

## PSYCHIATRIC ADVERSE EVENTS AND USE OF PSYCHOTROPIC MEDICATIONS BEFORE & DURING INTERFERON TREATMENT FOR HEPATITIS C (HCV)

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The speaker has no conflict to disclose.

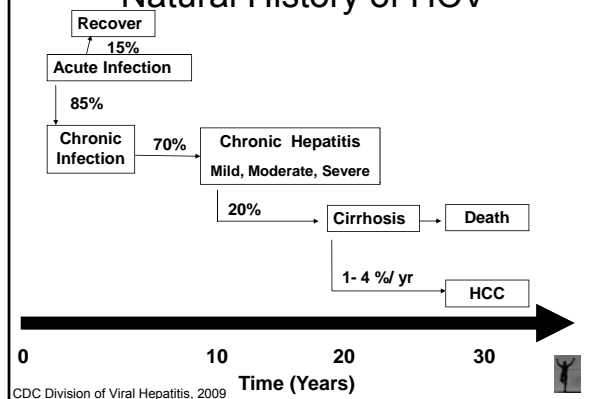


## Objectives

- List potential complications of untreated Hepatitis C virus (HCV)
- Describe the complications of psychiatric adverse effects that occur during HCV therapy
- Identify patients at higher risk for developing psychiatric adverse effects during HCV therapy



## Natural History of HCV



## HCV Treatment

- Goal: Achieve Sustained Virologic Response (SVR)
  - Undetectable viral load 24 weeks after treatment discontinuation
- Factors associated with a decreased likelihood of sustaining SVR
  - Genotype 1
  - High baseline viral load
  - African American ethnicity
  - Liver transplant recipient
  - Previous treatment failures
  - Uncontrolled diabetes

Muir et. al, 2004  
Ghany et al., 2009



## HCV Treatment

- Pegylated Interferon (PegIFN) & Ribavirin
  - PegIFN alfa-2a or 2b administered SC weekly
  - Ribavirin twice daily dose depends on PegIFN & HCV genotype

Genotype	Duration of Therapy
1, 4	48 weeks recommended (up to 72 weeks)
2, 3	24 weeks recommended (up to 48 weeks)
5, 6	No specific guidelines for the U.S.

Ghany et.al., 2009



## Adverse Effects of Treatment

### PegIFN

- Flu-like symptoms
- Injection site reactions
- Neutropenia
- Thrombocytopenia
- Thyroid dysfunction
- Insomnia
- Rash and pruritus
- Anorexia
- Diabetes
- Hyperlipidemia
- Psychiatric disorders
  - Depression, irritability

### Ribavirin

- Hemolytic anemia
- Dyspnea
- Chest pains
- Pruritus
- Rash
- Cough
- Anorexia
- Teratogenicity



## Depression & HCV Treatment

- In psychiatric patients, HCV prevalence is 6.8 - 8.5%
- Registration trials of PegIFN alfa-2a & 2b + Ribavirin
  - 10-14% dropout due to AEs
    - >50% flu-like symptoms
    - 22-31% psychiatric AEs
- Interferon-specific depression
  - Mood, anxiety, cognitive complaints
  - Fatigue, anorexia, pain, psychomotor slowing
- Psychiatric AEs correlate to poor treatment adherence
  - Impact on SVR is unclear



## Self Assessment Question

Which of the following factors make a patient a better candidate for achieving sustained virological response to HCV therapy?

- Genotype 1 disease
- African American ethnicity
- Uncontrolled diabetes
- HCV RNA level less than 300,000 IU/mL



## Self Assessment Question

True or False:

The incidence of psychiatric adverse effects associated with interferon or pegylated interferon therapy ranges between 5% to 20%.



## Study Objectives

- **Aim 1:** To assess the incidence of new onset psychiatric adverse events and new or increased psychotropic medication use after the initiation of interferon therapy
- **Aim 2:** To identify risk factors associated with psychotropic medication use and/or psychiatric adverse events in subjects receiving treatment for HCV



## METHODS



## Study Design

- Retrospective chart review
- Reviewed all subjects evaluated for HCV therapy at UIMC outpatient liver clinic from July 1999 through August 2009
- Utilized objective reporting of psychotropic medication use as surrogate marker for depressive or other psychiatric symptoms
- This study was IRB approved by our institution on 10/22/2009 prior to data collection



## Subject Selection

- Inclusion criteria
  - All patients  $\geq 18$  years old
  - Receiving PegIFN + Ribavirin
  - First round of HCV therapy at UIMC
- Exclusion criteria
  - HIV
  - Hepatitis B
  - HCV therapy from outside provider
  - Therapy taking place outside the pre-specified date range



## Data Collection

### Baseline

- Sex
- Age
- Race
- Height & Weight
- HCV Genotype
- Past Medical History
- Risk Factors for HCV

### All Visits

- Viral Load
- Psychotropic Medications
- Hemoglobin
- Weight



## Statistical Analysis

- Student's T-test was used to correlate new or worsened psychiatric effects with
  - Age
  - BMI
- Chi-squared test was used to correlate new or worsened psychiatric effects with
  - Sex
  - Race
  - Baseline psychotropic medication use
  - Treatment response



## Definitions

- Psychotropic medications: antidepressants, antipsychotics, mood stabilizers, anxiolytics, sedative hypnotics
- Psychotropic medication history: use of psychotropic medications prior to initiation of HCV therapy
- New/worsened psychiatric adverse events during therapy: addition of new medication, increased dose of current medication, or change of drug as surrogate marker for new/worsened psychiatric symptoms at any time during HCV treatment



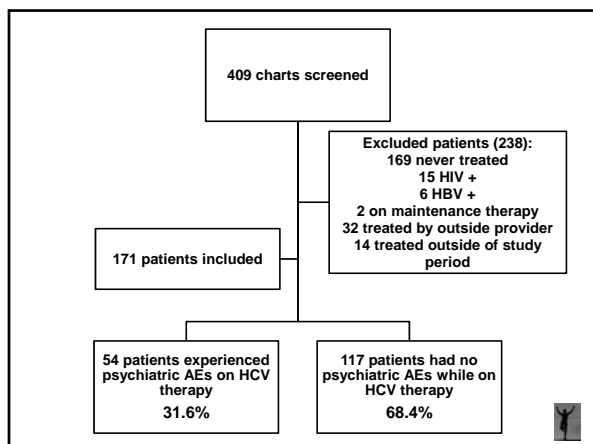
## Definitions

- Treatment response: achievement of undetectable viral load before discontinuation of therapy
- Non-response: undesirable change in viral load leading to discontinuation of therapy; change from treatment to maintenance dosing for PegIFN
- Lost to follow-up: patients who self-discontinued therapy for financial reasons or unknown reasons
- Side effects: therapy discontinued by patient or provider due to side effects (e.g. uncontrolled anemia, psychiatric hospitalization, hallucinations, anhedonia, severe anorexia, etc.)



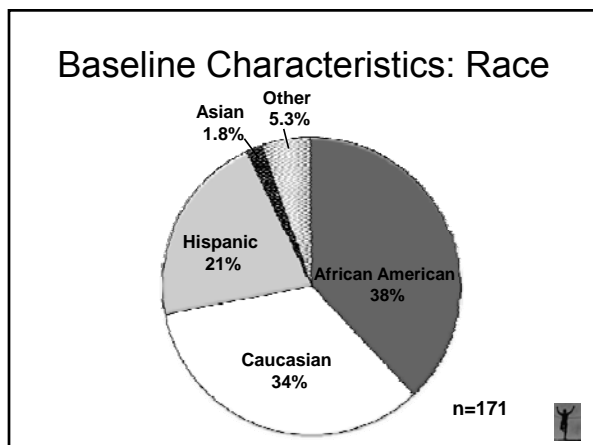
## RESULTS





### Baseline Demographics

Characteristic	Mean
Male	61%
Mean Age	49 yr
Mean BMI	29
Initial Drug	33.9%
Genotype (n=168)	
1	67.3% (113)
2	19.6% (33)
3	11.9% (20)
4	1.2% (2)
Stage (n=117)	
1	11.1% (11)
2	38% (45)
3	24% (28)
4	26% (31)
Treatment naïve (n=162)	63.4% (161)

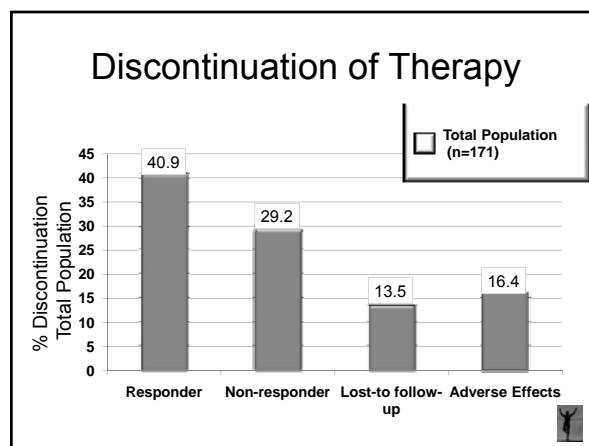


### Distribution by Race

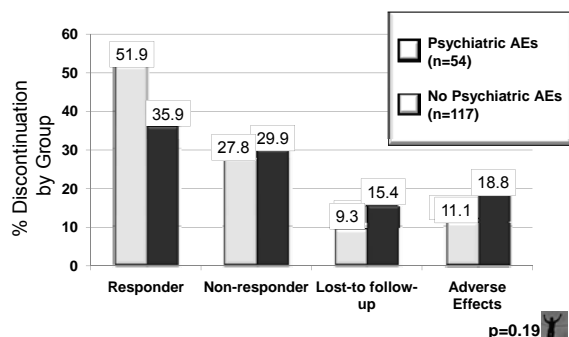
	Total (n=171)	New/ Worsened Psychiatric AEs (n=54)	No Psychiatric AEs (n=117)	p-value
Psychiatric AEs (%)		31.6	68.4	
African American (%)	38	29.6	41.2	0.23
Non-Hispanic White (%)	34	44.4	29.1	
Hispanic (%)	21	20.4	21.4	
Other (%)	7	5.6	7.7	

### Baseline Characteristics

	Total (n=171)	New/ Worsened Psychiatric AEs (n=54)	No Psychiatric AEs (n=117)	p-value
Psychiatric AEs (%)		31.6	68.4	--
Male (%)	61	64.8	59	NS
Mean Age (yr)	49	48.9 +/- 8.8	48.7 +/- 9.6	NS
Mean BMI	29	29 +/- 6.4	29.2 +/- 7	NS
Initial Drug (%)	33.9	46.3	28.2	0.02
Bipolar (%)	2.3	3.7	1.7	--
Anxiety (%)	2.3	5.6	0.9	--
Schizophrenia (%)	1.8	5.6	0	--



## Discontinuation of Therapy



## Conclusion

- Subjects using psychotropic medications prior to initiation of HCV therapy were statistically more likely to develop depression or other psychiatric symptoms while on HCV therapy
- No correlations were made between response to therapy or treatment discontinuation
- No correlation was made with new/ worsened psychiatric AEs
  - Sex, age, race, BMI, reason for discontinuation of HCV therapy

## Discussion

### Study Limitations

- Inconsistency of documentation
- Medication use as surrogate marker
- Depression vs other psychiatric AEs
- Referral center
- Inability to obtain SVR
- Exclusion of HIV+, Hepatitis B+ patients

Future Analysis: Genotype, previous treatment, trends in hemoglobin, duration of treatment

## Impact on Clinical Practice

- Proposed use of validated depression screening tools at baseline and follow-up visits for patients undergoing HCV therapy
  - Beck Depression Inventory
  - Zung Self-Rating Depression Scale

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