Long-term Monitoring of Patients Not on Hepatitis C Treatment

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Recorded on May 20, 2013

IAS–USA
International AIDS Society–USA

Noninvasive Tests of Fibrosis Likely To Be an Alternative in the Future

- **Blood tests**
  - Fibrotest
  - AST-to-platelet ratio index
  - Enhanced liver fibrosis
  - Forns index
  - FIBROSpect
  - Fibrometer
  - Hepascore
  - FIB-4 (coinfected patients)
- **Liver Imaging**
  - Transient elastography
  - Diffuse-weighted MRI
  - MRI elastography
  - MR spectroscopy

Reviewed in Nelson et al, *Clin Gastroenterol Hepatol*, 2009.

Reevaluating and Optimizing Readiness for Hepatitis C Virus (HCV) Treatment

Reevaluating and Optimizing Readiness for HCV Treatment

- Does patient want therapy?
- Is therapy contraindicated?
- Is therapy safe?

Contraindications to Triple Therapy

Interferon alfa:

- Major uncontrolled depressive illness
- Solid organ transplant (renal, liver, lung)
- Autoimmune diseases (exacerbated by interferon alfa)
- Untreated thyroid disease
- Decompensated cirrhosis

Ribavirin

- Pregnant or unwilling to comply with adequate contraception- male and female
- Severe anemia - concurrent medical disease

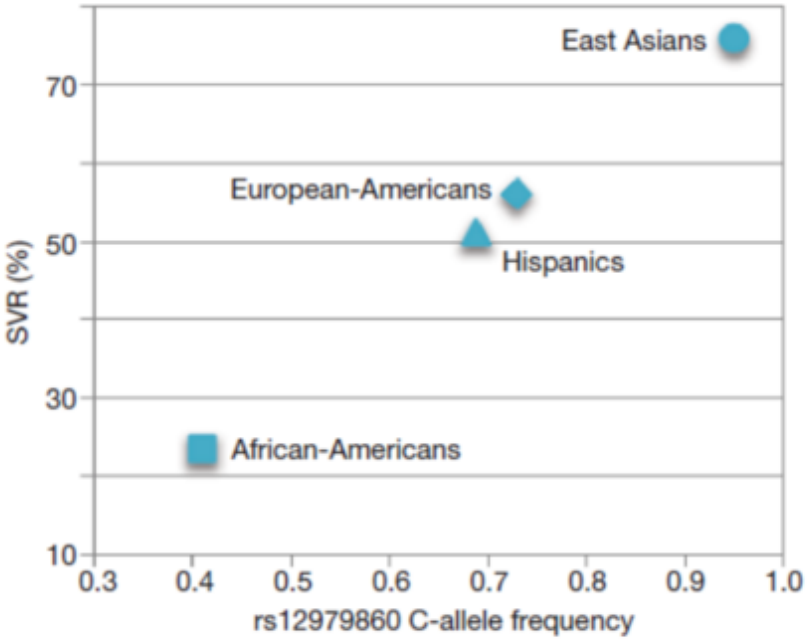
Protease inhibitor

- Drug-drug interactions
- Anemia

Testing Prior to Triple Therapy

- HCV RNA and genotype
- Liver tests: ALT, AST, Albumin, bilirubin, International Normalized Ratio (INR)
- Rule out other liver disease (eg, HIV, hepatitis B virus, autoimmune hepatitis, alcohol)
- Toxicities: complete blood cell count with differential, thyroid-stimulating hormone, antinuclear antibody, HbA1c, creatinine
- IL28B genotyping predicts interferon alfa responsiveness

C Allele Frequency Varies by Race/Ethnicity



Thomas, *Nature*, 2009.

Impact of IL28/29 on Direct-Acting Antiviral Therapy

- Impact of testing for *IL28B* is important with peginterferon alfa and ribavirin
- *IL28B* testing will need to be investigated when developing new direct-acting antiviral drugs
- *IL28B* testing for telaprevir and boceprevir suggests this is a less important predictor, especially in treatment-naive patients

Testing Prior to Triple Therapy

- Interferon alfa–based therapies:
  - If hypertension or diabetes: eye exam, stress test
- If cirrhosis: MELD, ultrasound, alpha-fetoprotein, EGD, orthotopic liver transplantation evaluation
- Assess psychiatric state
- Assess substance abuse: adherence, alcohol
- Counsel on contraception and drug-drug interactions
- Assess all medications and herbal supplements for drug-drug interactions

Summary

- Assess liver function: INR, albumin
- Assess inflammation: ALT/AST
- Ongoing assessment suitability for current and future therapies
- Assess if cirrhosis
- If cirrhosis
  - HCC screening even if cured (SVR)
  - EGD
  - Monitor for decompensation (ascites, encephalopathy, varices)
  - MELD every 3 months (INR, bilirubin, creatinine)

Disclosure Information

Dr Peters has reported the following financial relationships with commercial firms:

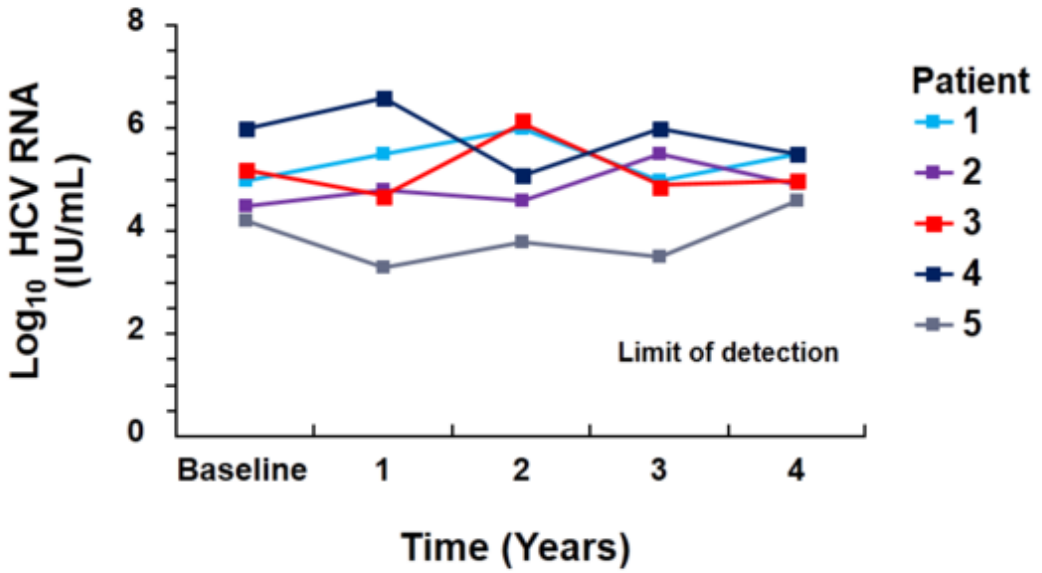
- Consultant: Merck & Co, Inc, Theravance, and Roche
- Data safety monitoring board: Biotron
- Scientific advisor: Clinical Care Options
- Her spouse is employed by Genentech (Roche)

Outline

- Laboratory monitoring and reassessment of liver fibrosis
- Reevaluating and optimizing readiness for hepatitis C virus (HCV) treatment

Laboratory Monitoring and Reassessment of Liver Fibrosis

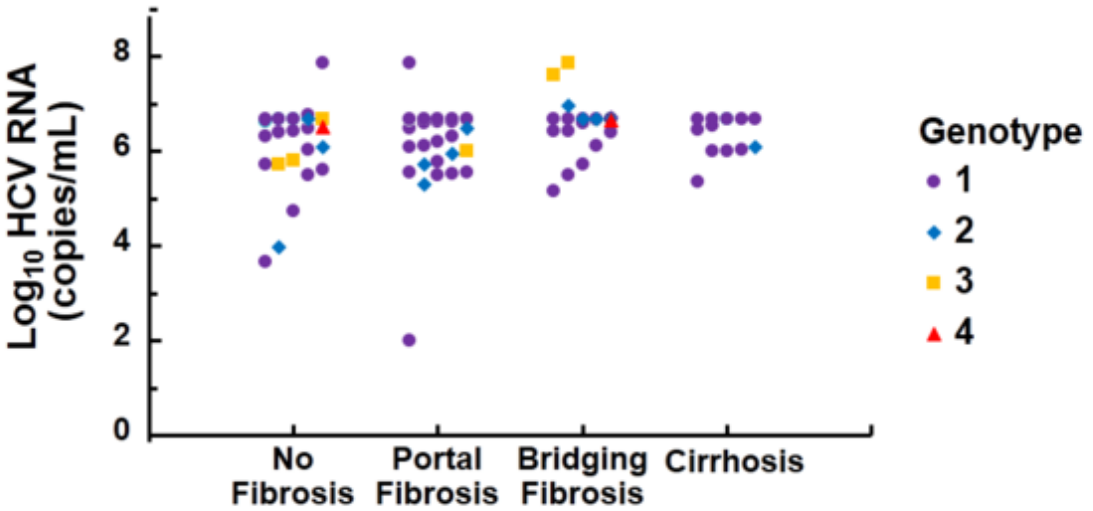
Serum HCV RNA Level
Stability Over Time



Ferreira-Gonzalez A et al, *Semin Liver Dis*, 2004.

HCV RNA and Liver Histology
Fibrosis

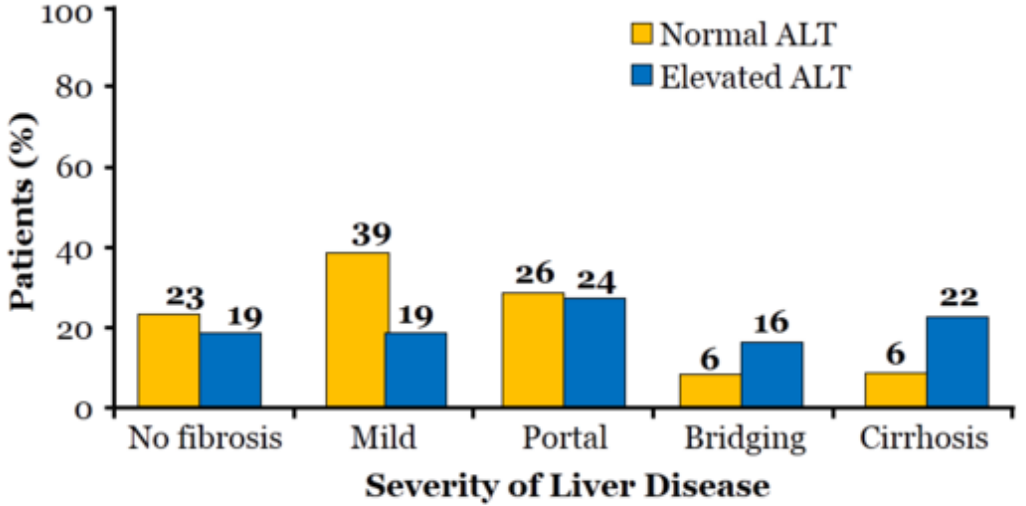
- Serum HCV RNA does not correlate with level of fibrosis



Ferreira-Gonzalez A et al, *Semin Liver Dis*, 2004.

Serum ALT Levels: An Imperfect Marker of Liver Disease Severity

- Distribution of hepatic fibrosis in 95 HCV-infected patients



Shiffman ML et al, *J Infect Dis*, 2000.

Laboratory Monitoring and Reassessment of Liver Fibrosis

- Assess if cirrhosis is present
  - Clinical
  - Laboratory
  - Noninvasive methods
  - Liver biopsy
- Cirrhotic patients need assessment for varices, hepatocellular carcinoma (HCC), and decompensation
  - Esophagogastroduodenscopy (EGD)
  - Ultrasound every 6-12 months
  - Model for End-Stage Liver Disease (MELD) score every 3 months

Staging of Liver Disease

- Not needed if no therapy required
- Less important prior to HCV treatment as treatment success increases
- Noninvasive markers improving
- Transient elastography now approved in United States
- Ultrasound, computed tomography (CT), magnetic resonance imaging (MRI) useful in cirrhosis but not useful to stage disease