Antiviral Drugs and Mood Disorders

Jerika T. Lam, Pharm.D., AAHIVE
Assistant Professor
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Disclosures

☐ This speaker has no conflicts of interest or commercial support to disclose.
Case

- A 32-year-old HIV-positive man with a CD4+ count of 288 cells/mm³ is initiated on his first antiretroviral regimen consisting of tenofovir/emtricitabine/efavirenz (Atripla®).
- His past history is notable for polysubstance abuse (in remission for the past year), depression (controlled) and chronic hepatitis C virus infection.

Case (cont’d)

- He takes his antiretroviral medication on an empty stomach at night before going to bed.
- One week after starting his antiretroviral regimen, he calls to complain that he is feeling dizzy and having difficulty concentrating at work.
Which of the following statements is most accurately related to the medication efavirenz (EFV)?

1. EFV levels are significantly lower when taken on an empty stomach. Patient may develop high plasma EFV levels b/c he is taking EFV on an empty stomach.
2. Development of early EFV-related CNS adverse effects usually improve within 4 weeks.
3. EFV drug levels should be monitored on a monthly basis during the first 6 months of therapy.
4. Patients with a h/o depression should never be prescribed EFV b/c of high likelihood of developing psychosis.

Objectives

- Review the epidemiology of HIV and hepatitis C transmission
- Identify the antiviral drugs used for the treatment of HIV and hepatitis C that cause mood disorders
- Describe the incidence and mechanisms of mood disorders associated with antiviral drugs
- Describe the drug interactions between psychotropic agents and antiviral drugs
- Discuss about the management and treatment of mood disorders
Adults and children estimated to be living with HIV, 2008

Total: 33.4 million (31.1 – 35.8 million)

December 2009

ARVs and the HIV Lifecycle
**Antiretroviral Agents**

- **Nucleoside RT Inhibitors**
  - zidovudine (ZDV, AZT)
  - lamivudine (3TC)
  - stavudine (d4T)
  - didanosine (ddl)
  - abacavir (ABC)
  - emtricitabine (FTC)
  - tenofovir (TDF): NiRTI

- **Protease Inhibitors**
  - saquinavir (SQV)
  - ritonavir (RTV)
  - indinavir (IDV)
  - nelfinavir (NFV)
  - lopinavir (LPV)
  - fosamprenavir (FPV)
  - atazanavir (ATV)
  - tipranavir (TPV)
  - darunavir (DRV)

- **Co-formulated combinations**
  - ZDV/3TC (Combivir®)
  - ZDV/3TC/ABC (Trizivir®)
  - LPV/RTV (Kaletra®)
  - 3TC/ABC (Epzicom®)
  - TDF/FTC (Truvada®)
  - EFV/TDF/FTC (Atripla®)

- **Non-nucleoside RT Inhibitors**
  - delavirdine (DLV)
  - efavirenz (EFV)
  - nevirapine (NVP)
  - etravirine (ETR)
  - rilpivirine—FDA approved 2011

- **CCR5 antagonist**
  - maraviroc (MVC)

- **Fusion inhibitor**
  - enfuvirtide (T-20)

- **Integrase inhibitor**
  - raltegravir (RAL)

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**DHHS Guidelines: Updated 2011**

**HAART regimen:** combination of 1 agent from Column A + 2 agents from Column B

<table>
<thead>
<tr>
<th>Column A (NNRTI, PI or INSTI Class)</th>
<th>Column B (NRTI Class: 2 agents)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Preferred</strong></td>
<td><strong>Preferred</strong></td>
</tr>
<tr>
<td>• NNRTI-based</td>
<td>• tenofovir/emtricitabine</td>
</tr>
<tr>
<td>efavirenz (EFV, Sustiva®)</td>
<td>(Truvada®)</td>
</tr>
<tr>
<td>• PI-based (boosted w/ritonavir)</td>
<td></td>
</tr>
<tr>
<td>atazanavir (ATV, Atazanavir®); OR</td>
<td></td>
</tr>
<tr>
<td>darunavir (DRV, Prezista®)</td>
<td></td>
</tr>
<tr>
<td>• INSTI-based</td>
<td></td>
</tr>
<tr>
<td>raltegravir (RAL, Isentress®)</td>
<td></td>
</tr>
</tbody>
</table>
Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTIs)

- Delavirdine (DLV, Rescriptor®)
- Nevirapine (NVP, Viramune®)
- Efavirenz (EFV, Sustiva®)
- Etravirine (ETR, Intelence®)
- Rilpivirine (TMC 278, Edurant®)
Adverse Effects: NNRTIs

- All NNRTIs
  - Rash
  - Drug-drug interactions
- Efavirenz (EFV, Sustiva®)
  - Neuropsychiatric effects
  - Teratogenic in primates (FDA pregnancy class D)
- Nevirapine (NVP, Viramune®)
  - Potential for hepatotoxicity & rash in patients with high CD4+ T cell counts at initiation

NNRTIs

- Efavirenz (EFV, Sustiva®)
  - CNS Side Effects
    - Dizziness, poor cognitive functioning
    - Vivid dreams
    - Depression
      - Use with caution in patients with history of serious mental illness
  - Rash
    - Generally mild and self-limiting
Efavirenz (EFV)

- Adult dose: 3 x 200 mg capsules or 600 mg tablet QHS
- Food Interactions
  - Take on an empty stomach or with low-fat meal
    - High-fat meals increase absorption by 50% → increases side effects
  - Consistent results: persistent activity after >5 years
- Never surpassed in clinical trials

Psychiatric Complications of Antiretroviral Agents

- CNS effects of efavirenz (EFV) demonstrated in cohorts, clinical studies
  - Up to 50% of patients in clinical studies experience dizziness, headache, confusion, impaired concentration, and abnormal or vivid dreams
    - Usually resolve in 2-4 weeks
  - Severe psychiatric symptoms reported in small percentage of patients in clinical trials
  - Current practice indicates close monitoring in EFV-treated patients with current or history of psychiatric illness; EFV not contraindicated
- Case reports with other agents
  - Zidovudine: mania, depression, insomnia, headaches
  - Abacavir: psychosis
  - Nevirapine: psychosis
Efavirenz CNS Profile

- **Symptoms:** confusion, insomnia, nightmares, poor concentration, mood change, dizziness, dysequilibrium, depression, psychosis

- **Onset:** within first week

- **Course:** usually resolves in 2-4 weeks

- **Causes:** possibly associated with high plasma EFV levels or CYP2B6 allelic variant

Efavirenz CNS Profile (cont’d)

- CNS toxicity may be associated with EFV plasma levels

- Patients who achieve higher plasma levels are at increased risk of developing long-term delayed neuropsychiatric adverse effects
Efavirenz-Induced Neuropsychiatric Adverse Effects

CNS Toxicity Related to Efavirenz Levels
CNS Toxicity Related to Efavirenz Levels

- Interindividual differences in EFV metabolism may also explain susceptibility to EFV CNS adverse effects.

- ACTG study 5097: differences in EFV exposure b/t different racial and ethnic populations
  - CYP2B6 allelic variant more common in African Americans than Caucasians
  - CYP2B6 is associated with significantly greater EFV exposure and acute CNS symptoms

CYP2B6 Polymorphism and Efavirenz Toxicity
CYP2B6 (G516T) Genetic Polymorphisms by Race

![Graph showing CYP2B6 (G516T) Genetic Polymorphisms by Race]

Efavirenz Levels According to Polymorphisms in the CYP2B6 (G516T) Genotype

![Graph showing Efavirenz Levels According to Polymorphisms in the CYP2B6 (G516T) Genotype]
Treatments for Depression

### Psychopharmacologic Treatments

<table>
<thead>
<tr>
<th>Tricyclic Antidepressants</th>
<th>Other Antidepressants</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Desipramine</em></td>
<td><em>Bupropion</em></td>
</tr>
<tr>
<td><em>Imipramine</em></td>
<td><em>Duloxetine</em></td>
</tr>
<tr>
<td><em>Nortriptyline</em></td>
<td><em>Mirtazapine</em></td>
</tr>
<tr>
<td><em>Doxepin</em></td>
<td><em>Nefazodone</em></td>
</tr>
<tr>
<td><em>Imipramine</em></td>
<td><em>Venlafaxine</em></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>SSRIs</th>
<th>Nonconventional Agents With Antidepressant Activity</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Citalopram</em></td>
<td><em>Dehydroepiandrosterone (DHEA)</em></td>
</tr>
<tr>
<td><em>Fluoxetine</em></td>
<td><em>S-adenosylmethionine (SAM-e)</em></td>
</tr>
<tr>
<td><em>Paroxetine</em></td>
<td><em>Testosterone</em></td>
</tr>
<tr>
<td><em>Sertraline</em></td>
<td></td>
</tr>
<tr>
<td><em>Escitalopram</em></td>
<td></td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Psychostimulants</th>
<th>Psychotherapeutic Treatments</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Dextroamphetamine</em></td>
<td><em>Psychotherapy (individual)</em></td>
</tr>
<tr>
<td><em>Methylphenidate</em></td>
<td><em>Cognitive behavioral psychotherapy (group and individual)</em></td>
</tr>
<tr>
<td><em>Modafinil</em></td>
<td><em>Cognitive behavioral stress management (group)</em></td>
</tr>
</tbody>
</table>

*Treatment for which there is randomized, controlled trial evidence of efficacy for depression in HIV-infected patients.

### Relationship Between Antidepressant Use and Adherence to Antiretroviral Therapy (ART)

- 1997-2001, retrospective review
- 1713 HIV-positive patients in an urban healthcare setting
  - 57% of patients were depressed
    - 46% of depressed patients received antidepressant treatment
    - 52% of depressed patients received ART
- Antiretroviral adherence lower among depressed patients not on antidepressants ($P < .005$) vs patients on antidepressants
- Nonadherence to ART more likely in patients nonadherent to antidepressants ($P = .0019$) and in patients who used alcohol ($P = .01$)

Practical Aspects of Treating Major Depression in Patients on ART

- No antidepressant has been shown to be clinically superior to all others
- Make adverse effects of drugs work for the patient
  - Ex: weight gain, constipation, and sedation can sometimes be beneficial
- Because of potential drug-drug interactions, clinically monitor drugs with a large therapeutic index
  - e.g.: SSRIs, newer atypical antidepressants
- Because of potential drug-drug interactions, monitor levels of drugs with a narrow therapeutic index
  - e.g.: tricyclic antidepressants and lithium

Drug-Drug Interactions
Cytochrome (CYP450)

- Present in liver, small intestine, lungs, and brain
- Primary function is to alter toxins (drugs) to speed excretion
- Isoenzymes: 1A2, 2C9/19, 2D6, 3A4 are primarily responsible for drug metabolism
- Also metabolize steroid hormones, vitamins, toxins, prostaglandins, fatty acids
- Knowledge of substrates, inhibitors and inducers helps predict drug interactions
  - Important as protease inhibitors and NNRTIs are metabolized 80-95% by the CYP450 isoenzymes in liver and small intestine

Proportion of Drugs Metabolized by Cytochrome P450 Enzymes

Goodman and Gilman’s The Pharmacologic Basis of Therapeutics. 9th ed.
Cytochrome P450 Enzymes

Patient Factors
- Genetics
- Diseases
- Diet/Nutrition
- Environment
- Smoking
- Alcohol

Outcome of Drug Interaction

Drug Factors
- Dose
- Duration
- Dosing Times
- Sequence
- Route
- Dosage Form

Variability

Adapted from Philip D. Hansten, Science & Medicine 1998

CYP P450 Drug-Drug Interactions

- Pharmacologic action of drug is altered by co-administration of second drug
- Co-administration may:
  - **↑** effect (e.g., ritonavir + saquinavir; ritonavir + simvastatin)
  - New effect (e.g., ritonavir + amitriptyline)
  - **↓** effect (e.g., rifampin + protease inhibitors, indinavir + coumadin)

No Consequences

Drug A → Drug B
CYTOCHROME P450: ANTIRETROVIRAL INTERACTIONS

Induced by: RTV, EFV, NVP

Inhibited by: RTV, NFV, EFV, IDV, APV, SQV, ATV, DLV, LPV/r

Induced by: RTV, DLV, ATV, NFV†, EFV

Induced by: NVP

Inhibited by: EFV, DLV, NFV

Induced by: RTV

Induced by: ATV, EFV*, NFV

Inhibited by: NFV‡

Induced by: RTV

Induced by: ATV, EFV*, NFV

Inhibited by: NFV‡

Induced by: ATV, EFV*, NFV

Inhibited by: NFV‡

Inhibited by: RTV, EFV*, IDV†, DLV

Inhibited by: EFV, DLV, NFV

2C19 2D6 2C9 3A4 1A2 2E1 2A6 2B6 2C8

*Only at concentrations well above those achieved clinically.
†May be a weak inhibitor.
‡ Did not inhibit at concentrations in the therapeutic range.

ARVs not listed are not known to be metabolized by cytochrome P450

Interactions Between Psychiatric Agents and Antiretroviral Agents

<table>
<thead>
<tr>
<th>Agent</th>
<th>Interacting Antiretroviral</th>
<th>Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Antidepressants</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>St John’s wort</td>
<td>All ARVs</td>
<td>ARV ↓</td>
</tr>
<tr>
<td><strong>Anxiolytics</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alprazolam</td>
<td>Delavirdine (DLV)</td>
<td>Alprazolam ↑</td>
</tr>
<tr>
<td>Midazolam</td>
<td>All PIs, DLV, EFV</td>
<td>Midazolam ↑</td>
</tr>
<tr>
<td>Triazolam</td>
<td>All PIs, DLV, EFV</td>
<td>Triazolam ↑</td>
</tr>
<tr>
<td><strong>Antipsychotics</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pimozide</td>
<td>All PIs, DLV</td>
<td>Pimozide ↑</td>
</tr>
</tbody>
</table>
CYP450 3A4 Substrates

- Anti-arrhythmics
  - Class IA
  - Class III
- Antidepressants
  - Amitriptyline
  - Nefazodone
  - Trazodone
- Benzodiazepines
  - Alprazolam
  - Midazolam: C/I with EFV and protease inhibitors
  - Triazolam: C/I with EFV and protease inhibitors

CYP450 3A4 Substrates (cont’d)

- HMG-CoA reductase inhibitors
  - Atorvastatin
  - Lovastatin
  - Simvastatin
- PDE5 drugs
  - Sildenafil
  - Vardenafil
  - Tadalafil
### CYP450 3A4 Inhibition

- **Azoles**
  - Ketoconazole, itraconazole, voriconazole, fluconazole
- **Macrolides**
  - Erythromycin, clarithromycin
- **Grapefruit juice**
- **Protease inhibitors:**
  - RTV > IDV/NFV/TPV/ATV/LPV > SQV

### CYP450 3A4 Induction

- **Rifamycins**
  - Rifampin: C/I with NNRTIs (NVP, ETR) and protease inhibitors
  - Rifapentine
  - Rifabutin
- **NNRTIs**
  - Nevirapine
  - Efavirenz
  - Etravirine
- **Anticonvulsants**
  - Phenobarbital, carbamazepine, phenytoin
- **Herbs**
  - St. John’s Wort (*Hypericum*): avoid use w/all NNRTIs and protease inhibitors
Selecting an Antidepressant: Potential for Drug-Drug Interactions

**Low P450 blockers:**
Likely to have little impact on metabolism of other drugs

- Citalopram
- Escitalopram
- Mirtazapine
- Venlafaxine
- Sertraline
- Duloxetine
- Bupropion

**Potent P450 blockers:**
Potential for strong impact on metabolism of other drugs

- Paroxetine
- Fluoxetine
- Fluvoxamine


Safety Considerations

<table>
<thead>
<tr>
<th>Type</th>
<th>Features</th>
</tr>
</thead>
<tbody>
<tr>
<td>SSRIs</td>
<td>• Sexual dysfunction, headache, dizziness, gastrointestinal adverse effects, tremor, anxiety</td>
</tr>
</tbody>
</table>
| TCAs       | • Potential for lethal overdose  
            | • Alpha-adrenergic effects  
            | • Delirium risk from anticholinergic/antihistamine adverse effects  
            | • Cardiac conduction prolongation |
| Venlafaxine| • Minimal protein binding  
            | • Blood pressure risk |
| Mirtazapine| • Risk of decreased white blood cell count  
            | • Risk of weight gain, sedation |
| Nelfzadone | • Risk of hepatic failure |
| Bupropion  | • May increase risk of interferon-associated seizures |
| Duloxetine | • Risk of liver toxicity |

TCAs, tricyclic antidepressants
Case

- A 32-year-old HIV-positive man with a CD4+ count of 288 cells/mm³ is initiated on his first antiretroviral regimen consisting of tenofovir/emtricitabine/efavirenz (Atripla®).
- His past history is notable for polysubstance abuse (in remission for the past year), depression (controlled) and chronic hepatitis C virus infection.

Case (cont’d)

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1. EFV levels are significantly lower when taken on an empty stomach. Patient may develop high plasma EFV levels b/c he is taking EFV on an empty stomach.

2. Development of early EFV-related CNS adverse effects usually improve within 4 weeks.

3. EFV drug levels should be monitored on a monthly basis during the first 6 months of therapy.

4. Patients with a h/o depression should never be prescribed EFV b/c of high likelihood of developing psychosis.

Prevention and Management of EFV-Associated CNS Effects

- Take EFV at bedtime and on empty stomach
- Address any past or current psychiatric issues prior to the patient starting therapy, as these disorders may worsen on EFV therapy
- Encourage patients, who have past or current psychiatric disorder, to obtain psychiatric consultation prior to initiating EFV therapy
- Patients with active, uncontrolled psychiatric disorders are not good candidates to receive EFV
Introduction: Hepatitis C Virus (HCV) Infection

- 170 million HCV infected individuals worldwide
- 4 million people are infected with chronic HCV in the US
- 50-70% of chronically infected individuals develop chronic liver disease
- HCV infection is responsible for an estimated 8,000 to 10,000 deaths annually in the US
- HCV-related disease is the leading indication for liver transplantation in this country

Hepatitis C - Epidemiology

Before 1985
- Illegal Drug Use
- Transfusion
- Sexual
- Other
- Unknown

1999

Hepatitis C Infection - Natural History

- **Acute infection**
  - Resolve 15%
  - Chronic infection 85%

- **Stable**
  - 80%
  - Cirrhosis 20%

- **Stable**
  - 75%
  - Mortality 25%


Mental Illness

- Demoralization
- Substance Use
- Depression

- Interferon

HCV
HCV and Depression

- More than 30% of chronic HCV-positive patients suffer from neuropsychiatric abnormalities
- HCV infection may lead to changes in brain metabolism with impairment in the serotonin-dopamine system, resulting in the following effects:
  1. reduction in the N-acetyl-aspartate/creatine ratio,
  2. increased choline and diminished N-acetyl-aspartate levels,
  3. hypometabolism of the prefrontal cortex
- These disturbances may contribute to the mechanism by which HCV produces mood disorders

HCV and Depression (cont’d)

- Statistically higher BDI scores in HCV patients compared with other liver diseases
- Mildly elevated Zung scores on all 96 HCV+ patients prior to IFN treatment
- 45.3% of HCV+ patients screened positive for depression on HADS vs. 4% of healthy controls
HCV and Depression (cont’d)

- Found major depression or dysthymia in 30% of patients prior to IFN therapy

- Depressive symptoms reported in 57.2% of HCV+ active drug users

- SCID on 50 patients prior to IFN
  - 7/50 (14%) with previous major depression

Interferons: Antiviral Cytokines

- Group of inducible cytokines synthesized in response to viral and other stimuli
  - Cytokines: soluble cellular mediators of immune system

- 3 classes of interferons (INFs):
  - INF-α, INF-β, INF-γ

- All INFs have antiviral activity
Interferons (cont’d)

- **MOA:** work by inducing, in the ribosomes of host cells, the production of enzymes that inhibit the translation of viral mRNA into viral proteins → stopping viral replication

- **Hepatitis C antiviral agents:**
  - INF-α-2a and 2b
  - Pegylated INF-α-2a and 2b

### Side Effects of Interferons (IFN)

<table>
<thead>
<tr>
<th>Flu-like symptoms</th>
<th>Psychiatric symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Headache</td>
<td>Depression</td>
</tr>
<tr>
<td>Fatigue or asthenia</td>
<td>Mood lability</td>
</tr>
<tr>
<td>Myalgia, arthralgia</td>
<td>Injection site reaction</td>
</tr>
<tr>
<td>Fever, chills</td>
<td>Autoimmunity</td>
</tr>
<tr>
<td>Nausea</td>
<td>Lab alterations</td>
</tr>
<tr>
<td>Diarrhea</td>
<td></td>
</tr>
<tr>
<td>Alopecia</td>
<td></td>
</tr>
<tr>
<td>Thyroiditis</td>
<td></td>
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<tr>
<td></td>
<td>Neutropenia</td>
</tr>
<tr>
<td></td>
<td>Thrombocytopenia</td>
</tr>
</tbody>
</table>
Interferon and Depression

- May influence the CNS directly (influencing neuron function) and indirectly (inducing cell-adhesion molecules and increasing the permeability of the blood-brain-barrier
  - Allows interferon and interferon-induced proinflammatory cytokines to enter the CNS and influence neuron function
- Plasma adrenocorticotropic hormone cortisol and IL-6 levels are elevated in patients receiving IFN treatment and experiencing depression
  - Reduction in plasma 5-hydroxytrptophan and serotonin levels correlates highly with the degree of depression during IFN-based treatment

PEG IFN/RBV-related Depression

**Patients Receiving PEG IFN and RBV**

- Manns et al. (2001)
  - HCV-infected patients: PEG IFN alfa-2b 1.5 µg/kg + 800 mg RBV
    - Depression: 31%
    - Irritability: 35%
- Fried et al. (2002)
  - HCV-infected patients: PEG IFN alfa-2a 180 µg + 1000-1200 mg RBV
    - Depression: 22%
    - Irritability: 24%

PEG IFN: pegylated interferon; RBV: ribavirin
Time Course of Adverse Effects Associated with Interferon Therapy

Incidence of Depression During Hepatitis C treatment

*P < .001 vs baseline.
Rapid Escalation of IFN-Induced Depressive Symptoms: *Threshold Effect*

![Graph showing BDI Score over time]

- Baseline/IFN Started
- Latency Period
- Time to Onset of MDD
- MDD Diagnosis Made
- Total Weeks of IFN Therapy Until MDD Diagnosis

IFN, interferon; MDD, major depressive disorder.

Prophylactic Citalopram: *PEG IFN/RBV-related Depression*

<table>
<thead>
<tr>
<th>History</th>
<th>Prophylactic antidepressant</th>
<th>On-therapy antidepressant</th>
<th>Depression rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>(n = 11) A</td>
<td>None</td>
<td>None</td>
<td>64%</td>
</tr>
<tr>
<td>Psych history (-)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(n = 11) B</td>
<td>None</td>
<td>None</td>
<td>55%</td>
</tr>
<tr>
<td>Receiving methadone substitution</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(n = 14) C</td>
<td>Citalopram 20 mg QD initiated</td>
<td>Citalopram 20 mg QD continued</td>
<td>14%</td>
</tr>
<tr>
<td>Receiving methadone substitution</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Schaefer et al. AASLD; October 24-28, 2003; Boston, Mass.
HCV Treatment Guideline Conundrum

**Is Depression a Contraindication?**

<table>
<thead>
<tr>
<th>Study</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Van Thiel <em>et al</em> (1995)</td>
<td>Patients with psychiatric illness successfully treated with IFN</td>
</tr>
<tr>
<td>Pariante <em>et al</em> (1999)</td>
<td>Patients with preexisting lifetime or current psychiatric disorders no more likely than controls to stop IFN for psychiatric symptoms</td>
</tr>
<tr>
<td>Schaefer <em>et al</em> (2003)</td>
<td>Preexisting psychiatric disorders should not be considered a contraindication to IFN therapy</td>
</tr>
</tbody>
</table>

IFN: interferon

Goals of Depression Treatment for IFN-treated Patients

- Alleviation of symptoms
- Adherence to dose and duration of IFN therapy

IFN, interferon.
Antidepressant prophylaxis can be considered for all of the following groups of patients initiating HCV therapy, EXCEPT which one?

1. Patients with previous INF-associated depression
2. Patients with increased depression scores just before starting IFN
3. Patients with a history of depression, but no current depressive symptoms

Managing Depression

- Take psychiatric history for mood disorders
- Treat pre-existing depression before starting PEG IFN
- Evaluate patients for development of depression at least every 2 weeks after initiation of PEG IFN therapy
QUESTIONS??

jtllam@llu.edu

References

- Fried et al. NEJM. 2002;347:975-982.
References (cont’d)