Harvoni: solution to HCV

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Hepatitis C (HCV)

- Inflammation of the liver, characterized by hepatocyte necrosis
- An enveloped, single stranded, positive sense RNA virus
- The most common chronic bloodborne infection in the United States
  - Prevalence: 1.6% (2.0*)
  - 3.2 (5.2*) million persons live with HCV infection
  - Genotype 1 (72%)
  - Genotype 2 (16% to 19%)
  - Genotype 3 (8% to 19%)

Goals of Pharmacological Treatment

- Sustained virological response (SVR)
  - Continued absence of detectable HCV RNA at least **12 weeks** after completion of therapy
  - SVR is a marker for cure of HCV infection and has been shown to be durable in large prospective studies in more than 99% of patients followed up for > 5 years\(^1\)

- Prevent complications from HCV infection
  - Necroinflammation
  - Fibrosis
  - Cirrhosis
  - Hepatocellular carcinoma
  - Death

History of HCV Treatment (genotype 1)

- Pegylated interferon + oral ribavirin
  - SVR 45-50%\(^2\)  
  - Relapse 13% to 18%\(^1\)
- 1\(^{st}\) gen protease inhibitors + pegylated interferon alfa-2a + ribavirin
  - SVR 67-75%\(^2\)
- 2\(^{nd}\) gen protease inhibitors e.g. simeprevir
  - SVR 79.2%\(^3\)
- RNA polymerase nonstructural protein (NS5B) inhibitor sofosbuvir
  - SVR 90%\(^4\)

\(^1\)http://www.scielo.br/scielo.php?script=sci_arttext&pid=S1413-86702007000600006
What is Harvoni?

- Fixed-dose combination in a single pill taken once daily:
  - Sofosbuvir 400 mg – NS5B Polymerase Inhibitor
  - Ledipasvir 90 mg – NS5A inhibitor
- Indicated for HCV genotypes 1, 4, 5, 6
- SVR 96% - 8 clinical trials that demonstrate >90% efficacy
- One tablet taken orally once daily with or without food
- Recommended treatment duration for GT 1:
  - Treatment-naïve with or without cirrhosis: 12 weeks
  - Treatment-experienced without cirrhosis: 12 weeks
  - Treatment-experienced with cirrhosis: 24 weeks
- Recommended treatment duration for other GTs: 12 weeks

Who is Harvoni being recommended by?

- Department of Veterans Affairs (VA) National Hepatitis C Resource Center Program and National Viral Hepatitis Program
- American Liver Foundation
- European Association for the Study of the Liver (EASL)
- 2016 AASLD/ISDA Guideline - American Association for the Study of Liver Diseases and Infectious Diseases Society of America
  - Harvoni (ledipasvir 90 mg/sofosbuvir 400 mg)
    - Rating: Class I, Level A
  - Daily sofosbuvir (400 mg) and weight-based RBV for 24 weeks
    - Rating Class IIb, Level A

Harvoni is cost-effective!

- Interferon and ribavirin overall combined cost: $25,000 for 48 weeks
  - SVR 50%, Relapse 18% → Cost / (SVR - Relapse) = $781.25
- Harvoni Cost: $94,500 for 12 week course
  - SVR 96%, Relapse 1% → Cost / (SVR – Relapse) = $994.74
- Cost and Medication Access: The wholesale acquisition cost (WAC) for ledipasvir-sofosbuvir is $1125 per pill.¹
  - Cost of 8-week course of therapy = $63,000
  - Cost of 12-week course of therapy = $94,500
- Annals of Internal Medicine cost effectiveness study - Harvoni vs. older standard of care requiring a protease inhibitor, interferon and ribavirin
  - 83% cost effective for treatment-naïve and 81% for treatment-experienced

¹ http://www.hepatitisc.uw.edu/page/treatment/drugs/ledipasvir-sofosbuvir
Why Harvoni?

- One course cure to HCV
- Once daily oral tablet formulation promotes patient adherence
- Sustained virological response 96% with low relapse 1%
- Pregnancy category B
- No need for IFN (flu-like syndrome) or ribavirin (preg cat X)
- Well tolerated – Fatigue, headache, nausea, diarrhea
- Cost-effective

The end