

A Study to Evaluate the Safety, Tolerability, Pharmacokinetics, and Immunogenicity of MEDI-524, a Humanized Enhanced Potency Monoclonal Antibody Against Respiratory Syncytial Virus (RSV), in Children With Hemodynamically Significant Congenital Heart Disease

Principal Investigator:

David Gremmels, MD, Pediatric Cardiologist

congestive heart failure and cyanotic heart disease, but could be broadened to include more minor diseases, if found to be beneficial in this group of patients.

Introduction

Respiratory syncytial virus (RSV) is common among young children during the winter. Most infants and young children become infected with RSV by age 3, developing a mild illness. However, because RSV can cause aggressive infection in the lower respiratory tract, it can be devastating for babies with congenital heart disease and premature infants. With compromised respiratory systems, these infants may be hospitalized or die from RSV infection.

An RSV medication called palivizumab (Synagis®) is available to prevent serious RSV disease and is recommended by the American Academy of Pediatrics. Its effectiveness is 70 to 75 percent. Under study is a new drug, MEDI-524, a modified form of Synagis in which one amino acid has been altered. Studied in 2005 among babies born prematurely, MEDI-524 is now being tested in North America and South America for infants with congenital heart disease.

Methods

Children's of Minnesota is part of a multicenter trial testing MEDI-524 on infants with congenital heart disease. Starting in November 2007, infants who participate in the study are receiving five monthly injections of Synagis or MEDI-524. The research is double-blinded, so that no one participating knows which medication is provided.

Infants are tracked for viral illness to determine whether they develop RSV. Side effects of the drugs, as well as kidney and liver function, are also being studied. Of particular interest is whether infants who develop RSV after treatment have an improved clinical course, which was found in trials with premature infants.

Future Direction

By defining the safety and efficacy of a new RSV preventive therapy, researchers hope to decrease the rates of illness and death from this infection in the high-risk group of children with cardiac disease. The future direction will then include clearly defining the population of children with cardiac disease who should receive the therapy. This medication currently has been restricted to children with significant

Gremmels: Pediatric Cardiology to Benefit From Greater Emphasis on Research

David Gremmels, MD, makes time in his busy clinical practice for researching better therapies for children with heart disease. Pediatric cardiology, he says, needs more research.

Research into pediatric cardiology treatments lags behind study of adult therapies, Gremmels explains, because there are far more adults with heart disease than children.

Gremmels joined the Children's Heart Clinic in 2003. He directs the echocardiography program, which handles evaluation of pediatric and fetal echocardiograms from hospitals around the Upper Midwest, including Children's of Minnesota.

During his fellowship in pediatric cardiology at the University of California, San Francisco (UCSF), Gremmels performed research on echocardiography screening for patients with transposition of the great arteries. His other research at UCSF included analyzing surgical outcomes for patients with Tetralogy of Fallot and infants undergoing the Fontan procedure to correct hypoplastic left heart syndrome.

At Children's, he's participating in research on the effectiveness of two therapies to prevent respiratory syncytial virus (RSV), a threat to babies with congenital heart defects and those born prematurely.

Gremmels points out the need for more research to support treatment recommendations for children with congenital heart defects. "We don't have the randomized, controlled studies for children," he explains. "A drug for a 70-year-old with heart disease may have been researched, but has it been studied for a 2-year-old? Usually the answer is no. We need careful studies to determine whether these treatments really work with children and are safe."