SANOFI PASTEUR

CDIFFENSE™ PHASE III TRIAL WITH SANOFI PASTEUR INVESTIGATIONAL VACCINE AGAINST *CLOSTRIDIUM DIFFICILE*

OVERVIEW

Sanofi Pasteur is developing a vaccine designed to produce an immune response to neutralize the effects of Clostridium *difficile* (C. *difficile*) toxins. Vaccination could be an efficacious, cost-effective and important public-health measure to help protect individuals from C. *difficile*, which is emerging as a leading cause of life-threatening, healthcare-associated infections (HAIs) worldwide. The candidate vaccine progressed through Phase I and II clinical studies. The Phase II data was presented at ECCMID in Barcelona and ASM in Boston in May 2014 and is expected to be published soon.

CDIFFENSE™ STUDY

***Cdiffense*™** is a randomized, observer-blind, placebo-controlled, multi-center, multi-national Phase III trial that began recruitment in August 2013. The trial will last approximately 4.5 years based on the incidence of CDI and necessary follow-up required with patients after vaccination.

The objective of the ***Cdiffense*™** trial is to evaluate the safety, immunogenicity and efficacy of a toxoid vaccine for the prevention of primary symptomatic C. *difficile* infection (CDI). The study will evaluate the use of C. diff Toxoids A and B, which are inactivated forms of C. diff bacterial toxins known to cause gastro-intestinal disease.

The primary endpoint of the trial is prevention of primary symptomatic CDI, defined as a change in bowel habits with passage of three or more loose stools per day for one or more days and either a positive C. diff stool toxin test (A, B or both) or a positive stool cytotoxicity assay and absence of another identified cause for diarrhea.

TARGET POPULATION AND INCLUSION CRITERIA

***Cdiffense*™** will seek to include up to **15,000 adults, age 50 or older,** who are at risk of symptomatic CDI, have given informed consent and fulfill at least one of the following requirements:

- Have had at least two hospital stays, each lasting more than 24 hours, and has received systemic (not topical) antibiotics in the previous year before enrollment.
- Are anticipated to have an in-patient hospitalization for a planned surgical procedure within 60 days of enrollment. The impending hospital stay should be anticipated to last more than 72 hours and include an elective surgery conducted on the kidney/bladder/urinary, musculoskeletal, respiratory, circulatory or central nervous system.

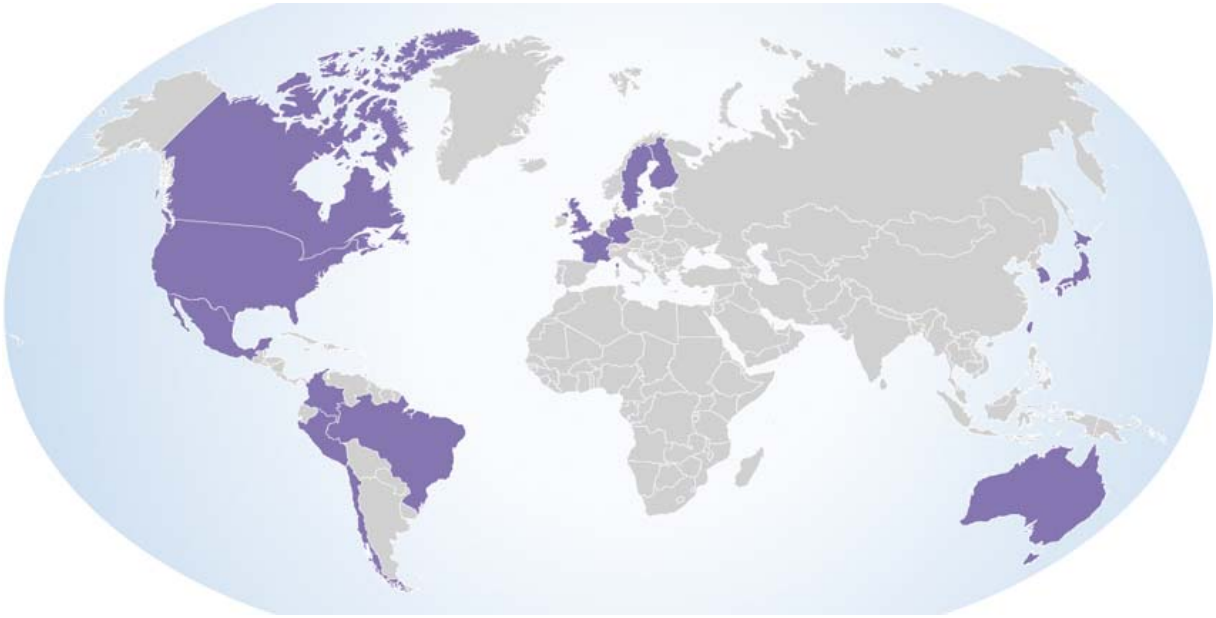
STUDY SIZE AND DOSING

A sample of up to 15,000 volunteers will be randomly assigned in a 2:1 ratio to either the vaccine or placebo group. The investigational vaccine will be tested as a three-dose immunization at 0, 7 and 30 days. The vaccine will be administered to 10,000 patients and the placebo to 5,000 patients. Of the up to 15,000 total volunteers, 1,500 will be enrolled into a subgroup that will test long-term immunogenicity of the vaccine.

CLINICAL TRIAL SITES

The trial will be held in **200 sites across 17 countries** from around the world, including:

- **North America**
  - U.S. and Puerto Rico
  - Canada
- **Europe**
  - United Kingdom
  - Finland
  - Sweden
  - France
  - Germany
- **Latin America**
  - Brazil
  - Mexico
  - Colombia
  - Peru
  - Chile
- **Asia Pacific**
  - South Korea
  - Australia
  - Taiwan
  - Singapore
  - And eventually in Japan



ABOUT *CLOSTRIDIUM DIFFICILE*

Clostridium difficile (C. *difficile*) is a potentially life-threatening, spore-forming bacterium that causes intestinal disease. The risk of contracting CDI increases with age, antibiotic treatment and time spent in hospitals or nursing homes, where multiple cases can lead to outbreaks.[1] A main source of C. diff is infected patients who release spores into the environment that can then infect other patients. When antibiotics disrupt the gut's normal flora and a person has ingested C. diff spores, the C. diff bacteria multiply and release potent toxins that can damage a patient's intestinal lining and cause C. diff disease. For more information about the ***Cdiffense***™ Phase III trial, please visit www.Cdiffense.org.

1. Centers for Disease Control and Prevention. Frequently Asked Questions about Clostridium difficile for Healthcare Providers. Centers for Disease Control and Prevention. http://www.cdc.gov/HAI/organisms/cdiff/Cdiff_faqs_HCP.html. Last Updated March 6, 2013. Accessed May 30, 2013.

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