients with improvement</td>
<td>11 (48%)</td>
<td>12 (55%)</td>
<td>0.9 (0.5 to 1.6)</td>
<td>0.65</td>
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<tr>
<td>Kleiner fibrosis stage</td>
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<tr>
<td>Change in score</td>
<td>-0.2 (0.8)</td>
<td>0.2 (1.0)</td>
<td>-0.4 (-0.8 to 0.1)</td>
<td>0.11</td>
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<tr>
<td>Patients with improvement</td>
<td>6 (26%)</td>
<td>3 (14%)</td>
<td>1.9 (0.5 to 6.7)</td>
<td>0.46†</td>
</tr>
<tr>
<td>Patients with worsening</td>
<td>2 (9%)</td>
<td>8 (36%)</td>
<td>0.2 (0.1 to 1.0)</td>
<td></td>
</tr>
</tbody>
</table>

* p values calculated using the Wilcoxon rank-sum test.
Summary

• NAFLD in HIV is similar to NAFLD
• NAFLD is not a benign disease
  – Increased liver mortality
  – Increased cardiovascular disease

• Full assessment requires
  – Evaluation of fibrosis
  – Identification of all clinical manifestations of metabolic syndrome

• Management should focus on
  – Weight loss
  – Cardiovascular / Cerebrovascular risk factors
  – Drug therapy