

HCV Management in the Presence of HIV Co-infection

Heather King, MSN, CFNP

University of Mississippi Medical Center

Division of Infectious Diseases

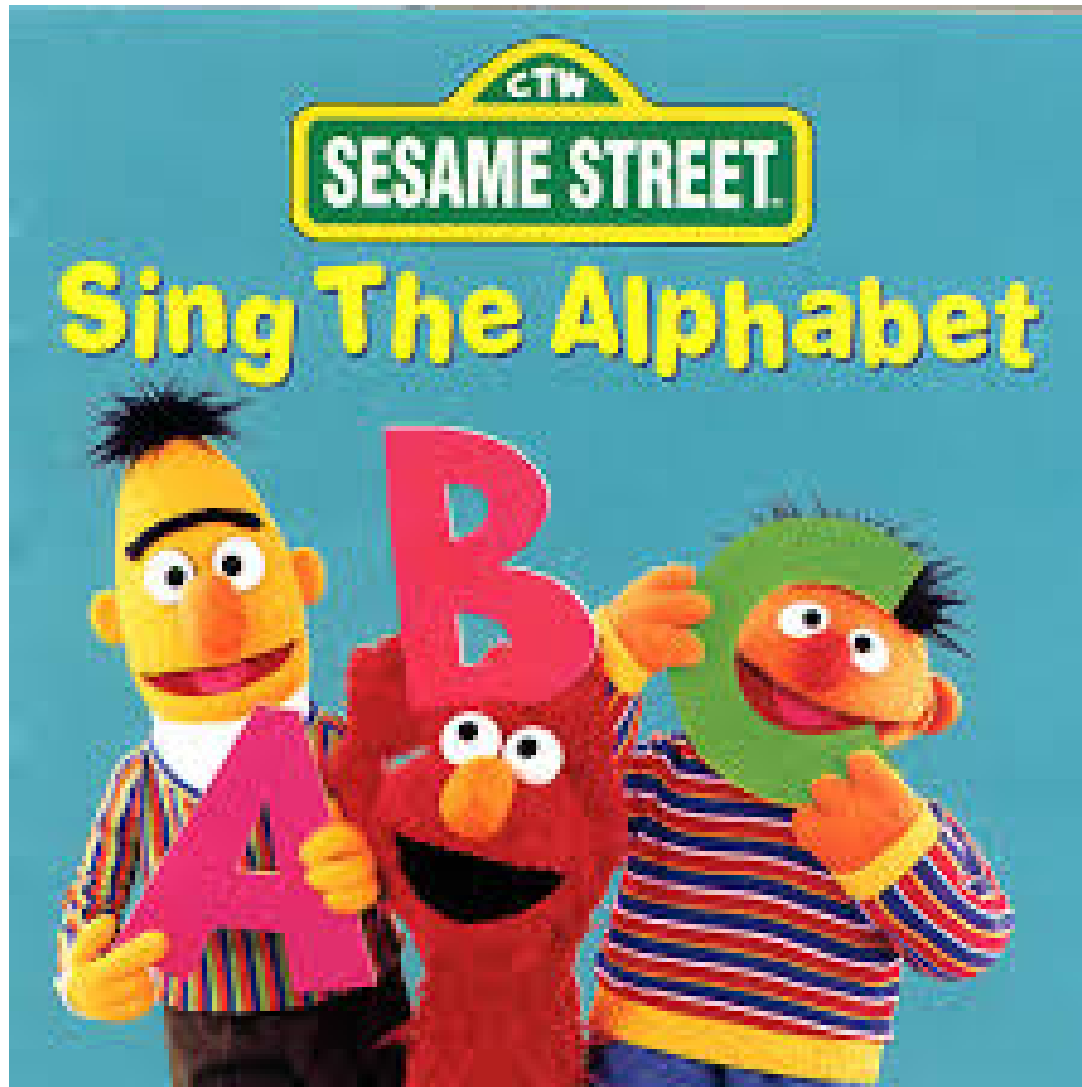
September 17, 2015

Acknowledgement

I would like to thank Dr. Svenja Albrecht, who provided, with consent, some of the slides in this presentation.

I do not have any conflicts of interest.

Outline



Objectives

- Objective 1: Discuss the differences between Hepatitis A, B, C, D, and E.
 - A. Route of infection
 - B. Symptoms
 - C. Serology
 - D. Screening Guidelines (Hepatitis B and C)
 - E. Recommended Vaccines (Hepatitis A and B)
 - F. Available treatment (Hepatitis B)

Objectives

- Objective 2: Discuss HCV treatment recommendations in the presence of HIV co-infection
 - A. Importance of providing HCV treatment in HIV co-infected patients
 - B. AASLD/IDSA Treatment Guidelines for HIV/HCV co-infected patients
 - C. Treatment considerations
 - D. Treatment specifics

Hepatitis A

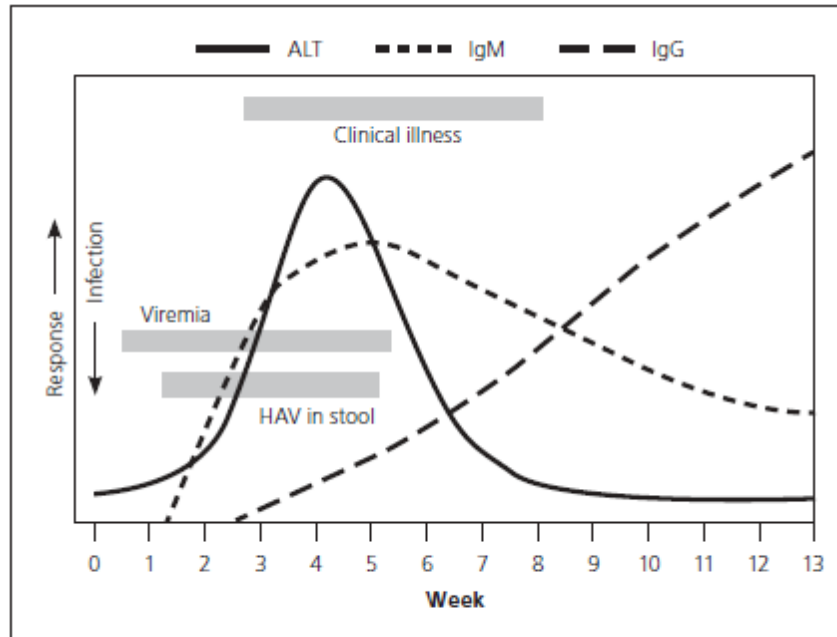


Figure 2. Timeline for hepatitis A manifestations. (ALT = alanine transaminase; HAV = hepatitis A virus; Ig = immunoglobulin.)

- *Enveloped RNA virus, worldwide distribution, fecal-oral transmission
- *Not chronic but can see relapse at 2-6 months
- *US prevalence decreased >90% since vaccine in 1995 (universal childhood vaccination in 2006)
- *Asymptomatic in 70% under age 6, icteric illness 70% adults
- ***HAV IgM** positive by day 5-10, sensitivity and specificity >95% for acute infection
- *Can check **HAV IgG (or total Ab)** to assess immunity prior to vaccination

Recommendations for Hepatitis A Vaccination (CDC)

Hepatitis A vaccination is recommended for all children at age 1 year, for persons who are at increased risk for infection, for persons who are at increased risk for complications from Hepatitis A, and for any person wishing to obtain immunity.

The following groups are recommended to receive Hepatitis A vaccination:

All children at age 1 year (i.e., 12–23 months).

Children and adolescents ages 2–18 who live in states or communities where routine Hepatitis A vaccination has been implemented because of high disease incidence.

Persons traveling to or working in countries that have high or intermediate rates of Hepatitis A.

Men who have sex with men.

Users of illegal injection and noninjection drugs.

Persons who have occupational risk for infection.

Persons who have chronic liver disease.

Persons who have clotting-factor disorders.

Household members and other close personal contacts of adopted children newly arriving from countries with high or intermediate hepatitis A endemicity

Licensed dosages and schedules for HAVRIX® ¹				
Age	Dose (ELISA units) ²	Volume (mL)	No. of doses	Schedule (mos) ³
12 mos–18 yrs	720	0.5	2	0,6-12
≥19 years	1,440	1.0	2	0,6-12

¹Hepatitis A vaccine, inactivated, GlaxoSmithKline.

²Enzyme-linked immunosorbent assay units.

³0 months represents timing of the initial dose; subsequent numbers represent months after the initial dose.

Licensed dosages and schedules for VAQTA® ¹				
Age	Dose (U.) ²	Volume (mL)	No. of doses	Schedule (mos) ³
12 mos–18 yrs	25	0.5	2	0,6-18
≥19 years	50	1.0	2	0,6-18

¹Hepatitis A vaccine, inactivated, Merck & Co., Inc.

²Units.

³0 months represents timing of the initial dose; subsequent numbers represent months after the initial dose.

TWINRIX®¹ (HepA/HepB) Vaccine Schedule (Not recommended for post exposure prophylaxis)

Licensed dosages and schedules for TWINRIX® ¹				
Age	Dose (ELISA units) ²	Volume (mL)	No. of doses	Schedule
≥ 18 yrs	720	1.0	3	0, 1, 6 mos
≥ 18 yrs	720	1.0	4	0, 7, 21–30 days + 12 mos ³

¹Combined Hepatitis A and Hepatitis B vaccine, inactivated, GlaxoSmithKline.

²Enzyme-linked immunosorbent assay units.

³This 4-dose schedule enables patients to receive 3 doses in 21 days; this schedule is used prior to planned exposure with short notice and requires a fourth dose at 12 months.

Hepatitis E

- Also RNA virus, predominantly fecal oral, mostly acute, mostly self limited in healthy hosts
- Can be fulminant with underlying liver dz, pregnancy
- Can be chronic, 2/2 transfusion, MTCT, other blood borne
- Consider in acute unexplained liver disease: IgM +/- PCR
- Consider in chronic hepatitis in severely immunocompromised if other causes are r/o.
 - Mostly solid organ transplant; **no special HIV risk to date**
 - Serology limited, needs PCR
- Ribavirin, interferon may be treatment option
- No vaccine available in US

Hepatitis D

The Hepatitis Deltas Virus

HBsAg

- HBsAg particles can self assemble
- HBV: 1 virion x 10^3 - 10^6 particles

HDV-RNA

- The smallest of all animal viruses
- Highly paired – rod like structure
- No enzymes but Ribozymes
- Only encodes S-HDAG

HDAG

- 2 forms: S-HDAG and L-HDAG
- S-HDAG: ↑ replication
- L-HDAG: ↑ assembly (↓ replication)

Heiner Wedemeyer:
Hepatitis Delta

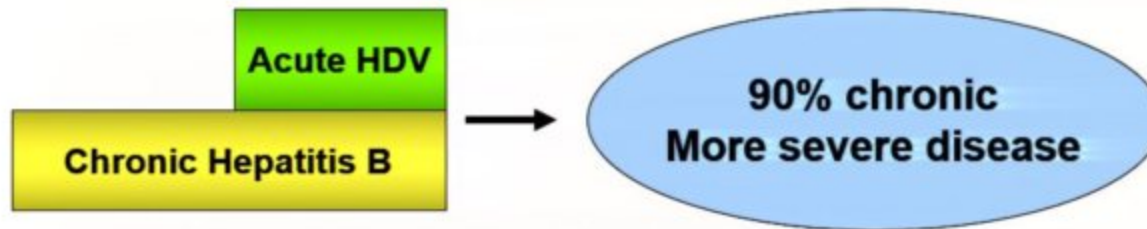
Calle Serrano, Manns & Wedemeyer, Seminars in Liver Disease 2012

- *Smallest virus known to infect humans
- *Defective satellite RNA virus; requires HBV for replication/assembly
- *Highest coinfection triple coinfection rates (HIV-HBV-HDV) in IVDA

Simultaneous Co-Infection



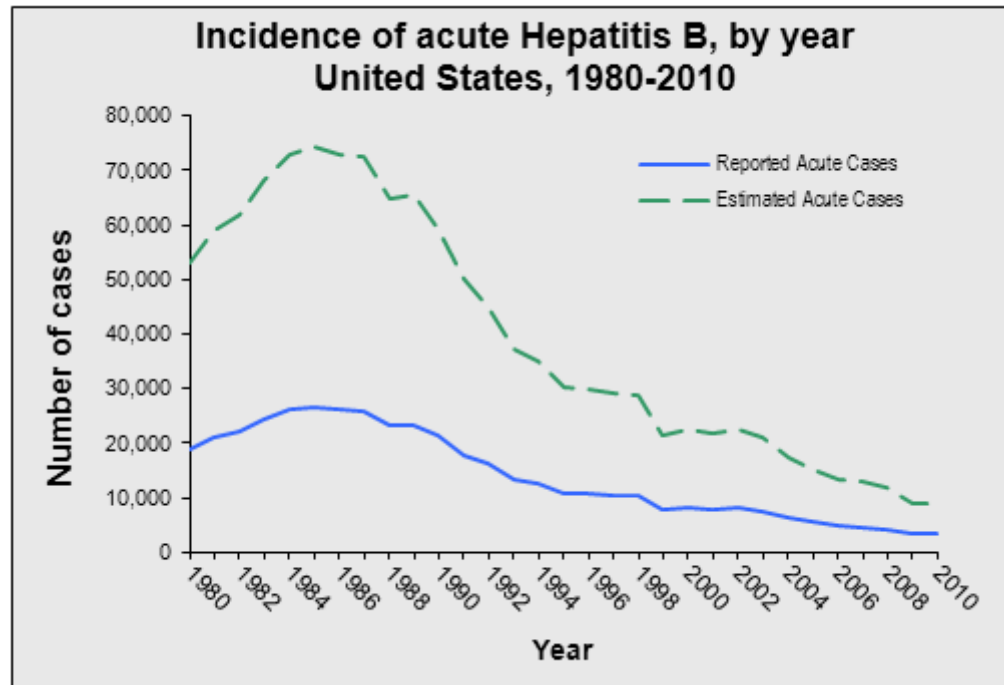
HDV Super-Infection



Hepatitis Delta 2010

- ***Consider coinfection in severe acute HBV (especially IVDA)**
- ***Consider HDV superinfection in unexplained exacerbation or progressive CHB**
- ***Screening = anti HDV-AB, confirmatory PCR (RNA)**
- *Treat HBV, only specific antiviral for HDV = PEG-IFNa
- *Phase 2a study of Lonafarnib (Prenylation inhibitor) promising in chronic HDV

Hepatitis B



- *DNA virus spread via sex, IVDA, MTCT, and other blood borne routes
- *Acute infection ranges from asymptomatic (most) to fulminant (1%)
- *High rates chronic infection if perinatal (90%), low if adult infection (5%)
- ***Chronic HBV infection = HBsAg positivity persisting for >6 months**

Hepatitis B Screening Guidelines

CHB SCREENING AND TESTING GUIDELINES SUMMARY SHEET

	AASLD
Who to screen	<ul style="list-style-type: none">• Persons born in countries with HBsAg prevalence >2% (intermediate to high HBV endemicity)• Unvaccinated children of persons from countries with ≥8% prevalence (high HBV endemicity)• Blood, organ, plasma, semen, tissue donors• Hemodialysis patients• All pregnant women• Infants born to HBsAg-positive women• Household contacts, needle-sharing or sex partners of HBV-infected persons• Sources of blood or body-fluid exposures that might warrant postexposure prophylaxis• HIV-infected and HCV-infected persons• Persons with select medical conditions (eg, elevated ALT or AST levels of unknown etiology)• Persons with behavioral exposures (eg, IDUs, MSM)
Which tests to use	HBsAg and anti-HBs

HIV coinfection: Screen EVERYONE; if negative: vaccinate!



Hepatitis B Serologies

HBsAg anti-HBc anti-HBs	negative negative negative	Susceptible
HBsAg anti-HBc anti-HBs	negative positive positive	Immune due to natural infection
HBsAg anti-HBc anti-HBs	negative negative positive	Immune due to hepatitis B vaccination
HBsAg anti-HBc IgM anti-HBc anti-HBs	positive positive positive negative	Acutely infected
HBsAg anti-HBc IgM anti-HBc anti-HBs	positive positive negative negative	Chronically infected
HBsAg anti-HBc anti-HBs	negative positive negative	Interpretation unclear; four possibilities: 1. Resolved infection (most common) 2. False-positive anti-HBc, thus susceptible 3. "Low level" chronic infection 4. Resolving acute infection

Hepatitis B e antigen (HBeAg):

A secreted product of the nucleocapsid gene of HBV that is found in serum during acute and chronic Hepatitis B. Its presence indicates that the virus is replicating and the infected person has high levels of HBV.

Hepatitis B e antibody (HBeAb or anti-HBe):

Produced by the immune system temporarily during acute HBV infection or consistently during or after a burst in viral replication. Spontaneous conversion from e antigen to e antibody (a change known as seroconversion) is a predictor of long-term clearance of HBV in patients undergoing antiviral therapy and indicates lower levels of HBV.

Treatment Algorithm for HBV in HIV Coinfection

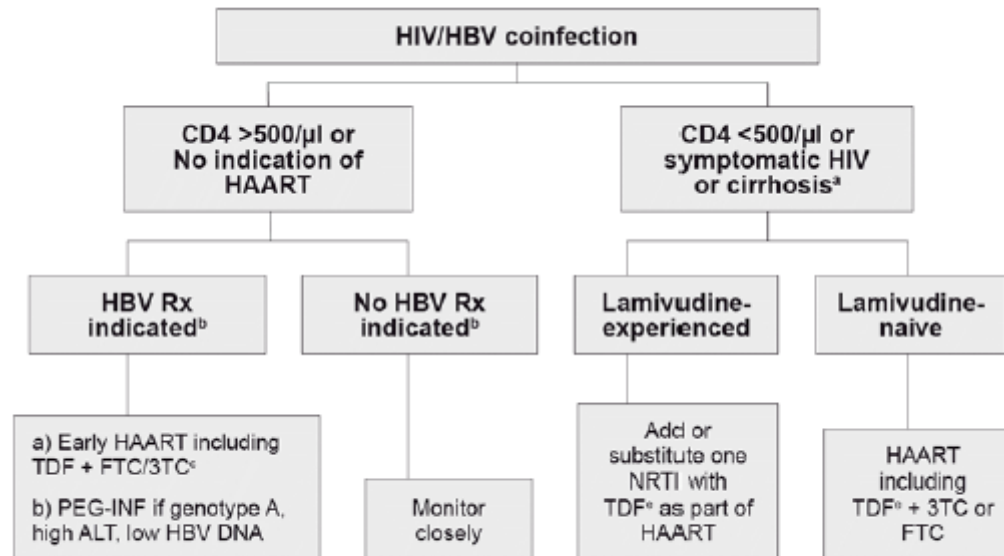


Figure 2. Treatment algorithm for HBV therapy in HIV-coinfected patients (EACS 2013)

***Treatment of one disease = indication to treat the other**

***Now that HAART indicated for (almost) every HIV infected patient = HBV treatment for all, most with TDF/FTC (Truvada)**

Treating with 2 active agents against both viruses is preferable.

- **TDF = tenofovir (Viread)**
- **FTC = emtricitabine (Emtriva)**
- **3TC = lamivudine (Epivir)**

Oral Antiviral Drugs for Hepatitis B

Table 3. Recommendations for the use of nucleos(t)ide analogs in clinical practice

Drug	Advantage	Disadvantage	Recommendation
Lamivudine (LAM)	<ul style="list-style-type: none"> • Low treatment costs • Oral solution available for children or individual dosage in case of renal impairment 	<ul style="list-style-type: none"> • High risk of resistance in long-term monotherapy • Cross-resistance to ETV and LdT 	<ul style="list-style-type: none"> • Use as first-line therapy only in selected patients with low viral load • Prevention of exacerbation in HBsAg+, HBV DNA- patients with immunosuppression • Preemptive therapy in case of HBsAg-negative, anti-HBc positive patients with immunosuppression • Use in pregnancy possible
Adefovir dipivoxil (ADV)	<ul style="list-style-type: none"> • Experience in combination with LAM • No cross-resistance to LAM 	<ul style="list-style-type: none"> • Moderate antiviral activity • Primary non-response in 10-20% of cases • Slow viral kinetics during therapy • Risk of viral resistance in long-term monotherapy • Nephrotoxicity 	<ul style="list-style-type: none"> • Not to be used as first-line therapy
Telbivudine (LdT)	<ul style="list-style-type: none"> • High antiviral efficacy • Potentially no cross-resistance to entecavir 	<ul style="list-style-type: none"> • Moderate risk for viral resistance in long-term monotherapy • Neuropathy and myopathy 	<ul style="list-style-type: none"> • First-line therapy • Can be combined with TDF
Entecavir (ETV)	<ul style="list-style-type: none"> • High antiviral efficacy • Low risk for viral resistance in long-term monotherapy in lamivudine-naïve patients • Combination therapy with TDF as rescue therapy • Oral solution available for individual dosage in case of renal impairment 	<ul style="list-style-type: none"> • In LAM-experienced patients high risk for the development of viral resistance and virologic failure in long-term monotherapy 	<ul style="list-style-type: none"> • First-line therapy • Can be combined with TDF
Tenofovir disoproxil fumarate (TDF)	<ul style="list-style-type: none"> • High antiviral efficacy • Low risk for viral resistance in long-term monotherapy 	<ul style="list-style-type: none"> • Rare Nephrotoxicity* • Decrease in bone mineral density 	<ul style="list-style-type: none"> • First- and any second-line therapy • Can be combined with ETV, LdT or LAM if needed

* in HBV-monoinfected patients no renal toxicity was observed in 5 years of TDF treatment

HBV Medication Selection

- Consider kidney function
 - Get baseline UA and BUN/Creatinine
 - If GFR<50 mL/min, avoid use of tenofovir (associated with proximal tubular injury and worsening chronic kidney disease)
- Obtain treatment history
 - Previously treated with lamivudine/emtricitabine?
 - Consider baseline HBV resistance panel
 - HBV resistance has been reported in patients using these agents (especially if they were used as monotherapy)

Monitoring on Antiviral Therapy

- HBV DNA quantitative
 - Every 3-6 months
 - Goal is to reduce HBV DNA levels to as low as possible, preferable below limits of detection. This reduces disease progression, helps prevent complications, and prolongs survival. Consider obtaining HBV resistance panel if HBV DNA increases >1 log during treatment. Assess for medication adherence first.
- LFTs
 - Every 3-6 months
- BUN/Cr
 - Every 3-6 months once (especially if tenofovir is used)
- **HCC screening every 6 months with liver ultrasound or CT/MRI (+/- AFP) regardless of cirrhosis!**

Hepatitis C

- Small, enveloped, positive-sense single-stranded RNA virus
- Most common blood-borne infection in the US
 - Estimates of chronic Hepatitis C range from 2.7 million to 3.9 million people
- Per CDC, of every 100 persons infected with HCV, approximately
 - 75–85 will go on to develop chronic infection
 - 60–70 will go on to develop chronic liver disease
 - 5–20 will go on to develop cirrhosis over a period of 20–30 years
 - 1–5 will die from the consequences of chronic infection (liver cancer or cirrhosis)
- There are 7 genetic variations of HCV, known as genotypes (GT). The GT can then further broken down into subtypes and then quasispecies.
 - GT1 is the most common in the United States and can be further broken down into subtypes a and b. GT1 and GT4 are less responsive to interferon based treatments than GT2 and GT3.
 - GT2 and GT3 are the next most common in the US.

Symptoms of Hepatitis C

- 20-30% of people acutely infected with Hepatitis C develop symptoms, usually 2-24 weeks after exposure
- Symptoms include:
 - Fever
 - Fatigue
 - Dark urine
 - Clay-colored stool
 - Abdominal pain
 - Loss of appetite
 - Nausea
 - Vomiting
 - Joint pain
 - Jaundice
- Patients with chronic Hepatitis C may not have any symptoms

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

Rating: Class I, Level B

Other persons should be screened for risk factors for HCV infection, and 1-time testing should be performed for all persons with behaviors, exposures, and conditions associated with an increased risk of HCV infection.

1. *Risk behaviors*

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

2. *Risk exposures*

- Long-term hemodialysis (ever)
- Getting a tattoo 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

3. *Other*

- HIV infection
- Unexplained chronic liver disease and chronic hepatitis including elevated alanine aminotransferase levels
- Solid organ donors (deceased and living)

Rating: Class I, Level B

*Regardless of country of birth

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.

Rating: Class IIA, Level C

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.

Rating: Class I, Level A

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 6 months; testing for HCV RNA can also be considered in persons who are immunocompromised.

Rating: Class I, Level C

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.

Rating: Class I, Level C

Quantitative HCV RNA testing is recommended prior to the initiation of antiviral therapy to document the baseline level of viremia (ie, baseline viral load).

Rating: Class I, Level A

Testing for HCV genotype is recommended to guide selection of the most appropriate antiviral regimen.

Rating: Class I, Level A

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.

Rating: Class I, Level A

Primary Care Guidelines for the Management of Persons Infected With HIV: 2013 Update by the HIV Medicine Association of the Infectious Diseases Society of America

Judith A. Aberg,¹ Joel E. Gallant,^{2,3} Khalil G. Ghanem,³ Patricia Emmanuel,⁴ Barry S. Zingman,⁵ and Michael A. Horberg⁶

¹Division of Infectious Diseases and Immunology, New York University School of Medicine, Bellevue Hospital Center, New York; ²Southwest CARE Center, Santa Fe, New Mexico; ³Johns Hopkins University School of Medicine, Baltimore, Maryland; ⁴Department of Pediatrics, University of South Florida Health, Tampa; ⁵Albert Einstein College of Medicine, Montefiore Medical Center, Bronx, New York and ⁶Mid-Atlantic Permanente Research Institute, Rockville, Maryland

25. HIV-infected patients should be **screened for hepatitis C virus (HCV) infection upon initiation of care** by a test for HCV antibody and **annually thereafter for those at risk** (strong recommendation, high quality evidence).

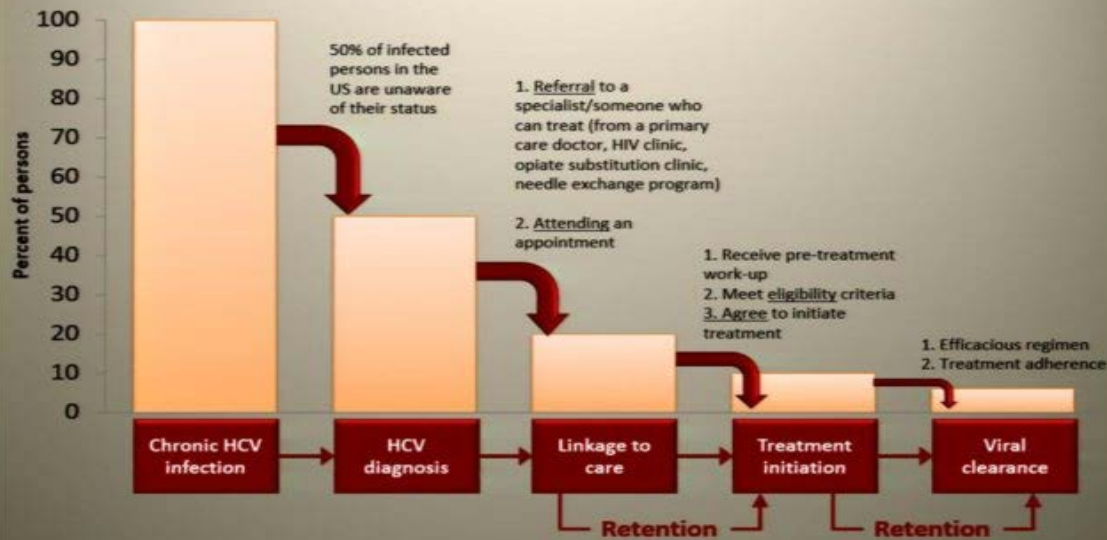
26. HCV RNA should be ordered on all those with a positive HCV antibody test to assess for active HCV disease (strong recommendation, high quality evidence).

***High risk includes all HIV positive MSM and active IVDU!**

Counseling to Avoid Transmission of Hepatitis B and Hepatitis C

- Avoid sharing toothbrushes and dental or shaving equipment
- Cover all bleeding wounds
- Stop using illicit drugs.
 - If IVDU is continued:
 - avoid reusing or sharing syringes, needles, water, and cotton or other paraphernalia
 - clean the injection site with a new alcohol swab
 - dispose safely of syringes and needles after one use
- Use condoms with all sexual activity
 - Risk of sexual transmission of Hepatitis C is low, but patient's with co-infection should be encouraged to use condoms to decrease transmission of HIV and Hepatitis C
- Do not donate blood, body organs, other tissues, or semen

The hepatitis C care cascade



Adeyemi 2004, Falck-Ytter 2002, Fishbein 2004, Fleming 2003, Grebely 2009, Groom 2008, Hall 2004, Hallinan 2007, Jowett 2001, Mehta 2006, Mehta 2008, Morrill 2005, Restrepo 2005, Rocca 2004, Stoope 2005

POC Tests for HCV Antibody Detection

Monoplex



Chembio



OraQuick

Multiplex



MedMira



mBio



*Spontaneous viral clearance after acute infection = 15%

*Screening = HCV AB

*Confirmation = RNA (Quant/Qual PCR)

*AB may be positive for life

Background: Advanced Disease Common at First Diagnosis

NHANES Evaluation of Fibrosis in Patients Aware or Unaware of HCV Status

45,000 Out of 62,000
Participants Tested for Anti-HCV

591 Positive for Anti-HCV

420 Positive for HCV RNA

418 Aged ≥ 20

417 with Available
AST, ALT, Platelets

163 Answered
Awareness Questions

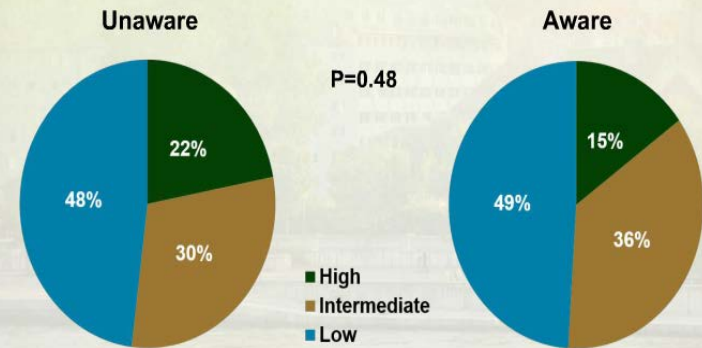
Hypothesis: Patients who have been diagnosed with HCV are more likely to have advanced disease

- HCV patients from 2001 – 2012
- 163 respondents versus 253 non-respondents
- Respondents representative clinically of overall population
- Questionnaire asked if aware versus unaware

Lazo M, et al. 50th EASL, Vienna, Austria, April 22-26, 2015. Abst. P0744.

NHANES: Probability of Advanced Fibrosis (FIB-4 Score)

- 10% Cirrhosis
- 20% Advanced Fibrosis
- Patients with undiagnosed HCV as likely to have advanced disease as those with known HCV



Lazo M, et al. 50th EASL, Vienna, Austria, April 22-26, 2015. Abst. P0744.

HIV/HCV Co-infection

- Persons with HIV/HCV:
 - Higher rate of HCV persistence
 - Faster progression of liver disease to cirrhosis and end-stage liver disease
 - Higher HCV RNA levels
 - Historically lower responses to pINF and RBV than mono-infected HCV pts
- HIV/HCV co-infection increases risk of:
 - liver-related morbidity and mortality
 - non-hepatic organ dysfunction
 - overall mortality
- Even with HIV antiretroviral therapy, HIV infection is independently associated with advanced liver fibrosis and cirrhosis in HIV/HCV co-infection
- Successful treatment of chronic Hepatitis C (SVR) decreases risk of hepatic decompensation, hepatocellular carcinoma, and liver-related mortality



AASLD/IDSA Guidance: When to Start Treatment in HCV/HIV-Coinfected Patients

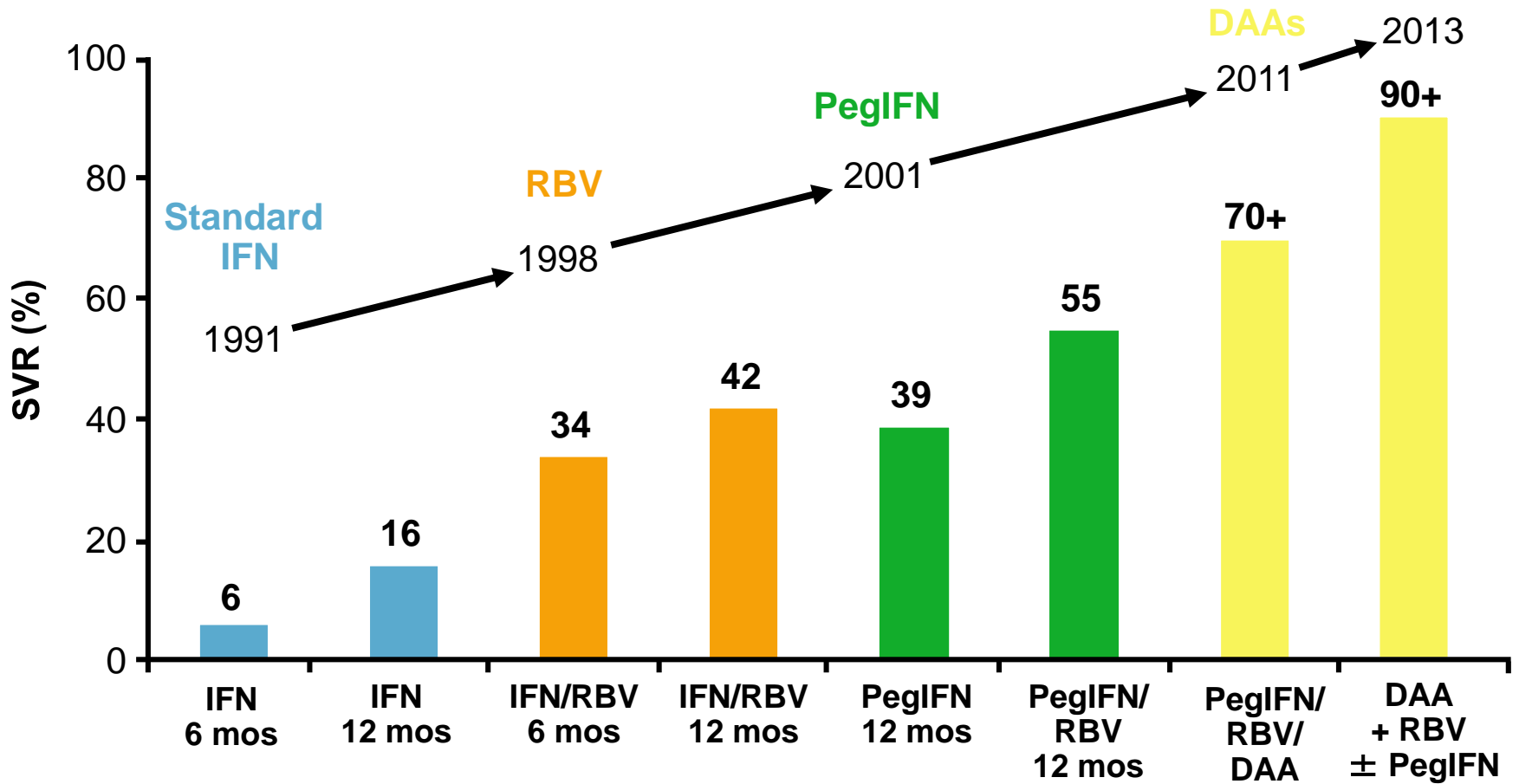
- Treatment is recommended for all patients with chronic HCV infection
- Treatment should be prioritized in patients at high risk for liver-related complications
 - Includes patients with HCV/HIV co-infection, regardless of fibrosis stage
- Treating patients at high risk for transmitting HCV to others may decrease transmission and HCV disease prevalence
 - Includes MSM with high-risk sexual practices and active injection drug users



Considerations Regarding Treatment Initiation in HCV/HIV-Coinfected Pts

- Is the pt ready and able to start therapy?
- Pts not receiving ART
 - Treat HCV now and defer ART?
- Pts receiving ART
 - Is there an HCV regimen available that can be coadministered with current ART or is ART switch needed?
 - Safe, maintain viral suppression, tolerable
 - If change HAART regimen, check HIV viral load after one month on new regimen to confirm viral suppression. Then may initiate HCV treatment.
 - Should ART interruption ever be considered?
 - Associated with increased risk of OI/death in HIV infected pts^[1]
 - Associated with increased risk of fibrosis progression in HCV/HIV-coinfected pts^[2]

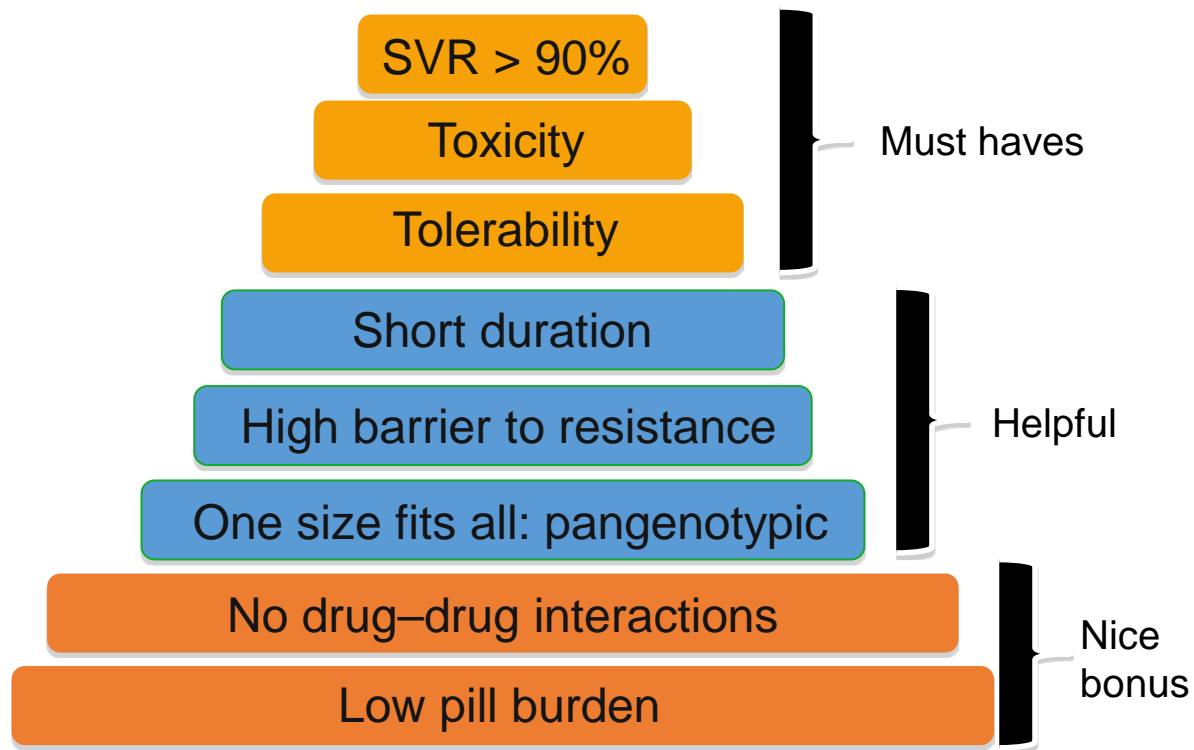
Sustained Virologic Response = "Cure"



Today's SVR Rates

- Now, recommended treatment regimens are interferon free, and most are ribavirin free with SVR rates >94% for most patients.
 - Regimens are easy to take, well tolerated, and of relatively short duration (12-24 weeks for HIV/HCV co-infected patients).

Requirements for HCV Therapy



Pre-treatment

- Hepatitis C genotype
 - GT1 is the most common in the United States and can be further broken down into subtypes a and b. GT1 and GT4 are less responsive to interferon based treatments than GT2 and GT3.
- Hepatitis C quantitative PCR (viral load)
- BMP
- Hepatic function panel
- CBC with diff
- HCV Fibrosure
- Hepatitis A Ab
- Hepatitis BsAb
- Hepatitis BsAg
- HIV screening (if HIV positive, CD4 and HIV viral load is needed)
- Liver US (with elastography is preferred)
 - If recent liver bx result is available, liver US and Fibrosure is not needed to evaluate level of fibrosis. If bx showed F3 or F4, liver US is still needed for HCC screen.

HCV Tx Selection in HIV/HCV Co-infected Patients

- Per AASLD/IDSA HCV tx guidelines updated 2/24/2016 (<http://hcvguidelines.org>)
- HIV/HCV co-infected patients should be treated/retreated the same as HIV negative patients. Specific HCV treatment regimens are not needed due to co-infection.
- Select HCV tx regimen based on HCV GT, level of Fibrosis, previous HCV tx and response, level of renal function, and possible DDIs with HAART regimen.
 - Be aware of complex drug interactions that can occur between antiretroviral medications and HCV DAAs.
- If antiretroviral switch is needed, do so prior to initiation of HCV tx, and do so in collaboration with an ID specialist.

GT1a, Tx Naïve, Non-cirrhotic

- Zepatier (fixed-dose combination of elbasvir 50mg/grazoprevir 100mg) x 12 weeks
 - For pts without baseline NS5A polymorphisms
 - For pts with baseline NS5A polymorphisms, ADD weight-based ribavirin and EXTEND tx to 16 weeks
 - Must test for NS5A polymorphisms prior to initiating HCV tx with Zepatier
- Harvoni (fixed-dose combination of ledipasvir 90mg/sofosbuvir 400mg) x 12 weeks
 - Harvoni x 8wks may be used in GT1, tx naïve, HIV negative patients who have minimal fibrosis and <6 million HCV copies at baseline. Harvoni x 8 weeks **cannot** be used to treat co-infected patients.

GT1a, Tx Naïve, Non-cirrhotic

- Viekira Pak (daily fixed-dose combination of paritaprevir 150mg/ritonavir 100mg/ombitasvir 25mg/ PLUS twice daily dosed dasabuvir 250mg) with weight-based ribavirin x 12 weeks
 - If HAART regimen contains Norvir, have pt HOLD HAART dose of Norvir, as it is included in Viekira Pak.

GT1a, Tx Naïve, Non-cirrhotic

- Olysio (simeprevir 150mg) with Sovaldi (sofosbuvir 400mg) x 12 weeks
- Daklinza (daclatisvir 60mg) with Sovaldi (sofosbuvir 400mg) x 12 weeks
 - Dose of daclatisvir may need to be adjusted when used concomitantly with cytochrome P450 3A/4 inducers and inhibitors.

GT1b, Tx Naïve, Non-cirrhotic

- Treatment of GT1B tx naïve, non-cirrhotic is the same as GT1A, EXCEPT for the following:
 - Zepatier (elbasvir 50mg/grazoprevir 100mg) x 12 weeks.
 - Do not need to check for NS5A polymorphisms.



GT1a, Tx Naïve, Cirrhotic

- Zepatier (fixed-dose combination of elbasvir 50mg/grazoprevir 100mg) x 12 weeks
 - For patients without NS5A polymorphisms
 - For pts with baseline NS5A polymorphisms, ADD weight-based ribavirin and EXTEND tx to 16 weeks
- Harvoni (fixed-dose combination of ledipasvir 90mg/sofosbuvir 400mg) x 12 weeks

GT1a, Tx Naïve, Cirrhotic

- Viekira Pak (daily fixed-dose combination of paritaprevir 150mg/ritonavir 100mg/ombitasvir 25mg/ PLUS twice daily dosed dasabuvir 250mg) with weight-based ribavirin x 24 weeks
 - If HAART regimen contains Norvir, have pt HOLD HAART dose of Norvir, as it is included in Viekira Pak.
- Sovaldi (sofosbuvir 400mg) and Olysio (simeprevir 150mg) once daily with or without Ribavirin x 24 weeks
 - Only for patients in whom no Q80K polymorphism is detected. Test for Q80K polymorphism prior to this regimen being used.

GT1a, Tx Naïve, Cirrhotic

- Olysio (simeprevir 150mg) with Sovaldi (sofosbuvir 400mg) with/without ribavirin x 24 weeks
- Daklinza (daclatisvir 60mg) with Sovaldi (sofosbuvir 400mg) with/without ribavirin x 24 weeks
 - Dose of daclatisvir may need to be adjusted when used concomitantly with cytochrome P450 3A/4 inducers and inhibitors.

GT1b, Tx Naïve, Cirrhotic

- Treatment of GT1B tx naïve, cirrhotic is the same as GT1A tx naïve cirrhotic, EXCEPT for the following:
 - Zepatier (elbasvir 50mg/grazoprevir 100mg) x 12 weeks. For GT1A, 16 weeks is needed.
 - Do not need to check for NS5A polymorphisms.
 - Viekira Pak (daily fixed-dose combination of paritaprevir 150mg/ritonavir 100mg/ombitasvir 25mg/ PLUS twice daily dosed dasabuvir 250mg) WITHOUT Ribavirin x 12 weeks. For GT1A, 24 wks with addition of RBV is needed.
 - If HAART regimen contains Norvir, have pt HOLD HAART dose of Norvir, as it is included in Viekira Pak.

GT2, Tx Naïve, Non-cirrhotic

- Sovaldi (sofosbuvir 400mg) PLUS Ribavirin (weight based) x 12 weeks
- Daklinza (daclatasvir 60mg) PLUS Sovaldi (sofosbuvir 400mg) x 12 weeks
 - Good for patients who cannot tolerate RBV
 - Dose of daclatisvir may need to be adjusted when used concomitantly with cytochrome P450 3A/4 inducers and inhibitors.

GT2, Tx Naïve, Cirrhotic

- Daklinza (daclatisvir 60mg) PLUS Sovaldi (sofosbuvir 400mg x 16-24 weeks)
 - Dose of daclatisvir may need to be adjusted when used concomitantly with cytochrome P450 3A/4 inducers and inhibitors.
- Sovaldi (sofosbuvir 400mg) PLUS Ribavirin x 16-24 weeks

GT3, Tx Naïve, Non-Cirrhotic

- Daklinza (daclatisvir 60mg) PLUS Sovaldi (sofosbuvir 400mg) x 12 weeks
 - Dose of daclatisvir may need to be adjusted when used concomitantly with cytochrome P450 3A/4 inducers and inhibitors.
- Sovaldi (sofosbuvir 400mg) PLUS Ribavirin PLUS weekly pINF x 12 weeks
- Sovaldi (sofosbuvir 400mg) PLUS Ribavirin x 24 weeks
 - For patients ineligible to receive pINF

GT3, Tx Naïve, Cirrhotic

- Daklinza (daclatisvir 60mg) PLUS Sovaldi (sofosbuvir 400mg) with/without RBV x 24 weeks
 - Dose of daclatisvir may need to be adjusted when used concomitantly with cytochrome P450 3A/4 inducers and inhibitors.
- Sovaldi (sofosbuvir 400mg) PLUS Ribavirin PLUS weekly pINF x 12 weeks
- Sovaldi (sofosbuvir 400mg) PLUS Ribavirin x 24 weeks
 - For patients ineligible to receive pINF

GT4, Tx Naïve, Non-cirrhotic/Cirrhotic

- Technivie (daily fixed-dose combination of paritaprevir 150mg/ritonavir 100mg/ombitasvir 25mg/ MINUS twice daily dosed dasabuvir 250mg) with weight-based ribavirin x 12 weeks
 - Same medication as Viekira Pak, except it does not contain dasabuvir.
 - If HAART regimen contains Norvir, have pt HOLD HAART dose of Norvir, as it is included in Viekira Pak.
- Zepatier (fixed-dose combination of elbasvir 50mg/grazoprevir 100mg) x 12 weeks
 - NS5A polymorphism test not needed
- Harvoni (fixed-dose combination of ledipasvir 90mg/sofosbuvir 400mg) x 12 weeks
- Sovaldi (sofosbuvir 400mg) PLUS Ribavirin PLUS weekly pINF 12 weeks

GT1a and GT1b, pINFL/RBV tx experienced, Non-cirrhotic

- Same recommended tx as GT1a tx naïve non-cirrhotic patients.

GT1a, pINFL/RBV tx experienced, Cirrhotic

- Recommended tx is the same as GT1A, tx naïve, cirrhotic EXCEPT:
- May also tx with Harvoni (ledipasvir 90mg/sofosbuvir 400mg) PLUS Ribavirin x 12 weeks

GT1b, pINFL/RBV tx experienced, Cirrhotic

- Recommended tx is the same as GT1A, tx naïve, cirrhotic EXCEPT:
- If using Harvoni (ledipasvir 90mg/sofosbuvir 400mg)
 - Extend tx to 24 weeks
 - OR add Ribavirin and tx for only 12 weeks

GT1 Tx Experienced with other regimens

- Previously failed tx with a NS3 protease inhibitor (Victrelis, Incivek, or Olysio):
 - Non-cirrhotic
 - Harvoni PLUS Ribavirin x 12 weeks
 - Daklinza and Sovaldi x 12 weeks
 - Zepatier PLUS Ribavirin x 12 weeks
 - Cirrhotic
 - Harvoni PLUS Ribavirin x 12 weeks
 - Harvoni x 24 weeks
 - Daklinza and Sovaldi with/without Ribavirin x 24 weeks
 - Zepatier PLUS Ribavirin x 12-16 weeks (depends on presence of NS5A polymorphism)

GT1 Tx Experienced with other regimens

- Previously failed tx with Sovaldi (sofosbuvir) PLUS Ribavirin (with/without pINr):
 - Non-cirrhotic
 - Harvoni PLUS ribavirin x 12 weeks
 - Cirrhotic
 - Harvoni PLUS ribavirin x 24 weeks
- Previously failed tx with other regimens:
 - Please discuss with an Infectious Disease Specialist, Gastroenterologist, or Hepatologist

GT2 and GT3, pINFL/RBV tx experienced, non-cirrhotic

- Same recommended tx as GT2 and GT3 tx naïve non-cirrhotic patients.

GT2 and GT3, pINFL/RBV tx experienced, Cirrhotic

- Same recommended tx as GT2 and GT3 tx naïve cirrhotic patients EXCEPT:
 - GT3 cirrhotic, MUST add weight-based Ribavirin to Daklinza/Sovaldi regimen x 24 weeks
 - For GT3 tx naïve cirrhotic, addition of Ribavirin was an option

GT2 and GT3 Tx Experienced with other regimens

- Previously failed tx with Sovaldi (sofosbuvir) PLUS Ribavirin (with/without pINF):
 - Daklinza (daclatasvir 60mg) and Sovaldi (sofosbuvir 400mg) with/without Ribavirin (must add in GT3) x 24 weeks
 - Sovaldi (sofosbuvir 400mg) PLUS Ribavirin PLUS pINF (weekly) x 12 weeks

GT4, pINF/RBV tx experienced, Non-cirrhotic/Cirrhotic

- Same recommended tx as GT4 tx naïve cirrhotic/non-cirrhotic patients EXCEPT:
 - Cirrhotic
 - If Zepatier is prescribed and the patient had prior ON TREATMENT VIROLOGIC FAILURE while on pINF/RBV, extend tx to 16 weeks and add Ribavirin
 - If Harvoni is prescribed, extend tx to 24 weeks

Harvoni

(ledipasvir/sofosbuvir)

- Fixed dose combination of an NS5A inhibitor (ledipasvir) and an NS5B polymerase inhibitor (sofosbuvir)
- Indication
 - Treatment of chronic Hepatitis C genotype 1,2,4,5, or 6
- Dosing
 - STR taken once daily with or without food
- Safety/tolerability
 - Treatment-related AEs: 45% SOF/LDV vs 71% SOF/LDV + RBV
 - Without RBV: < 1% d/c; < 1% serious AEs; headache, fatigue: ~ 20%, GI: ~ 8% to 10%; almost no anemia

Harvoni

(ledipasvir/sofosbuvir)

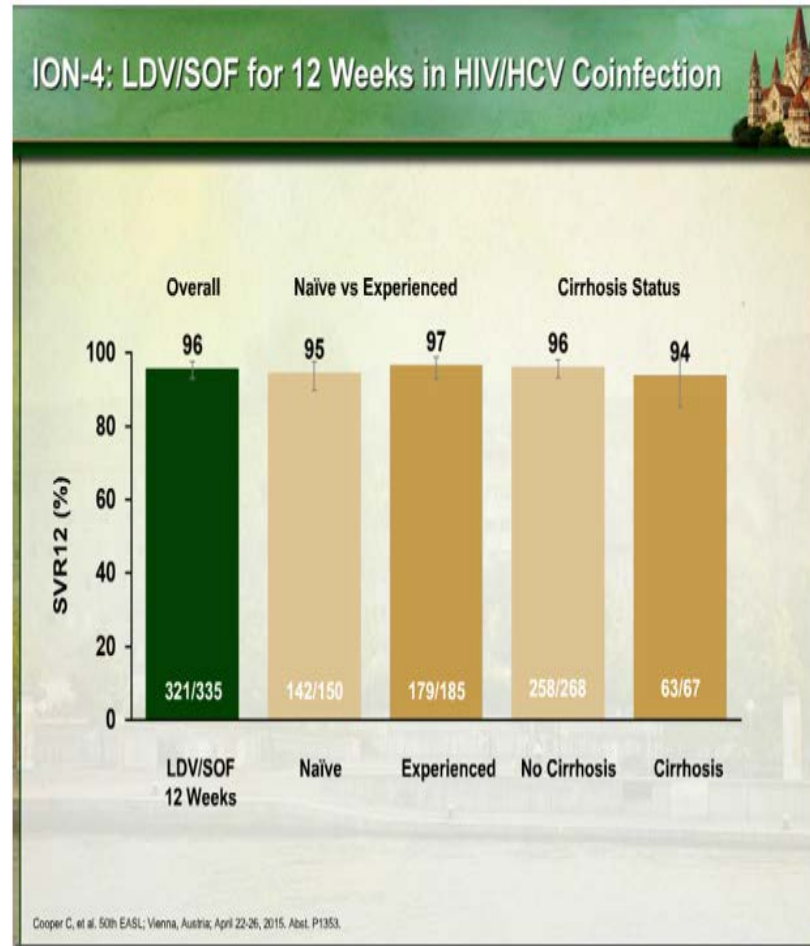
- DDIs
 - St John's wort, Rifampin (**AVOID**)
 - **Acid reducing agents:** high pH reduces LDV absorption
 - Separate antacids by 4 hours
 - Give an H2 with or 12 hours apart
 - PPI equivalent to omeprazole (Prilosec) 20mg or less must be coadministered with Harvoni on an empty stomach and then wait at least 30 min to eat
 - **Statins:** coadministration with rosuvastatin not recommended
 - **Seizure meds:** almost all contraindicated (**AVOID**)
 - Keppra is safe to use.
 - **Antiarrhythmics:**
 - Digoxin - be careful. May increase levels (monitor)
 - Amiodarone - black box warning. Causes severe bradycardia. (**AVOID**)


Harvoni

(ledipasvir/sofosbuvir)

- **ARVs:** most okay. DDI concerns with increased tenofovir levels depending on ARV combination
 - Potentiates tenofovir nephrotoxicity
 - Regimens containing tenofovir (TDF) without cobicistat or PI
 - Monitor
 - Regimens containing tenofovir (TDF) with a PI boosted with ritonavir or cobicistat, potentiates tenofovir nephrotoxicity
 - **AVOID**
 - Stribild – contains combination of TDF and cobicistat
 - **AVOID**
 - Aptivus (tipranavir) boosted with Norvir (ritonavir)
 - **AVOID**. It decreases the concentration of ledipasvir and sofosbuvir, leading to reduced therapeutic effect
 - Regimens containing new formulation of tenofovir (TAF) are okay to use, even in combination with cobicistat or boosted PI.

Harvoni: HIV Coinfected, 12 Week Duration





Daklinza (Daclatasvir)

- NS5A inhibitor
- Indication
 - Approved for use with sofosbuvir in tx of **GT1 and GT3 patients**
 - Also used as tx option in **GT2 pts (12 wks non-cirrhotic and 16-24 wks cirrhotic)**
- Length of therapy
 - 12 weeks duration for most patients
 - Decreased SVR in cirrhotic patients, so extend tx to 24 weeks
 - Add RBV for pts who previously failed tx with Sovaldi and RBV, regardless of cirrhosis status
- HCV genotype 1a with cirrhosis, consider testing for the presence of NS5A resistance-associated polymorphisms.

Daklinza (Daclatasvir)

- Overall SVR = 89%
 - Tx naïve = 90%
 - Tx experienced = 86%
- Non-cirrhotic
 - Overall non-cirrhotic = 96%
 - Tx naïve = 98%
 - Tx experienced = 92%
- Cirrhotic
 - Overall cirrhotic = 63%
 - Tx naïve = 58%
 - Tx experienced = 69%
- Adverse reactions
 - HA (14%), fatigue (14%), nausea (8%), diarrhea (5%)

Daklinza (Daclatasvir)

- Dose

- Recommended dose is 60mg once daily PO taken in combination with sofosbuvir x 12 weeks
 - Dose of daclatisvir may need to be adjusted when used concomitantly with cytochrome P450 3A/4 inducers and inhibitors.
 - Strong CYP3A inhibitors: reduce dose to 30mg once daily
 - » atazanavir/ritonavir (Reyataz/Norvir)
 - Moderate CYP3A inducers: increase dose to 90mg once daily
 - » Efavirenz (Sustiva), etravirene (Intelence)
 - Strong CYP3A inducers: **CONTRAINDICATED**
 - » Phenytoin, carbamazepine, rifampin, St. John's Wort
 - Moderate CYP3A inhibitors: monitor for adverse advents
 - » Unboosted atazanavir, darunavir/ritonavir (Prezista/Norvir), fluconazole

Sovaldi (sofosbuvir)

- Nucleotide analog NS5B polymerase inhibitor
- Indications:
 - Treatment of genotype 1, 2, 3 or 4 chronic hepatitis C virus (HCV) infection as a component of a combination antiviral treatment regimen.
- Dose:
 - 400mg tablet orally once daily with/without food
 - Use in combination with other antiviral treatment regimen (Olysio, Daklinza, RBV, pINF). It is a component of Harvoni (sofosbuvir/ledipasvir).

Sovaldi (sofosbuvir)

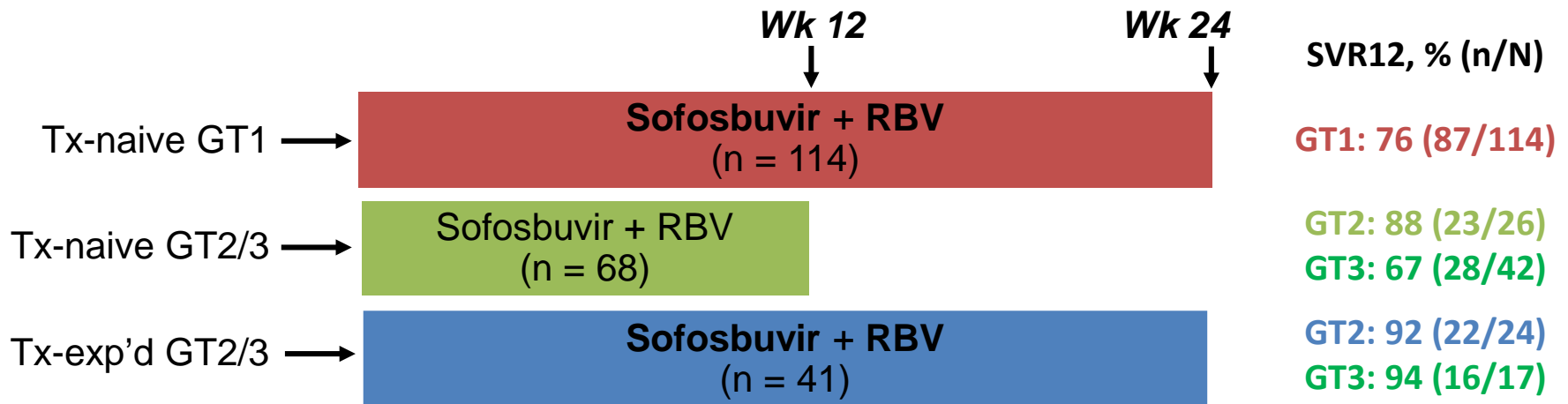
- Limitations of Use:
 - Severe renal impairment (eGFR <30) or ESRD requiring HD
 - Increases sofosbuvir metabolite
- Adverse reactions:
 - Studies did not evaluate Sovaldi alone, as it cannot be used as monotherapy.
 - For SOVALDI + ribavirin combination therapy, the most common ARs were fatigue and headache.
 - For SOVALDI + pINr+ ribavirin combination therapy, the most common ARs were fatigue, headache, nausea, insomnia and anemia.

Sovaldi (sofosbuvir)

- Do **NOT** coadminister Sovaldi with:
 - Aptivus (tipranavir/ritonavir) decreases the concentration of sofosbuvir, thereby reducing effectiveness
- ARVs safe to use with Olysio:
 - No DDIs expected with all other ARVs
- Other common medications safe to use with Olysio:
 - PPIs, H2-receptor antagonists, narcotic analgesics

PHOTON-1: Sofosbuvir + RBV in GT1-3 HCV Patients Coinfected With HIV

- Nonrandomized, open-label phase III study; primary endpoint: SVR12
- Stable ART (HIV-1 RNA < 50 copies/mL for > 8 wks before enrollment)
 - 95% on ART: TDF/FTC, 100%; EFV, 35%; ATV/RTV, 17%; DRV/RTV, 15%; RAL, 16%; RPV, 6%
- Cirrhosis at baseline: GT1, 4%; GT2/3 tx naive, 10%; GT2/3 tx-exp'd: 24%



Sofosbuvir 400 mg QD; weight-based RBV 1000 or 1200 mg/day

Olysio (simeprevir)

- NS3/4A protease inhibitor (PI)
- Indications:
 - the treatment of adults with chronic hepatitis C virus (HCV) infection:
 - in combination with sofosbuvir in patients with HCV genotype 1 without cirrhosis or with compensated cirrhosis
 - in combination with peginterferon alfa (Peg-IFN-alfa) and ribavirin (RBV) in patients with HCV genotype 1 or 4 without cirrhosis or with compensated cirrhosis.
- Dose:
 - 150mg capsule once daily, with food
 - Use in combination with other HCV medication (Sovaldi (sofosbuvir), RBV, pINF). Do NOT use as monotherapy.

Olysio (simeprevir)

- Limitations of Use:

- Efficacy of OLYSIO in combination with Peg-IFN-alfa and RBV is substantially reduced in patients infected with HCV genotype 1a with an NS3 Q80K polymorphism.
 - Strongly consider Q80K testing in patients with genotype 1a infection; if present, consider alternative therapies
- OLYSIO is not recommended in patients who have previously failed therapy with a treatment regimen that included OLYSIO or other HCV protease inhibitors.

- Adverse reactions:

- The most common (>10%) adverse reactions with OLYSIO® in combination with sofosbuvir **without RBV** were fatigue (25%), headache (21%), nausea (21%), dizziness (16%), diarrhea (16%), insomnia (14%), pruritus (11%), rash (11%), and photosensitivity (7%). The addition of RBV increases side effects associated with anemia, as hemolytic anemia is the most common adverse effect of RBV.

Olysio (simeprevir)

- Do **NOT** coadminister Olysio with:
 - Cobicistat containing products (Genvoya, Stribild, Evotaz, Prezcoibix)
 - Most NNRTIs (Sustiva, Viramune, Intelence, Rescriptor)
 - Edurant (rilpivirine) is safe to use
 - All PIs boosted/unboosted
- ARVs safe to use with Olysio:
 - Tivicay, Isentress, NRTIs, Maraviroc
- Other common medications safe to use with Olysio:
 - PPIs, H2-receptor antagonists, narcotic analgesics

Drug–Drug Interactions With ARVs

ARV	Simeprevir	Sofosbuvir
DTG (Tivicay)	No interaction expected	No interaction expected
RAL (Isentress)	Use standard doses	Use standard doses
EFV (Sustiva)	Do not coadminister	Use standard doses
DLV, ETR, NVP	Do not coadminister	Use standard doses
RPV (Edurant)	Use standard doses	Use standard doses
Any PI	Do not coadminister	
DRV/RTV (bPrezista)	Do not coadminister	Use standard doses
RTV (Norvir)	Do not coadminister	Use standard doses
TPV/RTV (Aptivus)	Do not coadminister	Do not coadminister
TDF (Viread)	Use standard doses	Use standard doses
COBI	Do not coadminister	Use standard doses

63. Sofosbuvir [package insert]. 64. Simeprevir [package insert]. 65. Kirby B, et al. AASLD 2012. Abstract 1877. 66. Ouwerkerk-Mahadevan S, et al. IDSA 2012. Abstract 49.



Viekira Pak

(Ombitasvir/Paritaprevir/Ritonavir and Dasabuvir)

- Approved for genotype 1 HCV infection only, with or without compensated cirrhosis
 - Approved for use in GT4 when dasabuvir is eliminated from the regimen
- **Regimen components**
 - **Ombitasvir: NS5A inhibitor**
 - **Paritaprevir: NS3/4 protease inhibitor with ritonavir boosting via CYP3A inhibition**
 - **Dasabuvir: non-nucleoside NS5B polymerase inhibitor** (vs SOF = nucleotide NS5B polymerase inhibitor)
- **Taken as 2 FDC ombitasvir (12.5 mg)/paritaprevir (75 mg)/ritonavir (50 mg) tablets QD and 1 dasabuvir tablet (250 mg) BID**
 - Taken with a meal; no specific limitations on fat or calorie content
 - **Weight-based ribavirin dosing: 1000 mg if ≤ 75 kg, 1200 mg if > 75 kg if indicated (all except non-cirrhotic 1B patients)**
 - Dosage divided and taken BID with food
 - No dose adjustment for hepatic or renal impairment or for HCV/HIV coinfection (may have to adjust HIV PIs)



Viekira Pak

(Ombitasvir/Paritaprevir/Ritonavir and Dasabuvir)

- **SVR**

- 92% overall for GT1, tx naïve/tx experienced with pINr/RBV
 - Turquoise I study. Had 63 participants. 5 did not achieve SVR (1 on tx failure, 1 dc'd tx, 1 relapse, and 2 were reinfected post tx)

- **AEs with Viekira + RBV (> 10% of pts):** Fatigue, nausea, pruritus, other skin reactions, insomnia, asthenia

- **AEs with Viekira only (\geq 5% of pts):** Nausea, pruritus, insomnia

- **Laboratory abnormalities in clinical trials:**

- ALT elevations of $> 5 \times$ ULN in $\sim 1\%$ of pts (women on ethinyl estradiol $>$ contraindicated)
- Bilirubin elevations $\geq 2 \times$ ULN in 15% of pts with RBV, 2% of pts without RBV
- Mean decrease in hemoglobin of 2.4 g/dL in pts with RBV, 0.5 g/dL without RBV

Viekira Pak

(Ombitasvir/Paritaprevir/Ritonavir and Dasabuvir)

- **Contraindicated medications:**

- Colchicine
- Dilantin
- St. John's wort
- Rifampin
- Ethinyl estradiol containing products
- Lovastatin and simvastatin
- **Efavirenz (Sustiva), Kaletra (lopinavir/ritonavir), Prezista/Norvir (darunavir/ritonavir), Edurant (rilpivirine), medications containing cobicistat (it is also a boosting agent)**

- **DDIs with ARVs:**

- If HAART regimen contains Norvir, have pt HOLD HAART dose of Norvir, as it is included in Viekira Pak.
- PPIs okay to co-administer but may need dose increase (reduced efficacy of omeprazole)
- - No dose adjustments needed with coadministration of the following:
- Digoxin, duloxetine, tenofovir DF/emtricitabine (Truvada), escitalopram, methadone, progestin only contraceptives, raltegravir (Isentress), warfarin, zolpidem

Zepatier

(elbasvir and grazoprevir)

- Fixed-dose combination containing an NS5A inhibitor (elbasvir) and an NS3/4A protease inhibitor (grazoprevir)
- Indication:
 - Treatment of chronic Hepatitis C GT1 and GT4 infections
 - **Must test for the presence of NS5A resistance associated polymorphisms in GT1a patients prior to treatment.**
- Dose:
 - One tablet orally, once daily. May be given with or without food. It is sometimes administered with Ribavirin, as part of a treatment regimen.
- Renal and Hepatic Impairment:
 - No dose adjustment needed in patients with renal impairment, including patients on hemodialysis. May be used in patients with mild hepatic impairment (Child-Pugh A), but is contraindicated in patients with moderate to severe impairment (Child-Pugh B and C).

Zepatier (elbasvir and grazoprevir)

- SVR:
 - Overall SVR rate for GT1 and GT4, with/without NS5A polymorphisms, treatment naive/treatment experienced was 94-100%
- AE's Zepatier: most common were fatigue, headache, nausea, insomnia, and diarrhea. Occurred in 5-7% of co-infected patients.
- AE's Zepatier + Ribavirin: most common were anemia, headache, fatigue, dyspnea, rash, irritability, abdominal pain, depression, and arthralgias. Occurred in 2-8%.
- DDIs with antiretrovirals:
 - Etravirine (dec levels of Zepatier) **CO-ADMINISTRATION NOT RECOMMENDED**
 - Stribild or Genvoya (co-admin with cobicistat containing regimens inc levels of Zepatier) **CO-ADMINISTRATION NOT RECOMMENDED**
 - Efavirenz (dec levels of Zepatier) **CONTRAINDICATED**
 - Protease inhibitors (atazanavir, darunavir, lopinavir, saquinavir, tipranavir) increases grazoprevir plasma concentrations, thereby inc. risk of ALT elevations. **CONTRAINDICATED**

Recommended Monitoring During Hepatitis C Tx

- Clinic visits or telephone contact
 - To ensure medication adherence, monitor for adverse events, and monitor potential DDIs.
- Labs at least 4 weeks after tx initiation:
 - CBC, creatinine level, eGFR, LFTs
 - If Zepatier is used, obtain LFTs again every 4 weeks until end of tx.
 - If Ribavirin is used, monitor CBC more frequently, as clinically indicated.
 - Quantitative HCV viral load
 - TSH every 12 weeks during tx if pINr is used.

Recommended monitoring after completion of Hep C Tx

- Labs:
 - Quantitative Hepatitis C viral load 12 weeks after tx completion to evaluate for SVR.
 - If HCV viral load is undetected 12 weeks after completion of treatment, SVR (sustained virologic response) will have occurred. SVR = cure. SVR does not confer immunity to Hepatitis C, so pt needs to avoid activities that increase the risk of HCV acquisition.
 - CBC, creatinine, eGFR, LFTs (and TSH if pINr used) to ensure resolution of lab abnormalities, such as anemia
- Baseline endoscopy to screen for esophageal varices (in pts with cirrhosis) if not previously done.

SVR

Now What???

- F0-F2
 - No additional follow-up needed.
- F3-F4
 - HCC surveillance every 6 months (Liver US, MRI abdomen with contrast, or 3-phase liver mass protocol CT)
 - Endoscopy to screen for varices if cirrhotic (if not previously done)
- Persistently elevated LFT's
 - Look for other causes of liver disease
 - Evaluate for re-infection if pt has ongoing risk factors. Obtain HCV RNA quantitative (viral load) in this case

No SVR

Next step???

- Evaluate for disease progression every 6-12 months
 - LFTs, CBC, INR
- HCC screening every 6 months via Liver US or CT if pt has advanced fibrosis/early cirrhosis (F3) or cirrhosis (F4)
- Evaluate other current treatment options
 - If another option is available, is patient ready for re-treatment?

No SVR

Next Step???

- Upcoming HCV therapies:
 - Sofosbuvir/velpatasvir is a once daily combination tablet made up of the nucleotide NS5B polymerase inhibitor sofosbuvir (Sovaldi), and velpatasvir, pan-genotypic NS5A inhibitor. The combination was submitted by Gilead for approval in October 2015 as a treatment for hep C genotype 1-6 infections. It is expected to be approved by the FDA at the end of 6/28/2016.
 - Per released data, 95-100% SVR after 12 weeks of tx in tx naïve/tx experienced without/with compensated cirrhosis. Lowest SVR (95%) was in GT3 tx naïve/experienced compensated cirrhotic patients. (ASTRAL-1, ASTRAL-2, ASTRAL-3).
 - ASTRAL-4 evaluated effectiveness in patients with decompensated cirrhosis. Best results occurred when RBV was added (12 weeks of tx). Lowest SVR is again, GT3 with SVR of 84%. Without RBV, SVR was 50% for GT3 when tx 12 or 24 weeks.

Thank-You!

???Questions???