

Liver Debate

Do not treat low stage genotype 1 HCV
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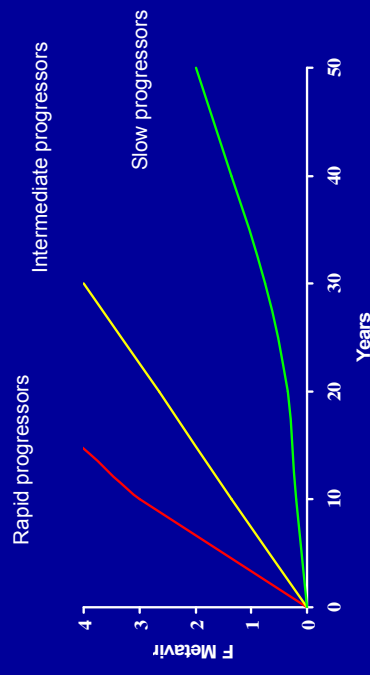
AASLD Recommendations: Treatment of Hepatitis C

“For patients whom liver histology is available, treatment is indicated in those with more-than-portal fibrosis” (Grade III)
 “Treatment decisions should be individualized based on severity of liver disease, the potential of serious side effects, the likelihood of treatment response and the presence of comorbid conditions” (Grade III)

Strader et al. Hepatology 2004;1147-1171

Most Patients with HCV Have a Benign Natural History

Chronic Hepatitis C (n=1157 patients)



Peynard et al, Hepatology 1999

Natural History: 25 Years

N=222 patients with acute transfusion associated HCV and n=377 controls
 Average age at transfusion 49 years
 Only 17% had cirrhosis at 25 years
 63% had some alcohol consumption, 23% heavy alcohol consumption (>175 gm/week)
 HCV group had marginally higher liver-related mortality (4.1% vs. 1.3%, p=0.05)
 No significant difference in all-cause mortality between groups

Seeff LB et al. Hepatology 2001;33:455-463

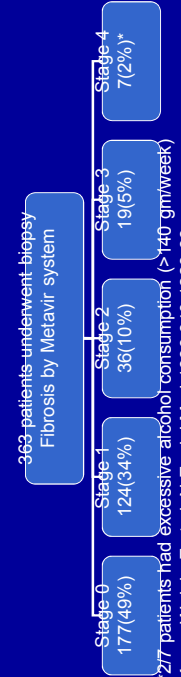
Natural History: 45 Years

45 year follow-up from serum stored by Veterans Hospital (unrelated to liver disease)
 17 of 8568 patients were HCV positive from the stored samples
 2/17 patients had liver disease
 1/17 patients died from liver disease

Seeff LB et al. Ann Intern Med 2000;132:105-111

Natural History in Young Women

62667 women screened after anti-D administered
 704 had past evidence of HCV infection (average time of infection was 17 years)
 390 still positive for HCV RNA
 363 underwent liver biopsy



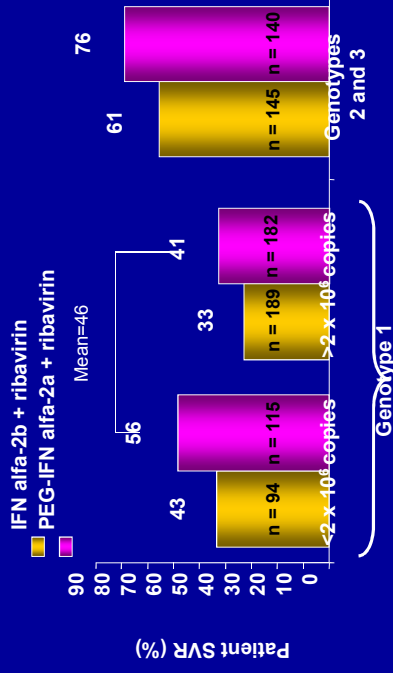
Conclusion Part I

Fibrosis progression is slow in most patients with hepatitis C
 Long-term natural history studies show that hepatitis C progresses to cirrhosis in <20% of patients over 25 to 45 years

Treatment Failure is at Least as Common As Success

Genotype 1 is difficult to treat

SVR by Genotype and Viral Load



Fried MW, et al. *N Engl J Med*. 2002;347:975-982.

Adverse Events

- Fatigue 54%
- Headache 47%
- Pyrexia 43%
- Myalgia 42%
- Insomnia 37%
- Nausea 29%
- Alopecia 28%
- Arthralgia 27%
- Irritability 24%
- Rigors 24%
- Pruritis 24%
- Depression 22%
- Dermatitis 21%

Fried MW et al. *N Engl J Med* 2002;347:975-82

Reduced Response Rates Occur in Many Different Populations

- African Americans SVR: 19-28%
 - Conjeevarum H et al. *Gastroenterology* 2006
 - Muir AJ et al. *N Eng J Med* 2004
 - Jeffers LJ et al. *Hepatology* 2004
- Hispanics
 - Munoz H et al. *Puerto Rico Health Sciences Journal* 2004
 - Cheung RC et al. *Am J Gastroenterol* 2005
- Older age
- Higher body weight
- Cirrhotics
 - Davis GL et al. *Hepatology* 1997

Treatment Site Impacts on Response

Studies conducted in academic centers have better response rates than elsewhere

Multi-center, retrospective cohort study (with interferon alpha-2b/ribavirin)

End-of-treatment viral response:

Academic centers 40%

Private centers 31%

Veterans' Affairs centers 17%

Jensen DM et al. Aliment Pharmacol Ther. 2004;19:69-77

Conclusion Part II

Treatment efficacy is limited for HCV genotype I

Interferon and ribavirin cause a number of side effects

Cost of Therapy

Costs

Annual cost of care for patients with chronic HCV

\$123

Compensated cirrhosis

\$895

Treatment of genotype 1 (Pegylated IFN and ribavirin)

\$18,507

It would take 150 years of HCV care to equal the cost of one year of treatment

Values reflect 2001
Salomon JA et al. JAMA 2003

Liver Biopsy Safety

3214 liver biopsies over 9 years

Complications requiring hospitalization
0.9%

Mortality 0.06%

Firpi RJ et al. Clin Gastroenterol Hepatol 2005.

CONCLUSIONS. Do No Harm

Benign Natural History
Can Monitor by Biopsy
Limited Efficacy
Side Effects
Cost
New Drugs in Development

Universal Treatment
"Treating Ourselves"

