UPDATE ON TREATMENT OF HEPATITIS C

SPRING EDUCATION SESSION
JUNE 10, 2017
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FINANCIAL DISCLOSURES

- Gilead – Speaker
- Merck - Speaker
OUTLINE

• Overview of hepatitis C
• Evolution of treatment
• Proposed Canadian Guidelines
• Brief review of drug coverage and criteria for coverage
• Overview of current treatment regimes
  • Harvoni
  • Sovaldi
  • Epclusa
  • Holkira Pak
  • Zepatier
  • Daklinza
OVERVIEW OF HEPATITIS C

- #1 infectious cause of lost years of life
- Estimated 0.5-1% Canadian population infected
- As few as 30% know about their infection
- Incidence is declining, severity is increasing
  - Peak in 2003 at 260,000
  - Estimated that by 2035
    - 205% increase in liver cancer
    - 160% increase in liver related death
    - 89% increase in compensated cirrhosis
    - 80% increase in decompensated cirrhosis
OVERVIEW OF HEPATITIS C

• Complications
  • Cirrhosis
  • Hepatocellular carcinoma
  • Porphyria cutanea tarda
  • Nephropathy, glomerulonephritis
  • Arthralgias
  • Mental complications
  • Vasculitis – mixed cryoglobulinemia
  • Lichen planus
  • Non-Hodgkin B cell lymphoma
GENOTYPES

- 6 main genotypes
- For now, genotype remains important for treatment selection
  - 1 – 65%
    - a – 56%
    - b – 33% (not in my NB experience)
    - Unable to subtype – 10% (not in my NB experience)
  - 2 – 14%
  - 3 – 32%
  - 4, 5, 6 - <1%
EVOLUTION OF TREATMENT

• 1989 – HCV identified
• 1991 – Interferon approved
• 1998 – Ribavirin approved
• 2001 – Pegylated interferon approved
• 2011- First generation protease inhibitors
• 2014 – Onward…..
  • 2nd
  • 3rd
  • And soon 4th generation
DECIDING ON TREATMENT REGIMEN

• Genotype
• Treatment experienced vs naïve
• Cirrhosis – decompensated vs compensated
• In some cases, viral load

• Drug-Drug Interactions
  • www.hep-druginteractions.org

• For now....
DRUG COVERAGE

• Public Formulary - Moving target
• Difference between what is covered and what I want to use....IFN....
COVERAGE CRITERIA

• Prescribed by a hepatologist, gastroenterologist or infectious disease specialist (or other physician experienced in treating a patient with hepatitis C infection)
• Genotype must be known
• Quantitative HCV RNA value in last 6 months
• F2 or greater.....or....
• Co-infection with HIV or HBV
• Post-organ transplant (liver or non-liver)
• Extra-hepatic manifestations
• Chronic kidney disease stage 3, 4 or 5
• Co-existent liver disease with diagnostic evidence for fatty liver disease
• DM on antihyperglycemic medications
• Women of childbearing age who are planning pregnancy within the next 12 months
DRUGS THAT ARE ON NB PUBLIC FORMULARY

- Elbasvir/grazoprevir (Zepatier)
- Daclatasvir (Daklinza)
- Sofosbuvir/velpatasvir (Epclusa)
- Ledipasvir/Sofosbuvir (Harvoni)
- Sofosbuvir (Sovaldi)
- Interferon ?!?!
Elbasvir/Grazoprevir

- Genotype 1 a/b
  - Treatment naïve or treatment experienced prior relapsers
    - 12 weeks (may consider 8 weeks in treatment-naïve geno 1b patients w/o significant fibrosis)
- Genotype 1b
  - Treatment-experienced on-treatment failures
    - 12 weeks
- Genotype 4
  - Treatment naïve or prior relapsers
    - 12 weeks
ELBASVIR/GRAZOPREVIR

- Genotype 1a
  - Treatment experienced on treatment failures
    - 16 weeks in combination with RBV
- Genotype 4
  - Treatment experienced on treatment failures
    - 16 weeks in combination with RBV
DACLATASVIR

- **Genotype 1b**
  - Without cirrhosis or with compensated cirrhosis
    - 24 weeks in combination with asunaprevir
- **Genotype 3**
  - Without cirrhosis
    - 12 weeks in combination with sofosbuvir
  - With compensated or decompensated cirrhosis
    - 12 weeks in combination with sofosbuvir and RBV
  - Post-liver transplant with no cirrhosis or with compensated cirrhosis
    - 12 weeks in combination with sofosbuvir and RBV
SOFOSBUVIR/VELPATASVIR

- Genotypes 1, 2, 3, 4, 5, 6 or mixed
  - Without cirrhosis or with compensated cirrhosis
    - 12 weeks
- Genotypes 1, 2, 3, 4, 5, 6 or mixed
  - With decompensated cirrhosis
    - 12 weeks in combination with RBV
SOFOSBUVIR/LEDIPASVIR

• Genotype 1
  • Treatment-naïve without cirrhosis with pre-treatment HCV RNA <6 million and mono-infected
    • 8 weeks
  • Treatment-naïve without cirrhosis, with pre-treatment HCV RNA >6 million
    • 12 weeks
  • Treatment-naïve with compensated cirrhosis
    • 12 weeks
  • Treatment-naïve with advanced liver fibrosis (F3-4)
    • 12 weeks
**SOFOSBUVIR/LEDIPASVIR**

- **Genotype 1**
  - Treatment-experienced without cirrhosis
    - 12 weeks
  - HCV/HIV co-infected without cirrhosis or with compensated cirrhosis
    - 12 weeks
  - Treatment-experienced with compensated cirrhosis
    - 24 weeks
  - Decompensated cirrhosis
    - 12 weeks in combination with RBV
  - Liver transplant recipients without cirrhosis or with compensated cirrhosis
    - 12 weeks in combination with RBV
DRUG COVERAGE

• Private plans
  • Plan specific but in general it mirrors the public formulary
  • Coverage generally occurs earlier than for public formulary
BRIEF REVIEW OF MAIN TREATMENTS

- Ledipasvir/sofosbuvir (Harvoni)
- Sofosbuvir (Sovaldi)
- Velpatasvir/sofosbuvir (Epclusa)
- Paritaprevir/ritonavir/ombitasvir + dasabuvir (Holkira Pak)
- Grazoprevir/elbasvir (Zepatier)
- Daclatasvir (Dacllinza)

- Drug-drug interactions
  - Hep-druginteractions.org
HARVONI

- Main side effects
  - Nausea
  - Fatigue
  - Headache
- Main drug-drug interaction
  - Antacids/PPI’s/H2 blockers
  - Amiodarone
  - Some anticonvulsants
    - Carbamazepine, phenobarbital, phenytoin
  - Rosuvastatin
  - Digoxin
- No bloodwork required on treatment unless used with RBV
SOVALDI

- Main side effects
  - Nausea
  - Fatigue
  - Headache

- Main drug-drug interaction
  - Amiodarone
  - Some anticonvulsants
    - Carbamazepine, phenobarbital, phenytoin

- No bloodwork required on treatment unless used with RBV
EPCLUSA

- **Main side effects**
  - Nausea
  - Fatigue
  - Headache*

- **Main drug-drug interaction**
  - Antacids/PPI’s/H2 blockers
  - Amiodarone
  - Some anticonvulsants
    - Carbamazepine, phenobarbital, phenytoin

- **No bloodwork required on treatment unless used with RBV**
HOLKIRA PAK

• Main side effects
  • Fatigue
  • Nausea
  • Hepatic decompensation

• Drug-drug interactions
  • Amiodarone
  • Anticonvulsants
  • Colchicine
  • Ethinyl estradiol
  • Gemfibrozil
  • Flagyl
  • Tamsulosin

• Bloodwork on treatment
  • Liver BW at baseline, recommended q4 weeks
ZEPATIER

- Main side effects
  - Headache
  - Nausea
  - Fatigue

- Drug interactions
  - Many
    - Anticonvulsants
    - Some antibiotics – clarithromycin
    - Plavix
    - Gemfibrozil
    - Statins
    - Colchicine
    - Warfarin

- Bloodwork on treatment
  - Do liver BW at baseline, week 8 and as clinically indicated
Daklinza

- Main side effects
  - Headache
  - Nausea
  - Fatigue

- Drug-drug interactions
  - Some anticonvulsants (carbamazepine, phenobarbital, phenytoin)
  - Dabigatran

- Bloodwork on treatment
  - No bloodwork required unless clinically indicated
THE FUTURE

- Pan-genotypic
- Shorter courses of treatment
- ?what to do with treatment failures
QUESTIONS, COMMENTS