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Hepatitis C in HIV/AIDS

November 2011

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This convenient pocket-sized guide is intended to assist clinicians in the diagnosis and management of chronic hepatitis C virus (HCV) infection in HIV coinfecting patients (pts). This guide summarizes guidelines for the detection of HCV infection, evaluation of pts for treatment (tx) of chronic HCV infection, contraindications to HCV tx, and recommendations for HCV tx in HIV coinfecting pts, including monitoring for response to tx and management of HCV tx complications.

Unless otherwise noted, tables and information in this card are adapted from Sulkowski, M. S., Cheever, L. W. & Spach, D. H. (2011, January 14). A Guide for Evaluation and Treatment of Hepatitis C in Adults Coinfected with HIV. Retrieved from <http://hab.hrsa.gov/deliverhivaidscafe/files/hepcocoinfectguide2011.pdf>

Background/US Epidemiology:

- 2.7-3.9 million with chronic HCV infection in the U.S.
- Of the 1.1 million living with HIV in the U.S., an estimated 300,000 are coinfecting with HCV
- Chronic HCV is a leading cause of morbidity and mortality in those coinfecting with HIV
- Effective tx for HCV exists and a cure is possible in a substantial portion of pts treated

The information contained in this publication is intended for medical professionals. If a serious adverse event occurs, please report the event to the FDA (www.fda.gov/Safety/MedWatch/HowToReport/default.htm), to help increase pt safety. Recognizing the rapid changes that occur in this field, clinicians are encouraged to consult with their local experts or research the literature for the most up-to-date information to assist with individual tx decisions for their pt.

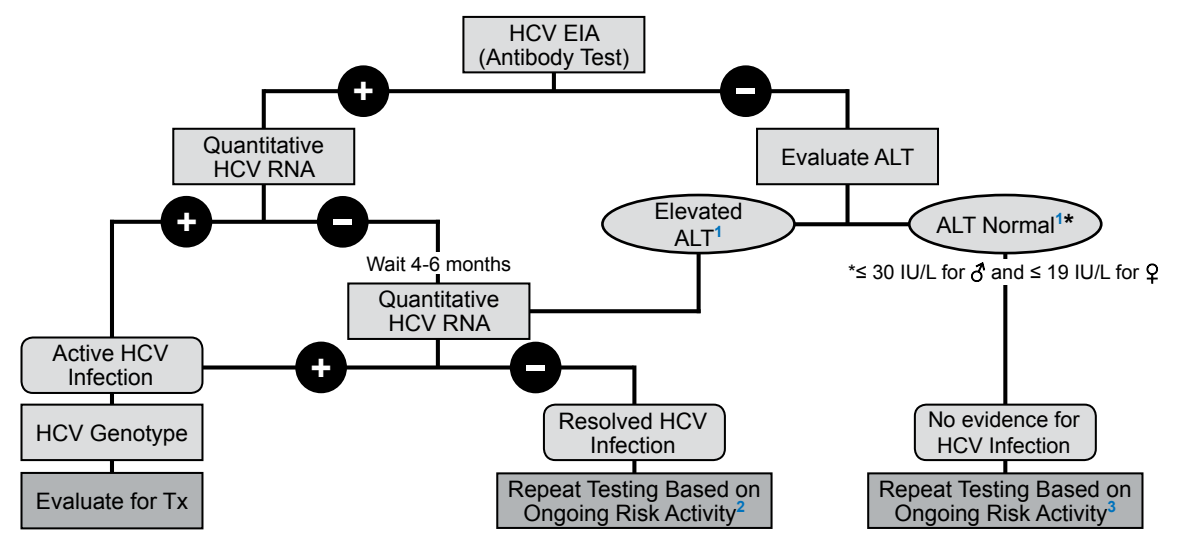
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Figure 1: HCV Testing Algorithm



1. Definitions of "normal and elevated" ALT (alanine aminotransferase level) vary. Most clinical laboratories and studies for persons coinfecting with HIV and HCV use ALT > 40 IU/L as the cut-off for elevated ALT. Prior studies in mono-infected pts have defined elevated ALT as > 30 IU/L (for men) and > 19 IU/L (for women).
 2. Positive HCV EIA, but confirmed negative RNA, indicates resolved HCV infection. Pts may become reinfected; repeat HCV RNA annually if pt has ongoing risk (e.g. unprotected sex, exposure to blood or instruments that could be contaminated with blood, risky behavior).
 3. For persons without HCV infection, repeat HCV EIA should be done annually only in those individuals with ongoing risk for acquiring HCV.

Evaluation of Liver Disease Stage

Liver Biopsy	Noninvasive Tests
<ul style="list-style-type: none"> Should be considered, but is not required Provides information on the state of intensity of liver inflammation, degree of fibrosis, amount of steatosis, and may identify other causes of liver disease May be most useful in pts in whom tx may not be as desirable, such as those with lower predicted response to tx (e.g. genotype 1 or 4 and HCV RNA > 400,000 International unit/mL or relative contraindications to tx - see "Contraindications to Therapy - Relative" table) 	<ul style="list-style-type: none"> Insufficient data to recommend routine use of these tests Most common noninvasive tests include HCV FibroSURE™, ALT, AST, platelet count, AST-Platelet Ratio Index (APRI), and FIB-4 Useful in differentiating minimal fibrosis from advanced fibrosis (i.e. cirrhosis), but not as useful in pts with intermediate stages Considered in pts who refuse liver biopsy (when recommended)

Monitoring of Patients not on HCV Therapy

- Repeat HCV RNA testing should not be done as it has no role in monitoring disease progression
- Counsel pts on the following:
 - Avoid alcohol consumption
 - Limit acetaminophen to < 2 g per day
 - Avoid nonsteroidal anti-inflammatory drugs (NSAIDs)
 - Do not ingest raw seafood (risk of infections due to Vibrio spp)
 - Maintain normal body mass index (BMI < 25 kg/m²)
 - Avoid iron supplements unless prescribed
- Evaluate pts yearly for consideration of HCV tx and document the decision in the pt's medical record
- Re-assess fibrosis staging at 2-4 yr intervals in pts who opt-out of tx due to minimal liver disease

Evaluating and Modifying Obesity

- See www.nhlbisupport.com/bmi to calculate BMI
- Pts with BMI > 25 kg/m² are considered overweight and should receive counseling on weight reduction
- Obesity is associated with development of nonalcoholic steatohepatitis (NASH). Insulin resistance may decrease response to peginterferon/ribavirin therapy.

Predictors of a Favorable Treatment Response	Favorable Indicators for Treatment
<ul style="list-style-type: none"> HCV genotype 2, 3 HCV RNA level < 400,000 IL-28B genotype CC Biopsy with chronic hepatitis with significant fibrosis (< portal fibrosis) Acute HCV infection Pt motivation 	<ul style="list-style-type: none"> Pt motivation Acute HCV infection Biopsy with chronic hepatitis with significant fibrosis (< portal fibrosis) Cryoglobulinemic vasculitis or kidney disease Stable HIV disease Compensated liver disease Body weight < 75 kg Age < 40 No insulin resistance Baseline ALT < 3 times upper limit of normal (ULN)

- Comorbid conditions (substance use and other psychiatric conditions)
- Safety issues
- Lack of efficacy despite adequate tx regimens
- Regimen may be too complex
- Pts may begin to feel better and decide they no longer need tx
- Adverse effects
- Pt's memory may be affected by either cognitive impairment or major depression or both
- Pt nonadherence: There are many reasons why pts may self-discontinue prescribed tx:
 - Tx intolerance
 - Several factors can affect whether a pt is given an adequate tx trial with a particular antidepressant, including psychiatrist or other mental health professional whenever possible
 - psychiatrist or other mental health professional whenever possible
 - should be assessed for suicidal ideation. Pts may require hospitalization for depression management. Manage pts in consultation with a
 - Monitor pts frequently for severity of depression (e.g. at least once a wk via phone or office visits). ALL pts with moderate or severe depression should be assessed for suicidal ideation. Pts may require hospitalization for depression management. Manage pts in consultation with a
 - Pts need to receive an adequate antidepressant dose for at least 4 wks for tx with the agent to be deemed adequate and not be considered a tx failure
 - additional 6-9 mos (even in pts with uncomplicated hx's) and at least 3 mos following completion of HCV tx
 - Treat the index episode of aggressively until remission is achieved within 10-12 wks. Following symptom remission, continue full tx for an
 - dosage range and ideally to the optimal dosage range
 - initiate therapy with the starting dose (given once daily) and increase the dose by that amount at weekly intervals to at least the adequate

7. Doses of bupropion > 100 mg per day should be given in 2 divided doses unless extended release (XR) formulation is used. All other agents can be dosed once a day.

8. Immediate-release formulation preferred in medical depressives

9. Instruct pt to take at bedtime to minimize daytime sedation

Medication	Starting Dose	Adequate Dose	Optimal Dose
Citalopram	10-20 mg once daily	20-40 mg	80 mg
Escitalopram	5-10 mg once daily	10-20 mg	40 mg
Fluoxetine	10-20 mg once daily	20-40 mg	80 mg
Paroxetine	10 mg once daily	20-40 mg	60 mg
Sertraline	25-100 mg once daily	100-150 mg	200 mg
Other Agents			
Bupropion SR ⁷	100 mg once daily	100-200 mg	300 mg
Duloxetine	20 mg once daily	30-60 mg	120 mg
Imipramine	25-50 mg once daily ⁸	150 mg	300 mg
Mirtazapine	7.5 mg once daily ⁹	15-30 mg	45-60 mg
Nortriptyline	10-25 mg once daily ⁸	75-100 mg	150 mg
Venlafaxine XR	37.5 mg once daily	150-225 mg	300 mg

DEPRESSION SCREENING AND MANAGEMENT

- Pts should be screened for depression at baseline and periodically during tx
- The 9-item pt health questionnaire (PHQ-9) is a useful depression screening tool and can be downloaded (www.phqscreeners.com/overview.aspx?Screen=02_PHQ-9) in several languages
- Propylactic serotonin-selective reuptake inhibitors (SSRIs) may be considered for some pts

The goal of tx for hepatitis C is to achieve a sustained virologic response (SVR). This is defined as an undetectable HCV RNA viral load 6 mos after completion of tx. An SVR is considered evidence of cure.

TREATMENT CONSIDERATIONS

- Pts with advanced fibrosis (e.g. bridging fibrosis and cirrhosis) should have hepatic ultrasound every 6 mos to assess for HCC
- Alpha-fetoprotein (AFP) alone is inadequate to assess for HCC and
- is not recommended

CARCINOMA (HCC)

EVALUATION FOR HEPATOCELLULAR

- Class A: Score 5-6; Class B: Score 7-9; Class C: Score > 9
- 4. Class A: Score 5-6; Class B: Score 7-9; Class C: Score > 9
- 5. Grade 1: mild confusion, anxiety, restlessness, fine tremor, slowed coordination; Grade 2: drowsiness, disorientation, asterixis; Grade 3: somnolent but rousable; marked confusion, incoherent speech, incontinent, hyperreflexia; Grade 4: coma, decerebrate posturing, flaccidity
- 6. Modified total bilirubin used to score pts with Gilbert's Syndrome or taking IDV or ATV

Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the Use of Antiretroviral Agents in HIV-1-Infected Adults and Adolescents. Department of Health and Human Services. October 14, 2011; 167. Available at <http://www.aidsinfo.nih.gov/ContentFiles/AdultandAdolescentGL.pdf>

Score	1	2	3
Encephalopathy ⁵	None	Grade 1-2	Grade 3-4
Moderate or refractory to diuretics	None	Grade 1-2	Grade 3-4
Albumin	> 3.5 g/dL	2.8-3.5 g/dL	< 2.8 g/dL
Total Bilirubin or Modified Total Bilirubin ⁶	< 2 mg/dL	2-3 mg/dL	> 3 mg/dL
Prothrombin Time	< 4	4-6	> 6
or INR	< 1.7	1.7-2.3	> 2.3

Table 1: Child-Pugh (CP) Score Calculation⁴

- Model for End-Stage Liver Disease (MELD) score and the Child-Pugh (CP) score can predict mortality risk and can be used to determine the need for liver transplantation referral
- Refer pt to hepatologist for transplantation evaluation if MELD < 10 and/or CP < 7
- See www.mayoclinic.org/medlineplus/model6.html for MELD score calculation and see table 1 below for CP score calculation
- Pts with documented or possible cirrhosis should have periodic assessment of liver status
- Model for End-Stage Liver Disease (MELD) score and the Child-Pugh (CP) score can predict mortality risk and can be used to determine the need for liver transplantation referral
- Refer pt to hepatologist for transplantation evaluation if MELD < 10 and/or CP < 7
- See www.mayoclinic.org/medlineplus/model6.html for MELD score calculation and see table 1 below for CP score calculation
- Uncontrolled active major psychiatric illness (hepatic encephalopathy, hepatic decompensation (hepatic encephalopathy, coagulopathy, or ascites)
- Uncontrolled HIV with advanced immunosuppression (CD4 < 100 cells/mm³)
- Allergy or severe adverse reaction to interferon and/or ribavirin
- Concurrent severe medical conditions including significant coronary artery disease (CAD), cardiac failure, severe hypertension, severe chronic obstructive pulmonary disease (COPD), poorly controlled diabetes, active TB, active cancer, untreated thyroid disease
- Women who are pregnant, nursing, or of child-bearing potential and/or men who have pregnant partners or partners of child-bearing potential and are unwilling, or not able to, practice contraception during tx and for 6 mos after tx ends
- Active, untreated autoimmune disease (e.g. systemic lupus erythematosus) known to be exacerbated by peginterferon and ribavirin
- Concomitant use of didanosine (ddI)

Contraindications to Therapy

- Significant hematologic abnormality
 - Hemoglobin < 10 g/dL, absolute neutrophil count < 1,000/ μ L
 - Platelet count < 50,000/ μ L
- Pts on hemodialysis \geq CrCl < 50 mL/min
- Uncontrolled diabetes mellitus
- Autoimmune disorders (systemic lupus erythematosus, rheumatoid arthritis)
- Active substance use \geq ongoing alcohol use \geq interference with adherence is anticipated
- Unrepaired mental health disorder
- Hemoglobinopathies (e.g. thalassemia major and sickle cell anemia)
- Sarcoidosis
- Solid organ transplantation pts
- Concomitant use of zidovudine (AZT)

- Substance abuse counselors
- Pt education
- Peer-based counseling
- Peer-based counseling
- Group counseling

Tools to Improve Treatment Success

- Initial Evaluation
- Initial Evaluation

- Alanine aminotransferase (ALT)
- IL28B (optional) CC > CT > TT for favorable tx response
- Albumin
- Aspartate aminotransferase (AST)
- Liver ultrasound[†]
- Pregnancy test if indicated
- Prothrombin time or international normalized ratio (INR)
- Hepatitis A antibody IgG: Hepatitis B surface antigen, Hepatitis B surface antibody, Hepatitis B core antibody IgG (begin vaccination series if indicated)

Table 3: HCV Therapy Recommendations Based on Genotype

Regimens for Genotype 1 and 4 for 48 weeks

Peginterferon alfa-2a and	Weight	Dosing
Ribavirin ¹⁰	≤ 75 kg	1000 mg/day in 2 divided doses
	> 75 kg	1200 mg/day in 2 divided doses
Peginterferon alfa-2b and	Weight	Dosing
	per kg	1.5 mcg/kg SC weekly
Ribavirin	≤ 65 kg	800 mg/day in 2 divided doses
	66-80 kg	1000 mg/day in 2 divided doses
	81-105 kg	1200 mg/day in 2 divided doses
	> 105 kg	1400 mg/day in 2 divided doses

Regimens for Genotype 2 and 3 for 48 weeks

(Peginterferon alfa-2a or Peginterferon alfa-2b) and	Weight	Dosing
	per kg	1.5 mcg/kg SC weekly
Ribavirin ¹⁰		800 mg/day in 2 divided doses

NOTE: If a pregnancy occurs during ribavirin therapy (either for a female pt or female partner of a male on ribavirin therapy), expert consultation should be obtained and the pregnancy reported to the Ribavirin Pregnancy Registry at **1-800-593-2214**.

10. Peginterferon alfa-2a (Pegasys®) and ribavirin doses should be reduced in pts with CrCL < 50 mL/min (See table 5). Do not use peginterferon alfa-2b (PEG-Intron®) and ribavirin combination tx in pts with CrCL < 50 mL/min

Table 4: Peginterferon and Ribavirin Dosage Forms

Drug	Brand	Dosage Forms
Peginterferon alfa-2a	Pegasys®	180 mcg/mL solution 135 mcg/0.5 mL solution (vials) or 180 mcg/0.5 mL (pre-filled syringes)
Peginterferon alfa-2b	PEG-Intron®	50, 80, 120, 150 mcg powder for injection (vials or Redipen®)
Ribavirin	Copegus®	200 mg tab
	Rebetol®	200 mg cap
	Ribasphere®	200, 400, 600 mg tab
	RibaPak®	800 mg/day, 1000 mg/day, and 1200 mg/day compliance packs containing 400 mg tabs

Table 5: Dosing in Renal Impairment

Peginterferon alfa-2b and ribavirin combination therapy should not be used in pts with CrCl < 50 mL/min

Creatinine Clearance	Peginterferon Alfa-2a dosing	Ribavirin dose
30-50 mL/min	180 mcg SC weekly	200 mg alternating with 400 mg every other day
< 30 mL/min	135 mcg SC weekly	200 mg daily
Hemodialysis	135 mcg SC weekly	200 mg daily

NOTE: Copegus® is the only ribavirin formulation approved for pts with CrCL < 50 mL/min

Table 6: Treatment Monitoring Labs and Visits

	Treatment Week											Post-Treatment Week		
	0	2	4 ¹¹	8	12 ¹¹	18	24 ¹¹	30	36	42	48 ¹¹	4	12	24 ¹¹
CBC	X	X	X	X	X	X	X	X	X	X	X	X	X	X
CMP	X	X	X	X	X	X	X	X	X	X	X	X	X	X
TSH	X				X	X		X		X				X
HCV RNA	X		X		X	X		X		X				X
CD4 Cell Count	X				X	X		X		X			X	X
HIV RNA	X		X		X	X		X		X	X	X	X	X
Depression Screen	X		X		X	X		X		X	X			
Clinic Visit	X		X	X	X	X	X	X	X	X	X	X		X

11. See table 7 below for definitions of virologic responses and response guide tx at these timepoints. Stop tx if EVR or cEVR (see definitions in table 7 below) are not achieved at wk 12. Consider prolonging tx to 72 wks to pts who are slow responders. If HCV RNA is detected in the post-tx period, following an end-of-tx response, the pt has experienced virologic relapse and no additional HCV RNA monitoring is indicated. See section on Managing HCV Treatment Failure or Relapse to the right

Table 7: Virologic Response Guided Therapy Terminology

Term	Weeks of Therapy	HCV RNA Viral Load
Rapid Virologic Response (RVR) ¹²	4	undetectable
Early Virologic Response (EVR) ¹³	12	≥ 2 log ₁₀ reduction from baseline
Complete Early Virologic Response (cEVR) ¹³	12	undetectable
Slow Response ¹⁴	24	undetectable (after a detectable 12 wk viral load)
End-of-Treatment Response (ETR)	end of therapy	undetectable
Sustained Virologic Response (SVR)	6 mos after therapy completed	undetectable

12. An RVR is associated with a significantly increased chance of tx success (SVR). In HCV monoinfected pts the length of therapy can be decreased with an RVR, but this is not yet a formal recommendation in HIV/HCV coinfecting pts

13. Therapy should be discontinued for pts who fail to achieve an EVR or cEVR at the end of 12 wks of therapy as there is minimal chance of achieving an SVR

14. Consider prolonging tx course to 72 wks to decrease chance for relapse

Table 8: Side Effect Management

Side Effect	Management
Influenza-like symptoms Manifestations often self-limited, with tachyphylaxis after first 2-3 injections	<ul style="list-style-type: none"> Prophylactic acetaminophen or NSAIDS <ul style="list-style-type: none"> Instruct pt to take acetaminophen 500 mg or ibuprofen 400-800 mg with mid-day peginterferon injection, repeat with dinner, at bedtime, and upon awakening in the morning Hydration
Dry, itchy skin	<ul style="list-style-type: none"> Moisturizing lotion Antihistamines <ul style="list-style-type: none"> Hydroxyzine 10-25 mg every 6 hrs as needed Diphenhydramine 25-50 mg every 6 hrs as needed
GI upset	<ul style="list-style-type: none"> Antiemetics <ul style="list-style-type: none"> Dronabinol 2.5 mg before lunch and dinner; can gradually increase to maximum dose of 10 mg twice daily Promethazine 25 mg every 4-6 hrs prn nausea
Injection-site reactions	<ul style="list-style-type: none"> Alternate injection sites; stomach and thighs are good places to inject Inject at 45-90 degree angle to skin Warm interferon in hand prior to injecting
Insomnia	<ul style="list-style-type: none"> Diphenhydramine 25-50 mg or Trazodone 25-50 mg or Temazepam 15 mg or Zolpidem 5-10 mg or Eszopiclone 2 mg One of the above can be taken at bedtime as needed for sleep

TREATMENT RELATED BONE MARROW TOXICITY

- Ribavirin therapy is primarily associated with anemia
- Interferon is most strongly associated with neutropenia and thrombocytopenia
- In many cases, dose reduction of the implicated drug can stabilize or reverse the cytopenia; however, in some cases colony stimulating factors [(epoetin alfa or darbepoetin alfa) and/or granulocyte colony-stimulating factor (G-CSF) (filgrastim)] are required. Eltrombopag is not recommended in managing tx-associated thrombocytopenia

Table 9: Anemia Ribavirin Dose Reduction

Indication	Baseline Ribavirin Dose	Dose Reduction
Hgb < 10	800-1200 mg/day	reduce by 200 mg
	1400 mg/day	reduce by 400 mg
Hgb < 10 unresponsive to initial dose reduction within 2 wks	any	further 200 mg reduction (do not reduce lower than 600 mg/day)
Severe acute Hgb drop in the first 4 wks of tx or Moderate to severe anemia symptoms or high cardiovascular risk	any	reduce dose to 600 mg/day

Use of Erythrocyte Stimulating Factors

Dosing

- Epoetin alfa 40,000 International Unit SC/wk **or**
- Darbepoetin alfa 200 mcg SC every other wk
- Goal: 1 g/dL or more increase in Hgb in 2 wks, if goal not achieved:
 - Epoetin alfa 60,000 International Units per wk **or**
 - Darbepoetin alfa 300 mcg every other wk

Outcome Goal

- Hgb between 10-12 g/dL, but not exceeding 12 g/dL
 - Hgb of > 13 g/dL resulting from erythrocyte stimulating agents has been linked to increased mortality and cardiovascular complications
 - Some experts will maintain the use of erythrocyte stimulating agents and slowly increase ribavirin dose when Hgb is between 10-12 g/dL

Table 10: Depression, Neutropenia, Thrombocytopenia Interferon Dose Reductions

Level 1 Dose Reductions			
Indications	Peginterferon alfa-2a dose	Peginterferon alfa-2b dose	Monitoring
Moderate to severe depression	135 mcg weekly	1 mcg/kg weekly	clinical/laboratory evaluation at least every 2 wks until stabilized
ANC < 500 cells/mm ³ ¹⁵			
Platelet count < 40,000 but > 25,000			
Level 2 Dose Reductions			
Indications	Peginterferon alfa-2a dose	Peginterferon alfa-2b dose	Monitoring
Severe depression	90 mcg weekly	0.5 mcg/kg weekly	clinical/laboratory monitoring at least every 2 wks until stabilized
ANC < 500 cells/mm ³ not responding to level 1 reduction within 2 wks ¹⁵			
Platelet count < 40,000 but > 25,000 not responding to level 1 reduction			

NOTE: When the clinical parameter stabilizes after dose reduction, the peginterferon dose should remain at the decreased level for the duration of therapy.

Stopping Therapy

- Neutropenia refractory to dose reduction **and** filgrastim (rare)
- Platelet count < 25,000 (tx should not be restarted if platelet count rebounds)
- Active suicidal ideation **or** rapid development of severe depression

15. The use of filgrastim (G-CSF) when the ANC falls below 500 cells/mm³ may limit the need for further peginterferon dose reductions and make the need for tx discontinuation unlikely (see below for use of filgrastim)

Use of Filgrastim (G-CSF)

- For ANC < 500 cells/mm³
- Neutropenia which does not respond to level 1 peginterferon dose reduction (many initiate at time of dose reduction)
- G-CSF 300 mcg SC once or twice weekly
- Monitor ANC at least once weekly
- Adjust dose based on response
- G-CSF may need to be dosed 2-3 times/wk to maintain ANC > 500 cells/mm³
- Hold G-CSF for ANC > 750 cells/mm³

MANAGING HCV TREATMENT FAILURE OR RELAPSE

Tx failure may be classified as one of the following:

- Partial Response - A partial EVR (> 2 log reduction in HCV viral load at wk 12) but detectable viral load at wk 24
- Null Response - Failure to achieve an EVR at wk 12
 - A longer tx course is not indicated; pts may benefit from retreatment with the addition of HCV direct acting antivirals
- Relapse - Detectable viral load after achieving an end of tx response (ETR)
 - Pts may benefit from tx extension to 72 wks, but may also be considered for retreatment with HCV directing acting antivirals
- Discontinuation due to side effects
 - Decision to retreat is based on whether the side effects may be modifiable. Depression and hematologic effects, like anemia and neutropenia, may be prevented upon retreatment with pretreatment strategies including antidepressant therapy and colony stimulating factors. Some side effects, such as severe thrombocytopenia, are not modifiable and should be managed with strategies to prevent liver disease progression.

DIRECT ACTING HCV ANTIVIRALS

Direct acting HCV antivirals (DAAs) directly inhibit the enzymatic activity of specific HCV proteins. This is in contrast to indirect acting antivirals, such as interferon and ribavirin which exhibit general antiviral activity which is not specific to HCV or its proteins. Two primary classes of DAAs are in development: HCV polymerase inhibitors and HCV serine protease inhibitors.

In May 2011 two HCV serine protease inhibitors (boceprevir, telaprevir) were approved for use in pts mono-infected with genotype 1 HCV. The drugs have demonstrated benefit in pts with prior tx failure, as well as tx-naïve pts, when used in combination with peginterferon and ribavirin. Demonstrated benefits of the first DAAs include significantly increased SVR rates in tx-naïve and retreatment pts as well as the potential for reduced tx duration based on response guided therapy.

Clinical trials are currently in-progress using both new HCV protease inhibitors in HIV/HCV coinfecting pts. Preliminary data shows improved virologic outcomes in these pts compared to those treated with only peginterferon and ribavirin. For those pts where initial or retreatment is not urgent, deferral of HCV tx until further data is available or approval of use in HIV/HCV coinfecting pts occurs may be reasonable.

Drug interactions between the HCV DAAs and HIV antiretrovirals are expected to be clinically relevant and may require dose adjustments of antiretrovirals, DAAs or both.

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