Complimentary CME

HCV Treatment in Patients With Advanced Liver Disease: Who, How, and When?

Developed in collaboration

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Med-IQ

Activity Overview

This activity provides an overview of the assessments needed before initiating direct-acting antiviral therapy, as well as an in-depth look at available methods for evaluating liver health in patients with HCV.

Target Audience

This activity is intended for primary care clinicians.

Accreditation / Designation Statements

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Paul Y. Kwo, MD

Consulting fees/advisory boards: AbbVie Inc., Gilead Sciences, Inc., Merck & Co., Inc.

The peer reviewers and activity planners have no financial relationships to disclose.

Acknowledgment of Commercial Support

This activity is supported by educational grants from AbbVie Inc. and Gilead Sciences, Inc.

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To receive credit, read the introductory CME material, listen to the audiocast, and complete the evaluation, attestation, and post-test, answering at least 70% of the post-test questions correctly

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Learning Objectives

Upon completion, participants should be able to:

- Describe treatment potential for patients with HCV and advanced liver disease

Faculty

Paul Y. Kwo, MD
Professor of Medicine
Chief of Hepatology
Stanford University
Stanford, CA

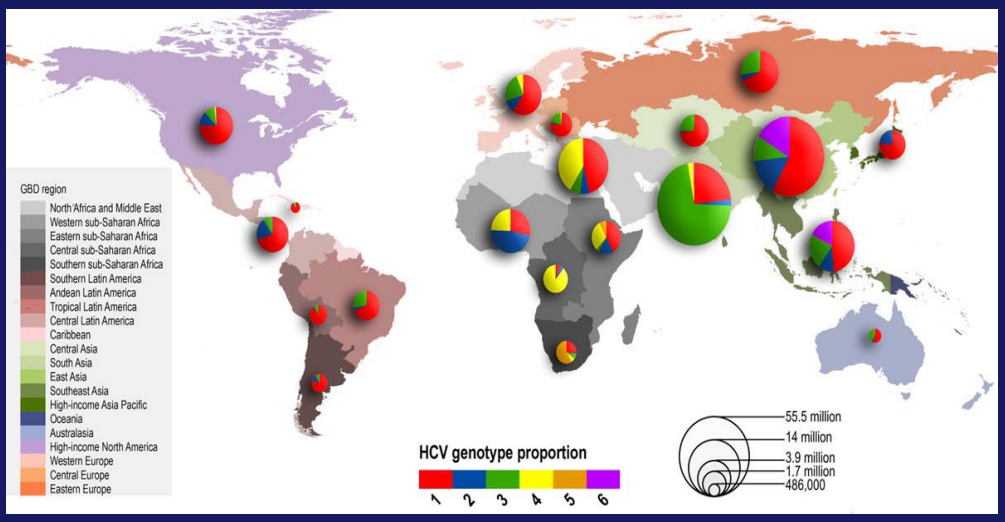
Activity Planners

Sara C. Miller, MS
Director, QI Institute, CE Strategy and Content
Med-IQ
Baltimore, MD

Jill Phillips
Compliance and Meeting Planning Specialist
Indiana University School of Medicine
Indianapolis, IN

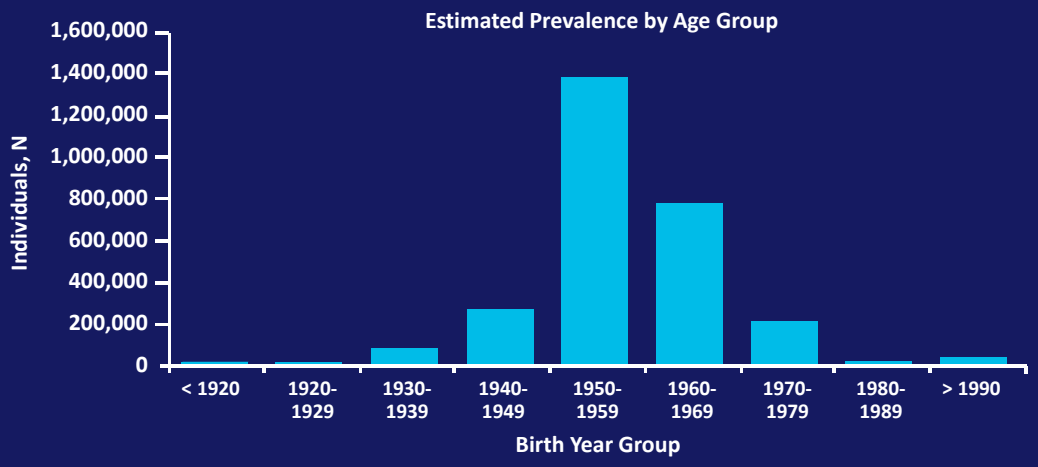
Samantha Gordon
CME Specialist
Med-IQ
Baltimore, MD

Global Distribution and Prevalence of HCV Genotypes



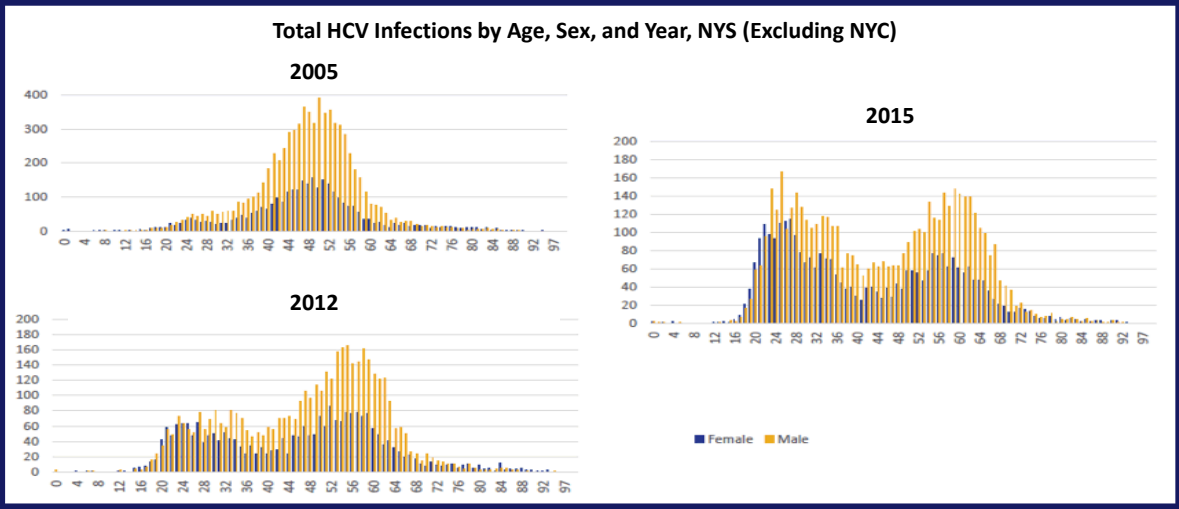
Messina JP, et al. *Hepatology*. 2015;61:77-87.

Historically, the Majority of Persons Chronically Infected With HCV Were Baby Boomers (Those Born Between 1945 and 1965)



Smith BD, et al. *MMWR Recomm Rep*. 2012;61:1-32.

In New York, HCV Is No Longer a Disease of Baby Boomers—Rates Are Higher in Those Aged 20 to 39 Years

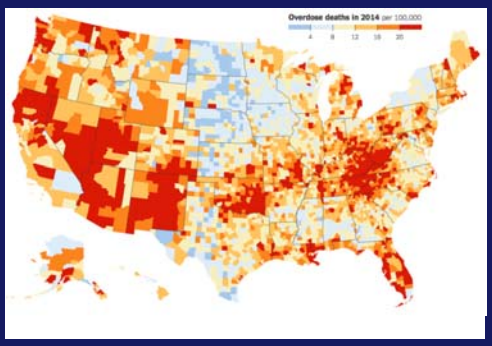


NYS DOH. health.ny.gov/statistics/diseases/communicable/index.htm.

Acute HCV Infections vs Deaths From Heroin Overdose

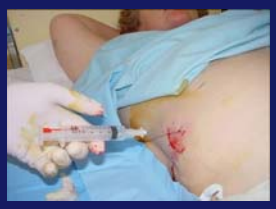
Acute HCV Infections, 2013, by State

Deaths From Heroin Overdose, 2014, by County

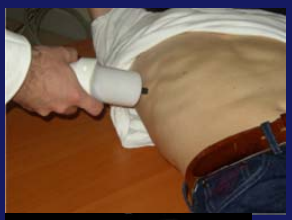


Adams D, et al. *MMWR Morb Mortal Wkly Rep*. 2015;62:1-122; CDC. cdc.gov/nchs/data-visualization/drug-poisoning-mortality.

Hepatic Fibrosis Staging: Do Not Miss F3 or Cirrhosis

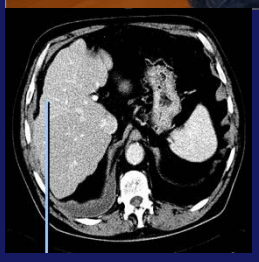


Liver Biopsy
- Gold standard
- Rarely done



Elastography
- > 12.5 kPa = cirrhosis

Fibrosis Serum Biomarkers
- APRI and FIB-4 have very good negative predictive value
- APRI < 0.5 and FIB-4 < 1.45 rule out cirrhosis
- Commercial serum fibrosis tests are also available in the US



Axial CT/MRI
- Cirrhotic morphology
- Portal hypertension

- F3/F4 fibrosis, screen for HCC
- F4 fibrosis, may need to screen for esophageal varices

AASLD-IDSA. hcvguidelines.org.

HCV Treatment: Assessing Fibrosis

- Is used by some payers to determine urgency of therapy
- Identifies patients with cirrhosis in need of additional screening
  - Varices
  - Hepatocellular carcinoma
  - Decompensated cirrhosis (cannot use protease inhibitors)
- Allows for the selection of a proper treatment plan and duration of therapy

AASLD-IDSA. hcvguidelines.org.

Child-Turcotte-Pugh Classification

	Points		
	1	**2**	**3**
Encephalopathy	None	Grade 1-2 (or precipitant-induced)	Grade 3-4 (or chronic)
Ascites	None	Mild/Moderate (diuretic-responsive)	Severe (diuretic-refractory)
Bilirubin (mg/dL)	< 2	2-3	> 3
Albumin (g/dL)	> 3.5	2.8-3.5	< 2.8
PT (see prolonged) or INR	< 4 < 1.7	4-6 1.7-2.3	> 6 > 2.3

- CTP score: Obtained by adding the score for each parameter
- CTP class: A = 5-6 points; B = 7-9 points; C = 10-15 points

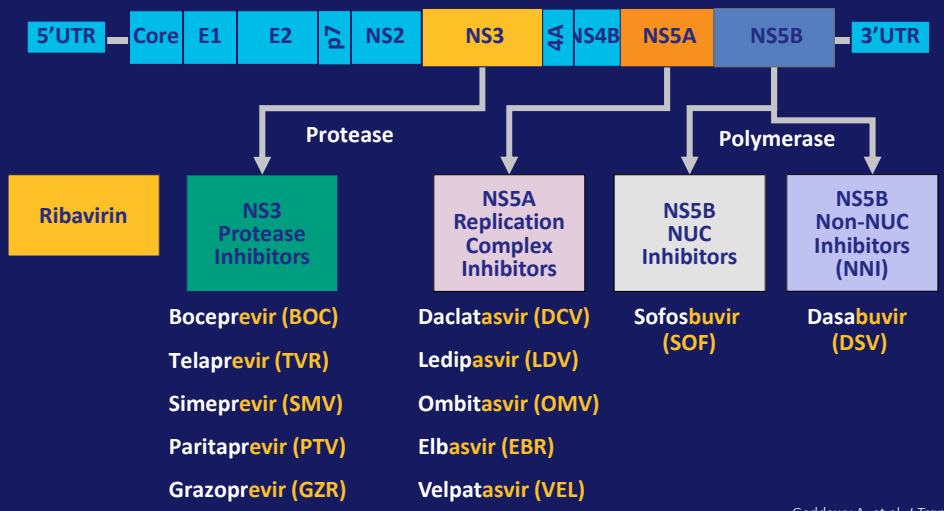
Pugh RN, et al. *Br J Surg*. 1973;60:646-9.

Many Special Populations Are No Longer Special

Population	SVR Rate
Black/Hispanic Race	> 95%
HIV/HCV Coinfection	> 95%
Post Orthotopic Liver Transplant	> 95%
CKD/Dialysis	> 95%
PWID/Opioid Agonist Treatment	> 95%

- Those with decompensated cirrhosis who have failed therapy remain one of the few special populations in need of additional therapies
- Protease inhibitors cannot be given in decompensated cirrhosis

FDA-Approved DAAs From Multiple Classes



Geddawy A, et al. *J Trans Int Med.* 2017;5:8-17.

All First-Line Treatment Options Lead to SVR Rates Greater Than 95%

HCV Genotype	No Cirrhosis		Compensated Cirrhosis		Adverse Events (occurring in ≥ 10% of patients)
1	EBR/GZR[a]	12 wk	EBR/GZR[a]	12 wk	Fatigue, headache, nausea
	GLE/PIB	8 wk	GLE/PIB	12 wk	Fatigue, headache
	LDV/SOF	8 or 12 wk	LDV/SOF	12 wk	Fatigue, headache, nausea
	SOF/VEL	12 wk	SOF/VEL	12 wk	Fatigue, headache, nausea, anemia
2/3	GLE/PIB	8 wk	GLE/PIB	12 wk	Fatigue, headache
	SOF/VEL	12 wk	SOF/VEL	12 wk	Fatigue, headache, nausea, anemia
4	EBR/GZR	12 wk	EBR/GZR	12 wk	Fatigue, headache, nausea
	GLE/PIB	8 wk	GLE/PIB	12 wk	Fatigue, headache
	LDV/SOF	12 wk	LDV/SOF	12 wk	Fatigue, headache, nausea
	SOF/VEL	12 wk	SOF/VE	12 wk	Fatigue, headache, nausea, anemia
5/6	GLE/PIB	8 wk	GLE/PIB	12 wk	Fatigue, headache
	LDV/SOF	12 wk	LDV/SOF	12 wk	Fatigue, headache, nausea
	SOF/VEL	12 wk	SOF/VEL	12 wk	Fatigue, headache, nausea, anemia

[a]No NS5A RAS.

AASLD-IDSA. hcvguidelines.org.

Recommended Assessments Prior to Starting Antiviral Therapy

- Patients scheduled to receive an HCV NS3 protease inhibitor should be assessed for a history of decompensated liver disease and for liver disease severity using the CTP calculator
  - Patients with current or prior history of decompensated liver disease or a current CTP score ≥ 7 should not receive treatment with regimens that contain NS3 protease inhibitors due to increased blood levels and/or lack of safety data
  - Similarly, patients with a CTP score of 5 or 6 who cannot be closely monitored for laboratory or clinical symptoms during treatment should not receive treatment with a regimen that contains paritaprevir/ritonavir
- Testing for the presence of RASs prior to starting treatment should be performed as recommended; rarely needed, but examples in which it would be warranted include:
  - In genotype 1a patients who are being considered for elbasvir, test for RAS at positions 28, 30, 31, or 93
  - For genotype 3 patients with cirrhosis who are being considered for velpatasvir, test for RAS at Y93
  - DAA failures

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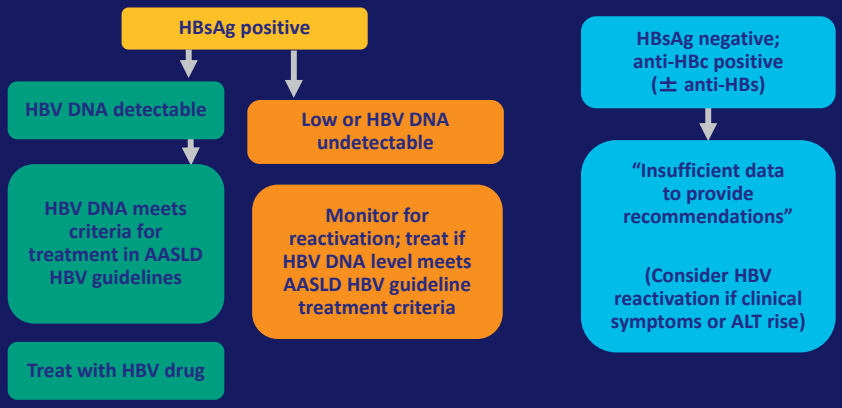
HBV Testing/Monitoring During HCV DAA Therapy

- Test all patients initiating HCV therapy for HBsAg, anti-HBc, and anti-HBs
  - Vaccinate if no HBV markers present; follow flowchart below if HBV markers present



AASLD-IDSA. hcvguidelines.org; graphic adapted from Ira M. Jacobson, MD.

Most Patients With HCV Viremia Should Be Considered Treatment Candidates if They Can Adhere to Therapy

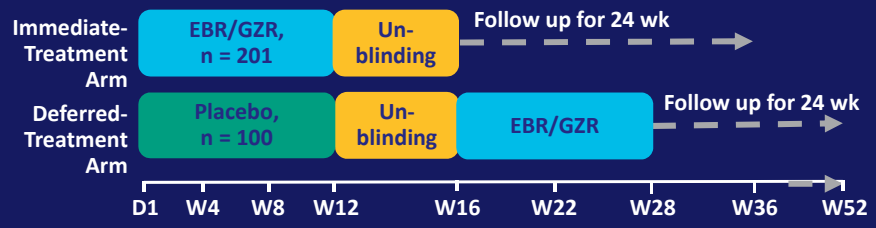
AASLD-IDSA Treatment Guidelines:

- Treatment is recommended for all patients with chronic HCV infection, except those with short life expectancies owing to comorbid conditions

AASLD-IDSA. hcvguidelines.org.

C-EDGE CO-STAR: Study Design

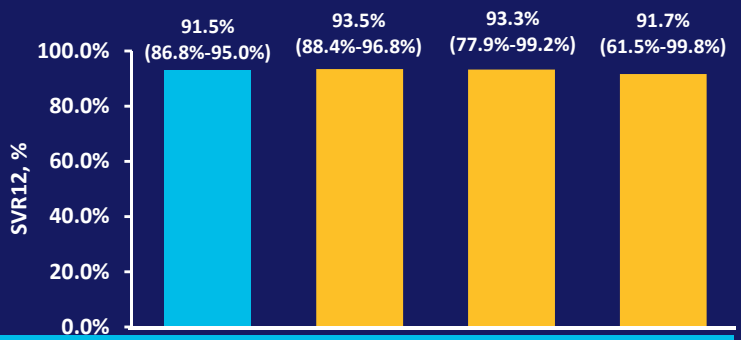
- Dedicated study in PWID



- Phase 3, randomized, parallel-group, placebo-controlled trial
- Patients:
  - Treatment naïve; genotypes 1, 4, and 6; ± cirrhosis (20%); ± HIV/HCV coinfection (7%)
  - On opioid agonist therapy for at least 3 months and consistently kept at least 80% of scheduled appointments while on opioid agonist therapy

Dore GJ, et al. *Ann Intern Med.* 2016;165:625-34.

C-EDGE CO-STAR: Efficacy Results (ITG)



	All GT 184/201	GT 1a[a] 144/154	GT 1b 28/30	GT 4 11/12
Relapse and discontinuation	7	6	1	0
Reinfection	5	3	0	0
LTFU or discontinuation unrelated to virologic failure	3	2	1	1

[a]Includes one subject with mixed infection (GT 1a and GT 1b) who achieved SVR12.

Dore GJ, et al. *Ann Intern Med.* 2016;165:625-34.

AASLD-IDSA HCV Treatment Guidelines: PWID

- "Recent and active IDU should not be seen as an absolute contraindication to HCV therapy"
- "Scale up of HCV treatment in PWID is necessary to positively impact the HCV epidemic in the United States and globally"

AASLD-IDSA. hcvguidelines.org.

Recommended Monitoring During Antiviral Therapy

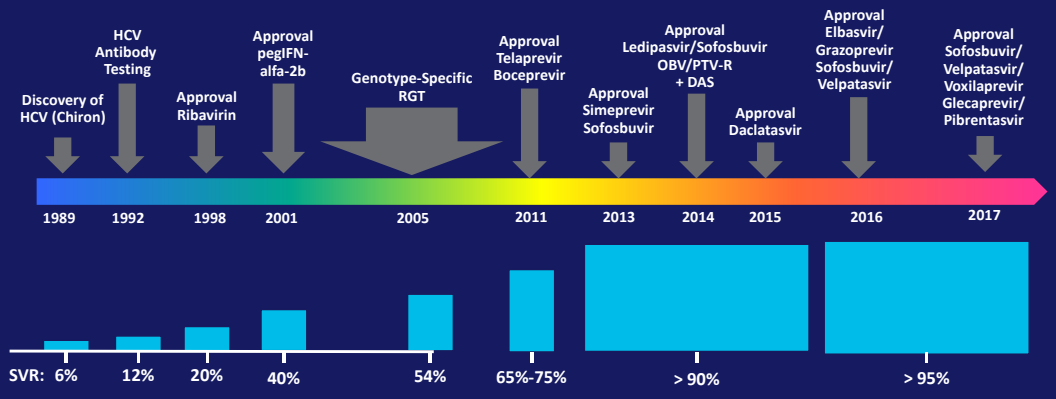
- Clinic visits or telephone contact is recommended as clinically indicated
  - Ensure medication adherence
  - Monitor for adverse events
  - Assess for potential drug-drug interactions with newly prescribed medications
- CBC, creatinine level, eGFR, and hepatic function panel are recommended after 4 weeks of treatment and as clinically indicated
- Quantitative HCV viral load testing is recommended 4 weeks after therapy initiation and 12 weeks after therapy completion
- Antiviral drug therapy should not be interrupted or discontinued if HCV RNA level evaluations are not performed or available during treatment

AASLD-IDSA. hcvguidelines.org.

Follow-Up of Sustained Response (SVR or Cure)

- SVR is durable
- Liver complications and HCV-related complications will decrease, not disappear
- If ALT is still elevated post SVR, it must be explained (eg, NAFLD, alcohol, drug, reinfection)
- Risk of HCC decreases markedly, but does not disappear entirely; screen F3/F4 patients for HCC (ultrasound and AFP every 6 months)
- Reinfection is possible; educate those with high-risk behaviors about risk reduction (PWID/MSM)
- Do not dismiss F3/F4 patients from clinic

History and Evolving Landscape of HCV Therapy



Houghton M. *Liver Int*. 2009;29:82-8; Carithers RL, et al. *Hepatology*. 1997;26:S83-8; Zeuzem S, et al. *N Engl J Med*. 2000;343:1666-72; Poynard T, et al. *Lancet*. 1998;352:1426-32; McHutchison JG, et al. *N Engl J Med*. 1998;339:1485-92; Lindsay KL, et al. *Hepatology*. 2001;34:395-403; Fried MW, et al. *N Engl J Med*. 2002;347:975-82; Manns MP, et al. *Lancet*. 2001;58:958-65; Poordad F, et al. *N Engl J Med*. 2011;364:1195-206; Jacobson IM, et al. *N Engl J Med*. 2011;364:2405-16; Lawitz E, et al. *N Engl J Med*. 2013;368:1878-87; Jacobson IM, et al. *Lancet*. 2014;384:403-13; Afdhal N, et al. *N Engl J Med*. 2014;370:1889-98; Nelson DR, et al. *Hepatology*. 2015;61:1127-35; Zeusem S, et al. *Ann Intern Med*. 2015;163:1-13; Feld JJ, et al. *N Engl J Med*. 2015;373:2599-607; Foster GR, et al. *N Engl J Med*. 2015;373:2608-17.

HCV Therapy Has Paralleled *Helicobacter pylori* Therapy

H. pylori

Select Long-Duration Regimens for *Helicobacter pylori* Eradication

Treatment Regimen	Duration	Eradication Rate (%)
Omeprazole (Prilosec) 20 mg twice daily, *plus* amoxicillin 1 g twice daily, *plus* clarithromycin (Biaxin) 500 mg twice daily	14 days	80-86
Lansoprazole (Prevacid) 30 mg twice daily *plus* amoxicillin 1 g twice daily, *plus* clarithromycin 500 mg twice daily	10-14 days	86
Bismuth subsalicylate (Pepto-Bismol) 525 mg four times daily, *plus* metronidazole (Flagyl) 250 mg four times daily, *plus* tetracycline 500 mg four times daily, *plus* histamine H_2 blocker	14 days (H_2 blocker alone for an additional 14 days taken once or twice daily)	80

HCV

All Oral Therapy

Duration 8-24 Weeks

Polymerase Inhibitor
±
Protease Inhibitor
±
NS5a
±
Non-Nucleoside Inhibitor
±
Ribavirin

Chey WD, et al. *Am J Gastroenterol*. 2017;112:212-39.

HCV Can Be Eliminated

- No non-human reservoir exists
- Simple and accurate diagnostic tools are available
- Transmission can be prevented
- Infection can be cleared from host
- Highly effective, safe drugs exist that are given for a finite period
  - Most unique populations are now routinely treated
- We are entering the era of pan-genotypic therapies
- HCV elimination can be achieved but only with screening and linkage-to-care strategies that lead to treatment

US DHHS. hhs.gov/sites/default/files/National%20Viral%20Hepatitis%20Action%20Plan%202017-2020.pdf.