Complimentary CME

Curing HCV in Treatment-Naïve Patients With Early Stage Liver Disease: Considerations for Treatment Selection, Monitoring, and Follow-Up

Developed in collaboration

INDIANA UNIVERSITY SCHOOL OF MEDICINE

Med-IQ

Activity Overview

This activity provides an overview of available therapeutic regimens for treatment-naïve patients with HCV infection and stage F2 or lower liver disease. Dr. Kwo also discusses the recommended monitoring that should occur during and after treatment, as well as the opportunity for cure among people who use injection drugs.

Target Audience

This activity is intended for primary care clinicians.

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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

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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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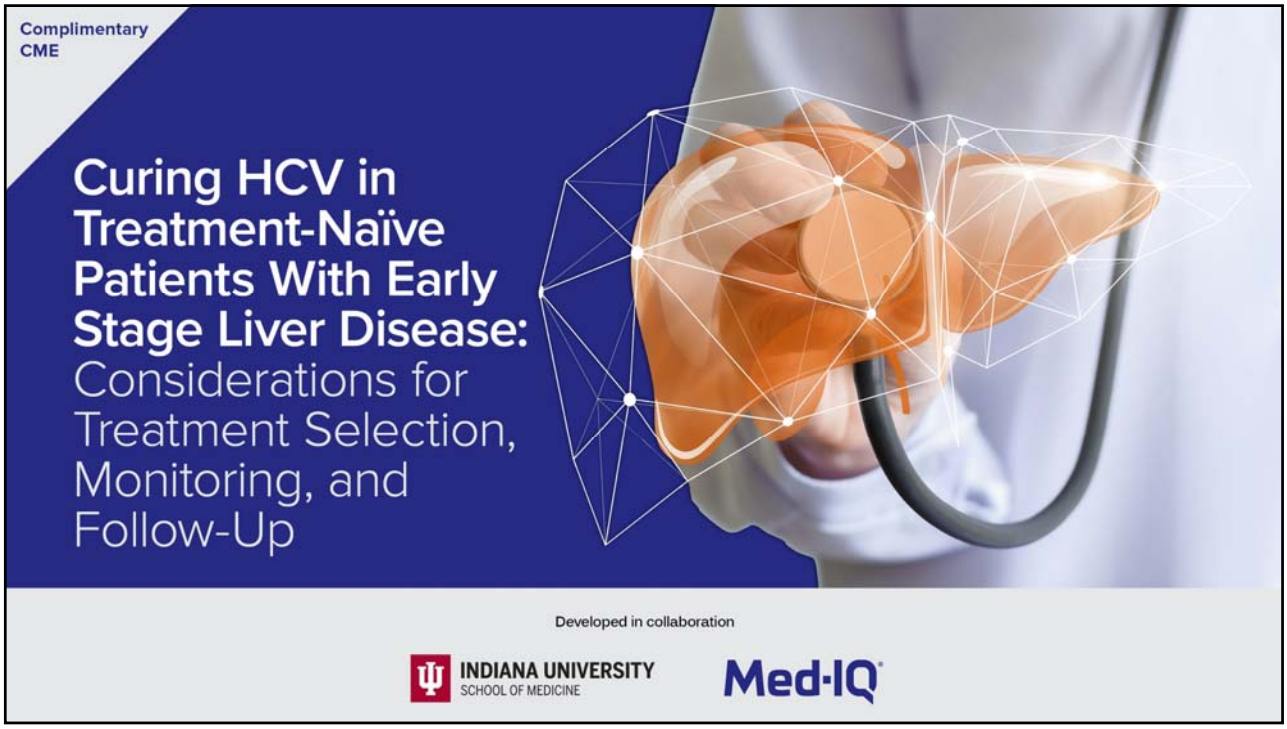

Learning Objectives

Upon completion, participants should be able to:

- Outline therapeutic options and expected outcomes in treatment-naïve patients with HCV infection and early stage liver disease

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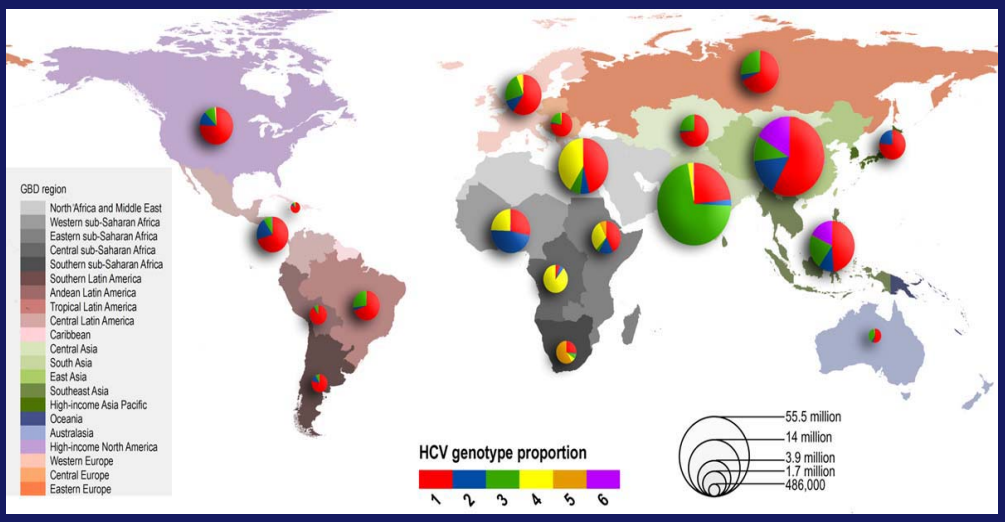
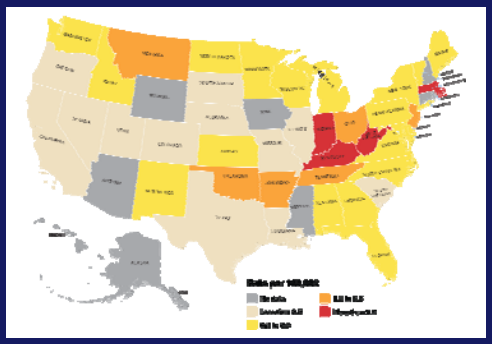
Global Distribution and Prevalence of HCV Genotypes



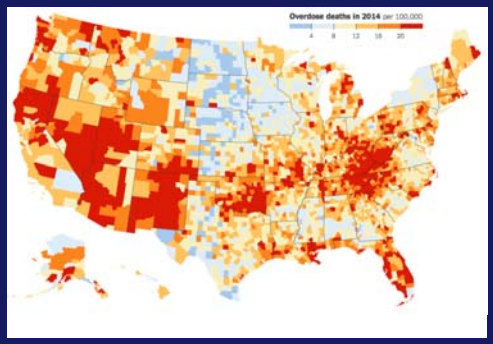
Messina JP, et al. *Hepatology*. 2015;61:77-87.

Acute HCV Infections vs Deaths From Heroin Overdose

Acute HCV Infections, 2013

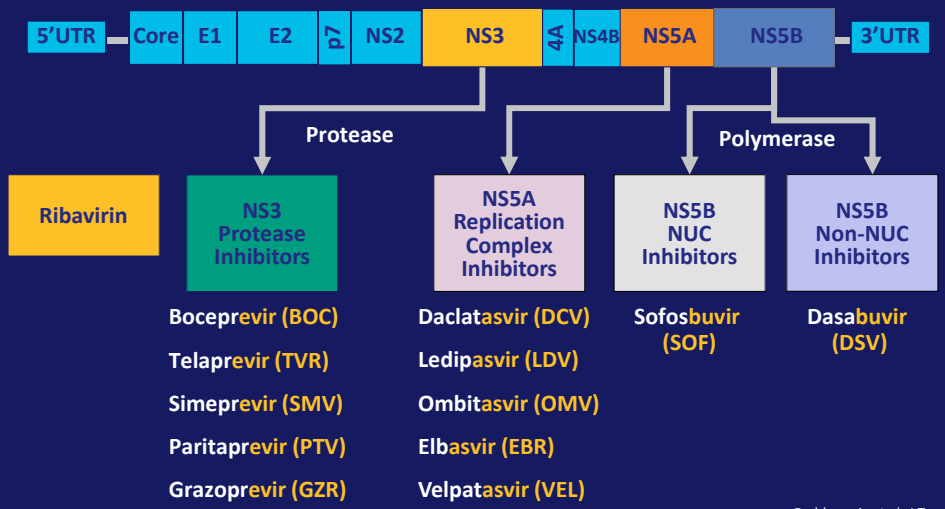


Deaths From Heroin Overdose, 2014 by County



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

FDA-Approved DAAs From Multiple Classes



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

HCV Genotypes 1a and 1b
Treatment Naïve, F0-F2

Regimen	Weeks	Study	SVR12	Adverse Events (occurring in ≥ 10% of patients)
Sofosbuvir + ledipasvir **(HCV RNA < 6 M IU/mL)** **(HCV RNA > 6 M IU/mL)**	8 12	ION-3	97% 95%	Fatigue, headache, nausea
Elbasvir/grazoprevir (1b) **(-) -NS5A RAVs (1a)**	12	C-EDGE	99% 99%	Fatigue, headache, nausea
Glecaprevir/pibrentasvir	8	ENDURANCE-1	99%	Fatigue, headache
Sofosbuvir + velpatasvir	12	ASTRAL-1	98%	Fatigue, headache, nausea, anemia

AASLD-IDSA. hcvguidelines.org; Kowdley KV, et al. *N Engl J Med*. 2014;370:1879-88; Afdhal N, et al. *N Engl J Med*. 2014;370:1889-98; Rockstroh JK, et al. *Lancet HIV*. 2015;2:e319-27; Ferenci P, et al. *N Engl J Med*. 2014;370:1983-92; Feld JJ, et al. *N Engl J Med*. 2015;373:2599-607; Zeuzem S, et al. *N Engl J Med*. 2018;378:354-69.

HCV Genotypes 2 and 3
Treatment Naïve, Noncirrhotic

Regimen	Genotype	Weeks	Study	SVR12	Adverse Events (occurring in ≥ 10% of patients)
Velpatasvir + sofosbuvir	2	12	ASTRAL-1	99%	Fatigue, headache, nausea, anemia
Glecaprevir/pibrentasvir	2	8	SURVEYOR-2	99%	Fatigue, headache
Velpatasvir + sofosbuvir	3	12	ASTRAL-3	98%	Fatigue, headache, nausea, anemia
Glecaprevir/pibrentasvir	3	8	ENDURANCE-3	95%	Fatigue, headache

Note: not head-to-head trials.

AASLD-IDSA. hcvguidelines.org; Feld JJ, et al. *N Engl J Med*. 2015;373:2599-607; Foster GR, et al. *N Engl J Med*. 2015;373:2608-17; Asselah T, et al. *Clin Gastroenterol Hepatol*. 2018;16:417-26; Zeuzem S, et al. *N Engl J Med*. 2018;378:354-69.

HCV Genotype 4
Treatment Naïve, Noncirrhotic

Regimen	Genotype	Weeks	Study	SVR12	Adverse Events (occurring in ≥ 10% of patients)
Velpatasvir + sofosbuvir	4	12	ASTRAL-1	100%	Fatigue, headache, nausea, anemia
Sofosbuvir + ledipasvir	4	12	SYNERGY	95%	Fatigue, headache, nausea
Elbasvir/grazoprevir	4	12	C-EDGE	97%	Fatigue, headache, nausea
Glecaprevir/pibrentasvir	4	8	ENDURANCE-4	99%	Fatigue, headache

Note: not head-to-head trials.

AASLD-IDSA. hcvguidelines.org; Feld JJ, et al. *N Engl J Med*. 2015;373:2599-607; Koli A, et al. *Lancet Infect Dis*. 2015;15:1049-54; Zeuzem S, et al. *Ann Intern Med*. 2015;163:1-13; Asselah T, et al. *Clin Gastroenterol Hepatol*. 2018;16:417-26.

HCV Genotypes 5 and 6
Treatment Naïve, Noncirrhotic

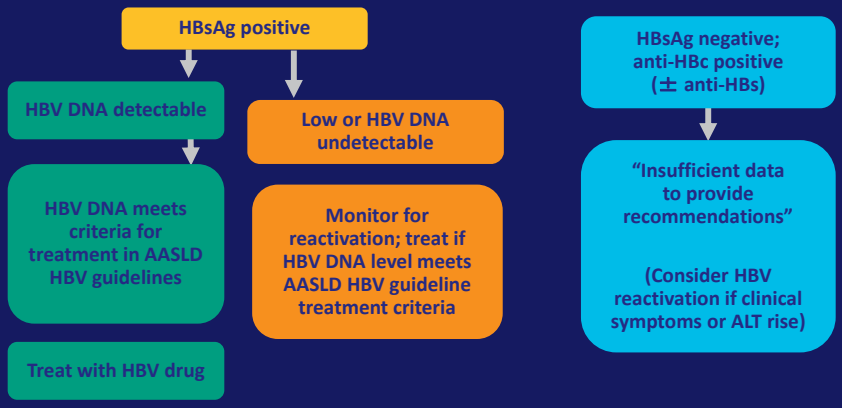
Regimen	Genotype	Weeks	Study	SVR12	Adverse Events (occurring in ≥ 10% of patients)
Velpatasvir + sofosbuvir	5	12	ASTRAL-1	96%	Fatigue, headache, nausea, anemia
Sofosbuvir + ledipasvir	5	12		95%	Fatigue, headache, nausea
Glecaprevir/pibrentasvir	5	8	SURVEYOR-2	100%	Fatigue, headache
Velpatasvir + sofosbuvir	6	12	ASTRAL-1	100%	Fatigue, headache, nausea, anemia
Sofosbuvir + ledipasvir	6	12	SYNERGY	100%	Fatigue, headache, nausea
Glecaprevir/pibrentasvir	6	8	EXPEDITION-1	100%	Fatigue, headache

Note: not head-to-head trials.

AASLD-IDSA. hcvguidelines.org; Feld JJ, et al. *N Engl J Med*. 2015;373:2599-607; Zeuzem S, et al. *Ann Intern Med*. 2015;163:1-13; Abergel A, et al. *Lancet Infect Dis*. 2016;16:459-64; Asselah T, et al. *Clin Gastroenterol Hepatol*. 2018;16:417-26.

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

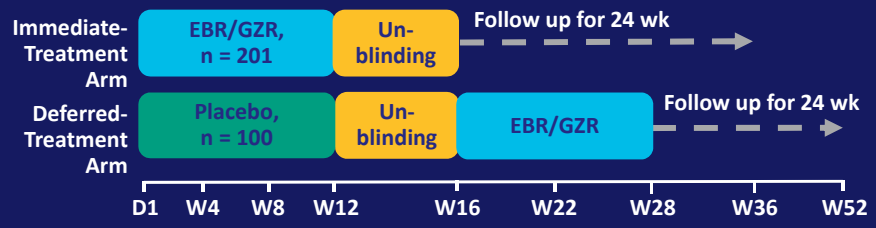
AASLD/IDSA Treatment Guidelines:

- 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

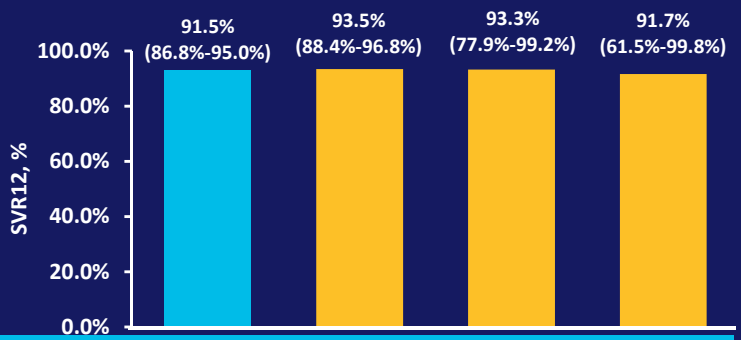
- Dedicated study in PWID



- 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

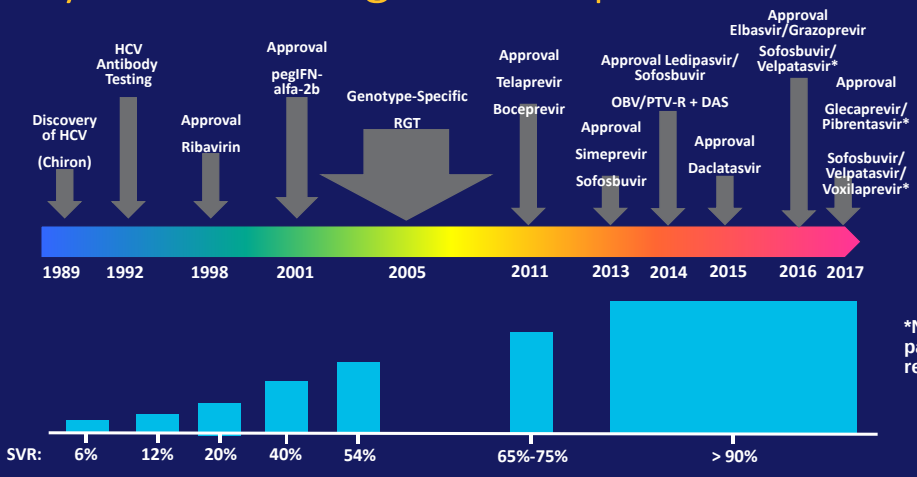
AASLD-IDSA. hcvguidelines.org.

Recommended Follow-Up for Patients Who Achieve an SVR

- For patients who do not have advanced fibrosis (METAVIR stage F0-F2)
  - Recommended follow-up is the same as if they were never infected with HCV
  - Verify that ALT normalizes (risk of NAFLD or alcohol-related liver disease and others may persist)
  - Assess for other causes of liver disease in patients who develop persistently abnormal liver tests after achieving SVR
- Assess for HCV recurrence or reinfection using HCV RNA testing only if the patient has ongoing risk factors for HCV infection or otherwise unexplained hepatic dysfunction develops

AASLD-IDSA. hcvguidelines.org.

History and Evolving Landscape of HCV Therapy



*Novel all-oral, pan-genotypic regimens

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.

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