Hepatitis C Drugs:
More Choices, More Hope

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11 December 2015
(word count 1,077)

Estimates suggest that more than million people in the United States, and 170 million people globally are chronically infected with the hepatitis C virus (HCV). Merck's development of a new hepatitis C therapy promises to deliver both hope and choice to hepatitis C patients. Prior to Sovaldi—a 'blockbuster' antiretroviral therapy produced by Gilead Sciences Inc.—hepatitis C patients faced low cure rates and debilitating side effects associated with treatments such as interferon and ribavirin. Moreover, many patients who suffer from hepatitis C eventually need a liver transplant.

Merck's once-daily, single-tablet combination of grazoprevir and elbasvir proved effective in treating even the sickest hepatitis C patients, without negative side effects. Treatment was well tolerated, with no significant difference in reports of headaches, nausea, fatigue, insomnia, dizziness and diarrhoea between the placebo group and the active treatment group (Alcorn). Moreover the grazoprevir/elbasvir combination safely and effectively delivered results in less time than existing therapies for the two most common HCV strains, genotypes (GT) 1 and 3. Preliminary clinical evidence indicates that the grazoprevir/elbasvir combination may substantially improve upon existing therapies with respect to one or more clinically significant endpoints (Merck 28 July 2015). Currently, both Sovaldi and Harvoni—a variant of Sovaldi also manufactured by Gilead—are available only for patients with mild or moderate kidney impairment, and thus not accessible to patients with severe kidney impairment or on dialysis (Koons & Chen). Although Sovaldi is approved for patients with hepatitis C GT 4, it must be taken in combination with another side-effect heavy drug.

The FDA granted grazoprevir/elbasvir combination therapy a Priority Review designation, pointing to a considerable unmet need in patient populations with chronic hepatitis C. The FDA also designated grazoprevir/elbasvir a breakthrough therapy in both the treatment of chronic HCV GT 4 infection, and chronic HCV GT1 infection in end-stage renal disease patients on hemodialysis (Vermes). Beyond testing grazoprevir/elbasvir in multiple chronic HCV genotypes, and HCV patients with HIV co-infection, grazoprevir/elbasvir is currently being studied in patients with stage 4 and 5 chronic kidney disease, inherited blood disorders, cirrhosis, and patients taking opiate substitution therapy (Vermes).

The grazoprevir and elbasvir combination therapy cured hepatitis C in 99% of people with advanced chronic kidney disease. This provides the first evidence that patients with chronic kidney disease may potentially be cured of hepatitis C if treated with an interferon-free regimen (Alcorn). Historically, existing treatments have been unsuitable for patients with kidney disease; notably ribavirin exacerbates the anemia suffered by many patients with chronic kidney disease. Sovaldi presents comparable risks and must be used with caution in patients with kidney disease, as the drug is cleared through the kidneys (Alcorn). Given that grazoprevir and elbasvir are broken down in the liver and not excreted through the kidneys, they may be used without dose adjustment in patients with kidney disease.

Merck's innovative therapy targets small, difficult-to-treat patient populations. In October, Merck announced that the grazoprevir/elbasvir combination therapy was effective against two hepatitis C genotypes after eight weeks of treatment, whereas many existing drugs required a 12-week treatment regimen of (Bloomfield, 14 November 2015). In addition, Merck's development of a triple therapy, grazoprevir and elbasvir in combination with MK-3682 (a drug in the same class as Sovaldi), achieved

cure rates exceeding 90% in HCV GT 1 and 2 after eight weeks of treatment, and a similarly high rate in GT 3 after 12 weeks of treatment (Reeves). These results are particularly striking when compared against Sovaldi, which has a lower success rate in treating HCV GT 2, 3 and 4, and typically requires a longer duration of treatment (Reeves).

First and foremost Merck's new hepatitis C drug delivers therapeutic value to patients. The grazoprevir/elbasvir combination therapy also benefits physicians, as it gives clinicians more options in treating diverse patient needs. In particular, therapeutic alternatives within the same drug class may differ in their metabolism, molecule, regimen, dosing schedules, speed of action, delivery system, adverse effects, therapeutic profile and/or interactions. Consequently, therapeutic alternatives may improve patient administration, allow for the elimination of treatment-limiting drug reactions or other side effects, and offer significant options to patients with different physiologic and pathophysiologic statuses.

Therapeutic choices also deliver cost savings, as price competition results from the greater availability of drugs within a therapeutic class. In a study of pharmaceutical innovation, DiMasi (2000) examined 20 new entrants to existing classes (1995-1999), finding that 80% were launched at a discount relative to the price leader and 65% were launched at a discount relative to the average price for the class. The average decrease in price (for new entrants) was 26 per cent below the price leader and 14 per cent below to the class average. DiMasi's analysis demonstrates that incremental innovation delivers cost savings, as well as therapeutic choice, to patients.

Ultimately, there are many reasons to celebrate Merck's development of a new hepatitis C therapy. The combination therapy promises hope to previously untreated patient populations, and provides others with a new choice. The health benefits and potential cost savings will benefit both patients and payers.

References

Alcorn, Keith. "Merck's grazoprevir/elbasvir combo cures 99% of hepatitis C in chronic kidney disease," Hepatitis C Trust, 2014. Available at: http://www.hepctrust.org.uk/news/may-2015/mercks-grazoprevirelbasvir-combo-cures-99-hepatitis-c-chronic-kidney-disease

Bloomfield, Doni. "Merck's Shorter-Treatment Hep C Drugs Work in Mid-Stage Trial," Bloomberg.com, 20 October 2015. Available at: http://www.bloomberg.com/news/articles/2015-10-20/merck-s-shorter-treatment-hep-c-drugs-works-in-mid-stage-trial

Bloomfield, Doni. "Study Shows Merck Hepatitis C Drug Cures Addicts," Bloomberg.com, 14 November 2015. Available at: http://www.bloomberg.com/news/articles/2015-11-15/merck-hepatitis-c-drug-cures-addicts-could-pressure-u-s-states

Chen, Angela. "Merck Gets Breakthrough Designation for Hepatitis C Drugs," Wall Street Journal, 8 April 2015. Available at: http://www.wsj.com/articles/merck-gets-breakthrough-designation-for-hepatitis-c-drugs-1428495376

DiMasi, Joseph A., "Price trends for prescription pharmaceuticals 1995-1999," a report prepared for the Conference on Pharmaceutical Pricing Practices, Utilization and Costs of the U.S. Department of Health and Human Services, 2000. Available at: http://aspe.hhs.gov/health/reports/Drug-papers/dimassi/dimasi-final.htm

Heitz, David. "Merck Challenges Harvoni with New Hepatitis C Treatment," Healthline, 24 April 2015. Available at: http://www.healthline.com/health-news/merck-challenges-harvoni-with-new-hepatitis-c-treatment-042415

Koons, Cynthia and Caroline Chen. "Merck Targets Toughest Cases to Gain Hepatitis C Foothold," Bloomberg.com, 28 July 2015. Available at: http://www.bloomberg.com/news/articles/2015-07-28/merck-targets-toughest-cases-for-foothold-in-hepatitis-c-market

Merck. "Merck Announces U.S. Food and Drug Administration Acceptance of New Drug Application for Grazoprevir/Elbasvir, an Investigational Therapy for Treatment of Chronic Hepatitis C Genotypes 1, 4 and 6 Infection," 28 July 2015. Available at: http://www.mercknewsroom.com/news-release/hepatitis-c-newsroom/merck-announces-us-food-and-drug-administration-acceptance-new-dru

Reeves, Amy. "Gilead, Merck Hepatitis C Rivalry Heats Up," Investor's Business Daily, 20 October 2015. Available at: http://news.investors.com/technology/102015-776473-gilead-gets-price-target-hike-merck-hepatitis-c-trial-succeeds.htm

Vermes, Krystle. "Merck's Hepatitis C Combination Candidate Receives Priority Review," PharmacyTimes, 1 August 2015. Available at: http://www.pharmacytimes.com/product-news/mercks-hepatitis-c-combination-candidate-receives-priority-review