Opportunities for improvement
HCV and Organ Transplantation

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Institute of Liver Studies
King’s College Hospital

ICVH 2016
When all think alike, no one thinks very much…

W Lippman

Pharma support:
AbbVie/Achillion/
Astellas/ BI/ BMS/
Gilead/ GSK/
Intercept/Janssen/
Merck/ Novartis/ Roche

Spectrum in audience

I will take the ‘Why not’ viewpoint but I have flip flopped
HCV-associated complications will increase markedly over the next 5–10 years.
Opportunities to treat HCV in patients undergoing liver transplantation

- Listed
- Transplant
- Chronic hepatitis
- Graft loss

- Prevent graft infection
- Prevent infection or ↓ risk of disease progression
- Prevent cirrhosis and graft failure

- Pre-transplant anti-viral therapy
- Prophylactic or pre-emptive therapies
- Antiviral therapy for recurrent disease
- Re-transplant
Traditional view of HCV post-LT treatment from a provider & patient perspective
Natural history of HCV post LT

D Joshi et al, Nat Rev Gas Hep, 2015
Donor pool is finite and under pressure
extended donors/ 24% waitlist mortality
different allocation systems – national waiting list
Timing of transplant is relatively inflexible

Hepatocellular carcinoma is increasingly the indication liver transplant listing among HCV infected patients in the United States

Incidences rate ratio* for HCC 1.118 95% CI 1.107 – 1.130; P < .001

Adjusted IR per 100,000

Fleming JA et al. The Liver Meeting 2013; Abstract 12

*Adjusted for age and sex
HCV-related healthcare costs relate to disease severity: EU and Asia Pacific

Median annual HCV-related sequelae costs (Converted to US dollars and adjusted to 2010 costs)

- **Liver Transplant**
  - Asia Pacific: $148,350
  - Europe: $132,040
- **Hepatocellular Carcinoma**
  - Asia Pacific: $21,180
  - Europe: $15,650
- ** Decompensated Cirrhosis**
  - Asia Pacific: $18,130
  - Europe: $14,660
- **Compensated Cirrhosis**
  - Asia Pacific: $800
  - Europe: $920

2010 US Dollars

Increase in number of deceased donors

**Donors after brain death (DBD)**
- 716
- 697
- 664
- 637
- 634
- 609
- 611
- 624
- 637
- 652

**Donors after circulatory death (DCD)**
- 61
- 73
- 87
- 127
- 159
- 200
- 288
- 335
- 373
- 436

**Increase in number of deceased donors**
- **DCD** – 2.5 organs per donor
- **DBD** – 3.9 organs per donor
HCV treatment landscape – 2015

Approved or imminent approvals: Protease¥, NS5B# and NS5A* inhibitors

95% cure rate in all populations safe

GT: genotype; IFN: interferon; RBV: ribavirin
HCV-TARGET: HCV RNA outcomes for SMV + SOF ± RBV in HCV genotype 1 post-transplant

Latest available HCV RNA BLOQ 91% (92/101)

Latest available HCV RNA quantified 9% (9/101)

SMV + SOF ± RBV N = 131

SVR4+ evaluable 68/101

SVR4+ (%)

- Non-cirrhotics: 94/31 (29/31)
- Cirrhotics: 86/37 (32/37)
- GT1a: 83/36 (30/36)
- GT1b: 95/19 (18/19)

Viral breakthrough 1% (1/68)

Relapse 6% (4/68)

Non-response 3% (2/68)

Lost to follow-up 0% (0/68)

SVR4+ 90% 61/68

Excludes prior PI-failures

SMV + SOF ± RBV: SVR4+ by baseline characteristics in post-transplant patients with HCV genotype 1

HCV-TARGET: AEs by Regimen

<table>
<thead>
<tr>
<th>Pts, n (%)</th>
<th>SOF + RBV (n = 24)</th>
<th>SOF + SMV (n = 83)</th>
<th>SOF + SMV + RBV (n = 24)</th>
<th>Total (N = 164)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total pts with AE</td>
<td>28 (85)</td>
<td>64 (77)</td>
<td>22 (92)</td>
<td>135 (82)</td>
</tr>
<tr>
<td>AEs in ≥ 10% of pts</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>▪ Fatigue</td>
<td>12 (36)</td>
<td>21 (25)</td>
<td>5 (21)</td>
<td>50 (30)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>▪ Anemia</td>
<td>10 (30)</td>
<td>1 (1)</td>
<td>9 (38)</td>
<td>35 (21)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>▪ Headache</td>
<td>2 (6)</td>
<td>16 (19)</td>
<td>7 (29)</td>
<td>28 (17)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>▪ Flulike symptoms</td>
<td>4 (12)</td>
<td>8 (10)</td>
<td>5 (21)</td>
<td>21 (13)</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>▪ Infections (any)</td>
<td>0</td>
<td>16 (19)</td>
<td>1 (4)</td>
<td>18 (11)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>▪ Diarrhea</td>
<td>4 (12)</td>
<td>6 (7)</td>
<td>3 (13)</td>
<td>14 (9)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>▪ Nausea</td>
<td>4 (12)</td>
<td>5 (6)</td>
<td>1 (4)</td>
<td>14 (9)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>▪ Insomnia</td>
<td>0</td>
<td>4 (5)</td>
<td>4 (17)</td>
<td>9 (6)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>▪ Cough</td>
<td>1 (3)</td>
<td>1 (1)</td>
<td>3 (13)</td>
<td>5 (3)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>▪ Emesis</td>
<td>1 (3)</td>
<td>0</td>
<td>3 (13)</td>
<td>4 (2)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>▪ Dehydration</td>
<td>0</td>
<td>0</td>
<td>3 (13)</td>
<td>3 (2)</td>
</tr>
</tbody>
</table>

- No episodes of acute rejection with any regimen

Brown RS, et al. AASLD 2014
SOLAR-2: Study Design

- GT 1 or 4 treatment-naïve or -experienced patients
- Main inclusion criteria: $\text{CL}_{cr} \geq 40 \text{ mL/min}$, platelets $>30,000 \times 10^3/\mu\text{L}$
- Main exclusion criteria: CPT 13-15
- RBV dosing
  - Metavir F0–F3 and CPT A cirrhosis: weight-based (1000 or 1200 mg/day)
  - CPT B and C cirrhosis: 600 mg/day

Manns et al, EASL; Forns et al. Lancet ID 2016
SVR12
GT 1 Pre- and Post-Transplant CPT B and C

LDV/SOF + RBV

12 Weeks 24 Weeks

GT 1 Pre-Transplant

- CPT B: 87% (20/23) with 3 relapses and 2 deaths.
- CPT C: 85% (17/20) with 1 relapse and 3 deaths.

GT 1 Post-Transplant

- CPT B: 95% (19/20) with 1 death.
- CPT C: 50% (1/2) with 1 death.

Error bars represent 2-sided exact 90% confidence intervals.

3 subjects (1 CPT B/24 Wk, 1 CPT C/12 Wk and 1 CPT C/24 Wk) excluded (transplant on study);
5 Pre- CPT C/24 Wk, 4 Post- CPT B/24 Wk and 1 post CPT C/24 Wk subjects have not reached SVR12.
SOF/VEL FDC for treatment of HCV in patients with decompensated liver disease: The Phase 3 ASTRAL-4 study

Charlton MR, et al. AASLD 2015, San Francisco. #LB-13

267 treatment naive or experienced G1–6 with Child B cirrhosis
– 65% treatment experienced
– MELD <15 = 95%
– Ascites 65–75%; encephalopathy 58–66%

<table>
<thead>
<tr>
<th>Week</th>
<th>SOF/VEL</th>
<th>SOF/VEL + RBV</th>
<th>SOF/VEL</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>n=90</td>
<td>n=87</td>
<td>n=90</td>
</tr>
<tr>
<td>12</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>24</td>
<td></td>
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<td></td>
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<tr>
<td>36</td>
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</tbody>
</table>

SVR12 (%)

<table>
<thead>
<tr>
<th>Overall</th>
<th>G1</th>
<th>G2, 4, and 6</th>
</tr>
</thead>
<tbody>
<tr>
<td>83/90</td>
<td>75/82</td>
<td>2/4</td>
</tr>
<tr>
<td>94/87</td>
<td>82/77</td>
<td>G3</td>
</tr>
<tr>
<td>96/90</td>
<td>65/68</td>
<td>4</td>
</tr>
<tr>
<td>92</td>
<td>65/68</td>
<td>G2</td>
</tr>
</tbody>
</table>

Safety
- d/c due to AE 3%; death 3% (9)
- AE more frequent with RBV
- Fatigue (29%); nausea (23%); HA (22%);
anemia (13%; 31% in RBV arm)
- RBV dose: Hb <10 = 23%; Hb <8.5 = 7%
- RBV decreased in 37% and d/c in 17%
- Bili <3 x ULN

Charlton MR, et al. AASLD 2015, San Francisco. #LB-13
Sofosbuvir/Velpatasvir Fixed Dose Combination For The Treatment Of HCV In Patients With Decompensated liver Disease: The Phase 3 ASTRAL-4 Study

MELD change: Baseline to follow-up Week 12

Patients with SVR12

Baseline MELD <15 (n=208*)

- **52% improved**
- **27% worsened**

Baseline MELD >15 (n=26)

- **84% improved**
- **8% worsened**

CPT shift

Patients with SVR12†

<table>
<thead>
<tr>
<th>CPT</th>
<th>Follow-up Wk 12, % (n/n)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>CPT A</td>
</tr>
<tr>
<td>Baseline</td>
<td></td>
</tr>
<tr>
<td>CPT A</td>
<td>71 (10/14)</td>
</tr>
<tr>
<td>CPT B</td>
<td>17 (34/205)</td>
</tr>
<tr>
<td>CPT C</td>
<td>10 (1/10)</td>
</tr>
</tbody>
</table>

†n=234; 5 pts had no follow-up Week 12 assessment

- **SOF/VEL ± RBV** for 12/24 weeks: High SVR12 in HCV pts with G1–6 and advanced liver disease
  - Extending duration to 24 weeks did not increase response rates
  - Addition of RBV has largest benefit in G3
- Virologic response was associated with improvements in CTP and MELD scores in Child’s cirrhosis
- **SOF/VEL ± RBV** for 12–24 weeks was safe and well tolerated in Child’s B patients

*No follow-up Week 12 assessment for 5 patients.

Charlton MR, et al. AASLD 2015, NEJM
ALLY-1: SOF + DCV + RBV in Cirrhotic or Posttransplant HCV-Infected Pts

- Multicenter, open-label phase III trial
- Enrolled advanced cirrhosis (n = 60) or post–liver transplant (n = 53) pts
  - 95% and 96% of pts were white, 40% and 42% were treatment naive, 75% and 77% were infected with GT1 HCV
- Treatment
  - All pts: 12 wks of daclatasvir 60 mg QD + sofosbuvir 400 mg QD + RBV
    - Initial RBV dose 600 mg/day, adjusted to 1000 mg/day based on hemoglobin levels and creatinine clearance
  - Pts with advanced cirrhosis who interrupted treatment due to liver transplantation could receive 12 additional wks of therapy immediately after transplantation
  - Individuals relapsing following 12 wks of daclatasvir + sofosbuvir + RBV offered re-treatment with the same regimen for 24 wks

ALLY-1: Key Results

- In subgroup analysis of pts in the advanced cirrhosis group, those who were Child-Pugh class C (n = 16) or had albumin < 2.8 g/dL (n = 18) had SVR12 rates of 56%.
- 10/10 pts who relapsed in the advanced cirrhosis group had NS5A RAVs at virologic failure; 4 of 10 pts had NS5A RAVs at baseline.
- 3/3 pts who relapsed in the posttransplantation group had NS5A RAVs at virologic failure; none had NS5A RAVs at baseline.

ANRS CUPILT: SOF + DCV Treatment for HCV Recurrence After Liver Transplant

- Multicenter, open-label, nonrandomized study

- Most pts were GT1a (27% to 29%) or GT1b (47% to 49%)

ANRS CUPILT: Efficacy Results

**From baseline to follow-up wk 24, albumin improved from 37 g/L to 40 g/L**

CORAL-I: study design and baseline characteristics

- Phase II study in 34 post-transplant patients with recurrent genotype 1 HCV and F0–F2 fibrosis

<table>
<thead>
<tr>
<th></th>
<th>3D + RBV (N=34)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time since liver transplant, months, median</td>
<td>39.5</td>
</tr>
<tr>
<td>Male, %</td>
<td>79</td>
</tr>
<tr>
<td>Age, years, mean</td>
<td>59.6</td>
</tr>
<tr>
<td>HCV subtype, %</td>
<td>85/15</td>
</tr>
<tr>
<td>1a/1b</td>
<td></td>
</tr>
<tr>
<td>HCV RNA $\log_{10}$ IU/mL, mean</td>
<td>6.6</td>
</tr>
<tr>
<td>Fibrosis stage, %</td>
<td>18/38/44</td>
</tr>
<tr>
<td>F0/F1/F2</td>
<td></td>
</tr>
</tbody>
</table>

CNI: calcineurin inhibitor; TAC: tacrolimus; CsA: cyclosporin A
3D: paritaprevir + ombitasvir + dasabuvir

Kwo P, NEJM 2015
CORAL-I: rates of response in post-transplant recurrent HCV 1 infection (F0–F2)

- One patient experienced relapse at 3 days after completing treatment
- At the time of relapse the patient had NS3, NS5A and NS5B RAVs that had not been present at baseline

P Kwo NEJM 2015
DAA Therapy in HCV-Infected Patients on the Transplant Waiting List: Is Delisting Possible?

French multicenter cohort study

183 patients

Cirrhosis
N=77

- LT
N=24 (31%)

- Delisting
N=14 (18%)

- Improvement
N=12 (16%)

- Other* N=2 (3%)

HCC
N=106

- LT
N= 57 (54%)

- Drop out
N=6 (6%)

MELD: 10
CPS: 45% A, 28% B
22% C

Mean follow-up: 68 wks (12-95)

- 84% achieved SVR
- Complete clinical and biochemical response achieved in 36%

AUC for Child-Pugh score: 0.814
- Best for predicting clinical and biochemical response

Coilly A, AASLD 2015, Abstract 95
‘Kings/ Belfast’ case- GM:

Pre –LT candidate
48 yr old male
GT3 - cirrhotic
Increased BMI
Blood group A
Failed 12 weeks sof /riba
MELD 25/ UKELD 64
Ascites/ renal impairment eGFR 32ml/min

Treat now or after LT?
‘priority’? What type of organ?
With what?
LT & HCV - timing of treatment is flexible

- What is the cost of failure?
- Role of ribavirin?
- Duration –12 vs 24 weeks?
- Early treatment post transplant 6-12 months
- Timing in relation to LT
- ‘MELD purgatory’ [Terrault] vs death
- Are we overstating ‘salvage’?
- Recipient- donor match
- Renal impairment
‘The illusion of knowledge is more dangerous than a lack of knowledge…’

D Bronstein
Hepatitis C virus infection and Chronic kidney disease

- Cryoglobulinemia and membranoproliferative GN → CKD\(^1\).
- Chronic HCV infection → risk factor for the development of CKD\(^2\).
- HCV infection → ↑ morbimortality in CKD and kidney transplants\(^3\).
- 10%–25% of candidates considered for kidney transplantation concurrently suffer from advanced liver fibrosis or cirrhosis\(^3\).

2. Tsui JL. Arch Int Med 2007; 167: 1271–1276 ;
Hepatitis C virus infection increases the risk of developing end-stage renal disease

The prevalence of HCV infection was 7.6% and it increased with the CKD stages (trend test, P<0.001), while the prevalence of HBV infection was 7.4% and no specific trend among CKD stages (trend test, P = 0.1).

Patients with HCV infection had higher cumulative rate of end-stage renal disease than cases without HCV infection (modified log-rank, P<0.001).
HCV is a risk factors for development of new-onset diabetes mellitus (NODM) after kidney transplantation

- From January 2004 to December 2005, 15,309 adult kidney transplants were identified in the OPTN/UNOS* database in the US. Among these, 1,581 patients developed NODM during the follow-up period.

<table>
<thead>
<tr>
<th>TABLE 2. Estimation of unadjusted and adjusted relative risks of developing NODM using univariate and multivariate Cox regression analyses</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Recipieent factors</strong></td>
</tr>
<tr>
<td>Female vs. male</td>
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<tr>
<td>Age (year)/10</td>
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<tr>
<td>Hypertension, yes vs. no</td>
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<tr>
<td>Black vs. others</td>
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<tr>
<td>BMI 25–30 vs. &lt;25</td>
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<tr>
<td>BMI &gt;30 vs. &lt;25</td>
</tr>
<tr>
<td>HCV antibody, positive vs. negative</td>
</tr>
<tr>
<td>Unadjusted RR (95% CI) P value</td>
</tr>
<tr>
<td>0.87 (0.79–0.97)</td>
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<tr>
<td>1.29 (1.24–1.34)</td>
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<tr>
<td>1.40 (1.23–1.59)</td>
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<tr>
<td>1.38 (1.23–1.54)</td>
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<tr>
<td>1.51 (1.35–1.71)</td>
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<tr>
<td>1.93 (1.71–2.19)</td>
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<tr>
<td>1.60 (1.31–1.96)</td>
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<table>
<thead>
<tr>
<th><strong>Donor factors</strong></th>
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<tbody>
<tr>
<td>ECD vs. SCD</td>
</tr>
<tr>
<td>Living vs. deceased</td>
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<tr>
<td>No. of HLA-A, B mismatch</td>
</tr>
<tr>
<td>Tacrolimus at discharge vs. others</td>
</tr>
<tr>
<td>Alemtuzumab vs. others</td>
</tr>
<tr>
<td>Adjusted RR (95% CI) P value</td>
</tr>
<tr>
<td>1.37 (1.18–1.59)</td>
</tr>
<tr>
<td>0.82 (0.74–0.90)</td>
</tr>
<tr>
<td>1.05 (1.01–1.09)</td>
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<tr>
<td>1.45 (1.29–1.63)</td>
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<tr>
<td>0.52 (0.40–0.67)</td>
</tr>
</tbody>
</table>

NODM, new-onset diabetes mellitus; RR, relative risk; CI, confidence interval; BMI, body mass index; HCV, hepatitis C virus; ECD, extended criteria donor; SCD, standard criteria donor; HLA, human leukocyte antigen.

*Organ Procurement Transplant Network/United Network of Organ Sharing database
HCV negatively affects graft and patient survival in kidney transplant recipients

- Renal Transplantation Cohort (n=7572):
  - Patient survival among HCVAb positive and HCVAb negative groups was
    - 77% vs. 90% at 5 years, respectively
    - 50% vs. 79% at 5 and 10 years, respectively
  - The aHR for patient death was 2.38 (95%CI, 1.69 –3.37).
  - Higher rates of death due to cardiovascular disease (aHR=2.74), malignancy (aHR=2.52), and hepatic failure (aHR=22.1) were observed.
  - The aHR for graft loss was 1.71 (95%CI, 1.28 –2.29) for HCVAb positive patients; and glomerulonephritis, chronic allograft neuropathy, and death were more frequent causes of graft failure.
Hepatitis C virus infection is associated with inferior kidney transplant outcomes

- A retrospective US study on 5703 patients undergoing renal transplant between 1996 and 2012 demonstrated that presence of HIV infection does not affect kidney or recipient survival, while presence of HCV infection negatively impacts both.

Sawinski K. The world transplant Congress 2014, t#2100
HCV is a risk factor for post-transplant de novo glomerulonephritis

- In a study by Özdemir, the influence of HCV infection on the occurrence of post-transplant de novo glomerulonephritis was assessed.
- Of 165 patients selected for the study, 44 were HCV positive and 121 HCV negative.
- Fifteen (34%) of 44 patients with HCV positive serology showed de novo GN at a mean time of 47 ± 22 months.
- Eight (6.6%) of 121 patients with HCV negative serology showed de novo GN at a mean time of 60 ± 39 months.
- The development of de novo glomerular disease had a significant negative influence on graft loss.

Özdemir BH. Transplantation Proceedings 2006; 38: 492–495
Antiviral treatment for HCV is associated with improved renal and circulatory outcomes

- The chance of survival was significantly higher in the treated than in the untreated cohort, with 93.28% and 84.43% at 8 years (p<0.001), respectively.

Hsu Y-C. Gut 2014;0:1–9
HCV infection is associated with increased aortic stiffness and cardiovascular event in dialysis patients

- Moreover, the Kaplan-Meier analysis indicated a significant difference in event-free rates between HCV-positive and HCV-negative patients.
‘Kings’ case- GH: ‘Focus and drive??’

Qualified lawyer senior SW
61 – Polycystic renal disease
CKD 6 now established dialysis 4 yrs – PD?
Usual spectrum of co-morbidities - asthma

G1b – non- cirrhotic
60 weeks peg interferon/rbv – responder/relapser
Pl + peg/rbv 10 weeks – sepsis/anaemia
Has a living donor!!! Who is getting older
Cross-match profile
Timing ?
Increase of ab mediated/ DM/ CVS with or without Renal Tx
**SOF Renal Insufficiency Study**

**SOF + RBV in patients with Severe Renal Impairment:** SOF not licensed <30ml eGFR

- Similar rapid virologic decline observed to those with normal renal function

- SVR4 and SVR12: 40%

**SOF and GS-331007 Pharmacokinetics**

- Comparable SOF and ~4-fold higher GS-331007 exposures compared with historical HCV-infected population

**Adverse Events**

<table>
<thead>
<tr>
<th>SOF 200 mg + RBV N=10</th>
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<tbody>
<tr>
<td><strong>Adverse Events</strong></td>
</tr>
<tr>
<td>Anemia</td>
</tr>
<tr>
<td>Headache</td>
</tr>
<tr>
<td>Pruritus</td>
</tr>
<tr>
<td>Rash</td>
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<tr>
<td>Muscle spasms</td>
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<tr>
<td>Hypoesthesia</td>
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<tr>
<td>Insomnia</td>
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<tr>
<td>Irritability</td>
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</tbody>
</table>

- Mean eGFR change from baseline to EOT (Week 24): -3.12 mL/min
- No treatment-emergent clinically significant ECG results

**SOF 200 mg + RBV was safe and relatively well tolerated in patients with severe renal impairment with exacerbation of anemia via RBV-induced hemolysis as primary AE**

Gane, AASLD, 2014, Poster #966
Abbvie: ongoing study in CKD

- **RUBY-I:**
  - Phase 3 study in 40 patients
  - Ombitasvir/ABT-450/ritonavir and dasabuvir +/- ribavirin in treatment-Naïve HCV genotype 1-infected adults with chronic kidney disease
  - Patients with eGFR <30, including those on hemodialysis
  - Final data collection date for primary outcome measure May 2015

ClinicalTrials.gov Identifier: NCT02207088
Efficacy

- All patients completing treatment to date had virologic response.
- Virologic response has been sustained in all patients who have reached post-treatment weeks 4 and 12 in this ongoing study.

<table>
<thead>
<tr>
<th>Timepoint</th>
<th>N</th>
<th>Virologic Response (n)</th>
<th>Percent</th>
</tr>
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<tbody>
<tr>
<td>End of Treatment</td>
<td>14</td>
<td>14</td>
<td>100</td>
</tr>
<tr>
<td>Post-treatment Week 4</td>
<td>10</td>
<td>10</td>
<td>100</td>
</tr>
<tr>
<td>Post-treatment Week 12</td>
<td>2</td>
<td>2</td>
<td>100</td>
</tr>
</tbody>
</table>

Adapted from the Paul Pockros presentation at ILC/EASL on April 25, 2015.
Safety and Efficacy of Grazoprevir (MK-5172) + Elbasvir (MK-8742) in Participants With Chronic Hepatitis C and Chronic Kidney Disease (MK-5172-052) (C-SURFER)

N = 110

• Intervention
  • Grazoprevir 100 mg + Elbasvir 50 mg (no ribavirin)
  • Immediate versus deferred treatment to facilitate assessment of safety (treatment blinded through week 16)

ClinicalTrials.gov Identifier: NCT02092350
SVR12: IMMEDIATE TREATMENT GROUP (ITG)

**GZR/EBR 12 weeks**

![Bar graph showing SVR12 results for GZR/EBR 12 weeks](image)

- **99%** for Modified Full Analysis Set
- **94%** for Full Analysis Set

**Patients, (%):**
- 115/116
- 115/122

**Relapse**
- **1***
- **1**

**Discontinued unrelated to Tx**
- **0**
- **6†**

MFAS = primary efficacy analysis; FAS was a secondary analysis

*Noncirrhotic, interferon-intolerant patient with HCV GT1b infection relapsed at FW12.
†Lost to follow-up (n=2), n=1 each for death, non-compliance, withdrawal by subject, and withdrawal by physician (due to violent behavior)
How do you balance risk and innovation?

Transplanting Hepatitis C–Positive Kidneys

Peter P. Reese, M.D., M.S.C.E., Peter L. Abt, M.D., Emily A. Blumberg, M.D., and David S. Goldberg, M.D., M.S.C.E.


New antiviral therapies for hepatitis C virus infection, with cure rates exceeding 95%, should prompt transplant-community leaders to view HCV-positive organs as a valuable opportunity for transplant candidates with or without preexisting HCV infection.
How do you balance risk and innovation?
Once you have tasted flight,
you will forever walk the earth
with your eyes turned skyward,
for there you have been,
and there you will always
long to return.

LEONARDO DA VINCI
Save the date!

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