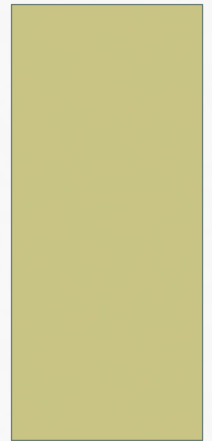


UPDATE ON TREATMENT OF HEPATITIS C

SPRING EDUCATION SESSION
JUNE 10, 2017
MEAGHAN O'BRIEN



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

COVERAGE CRITERIA

- 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 (Daclinzia)

- 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