FDA Panel: Study Hepatitis B Drug in Children

Entecavir was approved for chronic HBV infection therapy in adults subsequent to the panel meeting.

Dr. Schwartz and other pediatricians on the panel said they were concerned that entecavir would be used inappropriately in pediatric patients once approved because the appropriate studies were completed. The panel chair, Janet Englund, M.D., of the division of infectious diseases at Children’s Hospital and Regional Medical Center, Seattle, noted that how to dose children was not yet known. Lauren Wood, M.D., senior clinical investigator in the HIV and AIDS malignancy branch of the National Cancer Institute, Bethesda, Md., pointed out that a drug’s safety and efficacy can differ greatly in children, citing an example of an HIV drug that caused bone toxicity in children, but not in adults.

Mostly urban adolescents and international adoptees in the United States are infected with HBV, and children around the world have perinatally-acquired HBV, she noted. Babies with perinatally-acquired HBV have a high lifetime risk of hepatocellular carcinoma, as high as 40% in some studies, added Dr. Schwartz. And there also is a significant social stigma associated with having hepatitis B, Dr. Zimmerman said.

The safety profiles and malignancy rates were comparable in the entecavir and lamivudine-treated groups, according to the company. Entecavir also has a favorable resistance profile compared with lamivudine, according to Bristol-Myers Squibb.

During the discussion on adult use, Leonard Seeff, M.D., senior scientist for hepatology research at the National Institute of Diabetes and Digestive and Kidney Diseases, Bethesda, Md., said there was “no question” that entecavir is very effective at reducing viral load. “We need other treatments, and this drug has advantages that others don’t—namely, at least at this point, a lower rate of mutant strains developing and no nephrotoxicity,” he remarked.

Bristol-Myers Squibb has proposed a pharmacovigilance study that would aim to enroll 12,500 patients worldwide, randomize them to entecavir or another HBV drug treatment, and follow them for malignancies and progression of liver disease for 5-8 years. The panel agreed that the trial would be critical in determining whether the drug’s malignancy risk would increase, and whether resistant strains would develop with a longer duration of treatment.

Intracranial Infection Can Mimic Hypoxic Brain Injury on Imaging

Cabo San Lucas, Mexico — What looks like damage from hypoxic ischemic encephalopathy on neonatal brain imaging actually can be caused by intracranial infection, Robert A. Zimmerman, M.D., said at a conference on obstetrical, gynecologic, perinatal medicine, neonatology, and the law.

Always correlate clinical findings and laboratory results with images of brain abnormalities to detect intracranial infections and to avoid attributing the infant’s problems to hypoxic ischemic brain injury, said Dr. Zimmerman, chief of pediatric neuroradiology at Children’s Hospital of Philadelphia.

He described several infections that could be confused with hypoxic ischemic encephalopathy.

► Acute cytomegalovirus infection, the most common intracranial infection that occurs in utero, causes fetal brain abnormalities in the second and third trimesters. To lack of perfusion, which can look like a severe hypoxic ischemic brain injury. The clinical findings and cerebral spinal fluid analysis look quite different between the two problems, however. Close to half of patients with meningitis due to Citrobacter or Serratia also will show brain abscesses on imaging.

▶ Herpes encephalitis can result from infection in utero, from infection acquired at birth. Symptoms from infection at birth typically present as seizures or fever days or weeks after birth. Herpes encephalitis can be a focal or diffuse disease. The diffuse form of herpes encephalitis causes cytotoxic edema that can mimic a hypoxic-ischemic type of injury on imaging. Herpes usually is easily recognizable on good-quality brain studies and using gadolinium enhancement.

In general, MRI is the best modality for imaging the normal cerebral cortex. In addition, CT scans can help you for brain calcifications, Dr. Zimmerman commented.