

Gastroenterology and Hepatology Clinical Update

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Telaprevir for Previously Treated Chronic Hepatitis C Infection

McHutchison JG, et al. NEJM 2010: 362 (April 8): 1292 – 1303

Less than 50% of patients with Hepatitis C either fail to respond to standard treatment with Interferon (INF) and Ribavirin or relapse once treatment is finished. This is especially true in genotype I. A new generation of oral drugs is being studied for this group of patients. This class of medicines is the protease inhibitors and Telaprevir is one of them. In this study, 453 patients who were genotype I nonresponders or relapsers were entered. The end point of treatment was sustained virologic response (SVR) after treatment.

Results: Treatment with Telaprevir, PEG INF and Ribavirin resulted in an SVR in 39% of the nonresponders to standard therapy and a SVR in 69% - 76% of relapsers to standard of care treatment. Telaprevir did not work unless used with Ribavirin and Interferon; in addition side effects were more frequent when it was added.

Comments: This study is very encouraging in that it shows a quadrupling in the SVR when Telaprevir is added to treatment of nonresponders to standard of care therapy (PEG INF and ribavirin.) Will this regimen someday become the “standard of care” at the price of the noted higher side effect profile and potentially higher cost.

Rifaxamin Treatment in Hepatic Encephalopathy

Bass NM, et al. NEJM 2010: 362 (March 25): 1071 – 1081

Standard treatment of recurrent hepatic encephalopathy (HE) includes dietary modification and Lactulose. Recurrences are common, occurring in 20% - 30% of patients. As one of the theories for the cause of HE is the production of ammonia by bacteria in the gut, the use of the minimally absorbable antibiotic Rifaxamin is a candidate to alter the bacterial content of the bowel, thus helping prevent HE. Patients for this study were recruited from multiple medical centers in the USA, Canada and Russia. They had to have had at least 2 episodes of HE in the past 6 months and not have been encephalopathic at entry to the study. Patients were

placed on 550 mg of Rifaximin or placebo twice a day for 6 months. The use of Lactulose was permitted in both groups.

Results: More than 300 patients were enrolled and the study ran for 6 months. In the Rifaximin group, 22% of the subjects developed HE as compared to 46% of those who got placebo. Hospitalizations were less common in the Rifaximin treated patients versus placebo, 14% vs. 23%. Both groups used Lactulose with equal frequency. There were no differences in side effects in either group.

Comments: The treatment of HE is often difficult. Dietary restrictions are tough to adhere to and Lactulose is fraught with side effects (diarrhea) and potential noncompliance (frequent liquid dosing.) The addition of a twice a day pill such as Rifaximin is a welcome addition to treatment of this disabling condition.

Pioglitazone, Vitamin E or Placebo for Nonalcoholic Steatohepatitis

Sangal AJ, et al. NEJM 2010; 362 (May 6): 1675 – 1685

Nonalcoholic steatohepatitis (NASH), which is the variant of fatty liver that can be associated with end stage liver disease (cirrhosis), has been linked to oxidative stress and insulin resistance. In a double blind, placebo controlled multicenter study, the insulin sensitizer Pioglitazone (used on the treatment of diabetes) and the antioxidant Vitamin E were studied for use as monotherapy in patients with NASH who did not have diabetes.

84 patients were assigned to Vitamin E 800 IU or placebo, 80 to Pioglitazone 30 mg or placebo, while 83 received both placebos. The study ran for 96 weeks with medicine or placebo given once a day.

Major histologic improvement in NASH was statistically more frequent in the Vitamin E treated group when pre and post liver biopsies were compared. When improvement in liver function studies and other more subtle secondary endpoints were looked at, both Vitamin E and Pioglitazone were effective.

Conclusion: Vitamin E is superior to placebo in the treatment of NASH. Pioglitazone also improves secondary features suggesting that both drugs may have a place in treatment

Comments: Although Vitamin E seemed to have the best over all results, the study ran for only 96 weeks and the treatment of NASH would probably have to last longer than this. Some studies have also linked long term use of high dose Vitamin E with adverse events, so prescribing caution is advised.

Pioglitazone is used in the treatment of diabetes and could be used in the subset of patients with both diabetes and NASH.

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