Combining JIA Drugs May Add to Adverse Events

BY JANE SALODOF MACNEIL
Southwest Bureau

VERSAILLES, FRANCE — Preliminary data from a new drug safety registry suggest that the combination of etanercept and methotrexate might lead to more serious adverse events than either agent alone in patients with juvenile idiopathic arthritis.

"Some [adverse events] may not be surprising, but I think it is important as increasingly combinations of etanercept and methotrexate are used in severe arthritis," said Taunton Southwood, M.D.

Speaking on behalf of the British Society for Paediatric and Adolescent Rheumatology Biologics and New Drugs Registry, Dr. Southwood of the University of Birmingham (England) presented the preliminary report at the 12th European Pediatric Rheumatology Congress.

When the data were analyzed, 122 children on etanercept and 30 on methotrexate had been entered into the registry.

Children on both had nausea, abnormal liver function tests, hepatomegaly, menstrual problems, pancytopenia, flare, and eczema.

Although there is no registration category such as "both drugs," 28 children were reported to be on both agents.

Dr. Southwood urged caution in interpreting the findings, as they are based on less than a quarter of the data the investigators hope to collect from 12 participating centers, and the cases are not compared with a healthy population. He estimated about 300 children are on etanercept in the United Kingdom.

"It's not a controlled trial as such. It is a safety registry," he said, adding later with respect to individual adverse events, "We have no factual basis for suggesting they occur any more frequently in the registry patients than in a population of age-matched controls."

The registry is designed to capture adverse events occurring after the approval of etanercept, which he described as being of "undoubted benefit for treatment of JIA."

It was established in January 2004, but first began to accumulate substantial amounts of data in the 3 months leading up to August 2005.

Girls comprised about two-thirds of the population analyzed. The children on methotrexate were a mean age of 8 years versus a mean of 12 years for those on etanercept.

Dr. Southwood noted that children in the United Kingdom must be treated with methotrexate before they can start etanercept.

Overall, 197 adverse events were reported in 62 patients. These included 72 (36%) events in 35 patients on etanercept, 62 (31%) events in 20 patients on methotrexate, and 64 (32%) events in 28 patients taking both drugs. Some patients were listed more than once.

"This is an example of how difficult it is to interpret data at this stage," Dr. Southwood noted.

He categorized serious adverse events related to etanercept as skin conditions, such as eczema, and central nervous system conditions such as panic and anxiety.

Although they were not serious, side effects related to etanercept also included infection (paronychia, skin, respiratory), injection site reactions, rash, and nausea.

Serious adverse events associated with methotrexate included abdominal pain, anemia, abnormal liver function tests, and nausea.

Other related side effects included rash, injection site reactions, eosinophilia, hair loss, and menstrual problems.

The following serious adverse events occurred in children who were receiving both agents: nausea, abnormal liver function tests, hepatomegaly, menstrual problems, pancytopenia, flare, and eczema.

Dr. Southwood said that the combination of agents also was associated with impetigo, paronychia, chicken pox, upper respiratory tract infection, rash, allergic reaction, hair loss, mood, and injection site reactions.

While skin conditions had been reported previously in adults and by a German pediatric register, Dr. Southwood said that the German register had not detected menstrual problems. ■