KDIGO GUIDELINE UPDATE ON HEPATITIS C IN CKD

NEW EVIDENCE

NEW RECOMMENDATIONS

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Cliniques universitaires Saint-Luc
Université catholique de Louvain
Brussels, Belgium

GLOBAL SCIENCE. LOCAL CHANGE.
Hepatitis C

Daniel P Webster, Paul Klenerman, Geoffrey M Dusheiko

Direct-Acting Antiviral Agents (DAAs)

SVR

Interferon → Interferon + ribavirin → Peginterferon + ribavirin → Peginterferon + ribavirin + PI → Interferon-free combination

Figure 1: Changes in standard of care for HCV, and improvements in numbers of sustained virological responses

Data from references 9–12. PI=protease inhibitor.

*Lancet 2015; 385: 1124–35*
## WORK GROUP MEMBERSHIP

### Work Group Co-Chairs

| Work Group Co-Chairs | | |
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| Michel Jadoul, MD    | Paul Martin, MD, FRCP, FRCPI |
| Cliniques Universitaires Saint Luc | Miller School of Medicine |
| Université Catholique de Louvain | University of Miami |
| Brussels, Belgium    | Miami, USA |

### Work Group

<table>
<thead>
<tr>
<th>Marina C. Berenguer, MD</th>
<th>Bertram Kasiske, MD</th>
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<tbody>
<tr>
<td>La Fe University Hospital</td>
<td>Hennepin County Medical Center</td>
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<td>Valencia, Spain</td>
<td>Minneapolis, MN, USA</td>
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<tr>
<th>Wahid Doss, MD</th>
<th>Ching-Lung Lai, MD</th>
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<td>National Hepatology and Tropical Medicine Research</td>
<td>University of Hong Kong</td>
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<td>Cairo, Egypt</td>
<td>Hong Kong, China</td>
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<th>Fabrizio Fabrizi, MD</th>
<th>José M. Morales, MD</th>
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<td>Maggiore Policlinico Hospital</td>
<td>Hospital Universitario 12 de Octubre</td>
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<td>Milan, Italy</td>
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<tr>
<th>Jacques Izoporte, PharmD, PhD</th>
<th>Priti R. Patel, MD, MPH</th>
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<tr>
<td>Centre de Physiopathologie de Toulouse Purpan</td>
<td>Centers for Disease Control and Prevention</td>
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<tr>
<td>Toulouse, France</td>
<td>Atlanta, USA</td>
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<th>Vivekanand Jha, MBBS, MD, DM, PhD, FRCP</th>
<th>Stanislas Pol, MD, PhD</th>
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<td>George Institute</td>
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<td>New Delhi, India</td>
<td>Paris, France</td>
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<tr>
<th>Nassim Kamar, MD, PhD</th>
<th>Marcelo O. Silva, MD</th>
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<tr>
<td>CHU Rangueil, Toulouse, France</td>
<td>Hospital Universitario Austral</td>
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<td>Pilar, Argentina</td>
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Evidence Review Team
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KDIGO 2018 CLINICAL PRACTICE GUIDELINE ON THE PREVENTION, DIAGNOSIS, EVALUATION AND TREATMENT OF HEPATITIS C IN CKD

Chapter 1: Detection and Evaluation of HCV in CKD
Chapter 2: Treatment of HCV Infection in Patients with CKD
Chapter 3: Preventing HCV Transmission in Hemodialysis Units
Chapter 4: Management of HCV-Infected Patients before and after Kidney Transplantation
Chapter 5: Diagnosis and Management of Kidney Diseases Associated with HCV Infection
1.1 Screening patients with CKD for HCV infection

1.1.1: We recommend screening all patients for hepatitis C virus (HCV) infection at the time of initial evaluation of chronic kidney disease (CKD) (1C).

1.1.1.1: We recommend using an immunoassay followed by nucleic acid testing (NAT) if immunoassay is positive (1A).

1.1.2: We recommend screening all patients for HCV infection upon initiation of in-center hemodialysis or upon transfer from another dialysis facility or modality (1A).

1.1.2.1: We recommend using NAT alone or an immunoassay followed by NAT if immunoassay is positive (1A). To be repeated every 6 months as long as at risk (1B)
Hepatitis C virus itself is an independent risk factor for CKD onset, beyond traditional risk factors: a 6-year nationwide cohort study across Taiwan

- HCV new diagnosis 1998 to 2004 without CKD and associated comorbidities (N=3182)
- Compared to HCV negative without CKD and associated comorbidities (N=12728)

Chen et al, BMC Nephrol. 2013
Antiviral treatment for HCV infection is associated with improved renal outcomes in diabetic patients (Hsu et al)

Cumulative incidence of ESRD
Rationale for screening CKD non D patients for HCV

- HCV may cause MPGN
- Greater prevalence of HCV in late CKD stages
- Consistent association of
  - HCV+ with worse liver, kidney and CV outcomes
  - anti-HCV treatment with better outcomes (liver, kidney, CV)
- Low cost of single EIA for HCV
- Thus testing once for this modifiable risk factor is recommended (1C)
1.3.1: We recommend assessing HCV-infected patients with CKD for liver fibrosis (1A.)

1.3.2: We recommend an initial non-invasive evaluation of liver fibrosis (1B).

1.3.3: When the cause of liver disease is uncertain or non-invasive testing results are discordant, consider liver biopsy (Not Graded).

1.3.4: We recommend assessment for portal hypertension in CKD patients with suspected advanced fibrosis (F3-4) (1A).
HCV genotypes in the general population
HCV Virus – 9.6kb RNA

Polyprotein

- C
- E1
- E2
- p7
- NS2
- NS3
- NS4A
- NS4B
- NS5A
- NS5B

Protease Inhibitors
- Telaprevir
- Boceprevir
- Simeprevir
- Paritaprevir
- Grazoprevir

NS5A Inhibitors
- Ledipasvir
- Ombitasvir
- Daclatasvir
- Elbasvir

NS5B Polymerase Inhibitors
- Sofosbuvir
- Dasabuvir

-PREVIR   -ASVIR   -BUVIR
Key characteristics, variable between molecules:
- antiviral activity on some vs all HCV genotypes
- extent of elimination by the kidney
- potential to cause drug-drug interactions (liver)
- barriers to viral resistance (and thus need to add ribavirin)
- all regimens include at least 2 drugs (to reduce risk of HCV resistance)
2.1: We recommend that all CKD patients infected with HCV be evaluated for antiviral therapy (1A).

2.1.1: We recommend an interferon-free regimen (1A).

2.1.2: We recommend that the choice of specific regimen be based on HCV genotype (and subtype), viral load, prior treatment history, drug-drug interactions, glomerular filtration rate (GFR), stage of hepatic fibrosis, kidney and liver transplant candidacy, and comorbidities (1A).
2.2: We recommend that patients with eGFR > 30 ml/min/1.73 m² be treated with any licensed direct-acting antiviral (DAA)-based regimen. (1A)

2.3: We recommend that patients with eGFR < 30 ml/min/1.73 m² be treated with a ribavirin free DAA-based regimen (1B) as outlined in Table 1.
- Sofosbuvir cleared by the kidney
  - eGFR < 30 ml/’= off label use
  - some reports (case series) that sofosbuvir-based regimens safe and effective in late CKD
  - optimal dosage of SOF not fully clear
  - worsening of CKD progression by SOF not completely excluded
Grazoprevir plus elbasvir in treatment-naive and treatment-experienced patients with hepatitis C virus genotype 1 infection and stage 4–5 chronic kidney disease (the C-SURFER study): a combination phase 3 study


- First RCT of an oral, interferon-free DAA regimen in CKD stage 4 /5 patients
- <1% of grazoprevir and elbasvir renally excreted: no dose adjustment in CKD
- Single pill: Grazo 100mg/Elbas 50 mg
- primary endpoint = sustained viral response 12 weeks after stopping DAAs (SVR12)
PATIENTS CHARACTERISTICS

• HCV Genotype 1 infection (52% 1a, 48% 1b)
• treatment-naive and treatment-experienced patients
• CKD stage 4/5
  – CKD stage 4
  – CKD stage 5 non D, or on hemodialysis (76% of total n)
• Compensated cirrhosis allowed (6 %)
• All HBV and HIV negative
• Randomized, parallel-group, multi-site, placebo-controlled trial
• 12 weeks of study drug
• Stratification by diabetes (yes/no) and hemodialysis status (HD/non-HD)
• 11 patients in open-label GZR/EBR arm underwent intensive pharmacokinetic sampling

*Deferred open-label treatment arm (all randomized patients remained blinded to treatment until FW4)
GZR and EBR were administered as separate entities in the immediate and PK arms, and as a fixed
dose-combination in the deferred arm. CKD = chronic kidney disease; GT = genotype; HD =
hemodialysis; PK = pharmacokinetic
C-SURFER  SVR12 RESULTS
IMMEDIATE AND DEFERRED TREATMENT ARMS

<table>
<thead>
<tr>
<th></th>
<th>Immediate treatment</th>
<th>Deferred treatment</th>
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<tbody>
<tr>
<td>Relapse</td>
<td>1\textsuperscript{a}</td>
<td>1</td>
</tr>
<tr>
<td>D/c unrelated to treatment</td>
<td>6\textsuperscript{b}</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>2\textsuperscript{c}</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>3\textsuperscript{d}</td>
<td>0</td>
</tr>
</tbody>
</table>

\textsuperscript{a}Lost to follow-up (n = 2), n = 1 each for death, noncompliance, withdrawal by subject, and withdrawal by physician (owing to violent behavior).

\textsuperscript{b}Withdrawal by subject, n = 1; AE, n = 1; death, n =1

Roth et al Lancet 2015
Bruchfeld et al Lancet Gastroenterol Hepatol 2017
SAFETY SUMMARY

• Tolerance better or similar to placebo
• A single SAE possibly ascribed to study drug, vs one due to placebo
• Clear improvement in ALT/AST with study drug vs placebo
• No difference in bilirubin, or anemia parameters

Roth et al Lancet 2015
Bruchfeld et al. Lancet Gastroenterol Hepatol 2017
Glecaprevir and Pibrentasvir in Patients with HCV and Severe Renal Impairment

Edward Gane, M.D., Eric Lawitz, M.D., David Pugatch, M.D., Georgios Papatheodoridis, M.D., Norbert Bräu, M.D., Ashley Brown, M.D., Stanislas Pol, M.D., Ph.D., Vincent Leroy, M.D., Ph.D., Marcello Persico, M.D., Christophe Moreno, M.D., Ph.D., Massimo Colombo, M.D., Eric M. Yoshida, M.D., David R. Nelson, M.D., Christine Collins, Ph.D., Yang Lei, Ph.D., Matthew Kosloski, Ph.D., and Federico J. Mensa, M.D.

- Open-label multicenter phase 3 study
- \( N = 104 \), 79% males, 25% Black
- HCV Genotype: 1 \( n = 54 \)
  - 2 \( n = 17 \)
  - 3 \( n = 11 \)
  - 4 \( n = 20 \)
  - 5 \( n = 1 \)
  - 6 \( n = 1 \)
- 88% on HD
- 58% treatment naive

<table>
<thead>
<tr>
<th>Time of measurement</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>On-treatment response — no./total no. (%)</strong></td>
<td></td>
</tr>
<tr>
<td>Week 1</td>
<td>37/101 (37)</td>
</tr>
<tr>
<td>Week 2</td>
<td>77/100 (77)</td>
</tr>
<tr>
<td>Week 4</td>
<td>98/103 (95)</td>
</tr>
<tr>
<td>Week 8</td>
<td>103/103 (100)</td>
</tr>
<tr>
<td>Final treatment</td>
<td>104/104 (100)</td>
</tr>
<tr>
<td><strong>Posttreatment response — no./total no. (%)</strong></td>
<td></td>
</tr>
<tr>
<td>Sustained virologic response at posttreatment week 4</td>
<td>103/104 (99)</td>
</tr>
<tr>
<td>Sustained virologic response at posttreatment week 12</td>
<td>102/104 (98)</td>
</tr>
<tr>
<td>Sustained virologic response at posttreatment week 24</td>
<td>100/104 (96)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Event</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>no. of patients (%)</td>
</tr>
<tr>
<td>Any adverse event</td>
<td>74 (71)</td>
</tr>
<tr>
<td>Serious adverse event</td>
<td>25 (24)</td>
</tr>
<tr>
<td>Adverse event leading to discontinuation of trial drug</td>
<td>4 (4)</td>
</tr>
<tr>
<td>Adverse event reported in at least 10% of patients</td>
<td></td>
</tr>
<tr>
<td>Pruritus</td>
<td>21 (20)</td>
</tr>
<tr>
<td>Fatigue</td>
<td>15 (14)</td>
</tr>
<tr>
<td>Nausea</td>
<td>12 (12)</td>
</tr>
<tr>
<td>Death*</td>
<td>1 (1)</td>
</tr>
<tr>
<td>Alanine aminotransferase $&gt;3\times$ ULN, grade $\geq 2$</td>
<td>0</td>
</tr>
<tr>
<td>Total bilirubin $&gt;3\times$ ULN, grade $\geq 3$*</td>
<td>1 (1)</td>
</tr>
<tr>
<td>Hemoglobin $&lt;8.0$ g/dl, grade $\geq 3$*</td>
<td>5 (5)</td>
</tr>
</tbody>
</table>

*From the article N Engl J Med 2017;377:1448-55*
In most CKD patients the potential benefits of treating HCV outweigh potential harm.

Some patients, e.g., patients with metastatic cancer, may not live long enough to benefit from therapy.

No minimum life expectancy would justify treatment: inaccuracy of predictions, need to individualize decision. However as in the AASLD/IDSA guidance, life expectancy of at least 12 months should be anticipated.

Who should be treated?
Drug-drug interactions with DAAs

- 12 weeks treatment with DAAs
- Important to review the potential interactions, and available alternative drugs or need to reduce dosages of drugs coprescribed with DAAs
### HEP Drugs

<table>
<thead>
<tr>
<th>HEP Drugs</th>
<th>Co-medications</th>
</tr>
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<tbody>
<tr>
<td>Elbasvir/Grazoprevir</td>
<td>Atorvastatin</td>
</tr>
<tr>
<td>Elbasvir/Grazoprevir</td>
<td></td>
</tr>
</tbody>
</table>

### Drug Interactions

- **Elbasvir/Grazoprevir**
- **Atorvastatin**
- **Ergot**
- **Formoterol**
- **Ipratropium bromide**
- **Montelukast**
- **Omalizumab**
- **Salbutamol**
- **Salmeterol**
- **Theophylline**

**Summary:**
Co-administration of elbasvir + grazoprevir (50 + 200 mg once daily) with atorvastatin (10 mg single dose) increased atorvastatin AUC by 94% and increased Cmax by 4.34 fold. The dose of atorvastatin should not exceed a daily dose of 20 mg when coadministered with elbasvir/grazoprevir.

**Description:**
Co-administration of atorvastatin (20 mg single dose) and grazoprevir...
2.5: As hepatitis B reactivation has been described with DAA therapy, all treatment candidates should undergo testing for HBV infection prior to therapy. If hepatitis B surface antigen [HBsAg] is present, the patient should undergo assessment for HBV therapy. If HBsAg is absent but markers of prior HBV infection (HBcAb positive with or without HBsAb) are detected, monitor for HBV reactivation with serial HBV DNA and liver function tests during DAA therapy (Not Graded).
2.1.3: Treat kidney transplant candidates in collaboration with the transplant center to optimize timing of therapy. (Not Graded)
Impact of HCV treatment on timing of kidney TP!

• Renewed interest for the use of HCV+ grafts, especially in the USA.
• Waiting time for deceased donor frequently > 5 years, whereas HCV+ graft may be available within less than a year (local epidemiology!)
• Good long-term results of HCV+ kidneys to HCV+ recipients (Morales et al. AJT)
• Thus, anti-HCV treatment of renal transplant candidates should be undertaken in collaboration with the transplant center to optimize timing of therapy.
Treatment With Ledipasvir–Sofosbuvir for 12 or 24 Weeks in Kidney Transplant Recipients With Chronic Hepatitis C Virus Genotype 1 or 4 Infection

A Randomized Trial

Massimo Colombo, MD; Alessio Aghemo, MD; Hong Liu, PhD; Jie Zhang, PhD; Hadas Dvory-Sobol, PhD; Robert Hyland, DPhil; Chohee Yun, MD; Benedetta Massetto, MD; Diana M. Brainard, MD; John G. McHutchison, MD; Marc Bourlière, MD; Markus Peck-Radosavljevic, MD; Michael Manns, MD; and Stanislas Pol, MD
Median of 10 years after kidney TP
Cockroft: median 56 ml/min
Tacrolimus 47%, CsA 39%, MMF 61%, Steroids 98%
Cirrhosis: 15%  tolerance: OK

<table>
<thead>
<tr>
<th>Variable</th>
<th>Ledipasvir-Sofosbuvir</th>
<th>Total (n = 114)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>12 wk (n = 57)</td>
<td>24 wk (n = 57)</td>
</tr>
<tr>
<td>HCV RNA level less than the LLOQ during treatment, n/N (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>0/57 (0)</td>
<td>0/57 (0)</td>
</tr>
<tr>
<td>Week 1</td>
<td>9/57 (16)</td>
<td>7/57 (12)</td>
</tr>
<tr>
<td>Week 2</td>
<td>21/57 (54)</td>
<td>33/57 (58)</td>
</tr>
<tr>
<td>Week 4</td>
<td>50/57 (88)</td>
<td>52/57 (91)</td>
</tr>
<tr>
<td>Week 8</td>
<td>56/56 (100)*</td>
<td>57/57 (100)</td>
</tr>
<tr>
<td>Week 12</td>
<td>56/56 (100)*</td>
<td>57/57 (100)</td>
</tr>
<tr>
<td>Week 16</td>
<td>NA</td>
<td>57/57 (100)</td>
</tr>
<tr>
<td>Week 20</td>
<td>NA</td>
<td>57/57 (100)</td>
</tr>
<tr>
<td>Week 24</td>
<td>NA</td>
<td>57/57 (100)</td>
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</table>

<table>
<thead>
<tr>
<th>HCV RNA level less than the LLOQ after end of treatment, n/N (%)</th>
<th>Total (n = 114)</th>
</tr>
</thead>
<tbody>
<tr>
<td>SVR4</td>
<td>SVR12</td>
</tr>
<tr>
<td>57/57 (100 [94-100])</td>
<td>57/57 (100 [94-100])</td>
</tr>
<tr>
<td>Overall virologic failure (relapse), n/N (%)</td>
<td>Total (n = 114)</td>
</tr>
<tr>
<td>0/0 (0)</td>
<td>0/0 (0)</td>
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</tbody>
</table>

HCV = hepatitis C virus; LLOQ = lower limit of quantification; NA = not available; SVR4 = sustained virologic response at 4 wk; SVR12 = sustained virologic response at 12 wk.
* Excluding 1 patient in the 12-wk group who discontinued study treatment early at week 4 because of a serious adverse event. This patient achieved SVR12.

Annals of Internal Medicine
Table 1. Recommended DAA treatment regimens for patients with CKD G4-G5 and kidney transplant recipients, by HCV genotype

<table>
<thead>
<tr>
<th>Kidney function</th>
<th>HCV genotype</th>
<th>Recommended regimen(s)</th>
<th>Strength of evidence</th>
<th>Alternate regimen(s)</th>
<th>Strength of evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>CKD G4–G5</td>
<td>1a</td>
<td>Grazoprevir/elbasvir</td>
<td>1B</td>
<td>Ritonavir-boosted paritaprevir, ombitasvir, and dasabuvir (also known as PrOD or 3D regimen) with ribavirin</td>
<td>2D</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Glcaprevir/pibrentasvir</td>
<td>1B</td>
<td>Daclatasvir/asunaprevir</td>
<td>2C</td>
</tr>
<tr>
<td></td>
<td>1b</td>
<td>Grazoprevir/elbasvir</td>
<td>1B</td>
<td>Ritonavir-boosted paritaprevir, ombitasvir, and dasabuvir (also known as PrOD or 3D regimen)</td>
<td>2D</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Glcaprevir/pibrentasvir</td>
<td>1B</td>
<td>Daclatasvir/asunaprevir</td>
<td>2C</td>
</tr>
<tr>
<td></td>
<td>2,3</td>
<td>Glcaprevir/pibrentasvir</td>
<td>1B</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>Grazoprevir/elbasvir</td>
<td>2D</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Glcaprevir/pibrentasvir</td>
<td>1B</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>5,6</td>
<td>Glcaprevir/pibrentasvir</td>
<td>2D</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CKD G5 PD</td>
<td></td>
<td>n/a (reasonable to follow proposed regimens for HD)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>KTR</td>
<td>1a</td>
<td>Sofosbuvir with ledipasvir, daclatasvir or simeprevir</td>
<td>1B</td>
<td>Sofosbuvir/ribavirir</td>
<td>2D</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Glcaprevir/pibrentasvir#</td>
<td>1C</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>1b</td>
<td>Sofosbuvir with ledipasvir, daclatasvir or simeprevir</td>
<td>1B</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Glcaprevir/pibrentasvir#</td>
<td>1C</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>2, 3, 5, 6</td>
<td>Glcaprevir/pibrentasvir#</td>
<td>1D</td>
<td>Sofosbuvir/daclatasvir/ribavirin§</td>
<td>2D</td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>Sofosbuvir with ledipasvir, daclatasvir or simeprevir</td>
<td>1D</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>Glcaprevir/pibrentasvir#</td>
<td>1D</td>
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Algorithm 1. Treatment scheme for CKD G1-G5D
Recommendation grading is provided for each specific treatment regimen and HCV genotype.
CKD G, chronic kidney disease; GFR category; DAA, direct-acting antiviral; GFR, glomerular filtration rate; GT, genotype; HCV, hepatitis C virus; NAT, nucleic acid testing.
CHAPTER 3: PREVENTING HCV TRANSMISSION IN HEMODIALYSIS UNITS

3.1: We recommend that hemodialysis facilities adhere to standard infection control procedures including hygienic precautions that effectively prevent transfer of blood and blood-contaminated fluids between patients to prevent transmission of blood-borne pathogens (see Table 2) (1A).

3.1.1: We recommend regular observational audits of infection control procedures in hemodialysis units (1C).

3.1.2: We recommend not using dedicated dialysis machines for HCV-infected patients (1D).

3.1.3: We suggest not isolating HCV-infected hemodialysis patients (2C).

3.1.4: We suggest that the dialyzers of HCV-infected patients can be reused if there is adherence to standard infection control procedures (2D).
Table 2. Infection control practices ("hygienic precautions") particularly relevant in preventing HCV transmission

- Proper hand hygiene and glove changes, especially between patient contacts, before invasive procedures, and after contact with blood and potentially blood-contaminated surfaces/supplies
- Proper injectable medication preparation practices following aseptic technique and in an appropriate clean area, and injectable medication administration practice
- Thorough cleaning and disinfection of surfaces at the dialysis station, especially high-touch surfaces
- Adequate separation of clean supplies from contaminated materials and equipment
CHAPTER 4: MANAGEMENT OF HCV-INFECTED PATIENTS BEFORE AND AFTER KIDNEY TRANSPLANTATION

HCV-infected candidates for a kidney transplantation

Testing for liver fibrosis and if indicated, portal hypertension

F0 to compensated cirrhosis without portal hypertension

Living donor

Deceased donor

 Decompensated cirrhosis

SKLT before treatment
CHAPTER 4: MANAGEMENT OF HCV-INFECTED PATIENTS BEFORE AND AFTER KIDNEY TRANSPLANTATION

- Living donor
  - Short time to transplantation < 24 weeks
    - Treatment after transplantation
  - Expected time to transplantation > 24 weeks
    - Treatment before transplantation
- Deceased donor
  - Possibility of receiving an HCV+ kidney rapidly
    - No treatment prior to transplantation
    - Kidney from HCV + or – donor
      - Treatment after transplantation
  - No possibility of receiving an HCV+ kidney rapidly
    - Treatment before transplantation
4.4.1: We recommend all kidney donors be screened for HCV infection with both immunoassay and NAT (if NAT is available). (1A)

4.4.2: We recommend that transplantation of kidneys from HCV RNA-positive donors be directed to recipients with positive NAT. (1A)

4.4.3: After the assessment of liver fibrosis, potential HCV-positive living kidney donors who do not have cirrhosis should undergo HCV treatment before donation; they can be accepted for donation if they achieve sustained virologic response (SVR) and remain otherwise eligible to be a donor. (Not Graded)
Transplanting HCV-RNA(+) kidneys into HCV(-) recipients?

- Preliminary exciting results from UPenn and Hopkins (total: around 20 patients) (NEJM 2017, Annals Int Med 2018)
- DAAs soon after TP, with SVR12 in all pts
- Very short waiting time for TP (weeks)
- Strategy as yet investigational
5.1: We recommend that a kidney biopsy be performed in HCV-infected patients with clinical evidence of glomerular disease (*Not Graded*).

5.2: We recommend that patients with HCV-associated glomerular disease be treated for HCV (1A).

5.2.1 show initia

5.2.3.1: We recommend rituximab as the first-line immunosuppressive treatment (1C).

5.2.2 synd
treatment, with immunosuppressive agents and/or plasma-exchange (1C).

5.2.3: We recommend immunosuppressive therapy in patients with histologically active HCV-associated glomerular disease who do not respond to antiviral therapy, particularly those with cryoglobulinemic kidney disease (1B).

5.2.3.1: We recommend rituximab as the first-line immunosuppressive treatment (1C).
A Randomized Controlled Trial of Rituximab for the Treatment of Severe Cryoglobulinemic Vasculitis

S. De Vita,1 L. Quartuccio,1 M. Isola,2 C. Mazzaro,3 P. Scaini,4 M. Lenzi,5 M. Campanini,6 C. Naclerio,7 A. Tavoni,8 M. Pietrogrande,9 C. Ferri,10 M. T. Mascia,10 P. Masolini,1 A. Zabotti,1 M. Maset,1 D. Roccatello,11 A. L. Zignego,12 P. Pioltelli,13 A. Gabrielli,14 D. Filippini,15 O. Perrella,16 S. Migliaresi,17 M. Galli,18 S. Bombardieri,8 and G. Monti19
**Figure 2.** Survival curves in patients randomized to receive rituximab (RTX) therapy or conventional therapy (non-rituximab [non-RTX]), consisting of glucocorticoids, azathioprine, cyclophosphamide, or plasmapheresis.
A Randomized Controlled Trial of Rituximab Following Failure of Antiviral Therapy for Hepatitis C-Associated Cryoglobulinemic Vasculitis

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Laboratory of Immunoregulation (M.C.S.) and Biostatistics Research Branch (Z.H), National Institute of Allergy and Infectious Diseases, Bethesda, MD, and Cleveland Clinic, Cleveland, OH (C.A.L.)
Summary

• Exciting time for those involved in the battle against HCV in CKD/dialysis/ kidney TP

• Major progress in the treatment of HCV in CKD patients: impressive new evidence

• No complacency anymore: the right time to get rid of HCV in the nephrology field, in line with WHO commitment to eliminate viral hepatitis as a public health problem by 2030
Publication expected soon in KI suppl and on www.kdigo.org