



# Side Effects Management

## Hepatitis C Treatments

*November 14, 2008*

**SouthWest Viral Hepatitis Summit**

# Goals of Therapy

Primary  
Goal

Secondary  
Goals

- Eradicate HCV infection
- Slow disease progression
- Improve histology
- Reduce risk of hepatocellular carcinoma
- Improve health-related quality of life

The title is centered at the top of the slide. It is flanked by five circles: a solid light purple circle on the far left, a hollow light purple circle, a solid light purple circle, a hollow light purple circle, and a solid light purple circle on the far right.

# Two Reasons to Know How To Deal With Side Effects

- Enables patient to stay on therapy to achieve viral eradication
- Adherence increases probability of achieving sustained viral response

# Types of Events



- +Early side effects that do not require dose modification (40-90%)
- ++Adverse events that may require dose modification or discontinuation (2-10%)
- +++Severe, even life threatening side effects that may be irreversible (0.1 to 1%)

# Ways to Deal with Side Effects

- Dose Reduction
- Addition of other medications
- Changes in daily habits (diet, rest)
- Stop HCV treatment

# Before Initiating Treatment

- Remember: initiating a therapy now has the potential to affect ability to intervene down the road
- Make sure this is a good time for the patient to start therapy
- Thorough education essential to patient compliance and comfort

# While Waiting for Rx Approval

- Weight loss  
(if patient is obese weight loss is therapy)
- Smoking cessation
- Establish exercise program
- Hydration Habit
- Skin care
- Review other meds/herbals
- Dental care
- Health Maintenance – Colonoscopy, Pap, Mammogram, PSA, etc.

# Teratogenicity



- Ribavirin is Category X (Interferon is Category C)
- 2 Methods of Birth Control
- Avoid handling of capsules
- Studies show that 1.5% of women on therapy become pregnant!
- Same recommendations for female partners not on therapy
- Consider medications acknowledgement form!
- Pregnancy Registry

# AGENDA – Side Effects of Alpha Interferons

- Flu-like symptoms (headache, fatigue or asthenia, myalgia, arthralgia, fever, chills)
- Neuropsychiatric: Depression, emotional lability, insomnia
- Alopecia
- Thyroiditis
- Nausea
- Diarrhea
- Injection-site reaction
- Lab alterations (neutropenia, anemia, thrombocytopenia)



# Fatigue

- Fatigue is often a primary dose-limiting factor that prevents completion of therapy.
- Correlates closely with sleep disorders, anxiety, agitation, stress, and depression
- Look at hydration, diet and nutrition too
- Assessment, Preventive Strategies, Treatment Strategies important



# Headache / Migraine

- Common headaches can be caused by stress, tension, allergies, caffeine, onset of menstruation, foods, eyestrain, hunger and other triggers.
- Migraines more limiting
- Educate patient on preventive strategies, including regular meal and sleep patterns, avoiding triggers, adequate hydration, avoiding caffeine.
- Use of OTC analgesics (acetaminophen, ibuprofen)
- Role of RX medications (beta blockers, calcium channel blockers, antidepressants)

# Myalgia / Arthralgia



- Body aches and pains following administration of interferon are fairly predictable.
- Short lived and diminish after a few weeks
- Can also be caused from fibromyalgia to common muscle stress and strain.
- Assess for new onset or exacerbation of arthritis, lupus, hypothyroidism, etc.
- Use of analgesics

# Fever and Chills



- Severity tends to abate as treatment continues
- Educate patients about how to take a temperature
- Investigate infectious causes for high fever or persistent fever
- Ensure adequate hydration
- Use of Acetaminophen 325 to 650 Q6H PRN, not to exceed 2-3 g/d
- Use of Ibuprofen 200 to 800 mg TID, not to exceed 2400 mg/d



# Neuropsychiatric: Ranges of What to Expect...

- Depression 16-29%
- Emotional Lability 03-34%
- Insomnia 18-24%



# Neuropsychiatric

- **May present early in treatment**
- **Potential increase in severity over treatment duration**
- **Consider depression scales as guideline tools**
- **Understand patient's history prior to treatment (does this patient need psychiatric evaluation, etc)**
- **Apathy**
- **Irritability**
- **Mood changes (depression)**
- **Insomnia**
- **Cognitive changes**
- **Suicidal Ideation and Completed Suicides**

# Depression- Pre-Treatment

- 35% - 57% of all chronic viral hepatitis patients may have depression upon diagnosis and/or preceding treatment for their disease.
- Severe psychiatric adverse events, including depression and violent behavior (suicides, suicide attempts and suicidal ideations) have occurred during peginterferon/ribavirin therapy and with interferon monotherapy, both in patients with and without a previous history of psychiatric illness.
- Know symptoms of major depressive syndrome



# Depression

- CES Depression Scale
  - Objective Tool
  - 5<sup>th</sup> Grade reading level
  - Valid with repeated measures
  - Reliable with chronic illness
- Depression tools including Beck, Hamilton, and Zung are available online at [www.fpnotebook.com](http://www.fpnotebook.com)
- Early use of Antidepressants; consider pre-tx

# Prior to Treatment- Managing Depression



- Patients treated with interferon who complain of depression usually describe apathy, cognitive slowing, and fatigue.
- Treat/stabilize pre-existing depression before starting HCV treatment
- Educate patients and family members regarding risk of depression
- Help patients understand and incorporate preventive strategies, regular mealtimes, sleep patterns, regular exercise, avoiding excess sugar, etc.)

# Treating the Depression

- Drug class SSRIs block serotonin receptors on nerve cells in the brain. These are usually the first antidepressant prescribed when patients initiate therapy.
- Examples of SSRIs are Celexa, Lexapor, Prozac, Pacil, Luvox, Zoloft, Desyrel.
- Choose an antidepressant using clinical considerations and distressing symptoms.
- Other agent and drug classes may be helpful.



# Emotional Lability

- Can present early in treatment and increase in severity over time
- Unpredictable
- Tearfulness, fret easily, irrational, moody
- Assess daily habits (rest, delegating)
- Dose reduction if necessary



# Insomnia

- Can present early in treatment and increase over time
- Common – can precipitate depression
- Assess caffeine use
- Sleep hygiene
- Regular daily exercise (walking)
- Suggest music, meditation
- RX if necessary (Ambien, Sonata, Trazadone)



# Alopecia

- Interferon affects hair follicles and changes hair texture leading to breakage.
- Seen in up to 30% of patients - black hair color and Asian more common
- Typically manifests as thinning

## **Management of Alopecia**

- Shampoo less frequently
- Use Nioxin shampoo or Selsun Blue
- Limit use of gels and products that make hair stiff and difficult to comb through
- Use of Rogaine and like products not efficacious for interferon related hair-loss
- Recovery is spontaneous and occurs within 6 months after stopping interferon

# Thyroiditis



- Interferon is a pro-inflammatory cytokine that causes thyroid disease in some patients
- Interferon can unmask or exacerbate
- IFN induced disease may not be reversible after cessation of treatment
- Make sure you get a baseline TSH and retest every 3 months during treatment
- Hypothyroidism - easy to manage with replacement
- Hyperthyroidism - best to refer to endocrinologist



# Nausea

- Occurs intermittently in some patients
- Take ribavirin with food
- Avoid greasy or highly seasoned foods
- Allow rest period with the head and trunk elevated after eating
- Consume flat soda, anything with ginger
- Exercise
- Tigan or other medications if necessary



# Diarrhea

- Usually related to dose, tends to be mild and self-limiting
- Needs to be thoroughly assessed (onset, composition, fever, dizziness, abd exam)
- Eat small, frequent meals
- Maintain adequate hydration
- Avoid milk or milk products
- Try over-the-counter antidiarrheals (Pepto Bismol, Kaopectate, Imodium)

# Injection-Site Reaction



- Pre-treatment education on self-injection
- Pay attention to injection sites, noting reports of unrelieved pain, erythema
- Injection-site reactions usually present as erythema and rarely involve induration at the injection site.
- Inject drug more slowly; drug at room temperature
- Assess subcutaneous technique (bevel up, site rotation, etc.)

# Lab Alteration: Neutropenia

- Most common hematologic side effect of peginterferon.
- Ongoing assessment of lab values (ANC) and trends
- Teach patients signs and symptoms of infection and when to report
- Can use Neupogen as a treatment strategy
- No intervention, other than monitoring, is not uncommon.
- More frequent monitoring may be necessary depending on the immune status of the individual patient

# Lab Alteration: Anemia

- Primary toxicity of ribavirin is hemolytic anemia and is compounded by the bone marrow suppressive effects of interferon.
- Monitor blood counts, including iron level
- Assess for bleeding, monitor fatigue, instruct patient to report onset of shortness of breath or tachycardia.
- Consider erythropoetin treatment sooner than later.
- Consider antioxidants (vitamins C 100mg/d and E 800 IU/d)
- Dose reduction of ribavirin may be necessary in some cases.

# Use of Erythropoetin



- Usually 40,000 U subcutaneously
- Given weekly
- Must now follow Hgb weekly per new guidelines 2<sup>nd</sup> to risks of thromboembolism
- Monitor BP as well
- Erythropoetin is ineffective in the setting of iron deficiency. Low iron levels should be corrected prior to erythropoetin therapy.

# Lab Alteration: Thrombocytopenia

- An abnormally low platelet count may be seen in patients treated with interferon
- Regular lab monitoring
- Avoid use of aspirin or aspirin-containing products
- Instruct patients on reporting of bleeding, bruising, disorientation, blurred vision
- Dose reduce or hold dose of interferon until platelet count recovers
- Consider platelet transfusion (rarely necessary).



# Education

**EDUCATE** your patient about what to expect during treatment for HCV

**BEFORE THE RX IS  
WRITTEN**



# Schering Support

- Moving Forward
- Be-In-Charge
- Patient Care Consultant
- Commitment to Care
- Drug Information Service:
  - 1-800-526-4099
- Pregnancy Registry
  - 1-800-727-7064

# Roche Support



- **Pegassist Program**
- **One Stop Shopping**
  - **1-877-734-2797**
    - **Are you a patient?**
    - **Are you a pharmacist?**
    - **Are you a provider?**
  - **Website [www.pegasys.com](http://www.pegasys.com)**
- **Pregnancy Registry**
  - **1-800-526-6367**

# Support Groups and Web Resources

- Create a list of patient support groups in your area. Encourage your patient to visit a group.
- Put together a list of web resources that might be useful for your patients.
- Knowledge is power. You are part of this formula!



# **Remember...**

Current HCV treatment regimens  
can cause serious side effects  
and toxicities at therapeutic doses