

## **The First-in-Human Phase 1b Safety Clinical Trial of CuraVac's Potential Myasthenia Gravis Therapeutic Vaccine Successfully Meets its Safety Primary End Points.**

### **CV-0002 study: communication of results**

**Protocol:** EUDRACT 2015-002880-41: A first-in-human and proof-of-concept study to assess the safety, tolerability and immunogenic response after subcutaneous injections of CV-MG01, acetylcholine receptor mimetic peptides, as potential therapeutic vaccine, in patients with myasthenia gravis.

**Sponsor:** CuraVac Europe S.A. (Rixensart, Belgium); CEO: Dr. Stéphane Huberty (contact: [info@curavac.com](mailto:info@curavac.com))

**General information:** First-in-human clinical trial (phase 1b, I/II) testing the potential MG therapeutic vaccine, CV-MG01, against a placebo in patients with Myasthenia Gravis conducted at Antwerp University Hospital (UZA) in Belgium. The study consisted in 10 visits over 20 weeks (Part A) and is followed by a 2-year long term follow-up period (Part B-ongoing). Three cohorts of 8 patients were recruited. In each cohort, 6 patients randomly received the vaccine and 2 received a placebo (i.e. aluminium hydroxide). A low dose of vaccine (or placebo) was tested on the first cohort, and then a high dose (or placebo) was administered to the second and third cohorts. The main objectives were to evaluate the safety and the immunogenicity after 3 subcutaneous injections with the CV-MG01 vaccine.

**Population of subjects:** The therapeutic vaccine (or placebo) was tested on 24 patients with Myasthenia Gravis, a chronic autoimmune neuromuscular disorder (mean age: 42 years, 24 – 64 years; 18 females, 6 males) with low to moderate disease severity.

**Safety Results:** The safety profile was found to be excellent. Most of the adverse events were of mild to moderate severity. The most frequent adverse events were reactions at the site of injection (such as tenderness, pain, plaque, erythema or itching) that resolved spontaneously within days after injection. No serious adverse events occurred after injection of the study drug. No safety issues were identified one year after the last injection of the study drug.

**Overall results of the trial:** The vaccine was very well tolerated, and no patient showed any significant clinical deterioration after completion of the study. However, the immunogenic response (i.e. production of antibodies to the vaccine antigens) was found to be low after the three injections with CV-MG01. The immunogenic response was nevertheless higher in patients who received the high dose of vaccine compared to those who received the low dose. Overall, most patients improved. Some patients significantly improved based on their subjective impression and clinical scoring but a statistical significance on efficacy could not be inferred. Although the immunogenic response was low, the patients who developed a relatively higher level of antibodies against the vaccine were more likely to show a clinical improvement. No clear conclusion can be drawn at this stage given the low number of subjects and the clinical efficacy will need to be tested in a further trial with more patients.

**Conclusion:** CV-MG01, a potential therapeutic vaccine for Myasthenia Gravis, was tested in a phase 1b (I/II) clinical trial on 24 MG patients. The primary objectives (safety and immunogenicity) were reached even though the immunogenic response was found to be low. The study had several limitations (small sample size, different number of patients receiving the vaccine or placebo, sequential cohort tested with different doses, clinical scores very low at baseline for some patients, interference with acetylcholinesterase inhibitor intake, and variability in the moment of testing) that will need to be addressed in a subsequent larger trial. Additionally, strategies to increase the immunogenic potential of the vaccine will be implemented.