

Vaccine development against RSV

Development of a vaccine against RSV: what is the status?

Respiratory Syncytial Virus (RSV) is the leading cause of acute lower respiratory tract infections, such as pneumonia and bronchiolitis, in infants and young children. Although the mortality rate of RSV in Europe is low, the virus is the second most important cause of death in infants in developing countries. At the moment there is no vaccine or cure for RSV.

Currently there are several vaccines in development. These include maternal vaccines, which are used to vaccinate mothers in the third trimester of pregnancy, and vaccines containing antibodies to protect children against RSV.

Stages of vaccine development

Before a vaccine is approved for use, it needs to be tested in different stages. Before a candidate vaccine is tested in humans, it is first tested in laboratory and animal studies. During this stage, researchers gain more information on the safety and ability of the drug to provoke an immune response.

Once approved, the candidate vaccine will be tested in humans during the clinical phase, which is divided in different clinical stages:

- *Phase I:* the vaccine will be tested in a small number of healthy volunteers, to assess its safety and tolerability. Additionally, researchers gather information on the body's immune response after receiving the vaccine.
- *Phase II:* the safety of the vaccine will be confirmed by administering it to a larger group of volunteers, and the correct dose of the drug for an optimum immune response will be investigated. Those vaccines that are safe and cause a strong immune response, will move to the next phase.
- *Phase III:* in addition to the safety, the efficacy of the vaccine will be tested by administering the vaccine to thousands of patients. This is the most expensive phase of vaccine development.

The information gathered during the three clinical phases will be used by the Federal Drug Administration (FDA) to evaluate if the vaccine should be licensed, and for who. After permission is given for a vaccine to become available, research will continue: *phase IV* is conducted among others to detect any long-term effects and to evaluate if the drug may also be effective against other diseases.



Maternal vaccines

In 2019 data from a phase III trial of a maternal vaccine (ResVax™, developed by Novavax, Inc.) were published. In this trial 4000 healthy pregnant women were vaccinated. The data showed that the maternal vaccine failed to meet the primary objective, i.e. prevention of medically significant RSV lower respiratory tract infections (LRTI) through 90 days of life. However, the maternal vaccine did reduce RSV LRTI hospitalizations and RSV LRTI with severe hypoxemia.

In October 2020 another company, GlaxoSmithKline (GSK), reported positive results on a maternal RSV candidate vaccine from phase I/II clinical studies. The vaccine was tested in 3 different doses compared with a placebo in 502 healthy non-pregnant women over monthly visits. According to the data 1 month after immunisation all vaccine dose levels were well-tolerated, with no safety concerns being identified. Furthermore, the data showed that the vaccine was able to rapidly boost the pre-existing immunity at all dose levels, leading to high levels of protective neutralising antibodies against RSV. Because it is still uncertain if this vaccine is effective in pregnant women, the company started a phase III clinical program GRACE to investigate the safety and efficacy of the maternal vaccine. It will be tested in approximately 10.000 healthy pregnant women for preventing medically assessed RSV LRTI in their newborns.

Antibodies

In July 2020, promising results from a phase IIb trial on the novel monoclonal antibody 'nirsevimab' were published. The data showed that one injection with nirsevimab protects healthy preterm infants from RSV during a whole RSV season: there was a significant reduction of 70.1% in medically-attended RSV LRTI, and a 78.4% reduction of hospitalisations due to RSV LRTI through 150 days post-dose. In the next phase of the trial the efficacy and safety of this vaccine will be evaluated in a large population of patients, to gain FDA approval for entering the drug market. Currently nirsevimab is also being evaluated in healthy term infants. The results of this trial are expected to emerge in 2021.

RSV Bronchiolitis Patient Network is excited about the above results. Vaccine development is a long and challenging process, taking 10-15 years to get it licensed. It is quite special that currently multiple vaccines offering protection against RSV are so close to becoming available. Although the first results are expected during 2021 at the earliest, we are looking forward to the data from the phase III trials and hope a vaccine will become available on the drug market soon. Which vaccine will be first is unknown, but in any case important steps in the development of a vaccine against RSV have been taken.



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