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The VSV-ZEBOV experimental vaccine triggers the production of Ebola virus neutralising antibodies

The first results of the phase I clinical trial at Geneva University Hospitals (HUG) show that the VSV-ZEBOV vaccine candidate triggers the production of antibodies capable of neutralising the Ebola virus. These results – published today as a world first in the *New England Journal of Medicine* – are based on a total of 158 volunteers in Europe and Africa. Most of the observed side effects were mild to moderate (fever and muscle pain for one or two days), but around 20% of the volunteers reported mild to moderate joint pain for a couple of weeks. The vaccine was able to disseminate through the body and was detected in vesicles on the hands or feet of some of the volunteers. The phase III clinical trials recently launched in West Africa will determine whether the immune response triggered by this vaccine is able to protect the population against the Ebola virus, and if large-scale vaccination campaigns are feasible.

Since 10 November 2014, the Hôpitaux universitaires de Genève (HUG) have been testing the VSV-ZEBOV vaccine candidate in collaboration with other teams based in Europe and in Africa. The preliminary results published today in the *New England Journal of Medicine* derive from phase I clinical trials being carried out in Geneva, Lambaréné (Gabon), Kilifi (Kenya) and Hamburg (Germany). The comparison of doses tested by the various teams (doses range from 300'000 to 50 million vaccine particles) showed that even low doses of this experimental vaccine are able to trigger the production of antibodies against the Ebola virus. However, the higher doses, in particular those tested at the HUG, induce higher levels of antibodies. Complementary analyses 6 and 12 months after vaccination should determine whether a single injection is enough to induce a lasting immune response, or if this vaccine will require subsequent booster injections.

As is often the case with a live vaccine, the strong immune response triggered by VSV-ZEBOV was manifested by inflammatory reactions (fever, muscle pain, etc.) in almost all volunteers; these lasted no more than 24 to 36 hours, however. These reactions cleared the vaccine particles from the blood in a few days, but additional investigations carried out by the HUG showed that the particles could reach other parts of the body. In one in five volunteers, vaccine particles were traced to the joints where they caused pains similar to rheumatism. For about ten days, occasionally more, this caused mild to moderate joint pain, mostly in the hands, feet, knees and elbows.

Fortunately, most of the time these symptoms were moderate, and they decreased and disappeared spontaneously or after a few days of treatment. Not a single volunteer had to miss work or be hospitalized. In some volunteers, VSV-ZEBOV also reached the skin, causing rashes or small vesicles on the feet or hands; in these cases as well, symptoms disappeared spontaneously after two or three weeks.

The investigations carried out by the four African and European teams on a total of 158 volunteers, and by two American teams on a further 58 participants, allowed the selection of a high dose of VSV-ZEBOV (20 million vaccine particles), which increases the probability that this vaccine candidate will be effective. Phase III clinical trials, the first of which began in Guinea in early March under the aegis of the World Health Organization will recruit several thousand volunteers and, in particular, people who were exposed to patients infected by the Ebola virus. These trials should determine whether the immune response triggered by the VSV-ZEBOV experimental vaccine is sufficient to protect against the Ebola virus, and if the safety of this vaccine allows its use in large-scale vaccination campaigns.

"Implementing these complex clinical trials in such a short time has only been possible thanks to the extraordinary mobilization of the research teams and of all those who support them, especially the volunteers who have placed their trust in us", emphasises Professor Claire-Anne Siegrist, Principal Investigator and Head of the Vaccinology Centre at the HUG: "It is to them that my thoughts and my thanks are addressed today. They are the heroes of this unprecedented adventure."

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For more information: (+41 22) 372 60 06, www.vsv-ebola.ch