



NORTHWEST AIDS EDUCATION AND TRAINING CENTER

# HIV and Hepatitis C: Practical Aspects of Hep C Treatment

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# Outline

- **Getting Your Patient Ready**
  - Psychiatric and Substance Abuse Issues
  - Financial Issues
- **Monitoring and Stopping Rules**
- **Common Side Effects**

# Side Effects of Interferon/Ribavirin Therapy

- Cytopenias
- Depression, anxiety, insomnia
- Rashes
- Flu like syndrome
- Thyroid dysfunction
- Retinopathy
- Nausea, vomiting, diarrhea
- Cough



“Interferon Man”

# Check List before Starting Hep C therapy

- ✓ Psychiatrically stable?
- ✓ Substance abuse?
- ✓ Decompensated cirrhosis (CPT score > 7)
- ✓ Baseline cytopenias?
- ✓ Stable thyroid function?
- ✓ Well-controlled HIV?
- ✓ Good adherence and ability to comply with followup?
- ✓ If history of HTN or DM, recent dilated retinal exam?
- ✓ Adequate social support?



# Brief Review of IFN and Depression

- Estimates are that HCV tx-emergent depression is a complication in 33% of cases.
- Most of these cases occur in the first 12wks of HCV tx.
- Multiple studies have failed to find a difference in IFN tx-adherence / SVR rates comparing pts with a pre-tx h/o MDD v. control HCV pts
- The best ([and perhaps only validated](#)) predictor for HCV tx-emergent depression is baseline depressive symptoms just prior to starting tx

# Should I prophylaxe patients with SSRI prior to PegIFN and Ribavirin?

ORIGINAL RESEARCH

Annals of Internal Medicine

## Escitalopram for the Prevention of Peginterferon- $\alpha$ 2a–Associated Depression in Hepatitis C Virus–Infected Patients Without Previous Psychiatric Disease

A Randomized Trial

Martin Schaefer, MD; Rahul Sarkar, MD; Viola Knop, MD; Susanne Effenberger, MSc; Astrid Friebe, MD; Loni Heinze, MD; Ulrich Spengler, MD; Thomas Schlaepfer, MD; Jens Reimer, MD; Peter Buggisch, MD; Johann Ockenga, MD; Ralph Link, MD; Michael Rentrop, MD; Hans Weidenbach, MD; Gwendolyn Fromm, MD; Klaus Lieb, MD; Thomas F. Baumert, MD; Andreas Heinz, MD; Thomas Discher, MD; Konrad Neumann, PhD; Stefan Zeuzem, MD; and Thomas Berg, MD



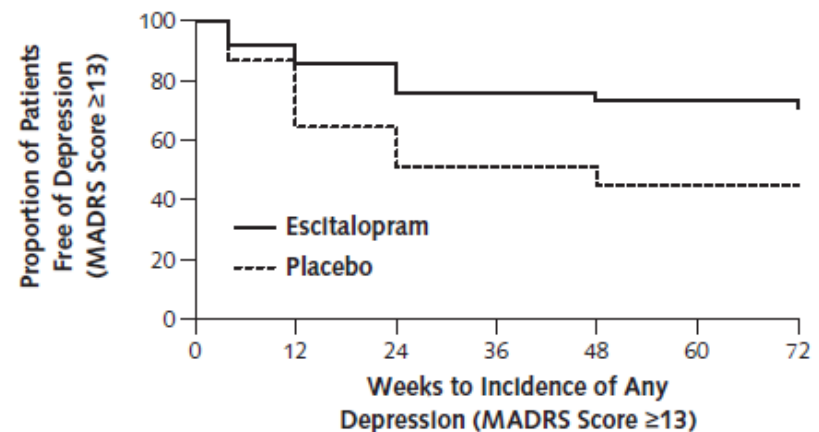
# Escitalopram pre-antiviral therapy

- Exclusions:
  - prior  $\Psi$  hx of a mood d/o or other Axis I condition;
  - illicit drugs w/in past 12mos
  - antidepressant use in past 3y
  - prior IFN tx history, prior immunotherapy, or prior h/o any other chronic
    - infection, autoimmune, or 'severe' medical comorbidity
- Double-blind, prospective, randomized, placebo-controlled, phase 3 study
- Identical appearing escitalopram (LEXAPRO) tabs & placebo tabs
- Pre-observation:
  - 12wks monitoring
- Antidepressant initiation:
  - escitalopram 10 mg/d, n=90 (or placebo, n=91)

# Results

- After imputation of missing data, 32% of the escitalopram group v. 59% of the placebo group became depressed (MADRS of 13+). NNT = 3.7,  $p < 0.001$ .

Figure 2. Cumulative Kaplan–Meier estimates of the time to first episode of depression during antiviral treatment.



Escitalopram, n	90	89	80	71	60	40
Placebo, n	91	91	79	56	40	25



# Results

- secondary outcomes (cont'd):
  - SVR

	Genotypes 1,4	Genotypes 2,3	Overall
Escitalopram	42%	73%	56%
Placebo	35%	86%	46%

- Mirtazapine rescue: 3% v. 18% (escitalo v. placebo),  $p=0.004$ .
- NO suicidal ideation, attempts, reported.
- Fewer escitalo pts developed fatigue ( $p=0.040$ ), insomnia ( $p=0.015$ )
- 87% of escitalo group completed HCV tx, 88% of placebo group.
- Medical complications:
  - 3 in escitalo (renal, brain tumor, jaundice)
  - 2 in placebo (retinopathy, brain tumor)

# FDA approved HCV Therapy in HIV+

## Peg-Interferon alfa

180 mcg SQ Qweek



## Ribavirin

400-600 mg PO BID



Longer Duration for HIV/HCV, regardless of GT

- Genotype 1 or 4: **48 weeks**
- Genotype 2 or 3: **48 weeks**

Management of hepatitis C. NIH Consensus State Sci Statements. 2002;19:1-46.  
Manns M, et al. Lancet. 2001;358:958-965. Fried MW, et al.  
N Engl J Med. 2002;347: 975-982.

# Financial Issues

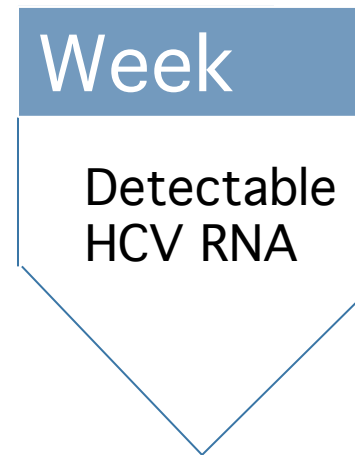
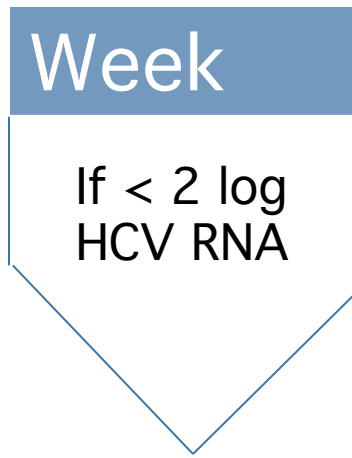
- Generous patient assistance programs available through manufacturers (Merck or Genentech)
- HCV RNA testing is not typically covered by these programs however
- For uninsured or underinsured, out of pocket expenses can be considerable
- About 20-25% of patients are unable to work during therapy

# Monitoring while on HCV therapy

Laboratory Tests	Wk 0	Wk 2	Wk 4	Wk 8	Wk 12
HCV RNA	X		X		X
CBC w/ diff	X	X	X	X	X
TSH	X				X
LFTs	X		X		X

- ✓ Consider more frequent CBC initially in cirrhotics
- ✓ CBC is typically q 1-2 mos after 12 wks
- ✓ LFTs, TSH q 3 mos after 12 wks

# Stopping Rules



# Management of Anemia

- ✓ RBV dose reduction
- ✓ Blood transfusion
- ✓ Addition of erythropoietin

# Anemia Management Recommendations

Agents	Hgb Value	Action
Peginterferon alfa-2a/ RBV	<10 g/dL in patient with no cardiac disease >2 g/dL decrease in Hgb during 4 wk period	Reduce RBV dose to 600 mg/d
	<8.5 g/dL	D/C PegIFN/RBV
	<12 g/dL despite 4 wks at reduced dose	D/C PegIFN/RBV
Peginterferon alfa-2b/ RBV	<10 g/dL	PEG-IFN: reduce 50% in cardiac disease RBV: dose reduce by 200 mg/d
	<8.5 g/dL	D/C PegIFN/RBV

# Take Home Points

- Psychosocial barriers are largest hurdle to overcome
- Lab monitoring is important to assess efficacy and safety, especially anemia
- Primary strategy for anemia initially is dose reduction of ribavirin



# Web Resources

- <http://hab.hrsa.gov/publications/hcvguide2011.pdf>
- [www.nlm.nih.gov/medlineplus/hepatitis](http://www.nlm.nih.gov/medlineplus/hepatitis)
- [www.nwaetc.org](http://www.nwaetc.org)
- [www.hepwebstudy.org](http://www.hepwebstudy.org)
- [www.hivwebstudy.org](http://www.hivwebstudy.org)
- [www.clinicaloptions.com](http://www.clinicaloptions.com)
- [www.cdc.gov/hiv](http://www.cdc.gov/hiv)
- [www.cdc.gov/hepatitis](http://www.cdc.gov/hepatitis)

**THANK YOU!!**

## HEPATITIS WEB STUDY

