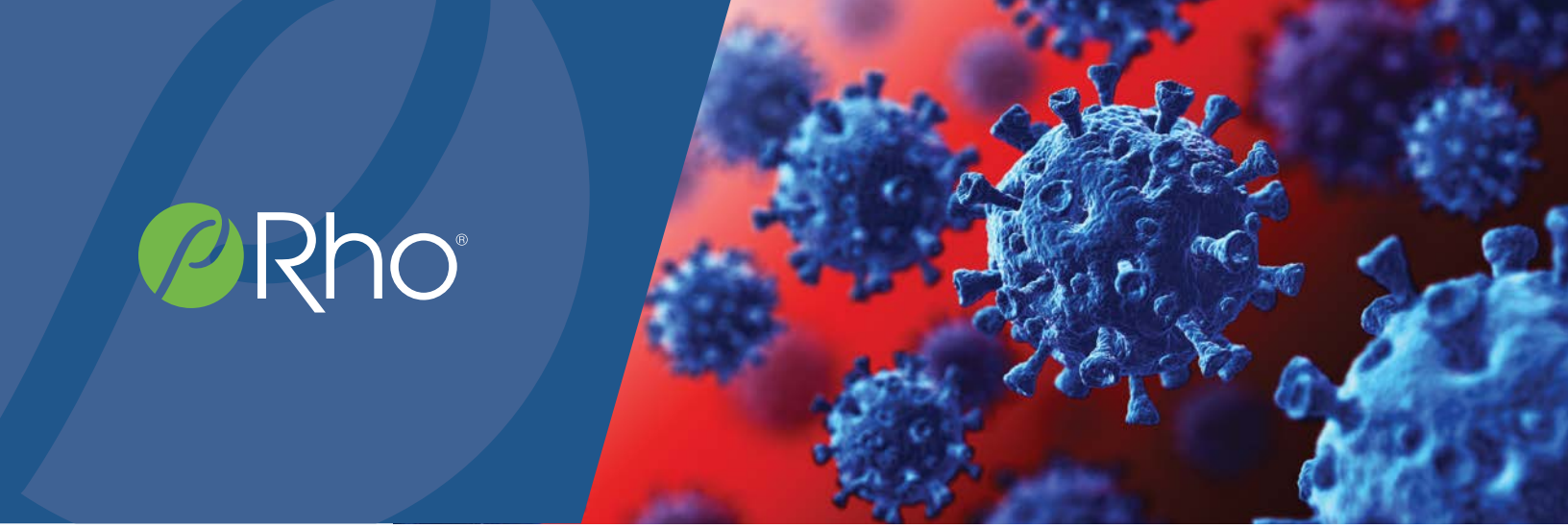

THE H1N1 STUDY

Conducting clinical research during a pandemic

EXECUTIVE SUMMARY

This article describes Rho's involvement in a clinical trial that assessed the safety and immunogenicity of the 2009 H1N1 vaccine in adults and children (aged 12-79 years) with severe asthma. In addition to providing important information for healthcare policymakers, this multi-center study represented an extremely successful research collaboration to design, implement, and publish study results against the backdrop of a global pandemic. In less than 18 months, the study team went from the initial study idea to publication of the primary study results in the Journal of Allergy and Clinical Immunology.

A NEW VIRUS

In late April 2009, the World Health Organization (WHO) reported that it was monitoring a new influenza virus that was responsible for a number of illnesses in the United States and Mexico. Only six weeks later, the WHO declared the start of the global H1N1 influenza pandemic.

From the outset, the rapid progression of the H1N1 pandemic challenged the healthcare community to react quickly to understand the virus and limit its impact. The development and distribution of an effective vaccine was of critical importance in the months following the WHO's announcement. As vaccine manufacturers raced to produce a viable vaccine, healthcare organizations began identifying the most susceptible at-risk populations and determining the optimum dosing for each population.

A VULNERABLE POPULATION

One of the most vulnerable populations identified were individuals with asthma. The Centers for Disease Control and Prevention (CDC) found that asthma was the most common underlying health condition for adults and children hospitalized with H1N1, with nearly a third of those hospitalized reporting having asthma. While healthcare organizations recognized the importance of vaccinating individuals with asthma, no one knew how well the vaccine would work in this unique population.There was even some concern that inhaled corticosteroids, a class of medications commonly used to treat asthma, might prevent the vaccine from achieving optimal protection against the virus. If this concern proved to be true, individuals with asthma might require a higher dose of the vaccine than the general population, or even multiple doses, to adequately protect against the H1N1 virus.

The National Institutes of Health recognized this problem and the urgency of the pandemic, and turned to Rho, a full-service contract research organization (CRO), to rapidly develop and coordinate a national, multi-site research project to evaluate the effectiveness and dosing of the vaccine for those with asthma. In collaboration with the National Institute of Allergy and Infectious Disease (NIAID), the National Heart Lung and Blood Institute (NHLBI), and the NHLBI's Severe Asthma Research Program (SARP), Rho investigators and project coordinators developed and implemented a new multi-center research protocol to address these urgent issues.

An Incredible Effort

In less than 18 months, the study team went from the initial study idea to publication of the primary study results in the Journal of Allergy and Clinical Immunology. For a multi-center, investigational new drug (IND) study enrolling 390 participants in a 7-site, 5-visit protocol to meet such an aggressive timeline, without sacrificing data quality or integrity, speaks to the incredible effort and productive collaboration of the researchers.

A NEW STUDY

The study protocol was designed to assess dosing requirements as well as the safety and immunogenicity of the 2009 H1N1 vaccine among participants with severe versus mild-to-moderate asthma. Study participants received an initial vaccination administration of either a 15µg dose (the standard dose recommended for the general population) or a 30µg dose. After three weeks, study participants either asthma severity group required a higher dose of vaccine and/or an additional dose of the vaccine to achieve adequate seroprotection against the virus.

STUDY RESULTS

The study protocol was designed to assess dosing requirements as well as the safety and immunogenicity of the 2009 H1N1 vaccine among participants with severe versus mild-to-moderate asthma. Study participants received an initial vaccination administration of either a 15µg dose (the standard dose recommended for the general population) or a 30µg dose. After three weeks, study participants received a second vaccine administration of the same dose received at baseline. Blood samples were collected before each vaccine administration, 8-10 days after each administration, and 21 days after the second administration to assess serum antibody levels. Results of the blood tests would indicate whether participants in either asthma severity group required a higher dose of vaccine and/or an additional dose of the vaccine to achieve adequate seroprotection against the virus.

STUDY SUCCESSES

The results of the trial not only contributed important information for individuals with asthma and the health care community; they also represented an extremely successful collaboration among the clinical trial researchers at 7 major medical institutions across the country and two different Institutions at the National Institutes of Health to address an urgent need during a global pandemic.

Less than 18 months after the first study protocol was developed, training and regulatory processes were completed, the study was conducted, analyses were finished, and the results were published in the Journal of Allergy and Clinical Immunology (JACI). For a multi-center, investigational new drug (IND) study enrolling 390 participants in a 7-site, 5-visit protocol to meet such an aggressive timeline, without sacrificing data quality or integrity, speaks to the incredible effort and productive collaboration of the researchers. The NIAID and NHLBI provided funding, scientific guidance, and medical oversight. The clinical research centers worked to aggressively recruit, screen, and enroll a unique study population and conduct hundreds of study visits in addition to their other ongoing clinical research projects. A broad project team at Rho provided end-to-end coordination and support for the project. A chart listing some of the project milestones and when they were accomplished is provided below.

Why Rho?

Rho was selected to coordinate the project based on our many years of experience conducting federally-funded asthma research and our reputation for providing exceptional customer service. Rho employees were closely involved in the project from conception to publication.

STUDY MILESTONES

Date	Milestone
August 2009	Only two months after the WHO declared a pandemic, the first version of the protocol was finished and seven clinical centers (drawn from existing SARP research locations) had agreed to participate.
September 2009	Over the course of two and a half weeks, Rho staff and NIH medical monitors conducted study initiation visits and protocol training at all seven clinical sites.
October 2009	By the time the first vaccines were available and the mandatory 30-day wait period for the IND was reached in mid-October, the first H1N1 study centers were enrolling participants.
December 2009	Only three months after the first study visit, the sites had enrolled all 390 participants and completed all dosing and in-person monitoring visits required by the protocol (follow-up phone calls continued throughout the spring of 2010 to continue safety monitoring of all participants).
December 2009 to October 2010	Analyses were planned and mock datasets were analyzed and prepared for final data lock.
September 2010	Study monitors conducted the final site closeout visit.
November 2010	The main outcome manuscript for the study was accepted for journal publication.
January 2011	The results of the study were published in JACI.

A FULL-SERVICE CRO

Rho was selected to coordinate the project based on our many years of experience conducting asthma clinical trials and our reputation for providing exceptional customer service. Rho employees were closely involved in the project from conception to publication:

- Rho investigators, scientists, statisticians, and project coordinators helped to develop the protocol, study manuals, and case report forms.
- Rho safety monitors tracked and managed all adverse events and serious adverse events.
- Rho project coordinators and study monitors conducted 28 site visits over the course of the project, including 7 site initiation visits over a two-and-a-half-week period at the start of the study.
- Rho statisticians and data managers monitored data trends and created data monitoring reports throughout the study.
- Rho data managers managed the clinical data and locked the database.
- Rho investigators, statisticians, data managers, and coordinators collaborated on the primary outcome manuscript.
- Study results were analyzed, published, and available to the scientific community in record time.

REFERENCES

Busse WW, Peters SP, Fenton MJ, Mitchell H, Bleecker ER, Castro M, et al. Vaccination of patients with mild and severe asthma with a 2009 pandemic H1N1 influenza virus vaccine. J Allergy Clin Immunol. 2011; 127(1):130-137.e3.

ADDITIONAL INFORMATION

- Abstract: http://www.jacionline.org/article/S0091-6749(10)01764-1/abstract
- ClinicalTrials.gov study description: http://clinicaltrials.gov/ct2/show/NCT00978120
- NIH Press Release: http://www.niaid.nih.gov/news/newsreleases/2010/Pages/H1N1VaxAsthmaResults.aspx

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