eP133
ePoster Viewing
Vaccine development

A PHASE II STUDY OF THE SAFETY AND IMMUNOGENICITY OF DIFFERENT VACCINATION SCHEDULES OF A CANDIDATE CLOSTRIDIUM DIFFICILE TOXOID VACCINE: VACCINATION SCHEDULE SELECTION FOR PHASE II

G. De Bruyn[1], G. Foglia[1], J. Saleh[2], D. Workman[3], R. Pollak[4], R. Gesser[1]

[1]Clinical Research & Development, Sanofi Pasteur, Swiftwater PA, USA ; [2]Northern California Research Center, Redding CA, USA ; [3]Jean Brown Research, Salt Lake City UT, USA ; [4]Endeavor Clinical Trials, San Antonio TX, USA

Objectives: Sanofi Pasteur is developing a toxoid vaccine for the prevention of first occurrence *Clostridium difficile* infection (CDI) in at-risk individuals. The data reported here constitute the second stage of a two-stage Phase II safety and immunogenicity study, with the objective of selecting the most appropriate vaccination schedule for use in subsequent Phase III clinical development. (The selection of the dose and formulation comprised a preceding first stage of the same study, and is presented in an accompanying abstract.)

Methods: Phase II, randomized, multi-center study (first stage was also placebo-controlled and double-blind) in adults aged 40-75 years and at risk of CDI (defined as those with impending hospitalization or residence in a long-term care facility). Subjects were randomized to receive high dose + adjuvant administered as 3 doses in one of three schedules: 0, 7, 30 days (Group 3, N=101); 0, 7, 180 days (Group 6, N=103; or 0, 30, 180 days (Group 7, N=103). (Groups 1 to 5 were defined in the first stage [dose and formulation selection] of the study.) Post-vaccination solicited and unsolicited adverse events were collected after each dose, and serious adverse events (SAEs) were monitored to Day 210. For the assessment of immunogenicity for vaccination schedule selection, IgG specific for *C. difficile* toxins A and B were assessed by ELISA and also toxin neutralization activity on Days 0, 7, 14, 30, 60, 180, and 210; the results were assessed using decision tree analysis, bootstrap composite analysis, geometric mean concentrations, seroconversion, and reverse cumulative distribution curves. All analyses were descriptive.

Results: Demographic characteristics were similar in each group. There were no safety concerns in any group: the incidence of Grade 3 solicited and unsolicited reactions was similar in each group and no SAE was considered to be related to vaccination. Based on the immunogenicity and ranking analyses, the optimum schedule was assessed to be 0, 7, 30 days (Group 3): this schedule provided the best immune response over Days 30, 60 and 180, the period during which recently hospitalized at-risk patients are most likely to develop CDI. There was no difference in the response in those aged 40-64 years and 65-75 years.

Conclusion: The candidate vaccine was well tolerated and immunogenic for toxins A and B. There was no safety concern, and with a high dose + adjuvant formulation an optimal schedule of 0, 7, 30 days was selected for further development of this novel *C. difficile* toxoid vaccine in a large-scale Phase III clinical study.