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Gastroenterology & Hepatology
Advanced Practice Providers

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Current Hep C Treatment Landscape

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Disclosures

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Disclosures

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No financial relationships to disclose.

Objectives

- Discuss the current hepatitis C landscape: screening, diagnosis, evaluation, treatment and follow-up
- Utilize case studies to highlight key factors in HCV treatment



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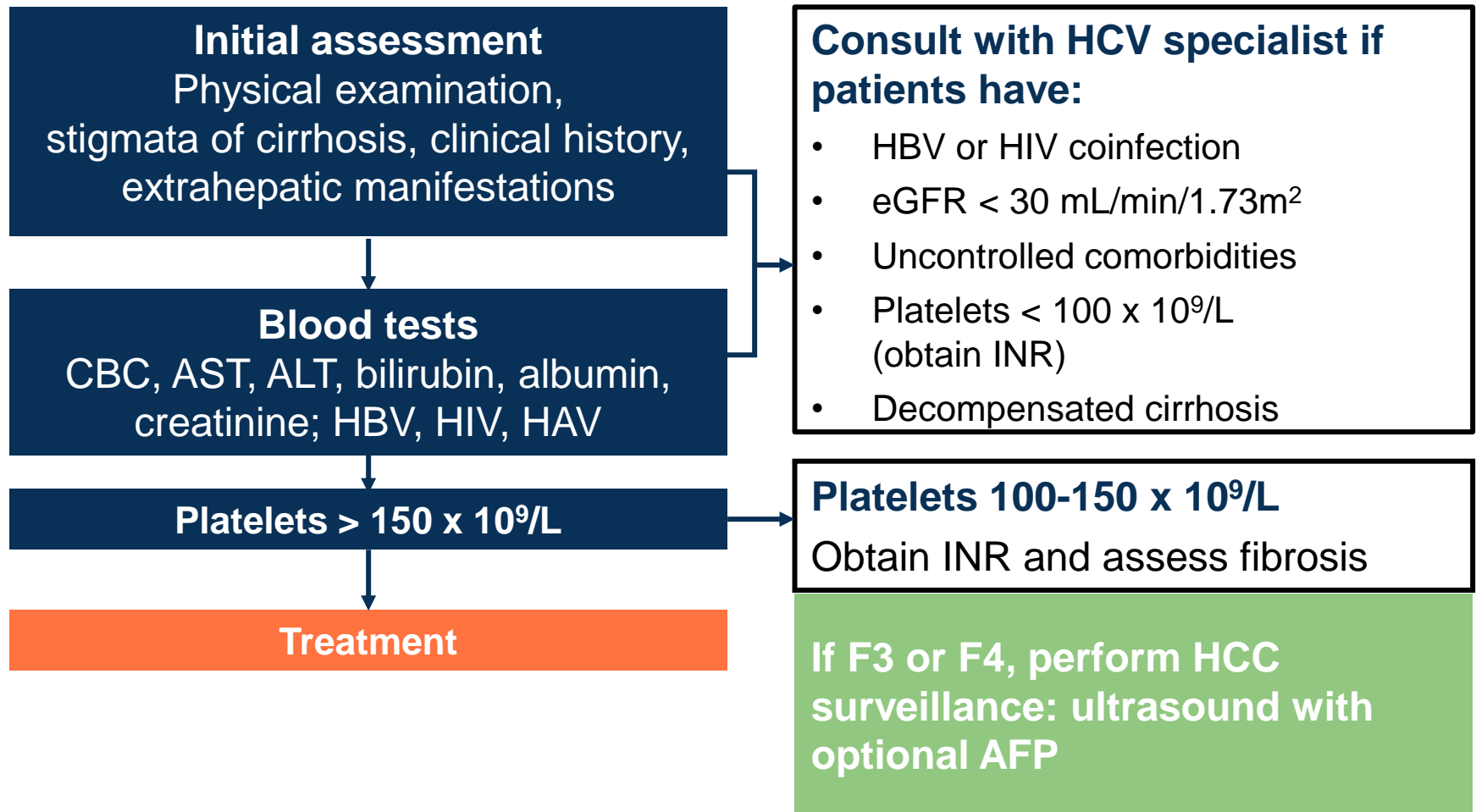
HCV Treatment in Individuals With Cirrhosis

Case Study #1

A 56-year-old male is referred to you after testing HCV Ab+ when screened by his PCP

- **What history and physical assessment would you do at this point?**
- **What tests would you order as part of his evaluation?**

Simplified Algorithm for HCV Pretreatment Assessment



Case Study #1: Results of Tests/Labs

- He has a history of heavy ETOH use for 35 years
- HCV viral load = 5,600,000 copies/ml with Genotype 1a
- Platelets = 78
- AST/ALT = 120/75
- FIB 4 = 3.75 (indicative of cirrhosis)
- Physical Assessment: palmar erythema, few spiders, no ascites
 - **Is any further workup necessary?**
 - **What is the diagnosis?**

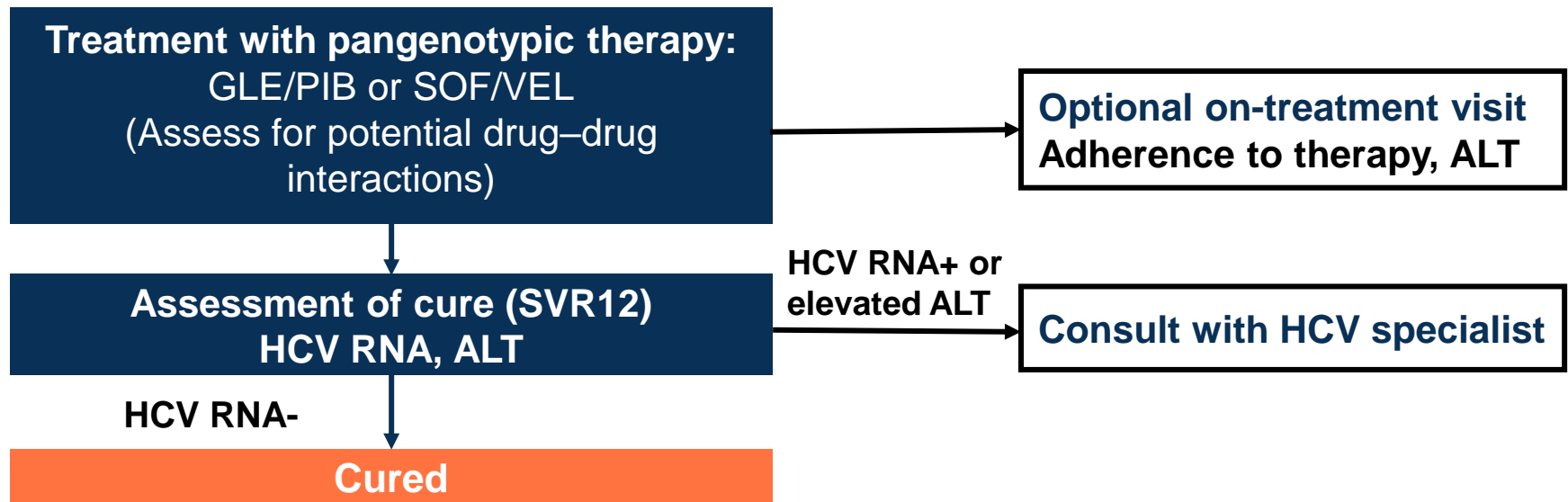
Case Study #1: Further Test Results

- Abdominal Ultrasound = No ascites, no liver lesions
- AFP = 7.8
- EGD = Signs of portal HTN with trace EV
- MELD score = 18

Case Study #1: Diagnosis

- Chronic HCV infection
- Naïve to HCV treatment
- Compensated cirrhosis
 - **What management options are available for this patient?**
 - **Medication considerations?**
 - **Any referrals at this point?**

Simplified Algorithm for HCV Treatment and Monitoring



Case Study #1: Patient Follow-Up

- He completes an 8-week course of GLE/PEB with EOT HCV PCR negative
 - **What is his short-term plan?**
 - **Additional labs, procedures, clinic visits**
 - **Do you continue to follow him?**
 - **Would you consider release back to PCP? If so, when and why?**
 - **Long-term plan?**
 - **What would indicate evidence of liver decompensation?**
 - **If he had signs of decompensated cirrhosis when referred to you, how would that change your treatment plan and decisions?**

Case Study #1: Patient Follow-Up

- He is referred to a liver transplant center for evaluation
- He continues to seek treatment for ETOH abuse and maintains sobriety in follow-up
- HCV PCR is negative 12 weeks post HCV treatment (SVR)



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HCV Treatment in Persons Who Inject Drugs (PWID)

Case Study #2

- 48-year-old Caucasian male with diagnosis of HCV complains of fatigue and joint pain
- Several years ago was diagnosed with HCV G2b with mild disease (stage 1-2 by Fibroscan[®])
- Was treated Sofosbuvir and Ribavirin for 12 weeks
- His HCV viral load was negative EOT with ALT of 23
- Office made multiple attempts to reach pt for WK 12 post treatment labs and f/u
 - **Which tests/labs should be offered?**

Case Study #2: Results of Tests/Labs

- HCV PCR = 16,290,000 copies/ml with Genotype 2b
- Fibroscan[®] = F4 or cirrhosis (kPA >12.5)
- Hgb = 12.1
- PLT = 110
- TB = 1.2
- AST/ALT = 132/157
 - **What is your differential diagnosis?**
 - **Is any further workup necessary?**
 - **What is the diagnosis?**

Case Study #2: Diagnosis

- A relapse of HCV vs. reinfection vs. acute HCV
- He reveals to you that he returned to injection drug use and never made it back for his post HCV treatment Week 12 SVR labs
- His abdominal ultrasound shows small nodular liver but no liver lesions
- EGD shows no EV or signs of portal HTN
 - **What management options are available for this patient?**

Case Study #2: Treatment Options

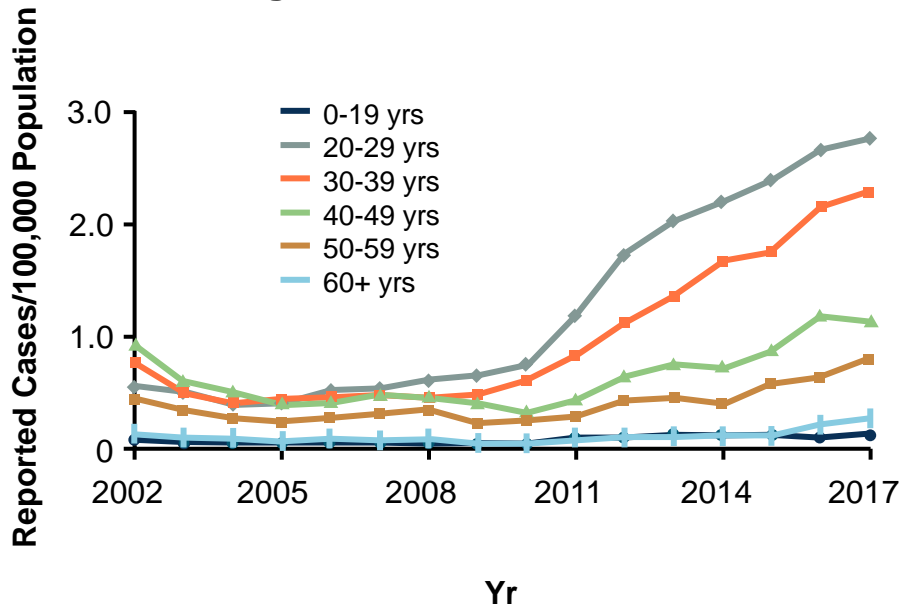
- Sofosbuvir 400mg and Velpatasvir 100mg for 12 weeks
- Glecaprevir 300mg and Pibrentasvir 120 mg for 12 weeks
- Alternative: Sofosbuvir with Velpatasvir with Voxilaprevir for 12 weeks
 - **What are the options to consider?**
 - **What are the factors that influence your treatment decisions?**

Case Study #2: Treatment Management

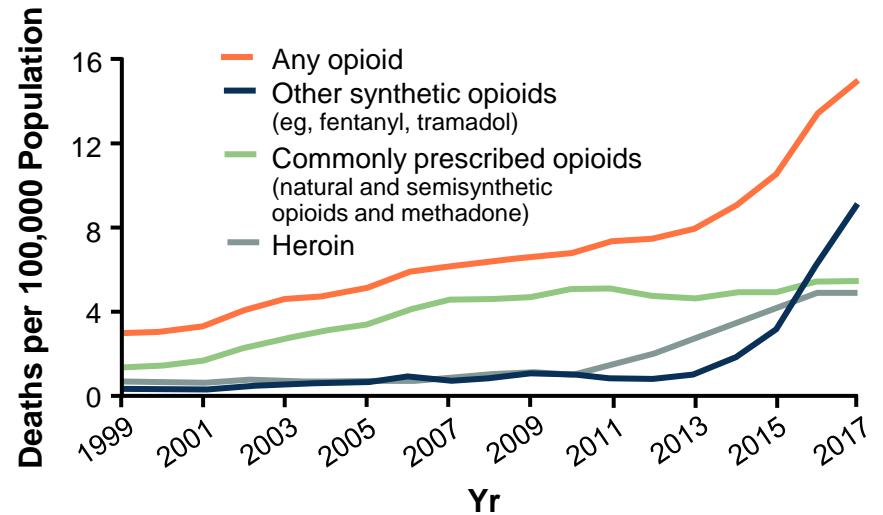
- How often would you follow this patient while on treatment?
- What labs or other tests would you order?
- Any referrals to consider?
- Would he be eligible for the simplified HCV treatment algorithm?

Twin Epidemics of HCV and Injection Drug Use

Rising Rates of Incident HCV^[1]



Rising Rates of Overdose Death^[2]



Slide credit: clinicaloptions.com.

1. CDC. Viral Hepatitis Surveillance. 2017; 2. CDC. Opioid Data Analysis and Resources.

People Who Inject Drugs (PWID)

- Increased HCV incidence in PWID
- Major cause of acute HCV infections
- Need for comprehensive care
 - HCV treatment with linkage to care
 - Need more frequent screening
 - Substance abuse treatment
 - Example: C-Change Philadelphia study (www.hepcap.org)

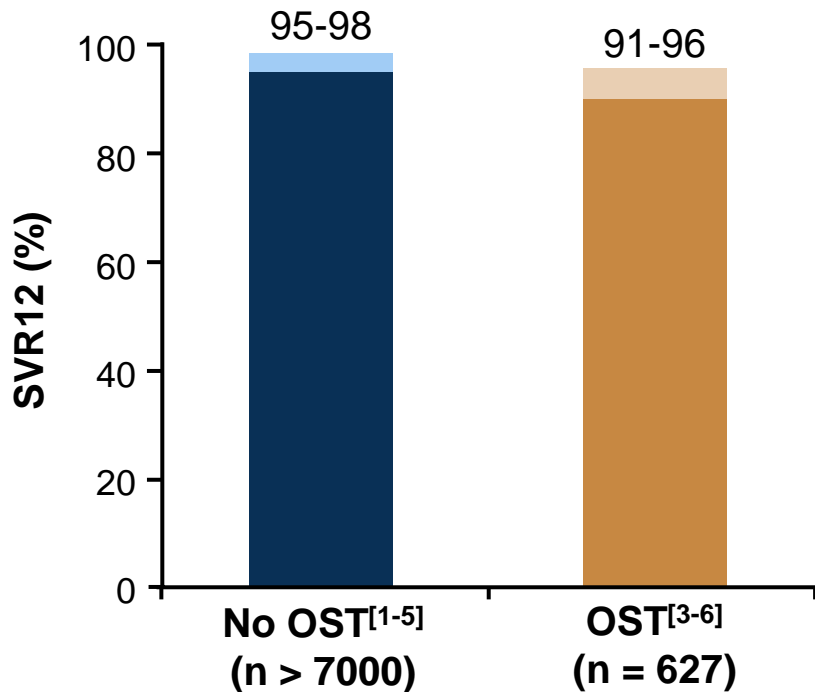
Antiviral Therapy Guidelines in PWID

AASLD/IDSA
Recent/active IDU
should *not* be seen
as contraindication
to HCV therapy¹



EASL
Treatment should
be prioritized in those
at risk of transmitting
HCV *including*
active PWUD²

Treating HCV Infection: SVR Rates High Among PWID, Even With Ongoing IDU



SVR12 rates > 90% among patients with current/recent IDU

- 90.4% in C-EDGE CO-STAR (n = 136)^[7]
- 94% in SIMPLIFY (n = 102)^[8]
 - Did not vary by adherence (90% cut off)
- 98% in pooled analysis from 6 phase III trials (mITT; n = 63)^[9]



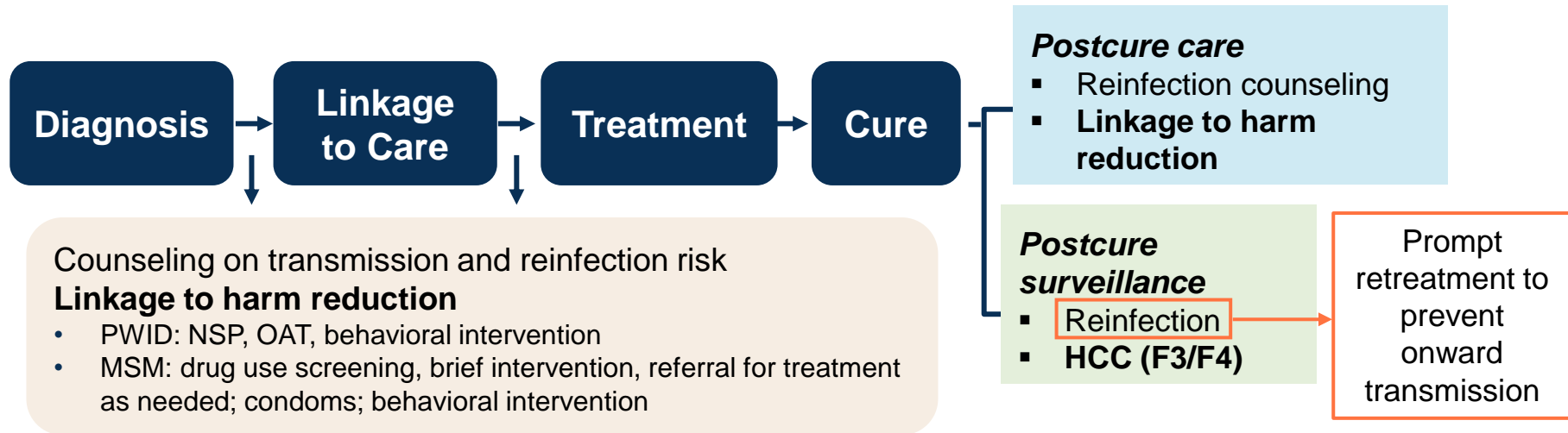
Slide credit: clinicaloptions.com.

1. Zeuzem. *Ann Intern Med*. 2015;163:1; 2. Feld. *NEJM*. 2014;370:1594; 3. Grebely. EASL 2017. Abstr FRI-236; 4. Grebely. *CID*. 2016;63:1405. 5. Grebely. *CID*. 2016;63:1479; 6. Puoti. AASLD 2014. Abstr 1938; 7. Dore. *Ann Intern Med*. 2016;165:625; 8. Grebely. EASL 2017. Abstr FRI-235; 9. Foster. AASLD 2017. Abstr 1182.

Addressing the Challenge of HCV Reinfection

- Reinfection should be viewed as a sign of engagement with populations at highest risk of sustaining the HCV epidemic
 - AASLD/IDSA guidelines recommend annual HCV RNA testing for PWID who achieve SVR^[1]
- Focus efforts to prevent, detect, and retreat reinfections

HCV Care Continuum^[2]



Case Study #2: Patient Follow-Up

- Patient Care Short-term Plan:
- He completes his 12-week regimen of sofosbuvir and velpatasvir (SOF/VEL)
- EOT HCV PCR is negative with ALT of 19
 - **When do you plan to check his HCV PCR again?**
- Patient Care Long-term Plan:
 - **Does the patient stay with you? If so, for how long?**
 - **Do you release back to PCP? If so, at what point?**



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HCV/HIV Co-infection

Case Study #3

- 65-year-old African American male with HIV, chronic Hepatitis C virus infection
- Genotype 1a
- He was first diagnosed with HCV around 2009
- He believes he may have contracted as a result of illicit drug use in the past
- Treated in April 2019 with Ledipasvir/sofosbuvir for 12 weeks
- Unfortunately had a relapse after his therapy was completed

Case Study #3

- He was then treated with Sofosbuvir with Velpatasvir with Voxilaprevir for 12 weeks, completing treatment in July 2020
- He did not achieve SVR
- HIV treatment
 - Emtricitabine / Tenofovir
 - Raltegravir



Case Study #3: Results of Tests/Labs

- FibroT-ActiTest = F2 bridging fibrosis with few septa
- Hepatitis B DNA = not detected
- GFR = 88
- Hgb = 15.3
- HCV RNA = 529,490
- AST/ALT = 29/26
 - Drug interactions to be concerned with?

Resistance

- **What labs would you order to test for resistance?**

HCV NS5a Subtype	1a
Daclatasvir Resistance	PROBABLE (A)
Ledipasvir Resistance	PROBABLE (A)
Ombitasvir Resistance	PROBABLE (A)
Elbasvir Resistance	PROBABLE (A)
Velpatasvir Resistance	PROBABLE (A)

HCV NS5b Subtype	1a
Sofosbuvir Resistance	NOT PREDICTED

Treatment Options

According to AASLD guidelines, patient should be retreated with daily fixed-dose combination of Sofosbuvir (400 mg) / Velpatasvir (100 mg) / Voxilaprevir (100 mg) plus weight-based Ribavirin for 24 weeks (1200 mg/day)

- **What are the options to consider?**
- **What are the factors that influence your treatment decisions?**
- **Drug resistance?**
- **Co-infection with HIV?**

Case Study #3: Treatment Management

- **How often would you follow this patient while on treatment?**
- **What labs or other tests would you order?**
- **Any referrals to consider?**

Case Study #3: Patient Follow-Up

- Patient Care Short-term Plan:
- He completes his 24-week regimen
- HCV viral load is negative
- ALT = 25
 - When do you plan to check his HCV PCR again?
- Patient Care Long-term Plan:
 - Does the patient stay with you? If so, for how long?
 - Do you release back to PCP? If so, at what point?

Hepatitis C by the Numbers



170 million
people worldwide

#1

blood-borne infection in US
indication for liver transplantation
cause of liver cancer in US



5.2 million
people in US



0 FDA-approved
vaccines

AASLD/IDSA HCV Screening Recommendations

Recommendations for One-Time Hepatitis C Testing ⁱ

RECOMMENDED

RATING

One-time, routine, opt out HCV testing is recommended for all individuals aged 18 years and older.

I, B

One-time HCV testing should be performed for all persons less than 18 years old with behaviors, exposures, or conditions or circumstances associated with an increased risk of HCV infection (see below).

I, B

Periodic repeat HCV testing should be offered to all persons with behaviors, exposures, or conditions or circumstances associated with an increased risk of HCV exposure (see below).

IIa, C

Annual HCV testing is recommended for all persons who inject drugs and for HIV-infected men who have unprotected sex with men.

IIa, C

World Health Organization (WHO) Goals

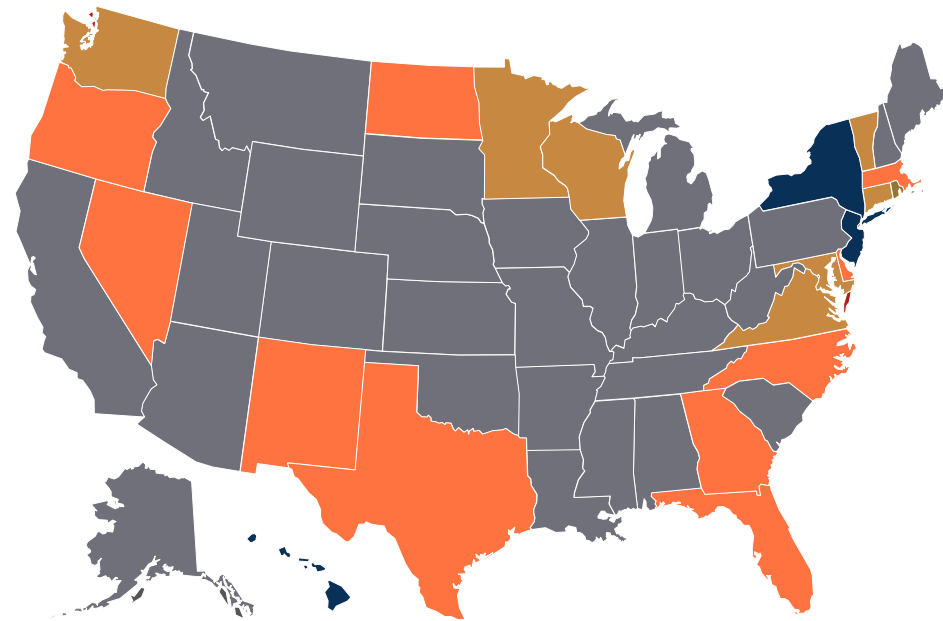
- Hepatitis C viral eradication by 2030
 - Requires screening and diagnosis
 - Increase access to treatment
 - Decrease mortality from ESLD

Effectiveness of HCV Screening in the US (2010 – 2016)

- To meet the 2030 diagnosis targets, must diagnose at least
 - 110,000 cases/year until 2020
 - 89,000 cases/year between 2020-2024
 - >70,000 cases/year between 2025-2030
- At current screening rate, 92% of US states are not on target

Timeline to Achieve WHO Screening Target for HCV Elimination

Reach WHO Target by: 2030 2040 2050 Beyond 2050



Claims data for HCV Ab screening from a single large commercial payer (CPT and ICD-9 codes): Screened (n=1,056,583); not screened (n=1,243,581).

Factors that increased the odds of getting screened: female gender, Medicare, presence of comorbidities.

Mehta D, et al. *J Hepatol.* 2018;68(suppl S1):S177. Abstract THU-113.

HCV Infection: Simplified Patient Evaluation and Treatment

Eligible Patients:

Chronic hepatitis C without cirrhosis and no previous HCV therapy

- **Assess cirrhosis (liver biopsy not required)**
 - Treat as though cirrhotic if any of the following suggest cirrhosis: FIB-4 > 3.25, platelet count < 150,000/mm³, APRI > 2.0, *FibroScan* > 12.5 kPa
- **Record medications and supplements, assess DDIs**
- **Conduct recommended baseline labs:** CBC, hepatic function panel*, eGFR, quantitative HCV RNA, HIV Ag/Ab, HBsAg, serum pregnancy test (for persons of child-bearing age)
- **Provide patient education**

Treatment Options:

GLE/PIB for 8 wks (3 pills QD, with food) or
SOF/VEL for 12 wks (1 pill QD, with or without food)



Slide credit: clinicaloptions.com.

*Hepatic function panel includes albumin, total and direct bilirubin, ALT, AST.

AASLD/IDSA HCV Guidance. 2019.

IDSA/AASLD Guidance Document Remains Current and Best Resource



HCV Guidance: Recommendations for Testing, Managing, and Treating Hepatitis C



Home

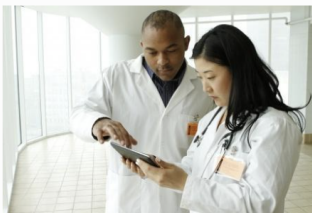
Test, Evaluate, Monitor

Treatment-Naive

Treatment-Experienced

Unique Populations

About



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Sep

What's New, Updates, and Changes to the Guidance

This version of the guidance has been updated to reflect several important developments,

Start Here: Choose a patient profile from the menu above. ↕

Welcome to HCVGuidelines.org

The AASLD and IDSA in partnership with the panel have created an updated web experience to facilitate easier and faster access to this important resource. Please select a patient profile from the menu above, click on a guidance section below, or use the search box to begin.

+ Contents and Introduction - *Select a Page*

+ Testing, Evaluation, and Monitoring of Hepatitis C - *Browse Topics*

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+ Retreatment of Persons in Whom Prior Therapy Has Failed - *Choose Patient Genotype*

+ Management of Unique Populations - *Review Recommendations*

HCV Researchers Win Nobel Prize in 2020

Congratulations for their groundbreaking work in the discovery of the Hepatitis C virus



Harvey J. Alter
National Institutes of Health

Michael Houghton
University of Alberta

Charles M. Rice
Rockefeller University



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Q&A



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Thank You