Parkinson's vaccine – clinical results boost prospects

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AFFiRiS AG announced today results of AFF008A, a Phase I clinical trial to assess boost immunizations with AFFITOPE PD01A, an active vaccine against Parkinson's disease (PD). The study was funded by a $1.04 million grant from The Michael J. Fox Foundation for Parkinson's Research.

The "boost" study AFF008A was designed to assess one boost immunization with AFFITOPE PD01A per patient with regard to safety/tolerability and immunological and clinical activity in those patients who had already received the vaccine (four "priming" vaccinations at four-week intervals) within the first-in-man clinical study AFF008. Six PD patients on best medical care, including standard symptomatic medication, served as a comparison group. In the "boost" study, two different doses of AFFITOPE PD01A (15 µg and 75 µg) were again safe and well tolerated, meeting the primary endpoint of the trial.

Patients belonging to the low-dose group of AFF008 were randomized in two equally distributed groups receiving either 15 µg or 75 µg AFFITOPE PD01A. The same was done with patients of the AFF008 high-dose group, in order to allow for evaluation of four different vaccination schedules.

Across all patients, no antibody concentration limiting toxicity was observed. Adverse events were similar across all five groups except injection site reactions, which only occurred in the active treatment groups, and psychiatric disorders, reported at a lower rate in the active

groups. All of the 28 patients completed the study and received all planned vaccinations. Only one serious adverse event was reported, which was classified as being not related to AFFITOPE PD01A administration.

An immune response against AFFITOPE PD01A was seen in 19 of 22 (86%) of vaccinated patients and 12 of 19 (63%) of these responders generated aSyn-specific serum antibodies. The immune response sustained throughout the entire observation period of 24 weeks. Patients on low dose and then high dose had a clear immunological boost. This data supports that further dose and scheduling may significantly influence antibody titer/concentration and further studies need to be performed. Additionally, vaccine-induced antibodies were detectable in cerebrospinal fluid. This induction of antibodies against aSyn supports the concept of the principle of AFFiRiS' proprietary therapeutic vaccine.

Parallel laboratory experiments using recombinant aSyn protein to assess selectivity showed that AFFITOPE PD01A-induced antibodies preferentially bind to aSyn fibrils, which are believed to be the toxic form of the protein, as compared to the monomeric form.

Due to the limitations of the Phase I trial design (the study was not double-blind, and assignment to the comparison group was not randomized), it is not known whether effects seen in the active groups are indicative of treatment effects or due to confounding factors. Efficacy variables were evaluated in an explorative manner with regard to the small sample size. Preliminary observations showed that in eight of the 19 (42%) immunological responders, no increase of the concomitant dopaminergic PD medication was needed throughout the observational period (on average three years per subject). Among the same group, five of eight (63%) patients had stable UPDRS III scores at the end of the "boost" study.

Continuous efforts are undertaken to follow this patient cohort and to further characterize their immunological and clinical response to treatment with AFFITOPE PD01A. The next study, AFF008AA, is focusing primarily on the long-term safety and, in addition, on the assessment of the immunological and clinical effects of a second boost vaccination ("reboost"). That study is also funded by The Michael J. Fox Foundation, as was the AFF008 trial. Recruitment of patients for AFF008AA has been completed; results are expected in Q2 2017.

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