In First Phase 3 Trial, Merck’s Investigational Inactivated Varicella-Zoster Virus Vaccine (V212) Reduced the Incidence of Confirmed Herpes Zoster Cases by an Estimated 64 Percent in Immunocompromised Subjects

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KENILWORTH, N.J.--(BUSINESS WIRE)--Merck (NYSE:MRK), known as MSD outside the United States and Canada, today announced the first Phase 3 study results for V212, the company’s investigational inactivated varicella zoster virus vaccine (VZV) for the prevention of herpes zoster or HZ, also known as shingles, in immunocompromised patients. This was a double-blind, randomized, placebo-controlled, multi-center trial to study safety, tolerability, efficacy and immunogenicity of inactivated VZV Vaccine in Recipients of Autologous Hematopoietic Stem Cell Transplants (auto-HSCT). In the trial, V212 met its primary endpoint and reduced the incidence of confirmed HZ cases by an estimated 64 percent (95% CI, 0.48, 0.75) in recipients of auto-HSCT. These results were presented today, as an oral presentation, at the combined annual meetings of the Center for International Blood & Marrow Transplant Research (CIBMTR) and the American Society for Blood and Marrow Transplantation (ASBMT) during a “Best Abstracts” session in Orlando, Florida.

Secondary endpoint findings from the study showed that V212 reduced the incidence of moderate-to-severe HZ pain by an estimated 69.5 percent, utilizing the Zoster Brief Pain Inventory (ZBPI) score. V212 demonstrated an estimated 83.7 percent reduction of the incidence of post-herpetic neuralgia (PHN) beyond 90 days after onset of HZ. In the study PHN was defined as pain in the area of the HZ rash with a “worst pain in the last 24 hours” score of 3 or greater (on a 0 to 10 scale) on the ZBPI that persists or appears 90 days or beyond after HZ rash onset following auto-HSCT.

In addition, V212 reduced the incidence of HZ complications by an estimated 73.5 percent. These other complications included hospitalization or prolongation of hospitalization due to HZ; disseminated HZ (including disseminated HZ rash or VZV viremia); visceral HZ; ophthalmic HZ; neurological impairment due to HZ; or administration of intravenous acyclovir therapy for treatment of HZ post auto-HSCT.

Because subjects receiving auto-HSCT are immunocompromised, they are at six-times greater risk of developing shingles than the general population. In 2014, an estimated 11,000 people underwent stem cell transplantation in the United States. ZOSTAVAX® (zoster vaccine live), the only approved vaccine indicated for the prevention of shingles in individuals 50 years of age or older, is contraindicated in immunocompromised patients. ZOSTAVAX is not indicated for the treatment of zoster or postherpetic neuralgia. ZOSTAVAX should not be used for prevention of primary varicella infection (Chickenpox).

“Patients undergoing auto-HSCT have an increased risk of HZ and associated complications due to impaired cellular immunity. These results indicate that V212 might offer a way to help reduce the risk of HZ and HZ-related complications in this vulnerable, immunocompromised patient population,” said Eliav Barr, M.D., senior vice president, Merck Research Laboratories. “We look forward to exploring these data further and to reviewing the results of an additional Phase 3 study that is underway in immunocompromised patients with malignancies.”

About the Study (NCT01229267)

The Phase 3 randomized, double-blind, placebo-controlled, multi-center trial included patients 18 years or older, undergoing auto-HSCT for malignancy or any other indication, with a history of varicella infection and/or seropositive for VZV antibody. Subjects had no malignancy with more than two disease relapses (except Hodgkin lymphoma), no planned tandem transplants, no previous VZV vaccination, no HZ infection within the previous year, and no intended antiviral prophylaxis for >6 months after auto-HSCT (antiviral prophylaxis for <6 months was allowed).

Eligible subjects (n=1,230) were randomly assigned to receive a 4-dose regimen of V212 from a consistency lot (a lot having a targeted potency as required by regulators in order to demonstrate that the vaccine can be manufactured consistently), a high-antigen lot (a lot having a higher antigen potency added to assess further the safety profile of V212), or placebo. Randomization was stratified by age (younger than 50 years vs. older than 50 years) and by intended duration of post-transplant antiviral prophylaxis (≤3 months vs. >3 to 6 months).

Dose 1 of V212 or placebo was given within approximately 30 days before auto-HSCT, and doses 2, 3, and 4 were given...
approximately 30, 60, and 90 days after auto-HSCT. Subjects were followed for the duration of the study for efficacy with cases of HZ confirmed by PCR and/or adjudicated by a blinded data monitoring committee. The average follow-up time for HZ surveillance was approximately 2.3 years (median: 2.6 years) post vaccination.

The most common systemic adverse events observed in both the vaccine and placebo arms of the study at a incidence rate of 15 percent or more in either group, included diarrhea, nausea, pyrexia, mucosal inflammation, thrombocytopenia, febrile neutropenia, vomiting, anemia, neutropenia, decreased appetite, fatigue, hypokalemia, and constipation.

Serious adverse events occurred in 216 (32.9%) subjects receiving the consistency lot or high-antigen lot and in 181 (32.7%) subjects receiving placebo for up to 28 days after the fourth vaccination dose. The most frequent serious adverse event observed was febrile neutropenia observed in 5.3 percent of the vaccine group and 4.9 percent in the placebo group. Serious vaccine-related adverse events occurred in 5 (0.8%) subjects receiving consistency lot or high-antigen lot and in 5 (0.9%) subjects receiving placebo.

About V212

V212 is Merck's investigational inactivated VZV vaccine for the prevention of HZ and HZ-related complications in immunocompromised subjects age 18 years and above. The Phase 3 trial in auto-HSCT recipients has been completed. Another Phase 3 trial in subjects with malignancies is ongoing.

About ZOSTAVAX® (zoster vaccine live)

ZOSTAVAX is a live attenuated virus vaccine indicated for prevention of herpes zoster (shingles) in individuals 50 years of age and older. ZOSTAVAX is not indicated for the treatment of zoster or postherpetic neuralgia. ZOSTAVAX should not be used for prevention of primary varicella infection (Chickenpox).

Select Safety Information

Vaccination with ZOSTAVAX does not result in protection of all vaccine recipients.

ZOSTAVAX is contraindicated in: persons with a history of anaphylactic or anaphylactoid reaction to gelatin, neomycin, or any other component of the vaccine; persons with a history of primary or acquired immunodeficiencies; persons on immunosuppressive therapy; pregnant women or women of childbearing age.

A reduced immune response to ZOSTAVAX was observed in individuals who received concurrent administration of PNEUMOVAX® 23 (Pneumococcal Vaccine Polyvalent) and ZOSTAVAX compared with individuals who received these vaccines 4 weeks apart. Consider administration of the two vaccines separated by at least 4 weeks.

Serious vaccine-related adverse reactions that have occurred following vaccination with ZOSTAVAX include asthma exacerbation and polyarthritis rheumatica. Other serious adverse events reported following vaccination with ZOSTAVAX (zoster vaccine live) include cardiovascular events (congestive heart failure, pulmonary edema). Common adverse reactions occurring in ≧1% of vaccinated individuals during clinical trials include injection-site reactions (erythema, pain/tenderness, swelling, hematoma, pruritus, warmth) and headache.

Transmission of vaccine virus may occur between vaccinees and susceptible contacts.

Deferral should be considered in acute illness (for example, in the presence of fever) or in subjects with active untreated tuberculosis.

About Merck

For 125 years, Merck has been a global health care leader working to help the world be well. Merck is known as MSD outside the United States and Canada. Through our prescription medicines, vaccines, biologic therapies, and animal health products, we work with customers and operate in more than 140 countries to deliver innovative health solutions. We also demonstrate our commitment to increasing access to health care through far-reaching policies, programs and partnerships. For more information, visit www.merck.com and connect with us on Twitter, Facebook, YouTube and LinkedIn.

Forward-Looking Statement of Merck & Co., Inc., Kenilworth, N.J., USA

This news release of Merck & Co., Inc., Kenilworth, N.J., USA (the “company”) includes “forward-looking statements” within the meaning of the safe harbor provisions of the U.S. Private Securities Litigation Reform Act of 1995. These statements are based upon the current beliefs and expectations of the company's management and are subject to significant risks and uncertainties. There can be no guarantees with respect to pipeline products that the products will receive the necessary regulatory approvals or that they will prove to be commercially successful. If underlying assumptions prove inaccurate or risks or uncertainties materialize, actual results may differ materially from those set forth in the forward-looking statements.

Risks and uncertainties include but are not limited to, general industry conditions and competition; general economic factors, including interest rate and currency exchange rate fluctuations; the impact of pharmaceutical industry regulation and health care legislation in the United States and internationally; global trends toward health care cost containment; technological advances, new products and patents attained by competitors; challenges inherent in new product development, including obtaining regulatory approval; the company's ability to accurately predict future market conditions; manufacturing difficulties or delays; financial instability of international economies and sovereign risk; dependence on the effectiveness of the company's patents and other protections for innovative products; and the exposure to litigation, including patent litigation, and/or regulatory actions.

The company undertakes no obligation to publicly update any forward-looking statement, whether as a result of new information, future events or otherwise. Additional factors that could cause results to differ materially from those described in the forward-looking statements can be found in the company's 2015 Annual Report on Form 10-K and the company's other
filings with the Securities and Exchange Commission (SEC) available at the SEC's Internet site (www.sec.gov).


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