Lilly Halts Pediatric Xigris Trial for Severe Sepsis

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Eli Lilly & Co. has halted a trial of Xigris in pediatric patients with severe sepsis, because the drug failed to show efficacy over placebo, according to a Food and Drug Administration MedWatch report.

An interim analysis showed that Xigris (drotrecogin alfa [activated]) was "highly unlikely to show an improvement over placebo in the primary end point of composite time to complete organ failure resolution over 14 days."

The mean time to resolution was 9.7 days in the Xigris group and 9.8 days in the placebo group.

An independent data monitoring committee also noted an increase in the rate of central nervous system bleeding in the Xigris group, officials at Eli Lilly & Co., which manufactures the drug, said in a statement. Over the 6-day infusion period, there were four intracranial hemorrhages among 201 Xigris-treated patients, compared with one among 198 placebo-treated patients.

Three of the four hemorrhages in the Xigris group occurred in patients aged 60 days or less.Over the 28-day study period, there were eight intracranial hemorrhages in the Xigris group, compared with five in the placebo group.

Mortality, the rate of serious adverse events, overall serious bleeding events, and major amputations appeared to be similar in the two groups of patients.

Xigris, a genetically engineered version of human activated protein C, is indicated only for adults with severe sepsis who are at high risk of death.

In March 2005, Lilly added a warning to the prescribing information for Xigris that it may not be appropriate for patients with single-organ dysfunction and recent surgery and should be administered only after careful consideration of the potential risks and benefits.

The warning was added after two studies indicated a small but clinically important increase in the rate of all-cause mortality among these patients treated with the agent, compared with those who received placebo. In the pediatric study, known as F1K-MC-EVBP, the 28-day all-cause mortality was 34 (17%) in the Xigris group vs. 36 (18%) in the placebo group. Data collection is ongoing in the pediatric study, and complete results are expected to be available in the latter part of 2005. ■

Nosocomially Acquired Case of KD Reported

SAN DIEGO — An 11-month-old Asian American boy acquired Kawasaki disease during an extended hospital stay, Wilbert H. Mason, M.D., reported in a poster session at an international Kawasaki disease symposium.

In a later interview, he said this marks the first case of nosocomially acquired Kawasaki disease that he is aware of.

"We think of Kawasaki disease as being developed in the community due to in an infectious agent of some sort," said Dr. Mason, professor of clinical pediatrics at the University of Southern California and head of the division of infectious diseases at Children's Hospital Los Angeles. "It's a lesson to us that there are a number of viral infections that can be nosocomially acquired, and you can add Kawasaki disease to the list of those."

The boy arrived at Children's Hospital after being transferred from another hospital with increasing lethargy and weak cry. He was diagnosed with infant botulism and required ventilation for 5.5 months in the ICU.

The boy was transferred to a rehabilitation unit 181 days after hospital admission. On day 32 following the transfer, Dr. Mason said the boy developed high fever, rash, conjunctivitis, red lips and buccal mucosa, palmar erythema, and tachycardia with an extra heart sound. The patient appeared toxic. On day 4 of fever, he was diagnosed with Kawasaki disease and received intravenous gamma globulin 400 mg/kg four times a day and aspirin 100 mg/kg four times a day. Echocardiogram was normal.

The patient responded well to therapy, and the repeat echo was normal.

Dr. Mason noted that the rug in the rehab unit had been replaced 42 days before the onset of Kawasaki disease.

—Doug Brunk