New Advances in Hepatitis C Treatment

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Assistant Professor in Medicine,
Mayo Clinic, College of Medicine
The presenter has nothing to disclose.
Session Objectives

* Identify two possible routes of transmission of Hepatitis C
* Name 4 new antiviral medications used to treat Hepatitis C
* State the goal of Hepatitis C treatment
Hepatitis C
A World Wide Issue

~180 Million Individuals Infected

Global Prevalence of HCV Infection

2.7-3.9 million

- <1.0%
- 1.0%-1.9%
- 2.0%-2.9%
- >2.9%
- Not included in a WHO region
Genotypes and Subtypes

Simmonds  J Hepatology 1999
Hepatitis C Genotypes Distribution

(Gower, Estes, Blach, Razavi-Shearer, & Razavi, 2014)
World Hepatitis Day - 28 July 2016

Know hepatitis - Act now

8 July 2016 -- Viral hepatitis infection is widely spread, affecting 400 million people worldwide – over 10 times the number of people infected with HIV. Globally, about 1.4 million people die each year from hepatitis. On World Hepatitis Day, celebrated on 28 July 2016, WHO calls on policy-makers, health workers and the public to "Know hepatitis - Act now".
Ways of Transmission

* Blood borne virus
* Most common transmission
  * IV drug use
  * Reuse of medical equipment without sterilization
  * Unscreened blood and blood product transfusions
* Other possible ways
  * Sexual transmission
  * Mother to baby
Assessment of the Patient with Viral Hepatitis

* Wide range of possibilities: asymptomatic to acute liver failure.
* Nausea, vomiting, decreased appetite, generalized malaise, fever, jaundice, dark or tea-colored urine, abdominal pain to the right upper quadrant, or clay-colored or light stools.
* Hepatomegaly, jaundice, icteric sclera
* Few are diagnosed acutely

(Hanson et al., 2015; WHO, 2016)
Progression of Infection

(CDC, 2016)
Baby Boomers Account for the Majority of HCV Cases in United States

Estimated Prevalence by Age Group

Number of HCV Infections (millions)

Birth Year Group

A one-time screening test for Hepatitis C virus (HCV) (antibody HCV) for all patients who were born between 1945 and 1965 and for individuals who meet high-risk criteria.

(CDC, 2016; USPSTF, 2016)
What test do I choose?

- Screening
  - HCV antibody
  - Also called Anti–HCV antibody
  - If +, then HCV RNA
HEPATITIS C SCREENING AND EVALUATION

CLINICAL DECISION SUPPORT TOOL

Screen at least once per lifetime

Adults born between 1945–1965 who have never been evaluated for HCV.1

OR

Patients with previous high risk factors, including any blood transfusions prior to 1992 or history of intravenous drug use.2

Screen at least once annually

Patients with current injection drug use.3

Conduct hepatitis C antibody testing.4

Result: Positive

Conduct quantitative HCV RNA testing.5

Result: Negative

Result: Negative

If patient has ongoing high risk behaviors, conduct counseling, retesting and other testing as appropriate.6

Allen, 2013
Further Medical Care

Testing, vaccinations and screening for confirmed HCV viremia

ORDER INITIAL LABORATORY TESTS
- Comprehensive metabolic panel
- HCV genotype
- INR
- CBC/diff/platelets
- HIV antibody
- HBV surface antigen

HAV & HBV VACCINATION
- Administer HAV vaccination
- HBV vaccination if the patient does not have documented immunity

ALCOHOL SCREENING/COUNSELING
- Conduct alcohol screening and intervention as clinically indicated

To learn more about the “Hepatitis C Screening and Evaluation: Clinical Decision Tool,” visit Gastroenterology at http://ow.ly/q3DZq.

Allen, 2013
What if I suspect Acute HCV infection?

<table>
<thead>
<tr>
<th>Test</th>
<th>Interpretation for Diagnosis of Acute HCV Infection</th>
</tr>
</thead>
</table>
| HCV antibody          | - May be negative in the first 6 weeks after exposure  
                        | - May be delayed or absent when the individual is immunosuppressed  
                        | - Presence alone does not distinguish between acute and chronic infection  
                        | - Low signal-to-cutoff ratio may be present during acute HCV infection or represent a false-positive result  |
| HCV RNA               | - Viral fluctuations greater than 1 \( \log_{10} \) IU/mL may indicate acute HCV infection  
                        | - May be transiently negative during acute HCV infection  
                        | - Alone does not distinguish between acute and chronic infection  |
| Alanine aminotransferase (ALT) | - Fluctuating peaks during acute HCV infection suggest acute infection  
                                     | - May be normal during acute HCV infection  
                                     | - May be elevated due to other liver insults such as alcohol consumption  |
Hepatitis C +: Now what to do?

* Additional lab work
* Vaccinate
* Patient Education
  * Alcohol
  * Drugs
* Imaging Studies
  * Ultrasound/Fibrosan®
* Check for further complications of Hepatitis C
* Compensated vs. Decompensated Cirrhosis
## METAVIR fibrosis and activity score

<table>
<thead>
<tr>
<th>METAVIR fibrosis score</th>
<th>METAVIR activity score</th>
</tr>
</thead>
<tbody>
<tr>
<td>No fibrosis</td>
<td>F0</td>
</tr>
<tr>
<td>Portal fibrosis without septa</td>
<td>F1</td>
</tr>
<tr>
<td>Portal fibrosis with few septa</td>
<td>F2</td>
</tr>
<tr>
<td>Portal fibrosis with numerous septa without cirrhosis</td>
<td>F3</td>
</tr>
<tr>
<td>Cirrhosis</td>
<td>F4</td>
</tr>
<tr>
<td>No activity</td>
<td>A0</td>
</tr>
<tr>
<td>Mild activity</td>
<td>A1</td>
</tr>
<tr>
<td>Moderate activity</td>
<td>A2</td>
</tr>
<tr>
<td>Severe activity</td>
<td>A3</td>
</tr>
</tbody>
</table>

**References:**

### Child Turcotte Pugh (CTP) Score

**Child Turcotte Pugh (CTP) classification of the severity of cirrhosis**

<table>
<thead>
<tr>
<th>Factor</th>
<th>Class A</th>
<th>Class B</th>
<th>Class C</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total points</td>
<td>5–6</td>
<td>7–9</td>
<td>10–15</td>
</tr>
<tr>
<td>Total bilirubin (μmol/L)</td>
<td>&lt;34</td>
<td>34–50</td>
<td>&gt;50</td>
</tr>
<tr>
<td>Serum albumin (g/L)</td>
<td>&gt;35</td>
<td>28–35</td>
<td>&lt;28</td>
</tr>
<tr>
<td>Prothrombin time/international normalized ratio</td>
<td>&lt;1.7</td>
<td>1.71–2.30</td>
<td>&gt;2.30</td>
</tr>
<tr>
<td>Ascites</td>
<td>None</td>
<td>Mild</td>
<td>Moderate to Severe</td>
</tr>
<tr>
<td>Hepatic encephalopathy</td>
<td>None</td>
<td>Grade I–II (or suppressed with medication)</td>
<td>Grade III–IV (or refractory)</td>
</tr>
</tbody>
</table>

Hcvguidelines.org
Hepatocellular carcinoma (HCC) screening

- Recommended for HCV patients
- Cirrhosis
- Stage 3 fibrosis
- Screening every 6 months
- Ultrasound
- AFP serum test
HCV: Extrahepatic Manifestations

Autoimmune Phenomena
- CRST Syndrome
- Lichen Planus
- Porphyria Cutanea Tarda

Dermatologic
- Cutaneous Necrotizing Vasculitis
- Lichen Planus
- Porphyria Cutanea Tarda

Hematologic
- Aplastic Anemia
- Mixed Cryoglobulinemia
- Non Hodgkin’s B-Cell Lymphoma
- Thrombocytopenia

Endocrine
- Diabetes Mellitus
- Hypothyroidism

Neuromuscular
- Arthritis/Arthralgia
- Myalgia/Weakness
- Peripheral Neuropathy

Neuropsychiatric
- Depression

Ocular
- Corneal Ulcer
- Uveitis

Renal
- Glomerulonephritis
- Nephrotic Syndrome

Vascular
- Necrotizing Vasculitis
- Polyarteritis Nodosa

CRST = Calcinosi, Raynaud’s phenomenon, Sclerodactyly and Telangiectasia

74% of HCV patients

Porphyria Cutanea Tarda
Mixed cryoglobulinemia syndrome (MCS)

- Vasculitis involves skin, major joints, peripheral nerves, renal disease
- 90% of MCS associated with HCV
- If HCV treated, remission of MCS
Membranoproliferative glomerulonephritis (MPGN)

- Cryoglobulin associated MPGN
- Non-cryoglobulin associated MPGN
- Resolution or improvement in successfully treated HCV
Increased risk of cardiovascular complications in HCV patients

- Early and advanced arthrosclerosis compared to general population
- Cardiovascular mortality
- Risk of Type 2 DM

(Kakinami, et al., 2013; Guiltinan, et al., 2008; Fukui, et al., 2003)
Gilead Gets FDA Approval for Combo Hepatitis C Drug

Biotech prices Epclusa drug below its older drugs that treat hepatitis C
The Goal of HCV Treatment

* A Cure = A sustained virologic response, or virologic cure
* An undetectable HCV RNA level for at least 12 weeks.

(Hanson, Pearson, & Kugelmas, 2015)
High Efficacy of Non-specialist Led HCV Treatment with DAAs - Methods

Two Urban Health Systems

16 Providers

5 NP
5 PCP
6 Specialist (ID/Hepatology)

Uniform 3-hour Training

600 Patients

LDV/SOF 8-24 Weeks

SVR12
Adherence

(Kattakuzhy, 2016)
### Results Interim Per Protocol SVR12 by Provider Type (n=382)

<table>
<thead>
<tr>
<th>Provider Type</th>
<th>Percentage with SVR12</th>
<th>Count</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>NP</td>
<td>95.2% (98/103)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PCP</td>
<td>97.3% (72/74)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Specialist</td>
<td>92.7% (190/205)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>94.2% (360/382)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

(Kattakuzhy, 2016)
History of HCV Treatment

- Difficult to treat special populations
- Interferon and Ribavirin
  - Weekly injections
  - 48 weeks of treatment
  - ~50% cure rate
  - Poor tolerance
  - Adverse reactions/side effects
Direct antiviral agents (DAA)

- Four classes of DAAs
  - Nonstructural proteins 3/4A (NS3/4A) protease inhibitors (PIs)
  - NS5B nucleoside polymerase inhibitors (NPIs)
  - NS5B non-nucleoside polymerase inhibitors (NNPIs)
  - NS5A inhibitors

(Pockros, 2016)
# Treatment of HCV

<table>
<thead>
<tr>
<th>Class</th>
<th>Drug</th>
</tr>
</thead>
<tbody>
<tr>
<td>NS3/4A Protease inhibitor</td>
<td>Simeprevir</td>
</tr>
<tr>
<td></td>
<td>Paritaprevir (ABT 450)+RTV</td>
</tr>
<tr>
<td></td>
<td>Asunaprevir (BMS 650032)</td>
</tr>
<tr>
<td></td>
<td>Grazoprevir (MK-5172)</td>
</tr>
<tr>
<td>NS5A Inhibitor</td>
<td>Daclatasvir</td>
</tr>
<tr>
<td></td>
<td>Ledipasvir</td>
</tr>
<tr>
<td></td>
<td>Elbasvir (MK-8742)</td>
</tr>
<tr>
<td></td>
<td>Ombitasvir</td>
</tr>
<tr>
<td>NS5B non-nucleoside polymerase inhibitor</td>
<td>Dasabuvir</td>
</tr>
<tr>
<td></td>
<td>Beclabuvir (BMS 791325)</td>
</tr>
<tr>
<td>NS5B nucleoside polymerase inhibitor</td>
<td>Sofosbuvir</td>
</tr>
</tbody>
</table>

**Pan-genotypic NS5A inhibitor**

**Velpatasvir**
Introduction to HCV protease inhibitors

- Boceprevir (Victrelis) and telaprevir (Incivek)
- No longer recommended

- 2013
  - Simeprevir (Olysio)
  - HCV NS3/4A protease inhibitor

(Dhawan, 2016).
History of HCV Treatment

* 2014
  * Simeprevir (Olysio) plus Sofosbuvir (Sovaldi)
  * All oral regimen
  * 12 weeks of treatment – without cirrhosis
  * 24 weeks of treatment – with cirrhosis
  * $150,000 for a 12 week course of treatment

(Dhawan, 2016; University of Washington, 2016)
History of HCV Treatment

- 2014
  - Polymerase inhibitors
  - Sofosbuvir (Sovaldi)
  - Ledipasvir + sofosbuvir (Harvoni)
  - Genotype 1, 4, 5, and 6
  - 12-weeks = $94,500

(Dhawan, 2016; University of Washington, 2016)
Combination Options

* Ombitasvir/paritaprevir/ritonavir and dasabuvir (Viekira Pak)
  * Approved in 2014
  * Genotype 1
* Ombitasvir/paritaprevir/ritonavir (Technivie)
  * Approved in 2015
  * Genotype 4
  * To be used in conjunction with ribavirin
* Elbasvir/grazoprevir (Zepatier)
  * Approved in 2016
  * Genotype 1 and 4
  * Clinical trials reflect 94-97% cure rate

(Dhawan, 2016; University of Washington, 2016)
<table>
<thead>
<tr>
<th>Drug Class</th>
<th>Drug(s) within Class that are Contraindicated</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alpha1-adrenoreceptor antagonist</td>
<td>Alfuzosin HCL</td>
</tr>
<tr>
<td>Anticonvulsants</td>
<td>Carbamazepine, phenytoin, phenobarbital</td>
</tr>
<tr>
<td>Antihyperlipidemic agent</td>
<td>Gemfibrozil</td>
</tr>
<tr>
<td>Antimycobacterial</td>
<td>Rifampin</td>
</tr>
<tr>
<td>Ergot derivatives</td>
<td>Ergotamine, dihydroergotamine, ergonovine, methylergonovine</td>
</tr>
<tr>
<td>Ethinyl estradiol-containing products</td>
<td>Ethinyl estradiol-containing medications such as combined oral contraceptives</td>
</tr>
<tr>
<td>Herbal Product</td>
<td>St. John’s Wort (<em>Hypericum perforatum</em>)</td>
</tr>
<tr>
<td>HMG-CoA Reductase</td>
<td>Lovastatin, simvastatin</td>
</tr>
<tr>
<td>Neuroleptics</td>
<td>Pimozide</td>
</tr>
<tr>
<td>Non-nucleoside reverse transcriptase inhibitor</td>
<td>Efavirenz</td>
</tr>
<tr>
<td>Phosphodiesterase-5 (PDE5) inhibitor</td>
<td>Sildenafil when dosed as <em>Revatio</em> for the treatment of pulmonary arterial hypertension (PAH)</td>
</tr>
<tr>
<td>Sedatives/hypnotics</td>
<td>Triazolam; Orally administered midazolam</td>
</tr>
</tbody>
</table>

*(University of Washington, 2016)*
<table>
<thead>
<tr>
<th>Drug Class</th>
<th>Drug(s) within Class</th>
<th>Contraindicated Class</th>
<th>Clinical Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alpha1-adrenoreceptor antagonist</td>
<td>Alfuzosin HCL</td>
<td></td>
<td>Potential for hypotension.</td>
</tr>
<tr>
<td>Anticonvulsants</td>
<td>Carbamazepine, phenytoin, phenobarbital</td>
<td></td>
<td>Ombitasvir, paritaprevir, ritonavir and dasabuvir exposures may decrease leading to a potential loss of activity for HCV therapy</td>
</tr>
<tr>
<td>Antihyperlipidemic agent</td>
<td>Gemfibrozil</td>
<td></td>
<td>Increase in dasabuvir exposures by 10-fold which may increase the risk of QT prolongation.</td>
</tr>
<tr>
<td>Antimycobacterial</td>
<td>Rifampin</td>
<td></td>
<td>Ombitasvir, paritaprevir, ritonavir and dasabuvir exposures may decrease leading to a potential loss of HCV therapeutic activity.</td>
</tr>
<tr>
<td>Ergot derivatives</td>
<td>Ergotamine, dihydroergotamine, ergonovine, methylergonovine</td>
<td></td>
<td>Acute ergot toxicity characterized by vasospasm and tissue ischemia has been associated with co-administration of ritonavir and ergonovine, ergotamine, dihydroergotamine, or methylergonovine.</td>
</tr>
<tr>
<td>Ethinyl estradiol-containing products</td>
<td>Ethinyl estradiol-containing medications such as combined oral contraceptives</td>
<td></td>
<td>Potential for ALT elevations.</td>
</tr>
<tr>
<td>Herbal Product</td>
<td>St. John’s Wort (Hypericum perforatum)</td>
<td></td>
<td>Ombitasvir, paritaprevir, ritonavir and dasabuvir exposures may decrease leading to a potential loss of HCV therapeutic activity.</td>
</tr>
<tr>
<td>HMG-CoA Reductase</td>
<td>Lovastatin, simvastatin</td>
<td></td>
<td>Potential for myopathy including rhabdomyolysis.</td>
</tr>
<tr>
<td>Neuroleptics</td>
<td>Pimozide</td>
<td></td>
<td>Potential for cardiac arrhythmias.</td>
</tr>
<tr>
<td>Non-nucleoside reverse transcriptase inhibitor</td>
<td>Efavirenz</td>
<td></td>
<td>Co-administration of efavirenz based regimens with paritaprevir, ritonavir plus dasabuvir was poorly tolerated and resulted in liver enzyme elevations.</td>
</tr>
<tr>
<td>Phosphodiesterase-5 (PDE5) inhibitor</td>
<td>Sildenafil when dosed as REVATIO for the treatment of pulmonary arterial hypertension (PAH)</td>
<td></td>
<td>There is increased potential for sildenafil-associated adverse events such as visual disturbances, hypotension, priapism, and syncope.</td>
</tr>
<tr>
<td>Sedatives/hypnotics</td>
<td>Triazolam Orally administered midazolam</td>
<td></td>
<td>Triazolam and orally administered midazolam are extensively metabolized by CYP3A4. Coadministration of triazolam or orally administered midazolam with VIEKIRA PAK may cause large increases in the concentration of these benzodiazepines. The potential exists for serious and/or life threatening events such as prolonged or increased sedation or respiratory depression.</td>
</tr>
</tbody>
</table>
## Drugs that are Contraindicated for Use with Elbasvir-Grazoprevir*

<table>
<thead>
<tr>
<th>Organic ion transporter polypeptide 1B (OATP1B) inhibitors</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Antimycobacterials</td>
<td>Rifampin</td>
</tr>
<tr>
<td>HIV medications</td>
<td>Atazanavir, Darunavir, Lopinavir, Saquinavir, Tipranavir</td>
</tr>
<tr>
<td>Immunosuppressants</td>
<td>Cyclosporine</td>
</tr>
</tbody>
</table>

**Strong CYP3A Inducers**

<table>
<thead>
<tr>
<th>Anticonvulsants</th>
<th>Phenytoin, Carbamazepine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Herbal products</td>
<td>St. John’s Wort (Hypericum perforatum)</td>
</tr>
<tr>
<td>HIV medications</td>
<td>Efavirenz*</td>
</tr>
</tbody>
</table>

*This is not a complete list of all drugs that inhibit OAT1B or strongly induce CYP3A

*Efavirenz is listed as a strong CYP3A inducer because it reduced grazoprevir exposure by ≥80%*
Since the approvals of Viekira Pak in December 2014 and Technivie in July 2015, at least 26 worldwide cases submitted to FAERS were considered to be possibly or probably related to Viekira Pak or Technivie. In most of the cases, liver injury occurred within 1 to 4 weeks of starting treatment. Some of the cases occurred in patients for whom these medicines were contraindicated or not recommended.

**RECOMMENDATION:** Health care professionals should closely monitor for signs and symptoms of worsening liver disease, such as ascites, hepatic encephalopathy, variceal hemorrhage, and/or increases in direct bilirubin in the blood.
Daclatasvir (Daklinza)

- Genotype 1 and 3
- Use with sofosbuvir with genotype 3
- Use with sofosbuvir, with or without ribavirin for genotype 1 or 3
- Use with HIV co-infection
- Decompensated cirrhosis
- After liver transplant

(Dhawan, 2016; University of Washington, 2016)
The first fixed-dose combination medication FDA approved for the treatment of chronic hepatitis C genotypes 1-6 infection in adults
Prior to Starting HCV Treatment

- Staging of liver fibrosis
- Evaluation of current medications
  - Aware of possible drug-drug interactions
- Patient education
  - **ADHERENCE TO THERAPY**
- Lab Tests, including genotype testing and HCV viral load
  - Repeat labs at 4 weeks, then as clinically indicated
  - Repeat viral load at 4 weeks and 12 weeks (completion of therapy)

www.hcvguidelines.org
Pretreatment Evaluation Before HCV Therapy

The following provides an overview of information needed to make choices regarding HCV therapy and to provide to most insurances when seeking prior authorization. Always consult individual company requirements before submitting applications for prior authorization.

Patient Identifier

<table>
<thead>
<tr>
<th>Required Information</th>
<th>Results and Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>HCV genotype and subtype</td>
<td></td>
</tr>
<tr>
<td>Recent HCV RNA quantitative</td>
<td></td>
</tr>
<tr>
<td>HCV treatment history: naive or experienced</td>
<td></td>
</tr>
<tr>
<td>• If experienced, what was the regimen(s) and the</td>
<td></td>
</tr>
<tr>
<td>outcome(s)?</td>
<td></td>
</tr>
<tr>
<td>Liver staging: biopsy, FibroSure, or FibroScan</td>
<td></td>
</tr>
<tr>
<td>• Note: some plans may not accept FIB-4 or APRI scores</td>
<td></td>
</tr>
<tr>
<td>Liver transplant status</td>
<td></td>
</tr>
<tr>
<td>For women of childbearing age receiving ribavirin:</td>
<td></td>
</tr>
<tr>
<td>• Pregnancy test results</td>
<td></td>
</tr>
</tbody>
</table>
Women of Childbearing Age

- Pregnancy test prior to the beginning of HCV treatment
- Newer regimens with Pregnancy B or C categories
- Ribavirin – Pregnancy X category
  - birth defects and miscarriages
- If taking regimen with ribavirin, advise patient to not become pregnant now and for up to 6 months after stopping
- Male partners should be advised as well
- Counsel regarding contraceptive use
Genotype 1a + 1b Treatment-Naïve Without Cirrhosis

- Daily fixed-dose combination of elbasvir (50 mg)/grazoprevir (100 mg) for 12 weeks
- Daily fixed-dose combination of ledipasvir (90 mg)/sofosbuvir (400 mg) for 12 weeks
- Daily fixed-dose combination of paritaprevir (150 mg)/ritonavir (100 mg)/ombitasvir (25 mg) plus twice-daily dosed dasabuvir (250 mg) with weight-based ribavirin for 12 weeks (1b- without ribavirin)
- Daily simeprevir (150 mg) plus sofosbuvir (400 mg) for 12 weeks
- Daily fixed-dose combination of sofosbuvir (400 mg)/velpatasvir (100 mg) for 12 weeks
- Daily daclatasvir (60 mg) plus sofosbuvir (400 mg) for 12 weeks

www.hcvguidelines.org
Genotype 1a Treatment-Naïve With Compensated Cirrhosis

- Daily fixed-dose combination of elbasvir (50 mg)/grazoprevir (100 mg) for 12 weeks
- Daily fixed-dose combination of ledipasvir (90 mg)/sofosbuvir (400 mg) for 12 weeks
- Daily fixed-dose combination of sofosbuvir (400 mg)/velpatasvir (100 mg) for 12 weeks

www.hcvguidelines.org
Genotype 1b Treatment-Naïve With Compensated Cirrhosis

- Daily fixed-dose combination of elbasvir (50 mg)/grazoprevir (100 mg) for 12 weeks
- Daily fixed-dose combination of ledipasvir (90 mg)/sofosbuvir (400 mg) for 12 weeks
- Daily fixed-dose combination of paritaprevir (150 mg)/ritonavir (100 mg)/ombitasvir (25 mg) plus twice-daily dosed dasabuvir (250 mg) for 12 weeks
- Daily fixed-dose combination of sofosbuvir (400 mg)/velpatasvir (100 mg) for 12 weeks

www.hcvguidelines.org
Genotype 2 Treatment-Naïve
Without Cirrhosis and with Compensated cirrhosis

Updated July 6th, 2016

* Daily fixed-dose combination of sofosbuvir (400 mg)/velpatasvir (100 mg) for 12 weeks
Genotype 3 Treatment-Naïve Without Cirrhosis

Updated July 6th, 2016

- Daily daclatasvir (60 mg) plus sofosbuvir (400 mg) for 12 weeks
- Daily fixed-dose combination of sofosbuvir (400 mg)/velpatasvir (100 mg) for 12 weeks
Genotype 3 Treatment-Naïve With Compensated Cirrhosis

Updated July 6th, 2016

* Daily fixed-dose combination of sofosbuvir (400 mg)/velpatasvir (100 mg) for 12 weeks

* Daily daclatasvir (60 mg) plus sofosbuvir (400 mg) for 24 weeks with or without weight-based ribavirin
Genotype 4 Treatment-Naïve
Without Cirrhosis and
With Compensated Cirrhosis

Updated July 6th, 2016

* Daily fixed-dose combination of paritaprevir (150 mg)/ritonavir (100 mg)/ombitasvir (25 mg) and weight-based ribavirin for 12 weeks
* Daily fixed-dose combination of sofosbuvir (400 mg)/velpatasvir (100 mg) for 12 weeks
* Daily fixed-dose combination of elbasvir (50 mg)/grazoprevir (100 mg) for 12 weeks
* Daily fixed-dose combination of ledipasvir (90 mg)/sofosbuvir (400 mg) for 12 weeks
Genotype 5 and 6
With and Without Cirrhosis

Updated July 6th, 2016

* Daily fixed-dose combination of sofosbuvir (400 mg)/velpatasvir (100 mg) for 12 weeks

* Daily fixed-dose combination of ledipasvir (90 mg)/sofosbuvir (400 mg) for 12 weeks

www.hcvguidelines.org
Regimens **NOT** Recommended in HCV Treatment

* Daily sofosbuvir (400 mg) and weight-based ribavirin for 24 weeks
* PEG-IFN/ribavirin with or without sofosbuvir, simeprevir, telaprevir, or boceprevir
* Monotherapy with PEG-IFN, ribavirin, or a direct-acting antiviral

www.hcvguidelines.org
Assessment for HCV recurrence or reinfection is recommended only if the patient has ongoing risk for HCV infection or otherwise unexplained hepatic dysfunction (abnormal LFTs, jaundice, etc.)

Surveillance for hepatocellular carcinoma with twice-yearly ultrasound examination is recommended for patients with advanced fibrosis who achieve a SVR.

Assessment of other causes of liver disease is recommended for patients who develop persistently abnormal liver tests after achieving an SVR.
Successful treatment of HCV reduces HCC risk, however still 0.33% per year

Risk factors for development of HCC include diabetes, older age and presence of cirrhosis

Need surveillance of HCC

Finding supports need for early HCV treatment before development of cirrhosis
Care after Completion of Therapy with SVR

Quick Reference Sheet: Care and Counseling of Patients Following SVR

This worksheet can be used to guide and document posttreatment care for patients who have achieved a sustained virologic response following HCV therapy.

Patient Identifier: _______________________

Cure characteristics and HCV RNA assessment

- HCV RNA negative 12 weeks posttreatment? _______________________
- HCV RNA negative 24 weeks posttreatment? _______________________
- HCV RNA negativity > 24 weeks posttreatment should be assessed if:
  - Patient is at risk for reinfection (i.e., engages in illicit drug use, high-risk sexual activity)*
    - If YES, document risk and assessment and counseling plan:
  - Patient is moving toward transplantation (document negative HCV RNA at time of referral)
    - If YES, describe and document plan:
  - Patient has a change in liver status or liver-associated enzymes become abnormal
    - If YES, describe and document plan:

*Assessment should occur every 6-12 months.

Posttreatment monitoring with hepatology team should occur in patients with confirmed cirrhosis

- Recommended interval every 6 months; consider alternating visits with PCP where appropriate
- Obtain comprehensive metabolic profile, INR, CBC; screen for HCC
- Screening for esophageal varices via endoscopy should occur at diagnosis of cirrhosis
  - Varices present? YES NO
  - If NO, further screening should occur every year for patients with decompensated cirrhosis and every 3 years for patients with compensated cirrhosis

Posttreatment HCC screening

- Hepatoma screening should be conducted every 6 months via ultrasound if YES for any of the following:
  - FibroScan > 12.5 kPa (possibly at 9.3 kPa or greater) YES NO
  - Liver biopsy 2 stage 3 YES NO
  - FibroSure/FibroTest 0.7 YES NO
  - APRI 0.7 YES NO
- Recommended HCC screening plan: ________________________

____________________
____________________
Life After a Cure

- Fibrosis regression
- Improvement in extrahepatic issues
- Improved quality of life
- Lower mortality
Resources

* Clinical Care Options – Hepatitis C
  * http://www.clinicaloptions.com/Hepatitis.aspx
  * http://www.clinicaloptions.com/Hepatitis/Treatment%20Updates/HCV%20Therapy/Worksheets/Pretreatment_Evaluation.aspx

* AASLD/IDSA
  * http://www.hcvguidelines.org/
Future Possibilities

* All genotypes have effective regimens with SVR rate > 90%
* Goals for future regimens
  * No need for Ribavirin
  * Shorter duration (as short as 6 weeks)
* Ideal regimen
  * Pangenotypic
  * Short duration
  * Well tolerated
  * One pill


Slide credit: clinicaloptions.com
Key Highlights

- Take the necessary precautions to screen for Hepatitis C when clinically indicated
- Treat Hepatitis C – use guidelines by hcvguidelines.org
- Hepatitis C can be cured
- Be aware of possible drug-drug interactions
- When in doubt or in the patient with cirrhosis, seek expert consultation
- Line up all the details to get the prior authorization from insurance companies for expensive HCV medications
References

References


Thank you

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Questions & Discussion