Hepatitis C Genotype 3: Hard to Have, Hard to Treat

February 2, 2015 By Lucinda K. Porter RN

When hepatitis C virus (HCV) genotyping became available, I learned that I had genotype 1a. Until recently, genotype 1 hepatitis C was the hardest to treat. However,genotype 1 is quite easy to treat now with the latest approved HCV drugs. Genotype 2 has always been fairly easy to treat too. Genotype 3 is the one causing problems. In this blog, I discuss genotype 3, review the current hepatitis C genotype 3 treatment recommendations, and look at what is ahead.

Genotype 3 is not only the most treatment-resistant, it is the most aggressive type of hepatitis C. Compared with other genotypes, people with genotype 3 tend to progress more rapidly to fibrosis and cirrhosis. Genotype 3's have a higher prevalence of severe steatosis (fatty liver), and a higher incidence of hepatocellular carcinoma (liver cancer).

Current HCV Treatment Recommendations for Genotype 3

The American Association for the Study of Liver Diseases (AASLD) and Infectious Diseases Society of America (IDSA) recommend the following treatment options for people living with genotype 3 HCV: Treatment-naÃ¯ve and Treatment-experienced for Patients Who Failed Prior Peginterferon and Ribavirin Treatment

- Sovaldi (sofosbuvir) + ribavirin for 24 weeks

Sustained virologic response rates at 12 weeks (SVR12) for treatment-naÃ¯ve: 93 percent for those without cirrhosis; 92 percent for those with cirrhosis. (VALENCE study) This small European study only had 13 treatment-naÃ¯ve cirrhotics. SVR12 rates for treatment-experienced: 87 percent for those without cirrhosis; 60

percent for those with cirrhosis. (VALENCE study)

- Sovaldi (sofosbuvir) + ribavirin + peginterferon (PEG) for 12 weeks

SVR12 rates: 87 percent (LONESTAR and VALENCE studies were very small and no data for cirrhosis vs non-cirrhosis were provided)

Discussion: The retreatment cure rates are low, but good for first-timers. Anything over 90 percent SVR is cause for celebration, but taking ribavirin is cause for commiseration. Ribavirin and side effects go together like peanut butter and jelly. Common side effects include: fatigue, impaired concentration, increased heart rate, insomnia, loss of appetite, mood issues (anxiety, depression, irritability, moodiness), nausea, rash/itching/dry skin, shortness of breath, taste perversion, upset stomach weakness, hemolytic anemia (low red cells), dizziness/lightheadedness.
Twenty-four weeks of this isn't fun. Moreover, real-world use of sofosbuvir and ribavirin might not yield cure rates as high as these. However, it is doable - hundreds of thousands of people endured 48 weeks of PEG plus ribavirin; some endured triple therapy with Incivek or Victrelis. So, if you undergo treatment, get support. The Hep Forums are a good place to start. (Shameless self-promotion, my books, especially *Hepatitis C One Step at a Time* may also be useful.)
What's Ahead

- Harvoni (sofosbuvir/ledipasvir) + ribavirin for 12 weeks: The ELECTRON-2 trial was very small with 51 treatment-naive genotype 3 hepatitis C subjects, of which only three had cirrhosis. In the treatment arm that used ribavirin, 100 percent achieved an SVR12, compared with 64 percent in the arm without ribavirin. In treatment-experienced patients, 89 percent of those without cirrhosis had an SVR; those with cirrhosis had a 73 percent SVR12. Harvoni is not FDA-approved to treat genotype 3 patients.

- Daclatasvir + sofosbuvir for 12 weeks: The ALLY-3 Phase 3 trial enrolled 152 genotype 3 subjects (101 treatment-naÃ¨ve/51 treatment-experienced). Of the treatment-naive subjects, 97 percent of those without cirrhosis had an SVR12; 58 percent SVR of those with cirrhosis.

Among treatment-experienced patients, 94 percent SVR12 in those without cirrhosis; 69 percent with cirrhosis). Daclatasvir is not FDA-approved in the U.S.

- GS-5816 + sofosbuvir with or without ribavirin: This is the combo to watch. GS-5816 is Gilead Sciences' next generation NS5A inhibitor (same class as ledipasvir). The ELECTRON-2 reported 96 to 100 percent SVR rates with the combination of sofosbuvir plus GS-5816, with or without ribavirin for 8 weeks in treatment-naÃ¯ve genotype 3 patients without cirrhosis. A similar study using GS-5816 + sofosbuvir without ribavirin for 12 weeks yielded 93 percent SVR rates.

The 50th International Liver Congress is April 22-26. Expect to see more data and perhaps genuine hope for people living with genotype 3.

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