Newly Diagnosed: HCV Treatment & What to Expect

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Today’s talk will include off label use and discussion of drugs under study
The views, comments and suggestions expressed are based on my years of experience in hepatology research-they are mine alone and not those of any entity, university, or pharmaceutical company.

My Disclosures

- I currently work with the following drug companies/organizations either as a consultant, or as a site coordinator in their research studies:
  - Roche, Bristol-Meyers Squibb, Novartis, Schering-Plough, Ortho-Biotech, Pfizer, Valeant, Zymogenetics, Wyeth, Astellas, Isotechnika, Berlex, and the NIH.
- My apologies to any entity I may have forgotten to list.

HEPATITIS

- The term “hepatitis” means inflammation of the liver. One does not have to have a hepatitis C virus infection to have hepatitis
- Other things cause hepatitis (inflammation of the liver): exposure to toxins, and fatty liver are two examples
- Hepatitis C virus does not cause the inflammation in your liver- your immune system does
Do You REALLY Have Hepatitis C?

A positive antibody test does not mean you have an active hepatitis C infection. A positive hepatitis C antibody is not a protective antibody.

To confirm infection, you should have a viral load test known as the "HCV RNA Qualitative" test. This test will tell you if there is hepatitis C virus in your blood.

Or, you can have the "HCV RNA Quantitative" test. This test will tell you how much hepatitis C virus is present in your blood.

HCV Tests

- Enzyme Immunoassay (EIA)-main screening assay for HCV antibody, 3rd generation test (EIA 3.0), 97% sensitivity.
- Polymerase Chain Reaction (PCR)-useful for confirming HCV diagnosis and for assessing antiviral response to treatment.

HCV Tests, cont.

- Quantitative Tests for HCV RNA - The "viral load test" useful for assessing and managing HCV infection.
- Genotype Determines "breed of HCV virus" useful for determining how long to treat a subject.

HCV Infection: Extrahepatic Manifestations

- Hematologic
  - Mixed cryoglobulinemia
  - Aplastic anemia
  - Thrombocytopenia
  - Non-Hodgkin's β-cell lymphoma
- Dermatologic
  - Porphyria cutanea tarda
  - Lichen planus
  - Cutaneous necrotizing vasculitis
- Renal
  - Glomerulonephritis
  - Nephrotic syndrome
- Endocrine
  - Anti-thyroid antibodies
  - Diabetes mellitus
- Salivary
  - Sialadenitis
- Ocular
  - Corneal ulcer
  - Uveitis
- Vascular
  - Necrotizing vasculitis
  - Polyarteritis nodosa
- Neuromuscular
  - Weakness/myalgia
  - Peripheral neuropathy
  - Arthritis/arthralgia
- Autoimmune Phenomena
  - CREST syndrome
IF HCV RNA +

- Make an appointment with your doctor to outline your plan of care and treatment (if needed)
- Stop drinking alcohol
- Complementary and alternative medicines are not proven to cure hepatitis C- don’t take them
- Get as much accurate information as you can and read, take notes, make a list of questions before you see your liver expert, so you can ask the right questions

What can I expect when I see the doctor?

- Meeting your liver expert, and possibly his/her team
- A discussion about what hepatitis C means and how it will personally affect you
- A test called a genotyping
- An appointment within the next month or two for a liver biopsy
- Possibly a discussion about treatment and its affects on you, your life, your family’s life and your co-workers’ lives
- Possibly a discussion about being in a study
- Your doctor should recommend a hepatitis A and B vaccine- take them

Role of Liver Biopsy in HCV Infection

- Confirm clinical diagnosis
- Assess severity of fibrosis and necroinflammation
- Evaluate possible concomitant disease processes (e.g., alcoholic liver disease, NASH)
- Assess therapeutic intervention

Cirrhosis of the liver

Macronodular cirrhosis

I had my liver biopsy and my genotype, now what?

- Based on your liver biopsy results, your doctor may/may not recommend treatment.
- Your genotype test is useful information for the doctor to have should you require treatment.
- You may be introduced to the nurse practitioner, clinic nurse, or physician’s assistant that will be your new best friend over the next 12-18 months should you require treatment.

Other Important Tests

- Liver Function Tests: ALT, AST, total bilirubin, albumin, INR
- CBC: hemoglobin, platelets, neutrophils
- Kidney Function Tests: BUN, creatinine (if history of renal insufficiency)- may need a GFR, 24 hour protein/creatinine clearance
- TSH (and other thyroid studies)
- Ferritin (and other iron studies)
- Reticulocyte counts, auto-immune tests

Test Frequency

- CBC (with platelets and a differential to include ANC) should be drawn at baseline, week 1, 2, 4, 6, 8, 12, 16, 20, 24, 28, 32, 36, 40, 44, and 48 of therapy. The follow-up period should be: post treatment week 4, 12, and 24.
- Liver enzymes/kidney function tests (ALT, AST, albumin, bilirubin, GGT, alk. Phos., protein, BUN, creatinine). These should be drawn every time a CBC is drawn.

Test Frequency, continued

- HCV RNA- a quantitative test should be drawn at minimum: baseline (if you do not have one less than 6 months old), week 12, week 24, week 48 and post-treatment follow-up week 24 to confirm SVR.
- HCV RNA- a qualitative test can be used once the patient becomes "undetectable" by a quantitative test to confirm the test. It is best to do both at weeks 12, 24, 48 and post-treatment follow-up week 24 to confirm SVR.
Other tests.....

- If the patient is diabetic, a glucose test should be done as often as the CBC and a Hgb A1C should be drawn every 8-12 weeks.
- A baseline eye exam should be done if there is a hx of HTN, diabetes, or chronic eye conditions.
- An ECG, stress test and an echocardiogram should be done at baseline if there is a cardiac history, or the patient is already anemic.
- A chest x-ray should be done if asthma, or another pulmonary or cardiac history is present.

What to do-or, know BEFORE you begin treatment:

- Hydrate yourself with non-caffeinated beverages for 24 hours before your first injection.
- Pre-medicate yourself with acetaminophen (Tylenol) at least one hour before your first injection.
- You WILL feel like you were hit by a truck after your first shot and the 2nd and 3rd aren’t that much better.

Treatments Available

- Interferon alfa-2a (Roferon)
- Pegylated interferon alfa-2a (Pegasys)
- Interferon alfa-2b (Intron-A)
- Pegylated interferon alfa-2b (Peg-Intron)
- Interferon alfacon-1 (Valeant)
- Ribavirin made by Roche (Copegus)
- Ribavirin made by Schering (Rebetol)
- Various generics: (4 generic ribavirins are available)

Things to do- or, know BEFORE treatment, cont.

- You will get to feel better after each subsequent injection.
- Take your ribavirin doses 10-14 hours apart.
- Do not take your ribavirin after 6pm, as it may cause you to be “wired” at bedtime.
- Take your ribavirin with food as it can upset your stomach.
Interferon will be the new classes of drugs approved for quite a while, even after the treatment for quite a while, even after the new classes of drugs are approved. Interferon will be the "backbone" of pharmaceutical companies. The new drugs directly attack the virus and have significantly fewer side-effects than interferon and ribavirin.

There are numerous drugs in the pipelines of pharmaceutical companies.

IFN Side Effects
- Fatigue
- Headache
- Fever
- Chills
- Muscle aches
- Sleeplessness
- Injection site reactions
- Moodiness
- Inflammation of the thyroid gland

RBV side effects
- Skin rash ("Ribavirin rash")
- Birth defects
- Itchy skin
- Cough
- Diarrhea
- Anemia
- Loss of appetite
- Shortness of breath
- Nausea
- Vomiting
- Itchy ears, dry throat
- Nasal Stuffy

Loss of appetite
In conclusion:

- Hepatitis C in most people is not a serious life-threatening infection
- When on treatment have your blood drawn on time, don’t be afraid to call your nurse/doctor and tell them everything (side-effects, etc.)
- Depression is evident in varying degrees in ~52% of patients on interferon therapy
- Anxiety is common in patients on ribavirin
- An informed patient is a patient who will tolerate treatment better-learn as much as you can

Yes, another conclusion slide...

- If you are interested in participating in a study, please ask your doctor or nurse, discuss it with your significant others
- Stay away from bad websites: the ones where patients talk about only the bad experiences, the ones that make treatment sound like it’s “as much fun as a barrel of monkeys,” and the ones that give inaccurate information.
- Most of all, remember, you are not alone, nor are you forgotten, the ALF has support groups-use them!!

Conclusion, cont.

- Hepatitis C is “curable” in up to 56% of patients
- Even if you don’t have a sustained response, you are still helping your liver by decreasing your chance of developing liver cancer
- There are new drugs in pharmaceutical pipelines-researchers are working hard on the Hepatitis C problem-

Thank you!

- I will entertain questions, comments and even rebuttals.