Hepatitis

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What is Hepatitis?

According to the WHO:

- Hepatitis is an inflammation of the liver, most commonly caused by a viral infection. There are five main hepatitis viruses, referred to as types A, B, C, D and E.
- Hepatitis A and E are typically caused by ingestion of contaminated food or water.
- Hepatitis B, C and D usually occur as a result of parenteral contact with infected body fluids.
- Types B and C lead to chronic disease in hundreds of millions of people and, together, are the most common cause of liver cirrhosis and cancer.

HBV

By some accounts, over 350 million people worldwide carry the hepatitis B virus. According to the WHO: More than 240 million people have chronic (long-term) liver infections, and more than 780,000 people die every year due to the acute or chronic consequences of hepatitis B.

A vaccine against hepatitis B has been available since 1982. The HBV vaccine is 95 percent effective in preventing infection and its chronic consequences, and was the first vaccine against a major human cancer.

HBV prevalence is highest in sub-Saharan Africa and East Asia, most infected during childhood, and between 5–10 percent of the adult population is chronically infected. High rates of chronic infections are also found in the Amazon and the southern parts of eastern and central Europe. In the Middle East and the Indian subcontinent, an estimated 2–5 percent of the general population is chronically infected. Less than one percent of the population in western Europe and North America is chronically infected.

There are seven FDA approved drugs for HBV, none of which are considered a cure, but they do significantly decrease the risk of liver damage by slowing down or stopping the virus from reproducing. The prices for some treatments are high. A new Medicines Patent Pool license for tenofovir alafenamide (TAF) as a treatment for Hepatitis B may offer a lower cost treatment option in some developing countries.

HDV: Studies reported in 1977 found that some patients with a more damaging form of HBV infection were also infected with a second virus that is known as hepatitis delta virus, hepatitis D virus or simply HDV. The genomes of HBV and HDV are very different and replicate by different mechanisms. An estimated 15-20 Million individuals are infected with HDV worldwide. Hepatitis delta is the most severe form of chronic viral hepatitis, and there is no testing or identification of HDV infection. Migrant populations and special risks groups show particular high HDV prevalences. Screening for HDV is limited, and the only available treatment for chronic HDV has a 25 percent success rate, involves at least weekly injections of high doses of pegylated interferons for one year.

HEV: According to WHO: Outbreaks and sporadic cases of hepatitis E occur around the world. These outbreaks frequently occur in resource-limited countries with limited access to essential water, sanitation, hygiene and health services, and may affect several hundred to several thousand persons. In recent years, some of these outbreaks have occurred in areas of conflict and humanitarian emergencies, such as war zones, and in camps for refugees or internally displaced populations (IDP). An estimated 20 million infections and 3.3 million acute cases occur annually worldwide with an estimated 56,600 deaths.

WHO on HCV

130–150 million people globally have **chronic** hepatitis C infection, and some experts suggest the infection rates are higher.

Some of those who are chronically infected will develop liver cirrhosis or liver cancer.

350,000 to 500,000 people die each year from hepatitis C-related liver diseases.

HCV Infection rates

According to the CDC, in many developed countries, including the United States, the prevalence of HCV infection is less than 2 percent.

Within Europe, some countries have infection rates below .5 percent, and others have infection rates between 3 and 5 percent.

The CDC estimates prevalence to be higher than 2 percent in several countries in Latin America, Eastern Europe, and the former Soviet Union, and certain countries in Africa, the Middle East, and South Asia, and the highest (greater than 10 percent) in Egypt.

HCV is a small, single-stranded RNA virus. The specific genetic makeup, or genotype, of the virus can vary and at least six genotypes have been characterized in HCV-infected patients, with over 50 sub-types identified. Genotypes are designated with numbers (genotypes 1-6) and subtypes with letters (e. g. genotype 1a).

HCV genotypes 1, 2, 3, and 4 are found worldwide, but their prevalence varies among geographic regions. Genotype 1, including its subtypes 1a and 1b, is the most common genotype globally, accounting for approximately 74% of all HCV infections.

It is estimated that patients with genotype 2 or 3 represent approximately 12% of the worldwide chronically infected HCV population, with approximately 6% comprised of genotypes 4 through 6 and the remaining 8% of patients in other undesignated categories.

The specific genotype and subtype of HCV in a patient appears to play a significant role in the degree of efficacy of standard of care therapy.

Genotype 1 is the most difficult genotype to treat and the most common in North America and Europe.

Treatments for HCV

- Diagnostic tools are expensive, not well suited for resource poor settings
- No vaccine exists
- Development of Sofosbuvir (SOF) by Pharmasset/Gilead was major breakthrough.
- When used with other drugs, SOF provide a cure.
    - SOF works with several drugs. Not all drugs are effective across all genotypes
    - Among the promising 2nd drugs, for use in an all oral combination, are BMS's DAC, and Gilead's LDV and GS-5816
    - SOF+GS-5816 possible oral pan-genotypic oral therapy for all HCV patients across genotypes.

Gilead's HCV voluntary license

- Drugs:
  - Includes SOF and LDV.
  - GS-5816 may be added in 2015.

- Licensed territory:
  - 91 countries with 2013 population of 3.26 billion persons, about 46 percent of the world population. (73 percent, when high income countries and China are excluded).
  - Per capita income of $1,879.
  - 54 percent of persons infected with HCV

- Countries outside of the licenses had a population of 3.87 billion persons, and a per capita income of $17,876.

Benefits of the Gilead License

The licenses were signed by seven strong generic manufactures

The availability of know-how, and the licensing of the test data will accelerate availability of inexpensive oral cures for HCV.

The licensed territory is large enough to induce entry and economies of scale.

Allows sales outside of territory where no patent or compulsory license is issued.

Permits coformulation with non-Gilead products

Criticism of the Gilead License

Did not go far enough in terms of geographic area

Creates uncertainty about cases where patents have been filed, but contested and not granted

Pricing of SOF, and SOF+LDV

- Super expensive in high income countries, and all members of the EU
- Deep discount in lower income countries
- Price negotiations everywhere.
- Voluntary license in 91 countries.
- Possibility to import drugs under compulsory licenses or where there is no patent.
- Drug registration a barrier in many countries

Misc access barriers

Lack of low cost point of care diagnostics

Drug registration will be a challenge

No affordable access to drugs from companies other than Gilead.

Case for patent buy-out/delinkage

- Benefits of treatment vary depending upon patent. Large differences in social benefits for treating patients who are infected, chronically infected, and suffering significant liver damage.
- Significant differences in infection rates, incomes and insurance across countries, regions.
- Treatment regimes cheap to manufacture, easy to administer.

Challenges for patent buy-out/delinkage

- Costs will be high.
- Health benefits will occur over long periods of time.
- Hard to organize buyers
- Reimbursement authorities face short term budget pressures

Potential trade issues

- ACTA/TPP/TTIP norms on damages for infringement
- ISDS and indirect expropriation claims
- Paragraph 6 implementation