NORTHWEST AIDS EDUCATION AND TRAINING CENTER

New IDSA/AASLD Guidelines for Hepatitis C

John Scott, MD, MSc
Associate Professor, UW SoM
Asst Director, Liver Clinic, Harborview Medical Center

Presentation prepared by:
Maggie Shuhart, MD and John Scott, MD
Last Updated: Dec 3, 2014

NW AETC | echo

Disclosures

- I have served on Advisory Boards for Gilead in the past year.
- I serve on the Data Safety and Monitoring Board for Tacere Therapeutics.
- The UW receives funding from AbbVie, Gilead, Merck and BMS for clinical trials on which I am an investigator.
- Many slides courtesy of Maggie Shuhart, MD

Objectives

- To understand the national guidelines on the prioritization of treatment of hepatitis C.
- To convey the appropriate monitoring of patients on antiviral therapy, including laboratory testing.

IDSA/AASLD Guidelines

AMERICAN ASSOCIATION FOR THE STUDY OF LIVER DISEASES
AASLD

IAS–USA
International Antiviral Society–USA

IDSA
Infectious Diseases Society of America

- Joint guideline by 3 expert societies
- Grading of data and recommendations
- Online, living document

http://hcv guidelines.org

NW AETC | echo

Grading System

Classification	Description
Class I	Conditions for which there is evidence and/or general agreement that a given diagnostic evaluation, procedure, or treatment is beneficial, useful, and effective
Class II	Conditions for which there is conflicting evidence and/or a divergence of opinion about the usefulness and efficacy of a diagnostic evaluation, procedure, or treatment
Class IIa	Weight of evidence and/or opinion is in favor of usefulness and efficacy
Class IIb	Usefulness and efficacy are less well established by evidence and/or opinion
Class III	Conditions for which there is evidence and/or general agreement that a diagnostic evaluation, procedure, or treatment is not useful and effective or if it in some cases may be harmful

Level of Evidence	Description
Level A	Data derived from multiple randomized clinical trials or meta-analyses
Level B	Data derived from a single randomized trial, or nonrandomized studies
Level C	Consensus opinion of experts, case studies, or standard of care

Adapted from the American College of Cardiology and the AHA Practice Guidelines

Sofosbuvir-Ledipasvir (*Harvoni*) Indications and Usage

Genotype 1 Patient Populations	Treatment Duration*
Treatment naïve with or without cirrhosis	12 weeks
Treatment experienced** without cirrhosis	12 weeks
Treatment experienced** with cirrhosis	24 weeks

*Consider treatment duration of 8 weeks in treatment-naïve patients without cirrhosis who have a pretreatment HCV RNA less than 6 million IU/mL

**Treatment-experienced patients who have failed treatment with either (a) peginterferon alfa plus ribavirin or (b) HCV protease inhibitor plus peginterferon alfa plus ribavirin

Hepatitis C Webstudy, Harvoni package insert

NW AETC | echo

Sofosbuvir (*Sovaldi*) and Ribavirin Indications and Usage

	Treatment*	Treatment Duration
Genotype 2	Sofosbuvir + RVN	12 weeks
Genotype 3	Sofosbuvir + RVN	24 weeks
Genotype 4	Sofosbuvir, PegIFN, RVN	12 weeks

*Ribavirin is dosed 1000 mg/d divided bid for individuals <75kg and 1200 mg/d divided bid for individuals >75kg.

Sovaldi package insert

When and In Whom to Start Antiviral Therapy

"…clinicians should treat HCV-infected patients with antiviral therapy with the goal of achieving SVR, preferably early in the course of their chronic HCV infection before the development of severe liver disease and other complications."

"Limitations of workforce and societal resources may limit the feasibility of treating all patients within a short period of time. Therefore, when such limitations exist, initiation of therapy should be prioritized first to those specific populations that will derive the most benefit or have the greatest impact on further HCV transmission. Others should be treated as resources allow."

When and in Whom to Initiate HCV Treatment

The goal of treatment is to reduce all-cause mortality and liver-related health adverse consequences, including ESLD and HCC, by the achievement of SVR (Class I, Level A)

Treatment is recommended for patients with chronic HCV infection (Class I, Level A)

- Treatment is assigned the highest priority for patients with advanced fibrosis, compensated cirrhosis, or severe extrahepatic HCV, and for LT recipients
- Based on available resources, treatment should be prioritized as necessary so that patients at high risk for liver-related complications and severe extrahepatic complications are given high priority

Complications and Extrahepatic Disease where Treatment is Most Likely to Provide the Most Immediate and Impactful Benefits

Highest Priority for Treatment Owing to Highest Risk for Severe Complications
Advanced fibrosis (Metavir F3) or compensated cirrhosis (Metavir F4) (Class I, Level A)
Organ transplant (Class I, Level B)
Type 2 or 3 essential mixed cryoglobulinemia with end-organ manifestations (eg, vasculitis) (Class I, Level B)
Proteinuria, nephrotic syndrome, or MPGN (Class IIa, Level B)

Complications and Extrahepatic Disease where Treatment is Most Likely to Provide the Most Immediate and Impactful Benefits

High Priority for Treatment Owing to High Risk for Complications
Fibrosis (Metavir F2) (Class 1, Level B)
HIV-1 coinfection (Class 1, Level B)
Hepatitis B virus (HBV) coinfection (Class IIa, Level C)
Other coexistent liver disease (eg, [NASH]) Class IIa, Level C)
Debilitating fatigue (Class IIa, Level B)
Type 2 diabetes mellitus (insulin resistant) (Class IIa, Level B)
Porphyria cutanea tarda (Class IIb, Level C)

Treating Persons at Risk of Transmitting HCV

"To guide implementation of hepatitis C treatment as a prevention strategy, studies are needed to define the best candidates for treatment to stop transmission, the additional interventions needed to maximize the benefits of HCV treatment (e.g., preventing reinfection), and the cost effectiveness of the strategies when used in the target population."

Persons Whose Risk of HCV Transmission is High and in Whom HCV Treatment may Yield Transmission Reduction Benefits

High HCV Transmission Risk*
MSM with high-risk sexual practices
Active IDUs
Incarcerated persons
Persons on long-term hemodialysis
(Rating: Class IIa, Level C)

*Patients at high risk of transmitting HCV should be counseled on ways to decrease transmission and minimize the risk of reinfection

Populations Unlikely To Benefit from HCV Treatment

- Limited life expectancy (< 12 months) where treatment would not improve symptoms or prognosis

Pre-Treatment Assessment

- Assessment of degree of liver fibrosis, using noninvasive testing or liver biopsy, is recommended (Class I, Level A)
  - Combine direct biomarkers (Fibrosure) and elastography[1]
    - Liver biopsy if tests are discordant for cirrhosis (one suggests cirrhosis, the other does not)
  - If Fibrosure/elastography are not available, use APRI or FIB-4
    - APRI>2.0 or FIB-4>3.25 are fairly specific for advanced fibrosis/cirrhosis, but have limited sensitivity[2]
      - FIB-4 = (Age x AST) / (Plt x (sqr (ALT))
      - http://gihep.com/calculators/hepatology/fibrosis-4-score/
  - Consider biopsy if more accurate staging would impact treatment decisions

http://hcv guidelines.org

1. Boursier J et al. Hepatology 2012;55:58-67.

2. Chou R, Wasson N. Ann Intern Med 2013;158:807-820.

Factors Associated with Fibrosis Progression

Host	Viral
Non-modifiable Fibrosis stage Inflammation grade Older age at infection Male sex Organ transplant	Genotype 3 Co-infection with HBV or HIV
Modifiable Alcohol consumption NAFLD Obesity Insulin resistance	

Pre-Treatment Monitoring

Recommended Assessments Prior to Starting Antiviral Therapy

Assessment of potential drug-drug interactions with concomitant medications is recommended (Class I, Level C)

Recommended within 6 weeks (Class I, Level B)

- CBC
- INR
- Hepatic function panel
- Thyroid-stimulating hormone (if IFN is used)
- Calculated GFR

Recommended within 12 weeks (Class I, Level B)

- HCV genotype and quantitative HCV viral load

On-Treatment Monitoring

Recommended Monitoring During Antiviral Therapy

Every 4 weeks
- CBC
- Creatinine and calculated GFR
- Hepatic function panel

Every 12 weeks for patients on IFN
- TSH

More frequent assessment for drug-related toxic effects (eg, CBC for patients receiving RBV) is recommended as indicated
(Class 1, Level B)

Quantitative HCV viral load testing is recommended
- After 4 weeks of therapy
- At the end of treatment
- At 12 weeks following completion of therapy.

(Class 1, Level B)

Four Week Viral Load Result

Recommended Monitoring During Antiviral Therapy

Quantitative HCV viral load monitoring at 4 weeks is recommended, but discontinuation of treatment because this test result is missing is NOT recommended. (Class III, Level C)

Additional Monitoring

Recommended monitoring for pregnancy-related issues prior to and during antiviral therapy that includes RBV
Women of childbearing age should be cautioned not to become pregnant while receiving RBV-containing antiviral regimens, and for up to 6 months after stopping. (Class I, Level C)
Serum pregnancy testing is recommended for women of childbearing age prior to beginning treatment with a regimen that includes RBV. (Class I, Level C)
Assessment of contraceptive use and of possible pregnancy is recommended at appropriate intervals during (and for 6 months after) RBV treatment for women of childbearing potential, and for female partners of men who receive RBV treatment. (Class I, Level C)

Post-Treatment Monitoring

Recommended monitoring for patients in whom treatment failed to achieve an SVR
Disease progression assessment every 6 -12 months with a hepatic function panel, CBC count, and INR is recommended. (Class I, Level C)
Surveillance for HCC with ultrasound testing every 6 months is recommended for patients with more advanced fibrosis (Metavir F3 or F4). (Class I, Level C)
Endoscopic surveillance for esophageal varices is recommended if cirrhosis is present. (Class I, Level A)
Evaluation for retreatment is recommended as effective alternative treatments become available. (Class I, Level C)

Additional Recommendations

Recommendations regarding monitoring for resistance-associated variants
Monitoring for HCV drug resistance-associated variants (RAVs) on and after therapy is NOT recommended. (Class III, Level C)

Post-Treatment Monitoring

Recommended follow-up for patients who achieve an SVR
For patients who do not have advanced fibrosis (Metavir F0, F1, or F2), recommended follow-up is the same as if they were never infected with HCV. (Class I, Level B)
Assessment for HCV recurrence or reinfection is recommended only if the patient has ongoing risk for HCV infection or otherwise unexplained hepatic dysfunction develops. In such cases, a quantitative HCV RNA assay rather than an anti-HCV serology test is recommended to test for HCV recurrence or reinfection. (Class I, Level A)
Surveillance for hepatocellular carcinoma with twice yearly ultrasound testing is recommended for patients with advanced fibrosis (ie, Metavir F3 or F4), who achieve an SVR. (Class I, Level C)

Post-Treatment Monitoring

Recommended follow-up for patients who achieve an SVR
A baseline endoscopy is recommended to screen for varices if cirrhosis is present. Patients in whom varices are found should be treated and followed up as indicated. (Class I, Level C)
Assessment of other causes of liver disease is recommended for patients who develop persistently abnormal liver tests after achieving an SVR. (Class I, Level C)

End of Slide Presentation
Questions?