Professor Mark Nelson
Chelsea and Westminster Hospital, London, UK
### Treatment should be prioritized

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Indicated</th>
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<tbody>
<tr>
<td></td>
<td>All naive and experienced pts with liver disease</td>
</tr>
<tr>
<td>Prioritized</td>
<td>• Pts with fibrosis (F3) or cirrhosis (F4) including compensated cirrhosis</td>
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<tr>
<td></td>
<td>• HIV coinfection, HBV coinfection</td>
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<tr>
<td></td>
<td>• Indication for liver transplantation</td>
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<tr>
<td></td>
<td>• HCV recurrence after transplantation</td>
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<tr>
<td></td>
<td>• Extra-hepatic manifestations</td>
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<tr>
<td></td>
<td>• Debilitating fatigue</td>
</tr>
<tr>
<td></td>
<td>• Risk of transmitting HCV</td>
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<tr>
<td>Justified</td>
<td>Pts with moderate fibrosis (F2)</td>
</tr>
<tr>
<td>Deferred</td>
<td>Pts with no or mild (F0-F1) disease and no extra-hepatic manifestations</td>
</tr>
<tr>
<td>Not recommended</td>
<td>Pts with limited life expectancy due to non-liver comorbidities</td>
</tr>
</tbody>
</table>

Summary of EASL and AASLD 2014/2015

100%
INTEGRATED SUMMARY OF RESULTS: SVR12 TREATMENT NAIVE PATIENTS

**EBR/GZR**
- HCV/HIV coinfected: 94.0% (233/248)
- HCV monoinfected: 94.8% (478/504)
- All: 94.5% (711/752)

**EBR/GZR + RBV**
- HCV/HIV coinfected: 96.6% (28/29)
- HCV monoinfected: 90.5% (95/105)
- All: 91.8% (123/134)

**Total**
- HCV/HIV coinfected: 94.2% (261/277)
- HCV monoinfected: 94.1% (573/609)
- All: 94.1% (834/886)

*Primary endpoint: SVR12 (HCV RNA <15 IU/mL)*
INTEGRATED SUMMARY OF RESULTS:
SVR12 TREATMENT EXPERIENCED PATIENTS

- HCV/HIV coinfectd
- HCV monoinfected
- All

<table>
<thead>
<tr>
<th>Treatment</th>
<th>HCV/HIV coinfected</th>
<th>HCV monoinfected</th>
<th>All</th>
</tr>
</thead>
<tbody>
<tr>
<td>GZR/EBR 12 weeks</td>
<td>100.0%</td>
<td>91.8%</td>
<td>91.8%</td>
</tr>
<tr>
<td>GZR/EBR+RBV 12 weeks</td>
<td>94.8% / 94.9%</td>
<td>93.9% / 93.4%</td>
<td>93.9% / 93.4%</td>
</tr>
<tr>
<td>GZR/EBR 16-18 weeks*</td>
<td>83.3%</td>
<td>97.8%</td>
<td>97.8%</td>
</tr>
<tr>
<td>GZR/EBR+RBV 16-18 weeks*</td>
<td>100.0%</td>
<td>100.0%</td>
<td>100.0%</td>
</tr>
<tr>
<td>Total</td>
<td>95.2%</td>
<td>94.4%</td>
<td>94.5%</td>
</tr>
</tbody>
</table>

*HCV/HIV coinfected patients treated for 16 weeks and HCV monoinfected patients treated for 18 weeks
Do HIV+ respond differently to mono-infected patients?

Karageorgopoulos, World J Hepatol, 2015; 7: 1936
### Baseline characteristics – GECCO Cohort: ledipasvir/sofosbuvir 8 weeks

<table>
<thead>
<tr>
<th></th>
<th>Overall (n=148)</th>
<th>HCV (n=120)</th>
<th>HIV-HCV (n=28)</th>
<th>p</th>
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</thead>
<tbody>
<tr>
<td>Male sex, n (%)</td>
<td>72 (49)</td>
<td>49 (41)</td>
<td>23 (82)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Median age [years] (IQR)</td>
<td>52 (44–58)</td>
<td>54 (45–62)</td>
<td>50 (42–62)</td>
<td>0.01</td>
</tr>
<tr>
<td>Transmission IVDU/MSM/blood, n (%)</td>
<td>46(31)/15(10)/36(24)</td>
<td>39(33)/1(1)/39(33)</td>
<td>7(25)/14(50)/0</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>HCV genotype 1/4, n (%)</td>
<td>144(97)/3(2)</td>
<td>120 (100)</td>
<td>24(86)/3(11)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Median HCV viral load [IU/mL] (IQR)</td>
<td>8.1x10^5 (2.5x10^5–1.7x10^6)</td>
<td>9x10^5 (3.4x10^5–1.7x10^6)</td>
<td>4.9x10^5 (8x10^4–9.8x10^5)</td>
<td>0.01</td>
</tr>
<tr>
<td>Median ALT [U/L] (IQR)</td>
<td>56 (37–89)</td>
<td>53 (36–80)</td>
<td>78 (49–166)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Prior HCV treatment, n (%)</td>
<td>26 (18)</td>
<td>22 (18)</td>
<td>4 (14)</td>
<td>ns</td>
</tr>
<tr>
<td>Fibroscan &gt;12.5kPa or APRI &gt;2, n (%)</td>
<td>5 (3)</td>
<td>3 (3)</td>
<td>2 (7)</td>
<td></td>
</tr>
<tr>
<td>HIV coinfection, n (%)</td>
<td>28 (19)</td>
<td>0 (0)</td>
<td>28 (100)</td>
<td></td>
</tr>
<tr>
<td>Median CD4 cell count [*/mm^3] (IQR)</td>
<td>531 (346–683)</td>
<td>NA</td>
<td>531 (346–683)</td>
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</table>

8 weeks of LDV/SOF is not within label for cirrhosis, GT4 or prior treatment

Ingiliz P et al. EACS 2015. Abstract PS7/5
Efficacy: SVR4 rates
Sofosbuvir/ledipasvir for 8 weeks in real-life, SVR 4: 99%

8 weeks of LDV/SOF is not within label for cirrhosis, GT4 or prior treatment

Ingiliz P et al. EACS 2015. Abstract PS7/5
Efficacy: SVR12 rates
Sofosbuvir/ledipasvir for 8 weeks in real-life, SVR 12: 98.5%

Metavir F4 defined as APRI > 2 OR Fibroscan > 12.5kPa, high VL load defined as > 2mio IU/ml (Abbott PCR) or 6 mio IU/ml (Roche PCR), pretreatment was interferon-based (in one case with sofosbuvir)

8 weeks of LDV/SOF is not within label for cirrhosis, GT4 or prior treatment

Ingiliz P et al. EACS 2015. Abstract PS7/5
Figure 2. Treatment Cascade for People with Chronic Hepatitis C Virus (HCV) Infection, Prevalence Estimates with 95% Confidence Intervals.

http://journals.plos.org/plosone/article?id=info:doi/10.1371/journal.pone.0101554
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There are multiple layered barriers

**Health care system issues**
- Accessibility of HCV antivirals & care locations
- Overburdened health systems
- Cost / insurance
- Segregated service delivery
- Criminalization of drug use
- Accessibility to drug use services

**Workforce issues**
- Inconsistent screening/treatment guidelines
- Insufficient number of providers who can treat HCV
- Insufficient resources for case managers, navigators, social workers

**Primary care provider barriers**
- Knowledge (misconceptions about who to screen, progression risk and treatment)
- Perceptions (may only refer good candidates who they perceive to need treatment)

**Specialist barriers**
- Knowledge (some providers may have limited HCV treatment experience)
- Perceptions (concerns about non-adherence, drug use, relapse, risk of re-infection)

**General barriers**
- General health care access (primary care provider, insurance, health literacy, patient provider-relationship, stigma)
- Competing health priorities (mental health, comorbidities)
- Stability factors (substance use, employment, income, housing, drug treatment, social support)

**HCV-specific barriers**
- Poor knowledge
- Lack of symptoms
- Fears about treatment
HIV/HCV co-infected patients are unique in some ways...

Multimorbid clinical conditions among HIV/HCV co-infected IDUs in Baltimore (n=362)

- Multimorbid conditions included diabetes (HbA1c and medication use), obstructive lung disease (Ratio of FEV to forced vital capacity), anemia (hemoglobin), obesity (BMI), kidney dysfunction (urine protein-creatinine, GFR), Hypertension (blood pressure and medication use), liver cirrhosis (Fibroscan)

Stability factors among HIV/HCV co-infected IDUs in Baltimore (n=560)

- Daily injection drug use, non-injection drug use, alcohol abuse, ≥1 mental health condition, suicidal ideation, incarceration, income < 5000 per year, lack of health insurance, no primary care

Survival estimates

Time at risk (years)

Proportion free from reinfection

- 95% CI
- Previous spontaneous clearance
- 95% CI
- Previous SVR
HCV re-infection incidence among HIV MSM changes over time
Response-guided Therapy - Study Design

<table>
<thead>
<tr>
<th>Day</th>
<th>0</th>
<th>2</th>
<th>21</th>
<th>35</th>
<th>105</th>
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- **Plasma HCV RNA < 500 IU/ml by Day 2**

**Group 1:**
- SOF + LDV + ASV N=12

**Group 2:**
- SOF + DCV + SMV N=6

**Group 3:**
- SOF + DCV + ASV N=8

Patients randomly assigned:
- GT-1b Non-cirrhotic Chinese N=26

Follow up

**Medications:**
- Sofosbuvir (SOF, nucleotide NS5B inhibitor) 400 mg / ledipasvir (LDV, NS5A inhibitor) 90 mg once daily
- Daclatasvir (DCV, NS5A inhibitor) 60 mg once daily
- Simeprevir (SMV, a protease/ NS3/4 inhibitor) 150 mg once daily
- Asunaprevir (ASV, a protease/ NS3/4 inhibitor) 100 mg twice daily