Clinical trial for rabies monoclonal antibody

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A pivotal clinical trial for an anti-rabies human monoclonal antibody (RMAb) being developed through a collaborative partnership between MassBiologics of the University of Massachusetts Medical School and the Serum Institute of India, Ltd., is starting to enroll patients. The study, sponsored by the Serum Institute, will evaluate the efficacy of post-exposure prophylaxis following rabies exposure with RMAb and vaccine compared to standard treatment of human rabies immune globulin (hRIG) and vaccine. Post-exposure prophylaxis for rabies that includes a monoclonal antibody should provide a more affordable, safer alternative to prevent the disease, which is a world-wide public health problem impacting 10 million people a year and resulting in some 55,000 deaths.

"We are extremely pleased that this potentially life-saving product has moved forward to the pivotal clinical trial phase," said Deborah Molrine, MD, deputy director of Clinical and Regulatory Affairs at MassBiologics and an associate professor of pediatrics at UMass Medical School. "Rabies is a major public health problem in Asia and Africa, and we are hopeful that the findings of this study may result in a treatment option readily available in those areas where it is needed most."

The randomized, comparator-controlled study being conducted in India will enroll 200 patients who have had a high-risk (category III as defined by the World Health Organization) exposure to a suspected rabid animal. Study participants will receive proper wound care followed by injections of either the investigational RMAb or standard hRIG treatment in combination with a five-dose rabies vaccine series.

The primary endpoint of the study is to demonstrate that the level of neutralizing antibody to rabies virus in the blood of participants who received RMAb and vaccine is at least as much as the level of anti-rabies neutralizing antibody in the blood of those who received hRIG and vaccine.

While deaths from rabies in the United States are rare, rabies remains a significant problem with approximately 95 percent of human deaths from rabies occurring in Asia and Africa. Death from rabies is preventable with timely post-exposure prophylaxis consisting of wound hygiene, administration of rabies immune globulin, and active immunization with rabies vaccine. In persons wounded by a suspected rabid animal, the vaccine works to stimulate the immune system to fight the rabies virus, while the rabies immune globulin provides immediate protection with neutralizing antibodies before the immune system begins making its own antibodies.

Human rabies immune globulin, derived from human blood, is an expensive product and carries a potential risk of contamination with blood-borne pathogens. Equine immune globulin (eRIG), derived from horse serum, is used in many parts of the world, but its use is associated with significant adverse effects such as anaphylaxis or serum sickness. Both products are often in short supply and costly for inhabitants of areas of the world where rabies is endemic. In India alone, it is estimated only 2 percent of patients whose wounds require the rabies immune globulin receive appropriate post-exposure treatment.

To address the supply and adverse effects issues, MassBiologics and the U.S. Centers for Disease Control and Prevention developed an anti-rabies monoclonal antibody with the goal that it might be used in place of hRIG or eRIG. MassBiologics then partnered with the Serum Institute to develop and manufacture the monoclonal antibody in India. "A monoclonal antibody for rabies has the advantage of being able to be

produced in large quantities, at much lower costs than blood products," said Prasad Kulkarni, MD, medical director at the Serum Institute of India, Ltd. "And since they are not derived from blood serum, they have none of the safety issues associated with human blood products. If the primary endpoint from this pivotal trial is met, a new therapy could become available to thousands of patients each year to prevent the too-often fatal outcome of this infection."

In a phase 1 trial at the King Edward Memorial Hospital (KEM) in Mumbai, India, 74 healthy volunteers were randomized into several groups that either received RMAb or of hRIG combined with vaccine. Results showed that the RMAb was well tolerated by all subjects, with no serious side-effects. A dose of RMAb was selected from this study that produced comparable levels of rabies virus neutralizing antibodies in the blood from volunteers who received RMAb and vaccine compared to those who received the standard regimen of hRIG and vaccine.

Based on these data, Serum Institute of India received regulatory approval to proceed with the current pivotal trial. Final results from the current study are expected in the second half of 2013. The trial is registered with Clinical Trials Registry-India (CTRI /2012/05/002709).

Provided by University of Massachusetts Medical School