Ready or Not, Here It Comes: Updates for Management of Hepatitis C Virus across Practice Settings

Moderator:
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Disclosure

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Gilead: Advisory Board

Michelle Martin
AbbVie: Stockholder/Ownership Interest (excluding diversified mutual funds); Gilead: Advisory Board, Stockholder/Ownership Interest (excluding diversified mutual funds); Merck: Stockholder/Ownership Interest (excluding diversified mutual funds)

All other planners, presenters, and reviewers of this session report no financial relationships relevant to this activity.
Learning Objectives

• Given a patient case, analyze emerging data on currently approved and anticipated hepatitis C virus (HCV) therapies.

• Discuss the challenges faced with HCV treatment across practice settings, including management of drug interactions, avoidance of treatment interruptions, and challenges encountered with specialty pharmacy medication coverage.

• Select resources for screening and management of HCV, medication selection, drug-drug interactions, pipeline agents, and continuing education.
Session Roadmap

• Dr. Martin
  – Overview of HCV / comparison of treatment options
    • Case studies in ambulatory care
• Dr. Spooner:
  – Management of HCV infection in the inpatient setting
    • Challenges/case studies
• Dr. Deming
  – Emerging data
  – Telemedicine
  – Anticipated challenges
Management of HCV Infection in the Ambulatory Care Setting

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Clinical Assistant Professor / Clinical Pharmacist
University of Illinois at Chicago College of Pharmacy
University of Illinois Hospital and Health Sciences System
Chicago, IL
Which resource offers guidance for HCV treatment selection?

A. https://www.clinicaloptions.com/Hepatitis.aspx
B. http://www.hep-druginteractions.org/checker
C. http://www.hcvguidelines.org/
D. http://www.hepatitisc.uw.edu/
Which of the following pieces of information is (are) necessary when selecting appropriate HCV treatment for a patient?

A. HCV genotype
B. HCV treatment history
C. Stage of disease (presence / absence of cirrhosis)
D. Concurrent medications
Which of the following is (are) an all-oral, pangenotypic, single tablet regimen(s) currently approved by the FDA for the treatment of adults with genotypes 1-6 chronic HCV infection?

A. Elbasvir/grazoprevir
B. Glecaprevir/pibrentasvir
C. Sofosbuvir/velpatasvir/voxilaprevir
D. Paritaprevir/ritonavir/ombitasvir/dasabuvir
Glecaprevir/pibrentasvir offers an 8-week treatment course for treatment-naïve, non-cirrhotic patients with any HCV genotype.

A. True
B. False
<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Definition</th>
<th>Brand (if applicable)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CTP</td>
<td>Child-Turcotte-Pugh</td>
<td></td>
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<tr>
<td>DAA</td>
<td>Direct-acting antiviral</td>
<td></td>
</tr>
<tr>
<td>DCV</td>
<td>Daclatasvir</td>
<td>Daklinza®</td>
</tr>
<tr>
<td>EBR/GZR</td>
<td>Elbasvir/grazoprevir</td>
<td>Zepatier®</td>
</tr>
<tr>
<td>ESLD</td>
<td>End-stage liver disease</td>
<td></td>
</tr>
<tr>
<td>G/P</td>
<td>Glecaprevir/pibrentasvir</td>
<td>Mavyret®</td>
</tr>
<tr>
<td>GT</td>
<td>Genotype</td>
<td></td>
</tr>
<tr>
<td>HCC</td>
<td>Hepatocellular carcinoma</td>
<td></td>
</tr>
<tr>
<td>LDV/SOF</td>
<td>Ledipasvir/sofosbuvir</td>
<td>Harvoni®</td>
</tr>
<tr>
<td>PegIFN</td>
<td>Pegylated interferon</td>
<td>Pegasys®, PegIntron®</td>
</tr>
<tr>
<td>PrOD</td>
<td>Paritaprevir/ritonavir/ombitasvir + dasabuvir</td>
<td>Viekira XR®</td>
</tr>
<tr>
<td>RBV</td>
<td>Ribavirin</td>
<td></td>
</tr>
<tr>
<td>SMV</td>
<td>Simeprevir</td>
<td>Olysio®</td>
</tr>
<tr>
<td>SOF</td>
<td>Sofosbuvir</td>
<td>Sovaldi®</td>
</tr>
<tr>
<td>SOF/VEL</td>
<td>Sofosbuvir/velpatasvir</td>
<td>Epclusa®</td>
</tr>
<tr>
<td>SOF/VEL/VOX</td>
<td>Sofosbuvir/velpatasvir/voxilaprevir</td>
<td>Vosevi®</td>
</tr>
<tr>
<td>SVR</td>
<td>Sustained virologic response</td>
<td></td>
</tr>
</tbody>
</table>
Hepatitis C Virus (HCV)

- Single-stranded RNA virus
- Multiple HCV genotypes and subtypes
- Most common blood-borne infection in the United States
  - Leading known reason for liver transplant
  - Main cause of liver-related death, end-stage liver disease (ESLD), and hepatocellular carcinoma (HCC)
- No vaccine available

<table>
<thead>
<tr>
<th>Global Prevalence</th>
<th>Global Death Rate</th>
<th>US Prevalence</th>
<th>US Death Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>~177.5 million</td>
<td>~399,000 / year</td>
<td>~2.5 – 4.7 million</td>
<td>19,629 in 2015</td>
</tr>
</tbody>
</table>

Progression of HCV

Acute Infection

Chronic Infection

Resolution 15%

Chronic Hepatitis Mild, Moderate, Severe

Cirrhosis

ESLD, transplant

Decompensation

HCC

Approximate Time (Years)

HCV Screening Recommendations

1. All patients with risk factors for HCV infection

2. Everyone born between 1945 and 1965 should get tested for HCV once regardless of risk factors

3. Annual testing of patients with ongoing risk factors
   - Persons who inject drugs
   - HIV+ men who have sex with men patients who have unprotected sex
HCV Treatment Cascade in US (2014)

- Chronic HCV Infection: 3,500,00
- Diagnosed and aware: 50%
- Access to Outpatient Care: 43%
- HCV RNA Confirmed: 27%
- Underwent Liver Biopsy: 17%
- Prescribed Treatment: 16%
- Achieved SVR: 9%

www.plosone.org/article/info%3Adoi%2F10.1371%2Fjournal.pone.0101554
Selecting HCV Treatment

• To ensure correct HCV agent and length of treatment, you need to know (at minimum):
  1) Genotype
  2) Previous treatment history
  3) Presence/absence of cirrhosis

• Also need to know:
  – Concomitant comorbidities (e.g., renal impairment, post-transplant)
  – Check concomitant medications to avoid/manage DDIs

→ Use HCV guidance to select appropriate regimen
HCV Guidance: Recommendations for Testing, Managing, and Treating Hepatitis C

- www.hcvguidelines.org
- First published on January 29, 2014
- Updated several times since
Drug-Drug Interaction Evaluation

HEP Drug Interaction Checker

Access our comprehensive, user-friendly, free drug interaction charts. Providing clinically useful, reliable, up-to-date, evidence-based information

Start Now
HCV Treatment Evolution

<table>
<thead>
<tr>
<th>Suffix</th>
<th>Medication Class</th>
<th>Example Medications</th>
</tr>
</thead>
</table>
| -previr | NS3/4A Protease Inhibitors (PIs) | • simeprevir  
• paritaprevir  
• grazoprevir  
• voxilaprevir  
• glecaprevir |
| -asvir | NS5A Replication Complex Inhibitors | • ledipasvir  
• ombitasvir  
• daclatasvir  
• elbasvir  
• pibrentasvir |
| -buvir | NS5B Inhibitors | • sofosbuvir  
• dasabuvir |
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<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Genotype (GT)</td>
<td>1</td>
<td>1, 4 – 6</td>
<td>1</td>
<td>1 – 3</td>
<td>1, 4</td>
<td>1 – 6</td>
<td>1 – 6</td>
<td>1 – 6</td>
</tr>
<tr>
<td>Length of Therapy: GT1, naïve, non-cirrhotic</td>
<td>12 weeks</td>
<td>8 – 12 weeks</td>
<td>12 weeks</td>
<td>12 weeks</td>
<td>12 – 16 weeks</td>
<td>12 weeks</td>
<td>12 weeks</td>
<td>8 weeks</td>
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<td>----------------</td>
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</tr>
<tr>
<td>Use in CKD, ESRD?</td>
<td>≥ 30 mL/min</td>
<td>≥ 30 mL/min</td>
<td>Used in dialysis</td>
<td>≥ 30 mL/min</td>
<td>Safe in dialysis</td>
<td>≥ 30 mL/min</td>
<td>≥ 30 mL/min</td>
<td>Safe in dialysis</td>
</tr>
<tr>
<td>Safety in cirrhosis CTP B, C</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
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</tbody>
</table>
# HCV Treatment Comparison

<table>
<thead>
<tr>
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</thead>
<tbody>
<tr>
<td><strong>Pill Burden</strong></td>
<td>2</td>
<td>1</td>
<td>3</td>
<td>2</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td><strong>Administration</strong></td>
<td>With food</td>
<td>+/- food</td>
<td>With food</td>
<td>+/- food</td>
<td>+/- food</td>
<td>+/- food</td>
<td>With food</td>
<td>With food</td>
</tr>
<tr>
<td><strong>ADRs</strong></td>
<td>Fatigue, HA, rash, photosensitivity, pruritus, nausea</td>
<td>Fatigue, HA</td>
<td>Nausea, pruritus, insomnia</td>
<td>Fatigue, HA</td>
<td>Fatigue, HA, nausea</td>
<td>Fatigue, HA</td>
<td>Fatigue, HA, nausea, diarrhea</td>
<td>Fatigue, HA</td>
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</tbody>
</table>
# HCV Treatment Comparison

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<tr>
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</thead>
<tbody>
<tr>
<td>Used</td>
<td>Used less after 2014</td>
<td>Highest used in 2015</td>
<td>DDIs limit use</td>
<td>Less use due to cost</td>
<td>1st approval for use in dialysis</td>
<td>1st pan-genotypic regimen</td>
<td>NS5A or NS3 failures (not both)</td>
<td>NS5A or NS3 failures (not both)</td>
</tr>
<tr>
<td>Role</td>
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<td>1st approval for use in dialysis</td>
<td>1st pan-genotypic regimen</td>
<td>NS5A or NS3 failures (not both)</td>
<td>NS5A or NS3 failures (not both)</td>
</tr>
<tr>
<td>Copyays</td>
<td>$$$$$ - 2 copays</td>
<td>$$ - 1 copay</td>
<td>$$ - 1 copay</td>
<td>$$$$$ - 2 copays</td>
<td>$ - 1 copay</td>
<td>$$ - 1 copay</td>
<td>$$ - 1 copay</td>
<td>$ - 1 copay</td>
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</tbody>
</table>
# HCV Treatment Comparison

<table>
<thead>
<tr>
<th>DDIs</th>
<th>SMV + SOF 2013</th>
<th>LDV / SOF 2014</th>
<th>PrOD 2014</th>
<th>DCV + SOF 2015</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>DDIs</strong></td>
<td>SMV: CYP 3A4 inhibitor, inducer, mild inhibitor of CYP 1A2, inhibitor P-gp, and OATP1B1/3 SOF: P-gp and BCRP substrates</td>
<td>LDV: Requires acidic environment for absorption; discuss antacid/H₂RA/PPI use SOF: P-gp and BCRP substrates</td>
<td>All: P-gp substrates; Paritaprevir: CYP 3A4 inhibitor, inducer; ritonavir: CYP 3A4, 2D6 substrate; Dasabuvir: CYP 2C8, 3A substrates; Ombitasvir: metab hydrolysis, oxidative</td>
<td>DCV: P-gp substrate and inhibitor; CYP 3A4 substrate (*decrease dose to 30 mg daily with strong inhibitors, increase dose to 90 mg daily with moderate inducers) SOF: P-gp and BCRP substrates</td>
</tr>
</tbody>
</table>

**Genetic Testing**

- Not for use in GT 1a with Q80K polymorphism
# HCV Treatment Comparison

<table>
<thead>
<tr>
<th>DDIs</th>
<th>EBR / GZR 2016</th>
<th>SOF / VEL 2016</th>
<th>SOF / VEL / VOX 2017</th>
<th>G/P 2017</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>EBR/GZR 2016</strong></td>
<td><strong>EBR:</strong> CYP 3A4 and P-gp substrate</td>
<td><strong>SOF/VEL:</strong> P-gp and BCRP substrates</td>
<td><strong>SOF/VEL/VOX:</strong> P-gp and BCRP substrates</td>
<td><strong>G/P:</strong> P-gp, BCRP, OATP1B1/3 inhibitors; weak inhibitors of CYP3A4, CYP1A2, and UGT1A1</td>
</tr>
<tr>
<td><strong>GRZ:</strong> Weak CYP 3A4 inhibitor, CYP 3A4, and P-gp substrate</td>
<td><strong>VEL:</strong> Requires acidic GI for absorption; discuss antacids/H₂RA/PPI use; inhibitor of P-gp and OATP181/3 (weak), BCRP (mod); substrate of OATP181/3; metab’d by CYP3A4, CYP2B6, CYP2C8</td>
<td><strong>VEL:</strong> discuss antacid/H₂RA/PPI use; see SOF/VEL for additional info</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>G/P 2017</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Genetic Testing</strong></td>
<td><strong>If GT1a – must check baseline NS5A resistance</strong></td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>
The Center of HCV Treatment

Providers

Pharmacists

Patients

Pharmacies
Sample Ambulatory Care Clinic Staff

HCV Treatment

- Physicians
- Physician Assistants
- Nurse Practitioners
- Nurses
- Social Workers
- Fellows / Residents / Students
- Medical Assistants
- Clinical Pharmacists
- Receptionists
Ambulatory Care
HCV Management Pearls

- Recommend screening, team involvement
- Aid in medication selection
  - Use guidance to confirm/select regimen
- Drug-drug interaction (DDI) screening and management
- Liaison for medication assistance programs

- Pt management
  - Clinic visits
  - Provide education – adverse drug reactions (ADRs), dosing, adherence, lifestyle changes
  - Monitor labs
Case Study 1

• DS is a 59-year-old African American woman with HCV GT 1b, stage F3. She is treatment-naïve and her HCV RNA is 799,715 IU/mL.
  – **PMH:** HCV, COPD, peripheral neuropathy, Non-Hodgkin’s Lymphoma; Laryngopharyngeal reflux
  – **SH:** Denies etoh, tob, illicits
  – **Labs:** tbili: 1.2; Alk Phos: 94; AST: 39; ALT 22; Albumin: 4; Hgb 15.3g/dL; PLT: 158; INR: 1.1; Scr: 0.56; CrCl 97.3 mL/min; Tox screen negative
  – Hep A IgG positive; Hep B surf Ag negative, Hep B surf Ab negative, Hep B core Ab total negative
  – **Vitals:** Wt: 79.3 kg; Ht: 68”, BMI 26.81
Case Study 1 (Continued)

- Stage F3 African American woman
  - HCV GT 1b
  - Treatment-naïve
  - HCV RNA 799,715 IU/mL
- All: None
- Insurance: Blue Cross Medicaid Managed Care

Medications:
- Albuterol HFA – 2 puffs every 4 hours as needed
- Fluticasone 44mcg HFA – 2 puffs every 12 hours
- Ranitidine 150mg twice daily
- Gabapentin 600mg three times daily
Case Study 1 (Continued)

Question 1: What potential struggles do you anticipate with obtaining treatment approval?

Question 2: What treatment regimen(s) is(are) appropriate for her?

Question 3: Any drug-drug interactions (DDIs) to manage?

Question 4: What is (are) the shortest HCV treatment regimen(s) available for this patient?

Question 5: What is the least expensive HCV treatment regimen available for this patient?
CT is a 62-year-old cirrhotic man (Child Pugh Class A) with HCV GT 1a. He relapsed after 12-weeks of treatment with ledipasvir/sofosbuvir in 2015. His HCV RNA is 7,956,694 IU/mL.

- **PMH:** HCV, HTN, T2DM, HL
- **SH:** Denies etoh, tob. Smokes marijuana 3x/week
- **Labs:** tbili: 0.4; Alk Phos: 116; AST: 70; ALT 93; Albumin: 3.7; Hgb 13g/dL; PLT: 270; INR: 1; Scr: 1.08; CrCl 36.3mL/min; NS5A Resistance: No mutations; Fibrosure (2016): F4
- **Hep A IgG positive; Hep B surf Ag negative, Hep B surf Ab positive, Hep B core Ab total positive**
- **Vitals:** Wt: 52.27 kg; Ht: 59”, BMI 23.29
Case Study 2 (Continued)

- Compensated cirrhotic man
  - HCV GT 1a
  - Treatment-experienced with NS5A
  - HCV RNA is 7,956,694 IU/mL
- ALL: penicillin (hives)
- Insurance:
  - State Medicaid

- Medications:
  - Amlodipine 10mg daily
  - Aspirin 81mg daily
  - Furosemide 40mg daily
  - Insulin glargine 22 units daily
  - Insulin lispro 10-15 units TID AC
  - Losartan 10mg daily
  - Metoprolol succinate 200mg daily
  - Simvastatin 20mg daily
Case Study 2 (Continued)

Question 1: What potential struggles do you anticipate with obtaining treatment approval?

Question 2: What treatment regimen(s) is(are) appropriate for him?

Question 3: Any drug-drug interactions (DDIs) to manage?

Question 4: If this patient had decompensated cirrhosis, what treatment regimen(s) is(are) appropriate for him?
Management of HCV Infection in the Inpatient Setting

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Professor of Pharmacy Practice
Massachusetts College of Pharmacy and Health Sciences (MCPHS) University
Worcester, Massachusetts
Optimizing Outcomes for Inpatients Receiving Treatment for HCV Infection

• Case study
• Overview
• Unique medication safety concerns
• Ideas for error prevention
Case Study 3

• JS is a 40 year old man with NKDA who presents to the Emergency Department (ED) complaining of a red, swollen left lower extremity and fever. He notes that 3 days ago, he fell forward on cement stairs and cut his leg, and that redness and warmth began to creep up his shin over the past day.
  – PMH:
    • HTN
    • Genotype 1a HCV infection, treatment-naïve, non-cirrhotic
      – Initiated treatment 2 weeks ago with ledipasvir/sofosbuvir
      – Plan is for 12 weeks of treatment
  • The admitting resident diagnoses JS with cellulitis, and decides he will be admitted to the general medical floor for IV antibiotics.
Case Study 3 (Continued)

• JS is admitted to the floor
  – Initial labwork shows normal renal and hepatic function
    • The resident orders an HCV RNA (viral load)
      – Results pending
  – The following orders are entered and verified:
    • Vancomycin 1250 mg IV Q12H
    • Hydrochlorothiazide 25 mg PO daily
    • Pantoprazole 40 mg PO daily
    • Patient’s own medication (ledipasvir/sofosbuvir, Harvoni®) once daily
    • Acetaminophen 1000 mg PO Q6H PRN headache
Discussion Questions

• How would you have performed medication reconciliation?
• Are there medication errors occurring here?
  – Underlying reasons for errors?
• How could these errors be prevented?
Medication Safety Concerns for Inpatients Taking HCV Pharmacotherapy

• Potential for treatment interruptions
  – At transitions of care
    • Admission to hospital
      – Documentation
      – Communication issues
      – Medication access
    • Discharge to home or rehabilitation facility
      – Lost medications
      – Communication issues
  – Why are interruptions problematic?
Medication Safety Concerns for Inpatients Taking HCV Pharmacotherapy

• Documentation as “Patient’s Own Med” in medication administration record (MAR)
  – Lack of automated drug interactions assessment
    • Missed drug interactions
  – Brand name or acronym use
    • Consistency
    • Confusion
  – Separate handling of the medication
    • Storage
    • Access
Medication Safety Concerns for Inpatients Taking HCV Pharmacotherapy

Drug interactions with inpatient medications

- Proton pump inhibitor (PPI)/H2-receptor antagonist/antacid issues
  - Ledipasvir/sofosbuvir
  - Sofosbuvir/velpatasvir
  - Sofosbuvir/velpatasvir/voxilaprevir
- Cytochrome P450 issues
  - Regimens containing protease inhibitors

- Enzyme/transporter induction
  - Antiepileptic drugs
  - Rifampin
- Antiarrhythmic medications issues
  - Amiodarone, digoxin
  - Sofosbuvir-containing regimens
- Autosubstitutions
  - Statins
  - PPIs
Medication Safety Concerns for Inpatients Taking HCV Pharmacotherapy

• Lack of familiarity with HCV medications
  – Regimens and durations used, drug interactions, patient counseling points
    • Potential for omission of ribavirin
  – Lack of knowledge varies among
    • Medical residents
    • Hospitalists
    • Nurses
    • Pharmacists
  – Look alike/sound alike names/acronyms
    • An issue with order entry, progress notes, discharge summaries
Ideas for Prevention of Medication Errors for Inpatients

• Education
  – Empowering patients
  – Interdisciplinary inservicing
• Pocket guides and wall charts
• Provision of electronic resources that are easy to access
• Order entry options
  – Customized order entry sets
  – Restricted prescribing
  – Entry of drug names from library rather than “patient’s own med”
  – Clinical pharmacist review
Case Study 3, Epilogue

• After 4 days in the hospital, JS is discharged home with orders to return to the infusion center daily for IV antibiotics.
  – How can the pharmacist assist with this transition of care?
  – What patient counseling points should be made?

• How can we apply lessons learned during JS’s hospitalization to improve care for our inpatients with HCV infection?
Challenges in HCV Treatment

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Associate Professor of Pharmacy- Clinician Educator
Assistant Director Hepatitis C Programs- Project ECHO
University of New Mexico Health Sciences Center
Albuquerque, New Mexico
Remaining Challenges in HCV Therapy

- HCV treatment in patients with decompensated cirrhosis
- Treatment interruptions
- HCV resistance
- Access to HCV therapy
Case Study 4: A 54 yo woman who previously failed HCV treatment with ledipasvir/sofosbuvir.

- Her past medical history is significant for cirrhosis, CTP Class A.
- What therapeutic options exist for retreatment?
Glecaprevir/Pibrentasvir: Indications and Duration of Therapy

<table>
<thead>
<tr>
<th>HCV Genotype</th>
<th>Prior Treatment Experience</th>
<th>Without Cirrhosis</th>
<th>With Compensated Cirrhosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>1,2,3,4,5,6</td>
<td>Naïve</td>
<td>8 weeks</td>
<td>12 weeks</td>
</tr>
<tr>
<td>1,2,4,5,6</td>
<td>Pegylated interferon, ribavirin and/or sofosbuvir</td>
<td>8 weeks</td>
<td>12 weeks</td>
</tr>
<tr>
<td>3</td>
<td>Pegylated interferon, ribavirin and/or sofosbuvir</td>
<td>16 weeks</td>
<td>16 weeks</td>
</tr>
<tr>
<td>1</td>
<td>NS3/4A (NS5A naïve)</td>
<td>12 weeks</td>
<td>12 weeks</td>
</tr>
<tr>
<td></td>
<td>NS5A (NS3/4A naïve)</td>
<td>16 weeks</td>
<td>16 weeks</td>
</tr>
</tbody>
</table>
Studies Evaluating the Efficacy of Mavyret in Patients with HCV GT1, 2, 4-6 Infection with or without Compensated Cirrhosis

Mavyret for 8 Weeks in TN/TE NC Patients: ENDURANCE-1 and SURVEYOR-2

- SVR12 (%): 98, 99, 98, 93, 100, 100
- N: 596, 348, 193, 43, 2, 10

Mavyret for 12 Weeks in TN/TE CC Patients: EXPEDITION-1

- SVR12 (%): 99, 99, 100, 100, 100, 100
- N: 145, 146, 89, 31, 16, 2, 7

Summary

- Overall Relapse: 1, 2
- Overall Non-VF*: 7, 2

All analyses are using the ITT population.

TN, treatment-naive; TE, treatment-experienced with IFN or pegIFN ± RBV, or SOF + RBV ± pegIFN; NC, non-cirrhotic; CC, compensated cirrhotic; ITT, intent-to-treat; BT, breakthrough; VF, virologic failure.

*Includes patients who discontinued due to adverse events, lost to follow-up, or withdrew.

Efficacy of Mavyret in GT1 Patients who have Previously Failed an NS3/4A PI or NS5A Inhibitor Containing DAA Regimen

Mavyret for 12 or 16 Weeks in GT1 Patients with Prior NS3/4A PI or NS5A Inhibitor Failure: MAGELLAN-1

G/P is not indicated for patients experienced to both NS5A inhibitors and NS3/4A PIs

All analyses are using the ITT population.
BT, breakthrough; PI, protease inhibitor; VF, virologic failure.
*Regimens containing simeprevir and sofosbuvir or simeprevir, boceprevir, or telaprevir with interferon or pegylated interferon and ribavirin.
†Regimens containing ledipasvir and sofosbuvir or daclatasvir with pegylated interferon and ribavirin.
#Includes patients who discontinued due to adverse events, lost to follow-up, or withdrew.

Sofosbuvir/Velpatasvir/Voxilaprevir Indications: DAA Treatment Experienced Patients

- Patients with genotype 1, 2, 3, 4, 5, or 6 who were previously treated with an NS5A inhibitor

- Patients with genotype 1a or 3 infection previously treated without an NS5A inhibitor
  - No advantage of using sofosbuvir/velpatasvir/voxilaprevir over sofosbuvir/velpatasvir for retreatment of patients with GT 1b, 2, 4, 5, or 6
POLARIS-1: SOF/VEL/VOX for 12 Weeks in NS5A Inhibitor-Experienced HCV GT 1–6

**SVR12 Results Overall and by Cirrhosis Status**

**Overall***
- 253/263
- 6 relapses
- 1 on-treatment failure**
- 2 withdrew consent
- 1 LTFU

**No Cirrhosis**
- 140/142
- 1 withdrew consent
- 1 LTFU

**Cirrhosis**
- 113/121
- 6 relapses
- 1 on-treatment failure**
- 1 withdrew consent

*p <0.001 for superiority compared with prespecified 85% performance goal for SOF/VEL/VOX

** Exposure was consistent with non-adherence**
SVR12 by Genotype and Cirrhosis Status

POLARIS-1: SOF/VEL/VOX for 12 Weeks in NS5A Inhibitor-Experienced HCV GT 1–6

*1/1 patient with GT unknown achieved SVR12; †4/4 patients with GT 1 other (cirrhosis, n=2; no cirrhosis, n=2) achieved SVR12; ‡Includes only GT 4 patients.

Data on file, Gilead Sciences
Case Study 5: 47 yo female with HCV GT3. She previously failed daclatasvir plus sofosbuvir. What are her treatment options?

- Currently on lactulose for encephalopathy and spironolactone and furosemide for ascites
- Laboratories: albumin 3.4 mg/dL, bilirubin 1.6 mg/dL, and INR of 1.11
Case Study 6: Which of the following is an effective approach to minimize the costs of HCV therapy?

A. Reauthorization of the therapy at week 4
B. Require HCV RNA viral load at week 4 prior to sending refill
C. Limit refills to 14 days to document adherence
D. None of the above
What’s the Big Deal?

• Interruptions in HCV therapy can lead to HCV resistance
• The development of resistance can compromise current treatment AND future attempts at retreatment
• Treatment interruptions compromise HCV therapy!
AASLD Guidelines Regarding HCV RNA Monitoring

“The significance of a positive HCV RNA test result at week 4 that remains positive, but lower, at week 6 or week 8 is unknown. No recommendation to stop therapy or extend therapy can be provided at this time”
## HCV Therapies

<table>
<thead>
<tr>
<th>HCV Class</th>
<th>Therapies</th>
</tr>
</thead>
<tbody>
<tr>
<td>NS3/4A inhibitors</td>
<td>Simeprevir, Paritaprevir, Grazoprevir, Voxilaprevir, Glecaprevir</td>
</tr>
<tr>
<td>NS5A inhibitors</td>
<td>Ledipasvir, Elbasvir, Ombitasvir, Velpatasvir, Pibrentasvir, Ruzasvir*</td>
</tr>
<tr>
<td>NS5B inhibitors</td>
<td>Sofosbuvir, Dasabuvir, Uprifosbuvir*</td>
</tr>
</tbody>
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*Investigational agents*
The Project ECHO (Extension for Community Healthcare Outcomes) Model

Moving Knowledge Instead of Patients
Hepatitis C in New Mexico (2004)

- More than 35,000 reported HCV cases
- Less than 5% had been treated
- Only one academic health center treated HCV
- Highest rate of cirrhosis deaths in the nation
Methods

• Use technology to leverage scarce healthcare resources (specialty knowledge and expertise)
  – Train physicians, nurses, pharmacists, and their teams in HCV care

• Share best practices- reduce variation in care
  – Conduct teleECHO clinics- “Knowledge Network”

• Case based learning (learning by doing)
  – Initiate case-based guided practice- “Learning Loops”

• Centralized database to monitor outcomes
  – Collect data and monitor outcomes centrally
Learning Loops

- Interactive Learning Environment
- Co-management of Cases
- Learning by doing
- Learning from didactics
- Learning from each other
- Collaborative Problem Solving
- ACPE continuing education credits for pharmacists
ECHO vs. Telemedicine

ECHO Supports Community Based Primary Care Teams

Patients reached with specialty knowledge & expertise

Traditional Telemedicine

Specialist Manages Patient Remotely
ECHO and Indian Health Services

- >70 sessions
- >130 new patient cases
- Predominantly pharmacists managing HCV patients
<table>
<thead>
<tr>
<th>Ambulatory Care</th>
<th>Inpatient</th>
<th>Community/Specialty</th>
</tr>
</thead>
<tbody>
<tr>
<td>Screening and referrals</td>
<td>Screening + linkage to care</td>
<td>Screening + linkage to care</td>
</tr>
<tr>
<td>Medication selection</td>
<td>Prevent interruption of treatment</td>
<td>Verify medication selection and length of treatment</td>
</tr>
<tr>
<td>DDI screening, management</td>
<td>DDI screening, management</td>
<td>DDI screening, management</td>
</tr>
<tr>
<td>Education</td>
<td>Education – adherence, administration, ADRs</td>
<td>Education – adherence, administration, ADRs</td>
</tr>
<tr>
<td>Liaison with pharmacy and assistance programs</td>
<td>Liaison with clinic</td>
<td>Liaison with clinic and assistance programs</td>
</tr>
<tr>
<td>Labs and follow-up</td>
<td>Labs</td>
<td>Refill management</td>
</tr>
</tbody>
</table>

Which resource offers guidance for HCV treatment selection?

A. https://www.clinicaloptions.com/Hepatitis.aspx
B. http://www.hep-druginteractions.org/checker
C. http://www.hcvguidelines.org/
D. http://www.hepatitisc.uw.edu/
Which of the following pieces of information is (are) necessary when selecting appropriate HCV treatment for a patient?

A. HCV genotype
B. HCV treatment history
C. Stage of disease (presence / absence of cirrhosis)
D. Concurrent medications
Which of the following is (are) an all-oral, pangenotypic, single tablet regimen(s) currently approved by the FDA for the treatment of adults with genotypes 1-6 chronic HCV infection?

A. Elbasvir/grazoprevir
B. Glecaprevir/pibrentasvir
C. Sofosbuvir/velpatasvir/voxilaprevir
D. Paritaprevir/ritonavir/ombitasvir/dasabuvir
Glecaprevir/pibrentasvir offers an 8-week treatment course for treatment-naïve, non-cirrhotic patients with any HCV genotype.

A. True
B. False
Key Takeaways

• Medication errors and drug interactions may occur in those patients taking HCV pharmacotherapy
  – Determining risk factors for your population will permit identification and prevention

• Maintaining current knowledge in HCV pharmacotherapy will permit optimal care of patients in all practice settings
  – Development of inservices, medication charts, pocket guides will facilitate accurate review of regimens
Q&A
## HCV Resources for Patients and Providers

**HCV Guidelines**
- American Association for the Study of Liver Diseases, Infectious Disease Society of America, and International Antiviral Society-USA: [www.hcvguidelines.org](http://www.hcvguidelines.org)

**Drug-Drug Interactions**
- University of Liverpool: [www.hep-druginteractions.org](http://www.hep-druginteractions.org)

**HCV Clinical Information**
- Clinical Care Options: [www.clinicaloptions.com/Hepatitis.aspx](http://www.clinicaloptions.com/Hepatitis.aspx)
- National AIDS Treatment Advocacy Project: [www.natap.org](http://www.natap.org)
- ViralEd: [www.viraled.com](http://www.viraled.com)

**Online Courses / Certificate Programs**
- University of Washington: [http://hepatitisc.uw.edu](http://hepatitisc.uw.edu)

**Free Online Hepatitis Textbook**

**Patient Support Groups**
- American Liver Foundation: [www.liverfoundation.org/support](http://www.liverfoundation.org/support)
- HCV Advocate: [http://hcvadvocate.org/resources/support-groups](http://hcvadvocate.org/resources/support-groups)
- HCV Support: [www.hcvsupport.org](http://www.hcvsupport.org)