Partnerships for Care

HIV TAC TEAM

P4C HIV TAC Collaborative Training: Hepatitis C Virus (HCV) Treatment Guidelines

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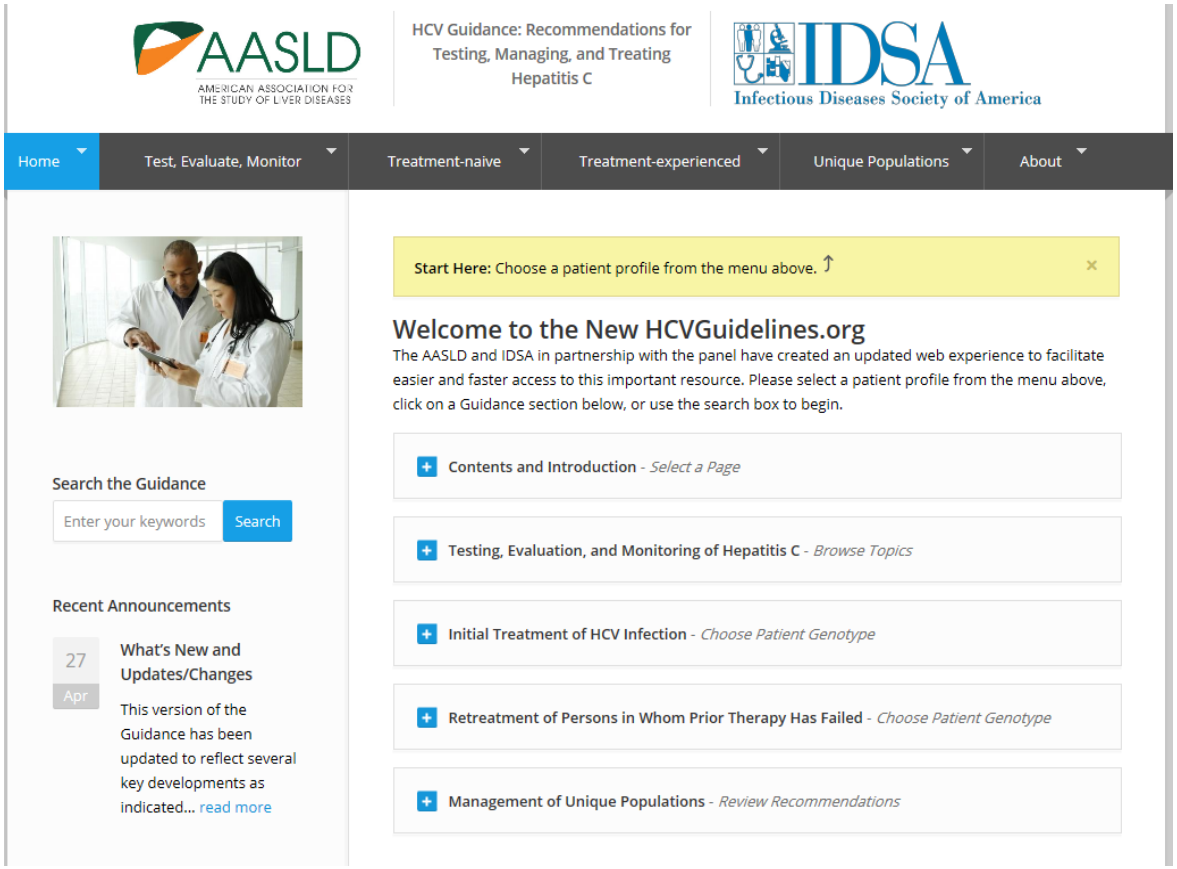
AASLD/IDSA Guidance

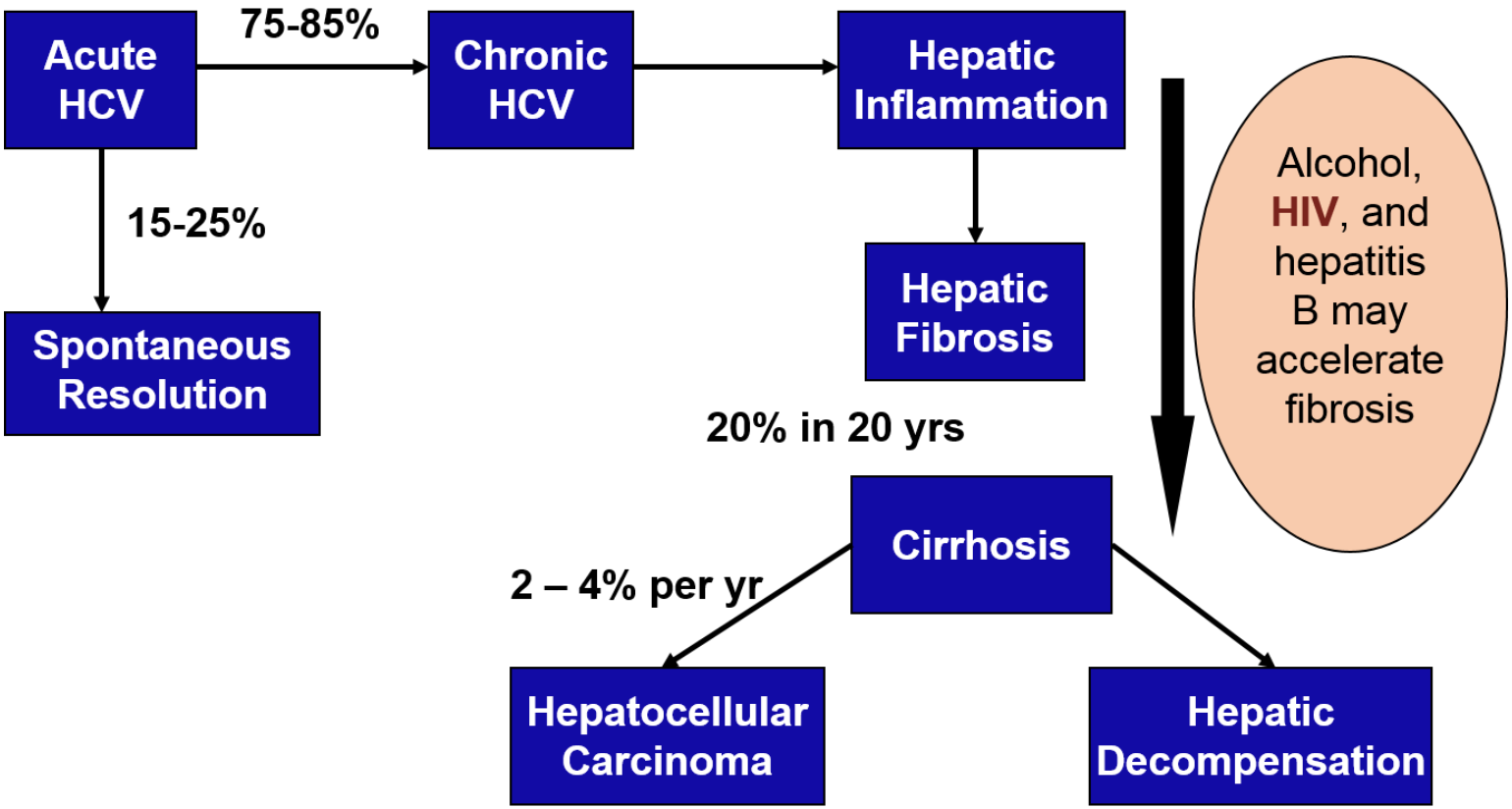
- This Guidance should be considered a "living document" and will be updated frequently
  - FDA-approved regimens
  - May also recommend off-label use of certain drugs or tests

NOTICE: Guidance for hepatitis C treatment in adults is changing constantly with the advent of new therapies and other developments. A static version of this guidance, such as printouts of this website material, booklets, slides, and other materials, may be outdated by the time you read this. We urge you to review this guidance on this website (www.hcvguidelines.org) for the latest recommendations.

AASLD/IDSA Homepage



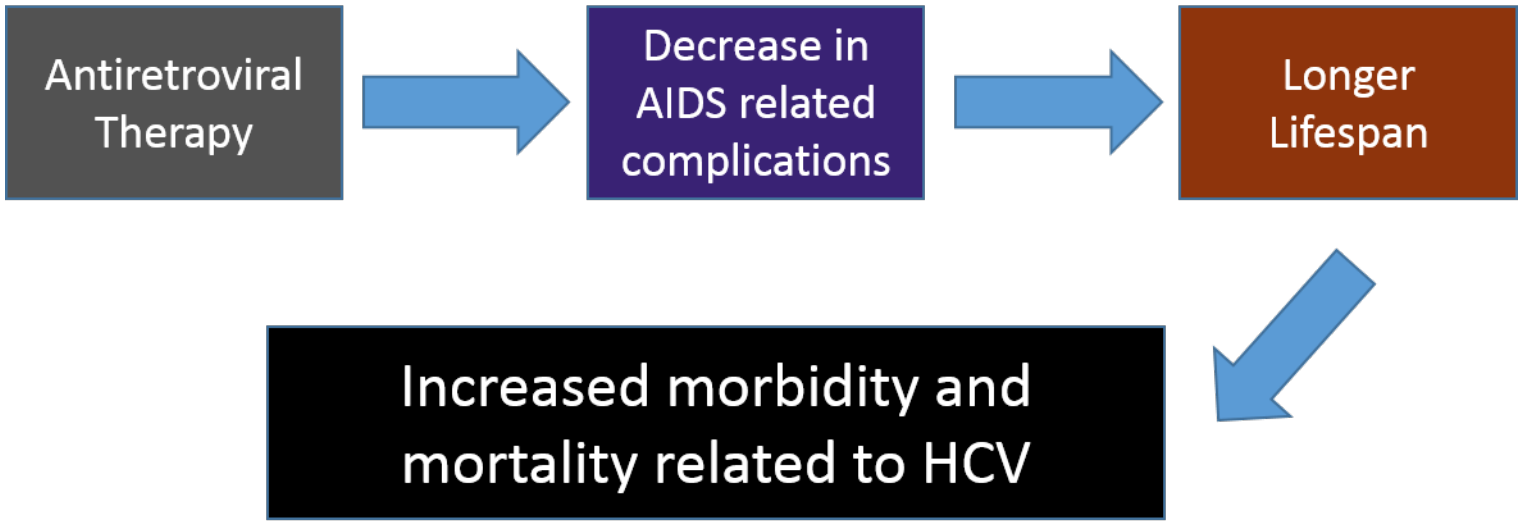
Hepatitis C History in Review



- **Prevalence of HIV/HCV coinfection is high**
- Shared routes of transmission
  - 30% of HIV+ are coinfected
  - ~400,000 HIV/HCV + in U.S.
- Prevalence of HCV in HIV+ individuals varies based on likely mode of acquisition
  - ~ 90% in IVDU
  - 60-85% in hemophiliacs
  - 4-8% in MSM

Sherman KE. Clin Infect Dis; 2002; 34:831–7
Rockstroh JK. J Infect Dis 2005; 192:992–1002

AntiRetroviral Therapy (A.R.T.) impact on HCV Treatment/Care

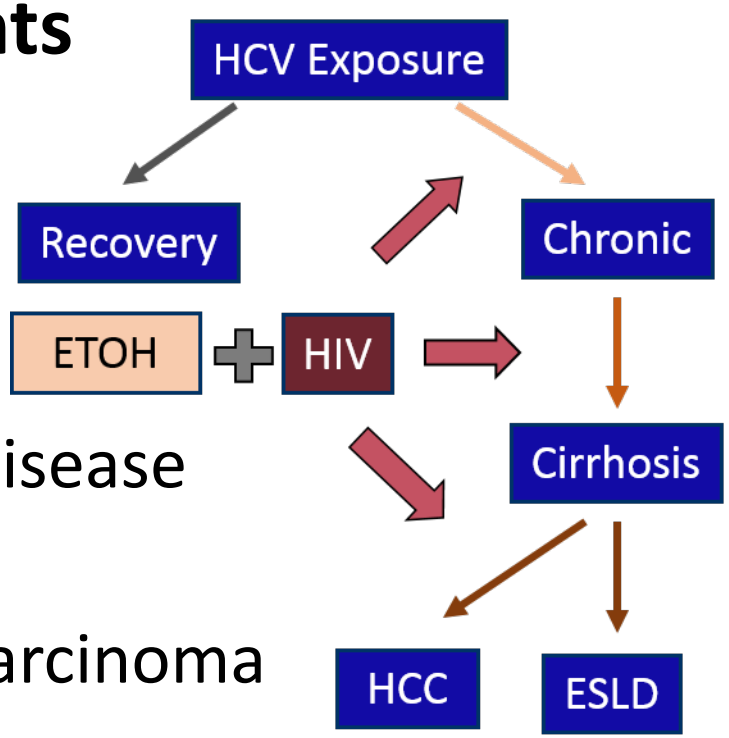


Liver disease is the second leading cause of death in HIV
Liver disease is primarily caused by chronic HCV

Sherman KE et al. *Clin Infect Dis* 2002;34:831-7
D:A:D Study. *Arch Intern Med* 2006;166:1632-41

HCV/HIV Co-infection Treatments

- decreased clearance of HCV
- increased HCV RNA levels
- increased risk of cirrhosis
- increased risk of end-stage liver disease and hepatic decompensation
- increased risk of hepatocellular carcinoma
- 30-50% of coinfected individuals have alcohol use disorders



Benhamou Y et al. *Hepatology* 1999;30:1054-1058.
Graham CS et al. *Clin Infect Dis* 2001;33:562-569.

Recommendations for One-time HCV Testing

RECOMMENDED

- One-time HCV testing is recommended for persons born between 1945 and 1965, without prior ascertainment of risk.

- Other persons should be screened for risk factors for HCV infection, and one-time testing should be performed for all persons with behaviors, exposures, and conditions associated with an increased risk of HCV infection.

Risk behaviors

- Injection-drug use (current or ever, including those who injected once)
- Intranasal illicit drug use

http://www.hcvguidelines.org/evaluate/testing-and-linkage

Recommendations for One-time HCV Testing (2)

Risk exposures

- Persons on long-term hemodialysis (ever)
- Persons with percutaneous/parenteral exposures in an unregulated setting
- Healthcare, emergency medical, and public safety workers after needlesticks, sharps, or mucosal exposures to HCV-infected blood
- Children born to HCV-infected women
- Prior recipients of transfusions or organ transplants, including persons who:
  - Were notified that they received blood from a donor who later tested positive for HCV infection
  - Received a transfusion of blood or blood components, or underwent an organ transplant before July 1992
  - Received clotting factor concentrates produced before 1987
- Persons who were ever incarcerated

http://www.hcvguidelines.org/evaluate/testing-and-linkage

Recommendations for One-time HCV Testing (3)

Other considerations

- HIV infection
- Sexually active persons about to start pre-exposure prophylaxis (PreP) for HIV
- Unexplained chronic liver disease and/or chronic hepatitis including elevated alanine aminotransferase levels
- Solid organ donors (deceased and living)

http://www.hcvguidelines.org/evaluate/testing-and-linkage

Recommendation for HCV Testing Those with Ongoing Risk Factors

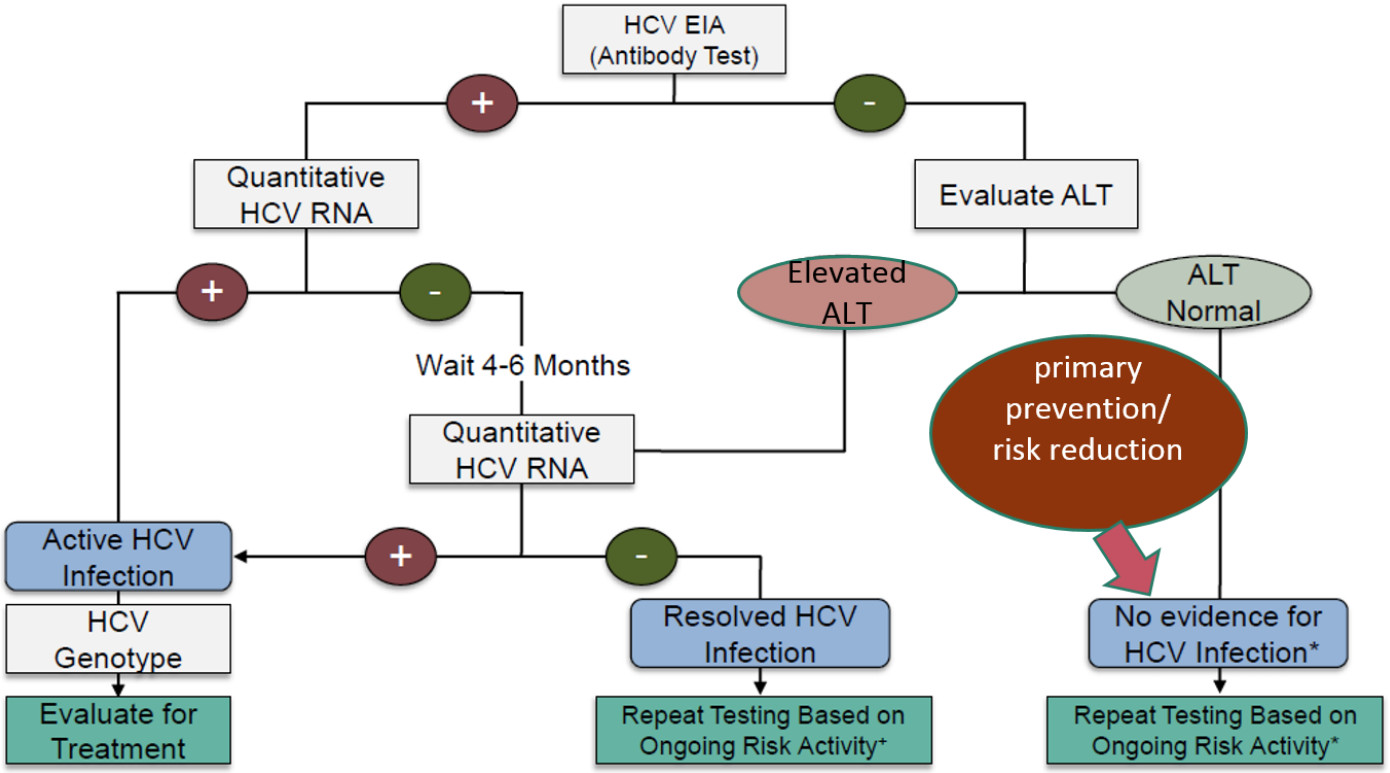
Annual HCV testing is recommended for persons who inject drugs and for HIV-seropositive men who have unprotected sex with men. Periodic testing should be offered to other persons with ongoing risk factors for exposure to HCV.

http://www.hcvguidelines.org/evaluate/testing-and-linkage

Recommendations for Follow-up of Initial Testing

- An anti-HCV test is recommended for HCV testing, and if the result is positive, current infection should be confirmed by a sensitive HCV RNA test.
- Among persons with a negative anti-HCV test who are suspected of having liver disease, testing for HCV RNA or follow-up testing for HCV antibody is recommended if exposure to HCV occurred within the past six months; testing for HCV RNA can also be considered in persons who are immunocompromised.
- Among persons at risk of reinfection after previous spontaneous or treatment-related viral clearance, initial HCV-RNA testing is recommended because an anti-HCV test is expected to be positive.
- Quantitative HCV-RNA testing is recommended prior to the initiation of antiviral therapy to document the baseline level of viremia (ie, baseline viral load).
- Testing for HCV genotype is recommended to guide selection of the most appropriate antiviral regimen.
- If found to have positive results for anti-HCV test and negative results for HCV RNA by polymerase chain reaction (PCR), persons should be informed that they do not have evidence of current (active) HCV infection.

HCV Testing Algorithm



Sulkowski M. 2011.
https://hab.hrsa.gov/sites/default/files/hab/clinical-quality-management/hepccoinfectguide2011.pdf

Recommendations for Counseling Those with Current (Active) HCV Infection

Persons with current (active) HCV infection should receive education and interventions aimed at reducing progression of liver disease and preventing transmission of HCV.

- 1. Abstinence from alcohol and, when appropriate, interventions to facilitate cessation of alcohol consumption should be advised for all persons with HCV infection.
- 2. Evaluation for other conditions that may accelerate liver fibrosis, including HBV and HIV infections, is recommended for all persons with HCV infection.
- 3. Evaluation for advanced fibrosis using liver biopsy, imaging, and/or noninvasive markers is recommended for all persons with HCV infection, to facilitate an appropriate decision regarding HCV treatment strategy and to determine the need for initiating additional measures for the management of cirrhosis (eg, hepatocellular carcinoma screening) (see When and in Whom to Initiate HCV Therapy).
- 4. Vaccination against hepatitis A and hepatitis B is recommended for all susceptible persons with HCV infection.
- 5. Vaccination against pneumococcal infection is recommended to all patients with cirrhosis (Marrie, 2011).
- 6. All persons with HCV infection should be provided education on how to avoid HCV transmission to others.

http://www.hcvguidelines.org/evaluate/testing-and-linkage

Additional Laboratory Testing

The following laboratory tests are recommended within 12 weeks prior to starting antiviral therapy:

- Complete blood count (CBC); international normalized ratio (INR)
- Hepatic function panel (albumin, total and direct bilirubin, alanine aminotransferase, aspartate aminotransferase, and alkaline phosphatase levels)
- Calculated glomerular filtration rate (GFR)

The following laboratory testing is recommended at any time prior to starting antiviral therapy:

- HCV genotype and subtype
- Quantitative HCV RNA (HCV viral load)

Additional Laboratory Testing (cont)

All patients initiating HCV DAA therapy should be assessed for HBV coinfection with HBsAg, anti-HBs, and anti-HBc.

Testing for the presence of resistance-associated substitutions (RASs) prior to starting treatment should be performed

See recommendations in the Initial Treatment and the Retreatment Sections of the Guidance.

Patients scheduled to receive an HCV NS3 protease inhibitor should be assessed for a history of decompensated liver disease and for severity of liver disease using CTP score.

- CTP score of 7 or > should NOT receive treatment with NS3 protease inhibitors
- 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.

Staging HCV Liver Fibrosis

Important part of chronic HCV work-up

Identify cirrhosis:

- Increased hepatocellular carcinoma risk: need to screen
- Monitor for hepatic decompensation
- Consider liver transplant evaluation

Determine cirrhosis by:

- Liver biopsy
- Non-invasive tests

Monitoring for HCC

Advanced fibrosis and cirrhosis

Hepatic ultrasound +/- AFP every 6 months

- Suspicious mass lesion requires more specific testing with a multi-phase contrast CT or MRI
- AFP alone is inadequate screening test for HCC

Routine screening for HCC without advanced fibrosis is not recommended

The Cirrhotic Patient

Evaluate for encephalopathy & ascites

- If ascites refer to hepatologist
  - Diagnostic paracentesis
  - Evaluation for liver transplant

Endoscopy to evaluate for the presence of esophageal varices

- need for prophylaxis with a non-selective beta blocker

Goal of Treatment

The goal of treatment of HCV-infected persons is to reduce all-cause mortality and liver-related health adverse consequences, including end-stage liver disease and hepatocellular carcinoma, by the achievement of virologic cure as evidenced by a sustained virologic response.

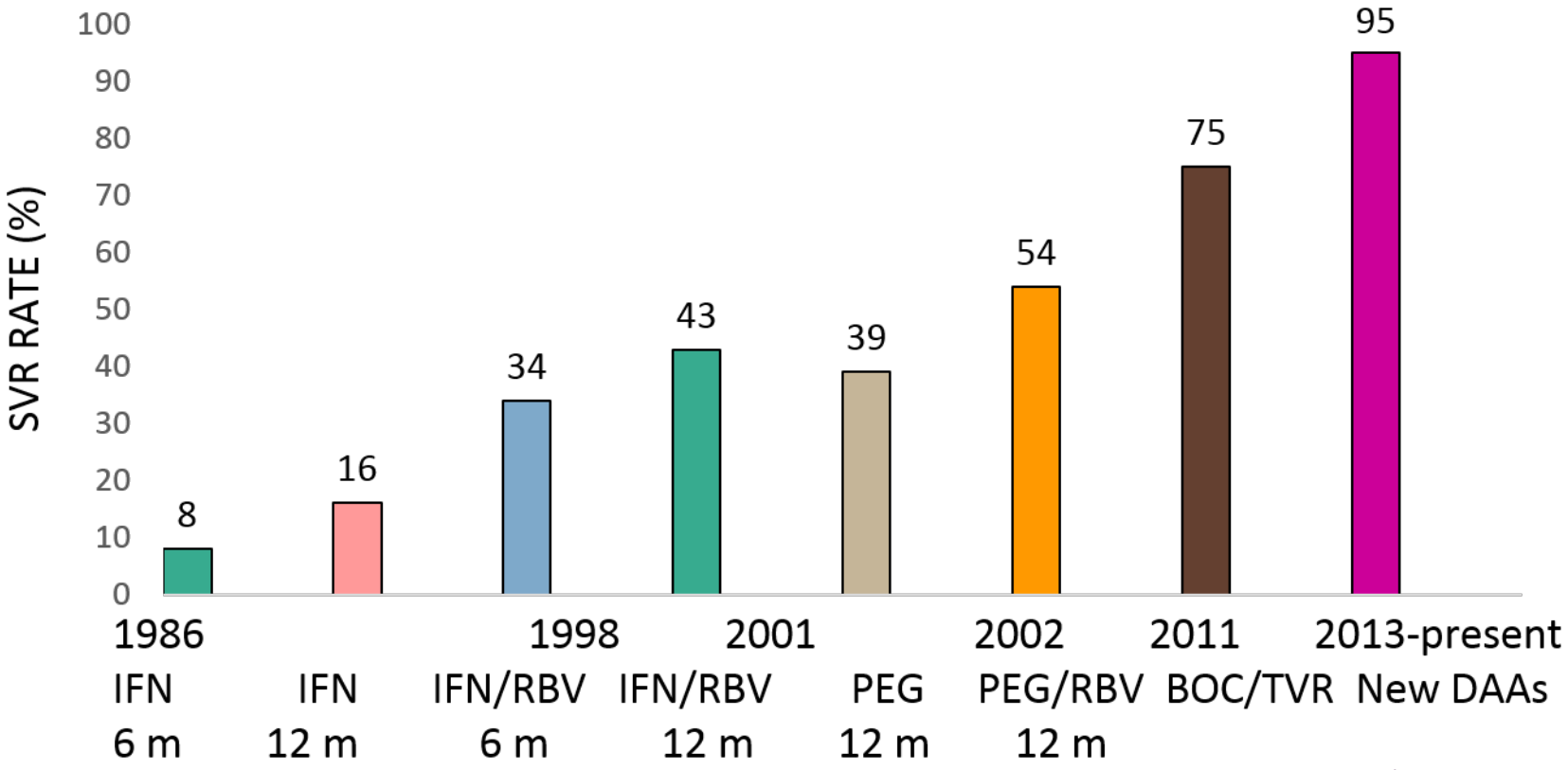
http://www.hcvguidelines.org/evaluate/when-whom

Recommendation for When and in Whom to Initiate Treatment

Treatment is recommended for all patients with chronic HCV infection, except those with short life expectancies that cannot be remediated by treating HCV, by transplantation, or by other directed therapy. Patients with short life expectancies owing to liver disease should be managed in consultation with an expert.

http://www.hcvguidelines.org/evaluate/when-whom

SVR rates for patients with HCV infections (genotypes 1–3) according to the treatment regimens and durations



Adapted from Strader DB. Clin Liver Disease 2012, 1:1; 6-11.

DAA: Direct Acting Antiviral

NS3/4A Inhibitors

- High Potency
- Limited genotypic coverage
- Low barrier to resistance

NS5A Inhibitors

- High potency
- Multi-genotypic coverage
- Intermediate barrier to resistance

NS5B Nucleos(t)ide Inhibitors (NI)

- Intermediate potency
- Pan genotypic coverage
- High barrier to resistance

NS5B Non Nucleoside Inhibitors (NNI)

- Intermediate potency
- Limited genotypic coverage
- Low barrier to resistance

Mnemonic to Remember DAAs

Look at end of the drug's name

PREvir = **PR**ot**E**ase inhibitor

- Tela**pre**vir, boce**pre**vir, sime**pre**vir, grazo**pre**vir

Uvir = n**U**cleotide or non-n**U**cleotide polymerase inhibitor

- Sofosb**uvir**, dasab**uvir**

Asvir = NS5**A** inhibitor

- Ledip**asvir**, ombit**asvir**, daclat**asvir,** velpat**asvir,** elb**asvir,**

Factors Associate with Treatment and Cure

HCV Genotype

- 1, 2, 3, 4, 5, 6
- Subtype: 1a, 1b

Stage of liver fibrosis

- Cirrhosis versus no cirrhosis
- Metavir score F0-F4

HCV treatment status

- Naïve versus treatment experienced

Special populations

- Transplant, chronic kidney dis, children

Medications Currently FDA Approved

Medication	Genotype	Genotype	Genotype	Genotype	Genotype	Genotype
Elbasvir/grazoprevir	GT1a	1b			4	
Ledipasvir/ Sofosbuvir	1a	1b			4	5/6
Paritaprevir/ritonavir/ ombitasvir/dasabuvir	1a	1b			4	
Simeprevir + sofosbuvir	1a	1b				
Sofosbuvir/velpatasvir	1a	1b	2	3	4	5/6
Daclatasvir + sofosbuvir	1a	1b	2	3		

Regimens NOT recommended for HIV/HCV coinfected patients

	Tipranavir	Cobisistat	Efavirenz	Etravirine	Nevirapine	Rilpivarine	Any PI	Other
Elb/Graz		x	x	x	x		x	
Sof/Vel	x		x	x	x			
Sof/Led	x							
PrOD*	x (r)	x	x	x	x	x		Darunavir Lopinavir (r)
Simeprevir		x	x	x	x		x	

Antiretroviral treatment interruption to allow HCV therapy is NOT recommended

*Ombitasvir/paritaprevir/ritonavir ± dasabuvir (PrOD) should not be used in HCV/HIV-coinfected patients who are not taking ART

AASLD and IDSA. http://www.hcvguidelines.org/full-report-view
Version July 15, 2017.

Ribavirin Drug Interactions

Do not use zidovudine with ribavirin

- Greater decrease in hemoglobin
- Higher risk of anemia

Do not use didanosine with ribavirin

- Risk of mitochondrial toxicity

Do not use stavudine with ribavirin

Abacavir

- May compete intracellularly with ribavirin
- No decrease in SVR with weight-based ribavirin

Alvarez D et al. *J Viral Hepat* 2006;13:683-9
Amorosa VK et al. *Antivir Ther* 2010;15:91-9

Partnerships for Care

HIV TAC TEAM

*probably ok **atazanavir ok † maraviroc ok

	Abacavir	Emtricitabine	Enfuvirtide	Lamivudine	Raltegravir	Dolutegravir	Rilpivirine	Tenofovir (TDF)
Elb/Graz	✔	✔	✔	✔	✔	✔	✔	✔
Sof/Vel	Can be used with most antiretrovirals							⌘
Sof/Led								✕
PrOD**		✔	✔	✔	✔	✔		✔
Simeprevir †	✔	✔	✔	✔	✔	* ✔	✔	✔

⌘ Vel and Led increase tenofovir levels when given as TDF. Avoid in those with CrCl below 60 mL/min. Renal monitoring is recommended during the dosing period

✕ Avoid Led+ TDF + ritonovir or cobi

Recommended Regimens for HIV/HCV-coinfected Individuals

- HIV/HCV-coinfected persons should be treated and retreated the same as persons without HIV infection, after recognizing and managing interactions with antiretroviral medications (see Initial Treatment of HCV Infection and Retreatment of Persons in Whom Prior Therapy Has Failed).

- Daily daclatasvir (refer above for dose) plus sofosbuvir (400 mg), with or without ribavirin (refer to Initial Treatment of HCV Infection and Retreatment of Persons in Whom Prior Therapy Has Failed sections for duration) is a Recommended regimen when antiretroviral regimen changes cannot be made to accommodate alternative HCV direct-acting antivirals.

Regimens Not Recommended for Patients with HIV/HCV Coinfection

- Treatment courses shorter than 12 weeks, such as the use of 8 weeks of ledipasvir/sofosbuvir.

Monitoring Guidance

- Clinic visits or telephone contact as clinically indicated
- CBC, Cr level, GFR, hepatic function panel after 4 weeks and as clinically indicated
- Patients receiving elbasvir/grazoprevir should be monitored with hepatic function panel at 8 weeks (and again at 12 if receiving 16 weeks treatment)
- 10 fold increase in ALT at week 4 <10 fold increase with symptoms should prompt discontinuation
- If <10 fold and no symptoms, repeat ALT at week 6 and 8

Monitoring Recommendations

- Quantitative HCV testing at 4 weeks of therapy and 12 weeks following completion of therapy
- Antiviral therapy should NOT be interrupted or discontinued if viral load testing is not able to be done
- Viral load testing can be considered at the end of treatment and 24 weeks or longer following completion
- Patients with compensated cirrhosis on paritaprevir/ritonavir based regimen should be monitored per guidelines
- For HBsAg+ patients who are not already on HBV suppressive therapy, monitor HBV DNA levels during and immediately after treatment and antiviral treatment should be given if criteria are met

Testing Recommendations

- If HCV RNA is detectable at week 4 of treatment, repeat quantitative HCV RNA viral load testing is recommended treatment week 6
- If quantitative HCV viral load has increased by greater than 10-fold (>1 $\log_{10}$ IU/mL) on repeat testing at week 6 (or thereafter), then discontinuation of HCV treatment is recommended

NEXT SESSION:

HIV TAC COLLABORATIVE TRAINING

Challenges in Access to HCV Care

Date: Wednesday, August 23, 2017

Time: 12:00PM – 1:00 PM EDT

Register Here:

https://attendee.gotowebinar.com/register/7335664884775362305

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Participate as Health Center co-presenter.

Contact:

Victor Ramirez,
P4C HIV TAC Collaborative Training Coordinator
vramirez@mayatech.com

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P4CHIVTAC@mayatech.com