HIGHLIGHTS FROM AASLD 2013

By Dee Rapposelli

Interim Results of Investigational NS3/4A Protease Inhibitor/NS5A Replication Complex Inhibitor Combo in HCV GT 1a/b Infection

Interim results of the C-WORTHY trial of the nonstructural (NS) 3/4A protease inhibitor MK-5172 and the NS5A replication complex inhibitor MK-8742 suggest that the combination exerts robust virologic suppression in treatment-naive patients with genotype (GT) 1 hepatitis C virus (HCV) infection. Interim results of C-WORTHY, a phase 2b trial, were reported by Eric Lawitz, MD, of the University of Texas Health Science Center and the Texas Liver Institute in San Antonio, at the annual scientific meeting of the American Association for the Study of Liver Diseases Liver Meeting 2013, which took place on November 1 to 5 in Washington, DC.

Sixty-five treatment-naive, noncirrhotic patients with HCV GT 1a or 1b infection were randomly assigned to receive 12 weeks of either 100 mg/d MK-5172 plus 20 mg/d MK-8742 plus ribavirin (n=22), 100 mg/d MK-5172 plus 50 mg/d MK-8742 plus ribavirin (n=24), or 100 mg/d MK-5172 plus 50 mg/d MK-8742 (n=12). The ribavirin-free regimen included only GT 1b-infected patients.

All of the patients in the triple therapy regimen that included MK-8742 at 20 mg/d and all of the patients receiving the ribavirin-free regimen who reached 12 weeks posttreatment had a sustained virologic response (SVR12). Of patients receiving triple therapy that included MK-8742 at 50 mg/d, 96% of the 23 patients who reached 12 weeks posttreatment had a SVR.

Enhanced Bottle Labeling Not Enough to Halt Misuse of Acetaminophen

Enhanced bottle labeling and written information about acetaminophen may not be sufficient to promote safe use of over-the-counter (OTC) and prescription products containing the widely used analgesic/antipyretic, concluded Marina Serper, MD, of the Division of Gastroenterology and Hepatology at Northwestern University in Chicago, Illinois. Dr Serper and a multicenter team conducted a study in which 662 patients presenting to general medical health clinics between August 2012 and February 2013 received either usual care; medication labeled with an icon stating that acetaminophen was an active ingredient and a flyer explaining the safe use of acetaminophen; or medication labeled with an icon, a flyer, and verbal counseling about use of acetaminophen. The strategies were meant to simulate scenarios that a patient might encounter in a pharmacy when picking up a prescription. Structured interviews were then conducted to assess participants' knowledge about safe use of acetaminophen and the risks of concomitant use of acetaminophen-containing products. The mean age of participants was 47 years, 73% were African American, 68% had limited literacy, and 52% had used an OTC analgesic in the past month.

The researchers found that participants receiving written and verbal instructions were most likely to understand the risks of concomitant use of acetaminophen-containing products, but no more than 50% of participants in this arm of the study did so. Nevertheless, this 50% rate represented a nearly 2-fold increase in awareness compared with participants given no intervention (P<.001).

Given that unintentional misuse of acetaminophen, including concomitant use of acetaminophen-containing products, is the leading cause of liver failure in the United States, more intensive public health measures are needed to promote consumer understanding of safe use of this agent, concluded Dr Serper. She recommended that clinicians routinely obtain detailed medication histories from patients and counsel them on the maximum, safe, daily dose and risks of taking multiple acetaminophen-containing medications at the same time.

Herbal and Dietary Supplement–Induced Hepatotoxicity on the Rise

Herbal and dietary supplements are increasingly being implicated in hepatotoxicity in the United States, according to findings from the Drug-Induced Liver Injury Network. Bodybuilding products are the most common cause of herbal and dietary supplement–related liver injury, and the rates of liver transplantation and death among persons with supplement-related liver injury were found to be twice those seen in persons with conventional drug-induced liver injury.

The study, reported by Victor J. Navarro, MD, of the Division of Hepatology at Einstein Medical Center in Philadelphia, Pennsylvania, examined 1035 cases of liver injury occurring over a 10-year period (2003-2013). Of these cases, 845 were considered to be either probably, very likely, or definitely caused by a drug or supplement. The product in 136 (16%) cases was the latter, an herbal or dietary supplement. Of these cases, the cause in 44 (35%) was specifically attributed to bodybuilding products, the cause in 85 (62%) was attributed to various other products, and the cause in 7 (5%) was attributed to a combination of agents.

In addition, said Dr Navarro, the proportion of cases of liver injury attributed to herbal or dietary supplements is on the rise, increasing from 7% in 2004/2005 to 20% in 2010/2012. Most cases involved women (65%), and the average age of the study cohort was 48 years. Thirteen percent of supplement-associated cases of liver injury required transplantation compared with only 3% of cases of drug-induced liver injury. Death occurred in 2% of supplement-associated cases and 3% of drug-associated cases. The findings suggest a need for further study of the elements of herbal and dietary supplements that have been associated with liver injury.

Patients with HCV Infection Plus Cirrhosis Are More Likely to Discontinue Triple Therapy Due to Adverse Events

HCV-TARGET (HCVT), a multicenter consortium involved in a longitudinal observational study of patients receiving direct-acting antivirals for HCV infection, confirmed that rates of intolerance to telaprevir (Incivek, Vertex)– and boceprevir (Victrelis, Merck)–containing triple therapy regimens are higher in patients with cirrhosis. Of 2212 patients enrolled in the HCVT program, the 970 who completed at least 26 weeks of treatment comprised the study population. Although treatment discontinuation of any HCV drug was similar between cirrhotics and noncirrhotics (28% vs 23%), cirrhotics more frequently discontinued therapy due to adverse events (13% vs 7.5%), reported Nezam H. Afdhal, MD, of the Department of Hepatology at Harvard Medical School in Boston, Massachusetts. Low platelet counts or albumin levels were predictive of treatment discontinuation, and decompensating events occurred in 12% of cirrhotic patients.

Immediate Treatment with a Nucleos(t)ide Analogue Avoids Transplantation in Patients with HBV-Induced Acute Liver Failure

Immediate administration of nucleoside or nucleotide analogues to patients with hepatitis B virus–induced acute liver failure can avoid liver transplantation and does not negatively influence hepatitis B surface antigen (HBsAg) clearance, reported Felix Maischack, MD, of the Duisburg-Essen University in Essen, Germany. Dr Maischack and colleagues retrospectively studied outcomes of 24 patients with acute liver failure admitted to the university hospital of Essen between 2009 and March 2013. Twenty-two patients received either entecavir (16), lamivudine (2), or tenofovir (4) at a median of 1.5 days after admission (range, 1 to 28 days), and 2 patients did not receive any specific treatment. All patients who received treatment survived and did not require liver transplantation, whereas 1 of the 2 patients who did not receive treatment died before transplantation could be performed. (The other was lost to follow-up.)

Pathologic signs and symptoms rapidly subsided for all treated patients, and laboratory values returned to normal within 3 months. HBsAg clearance occurred in 16 patients between 1 to 12 months after diagnosis (median, 95 days). Seroconversion to anti-HBsAg occurred in 9 of the 16 patients between 59 and 168 days (median, 123 days). Five of the 6 patients who received treatment but did not have HBsAg clearance were lost to follow-up. The remaining patient achieved HBsAg clearance at 1 year.