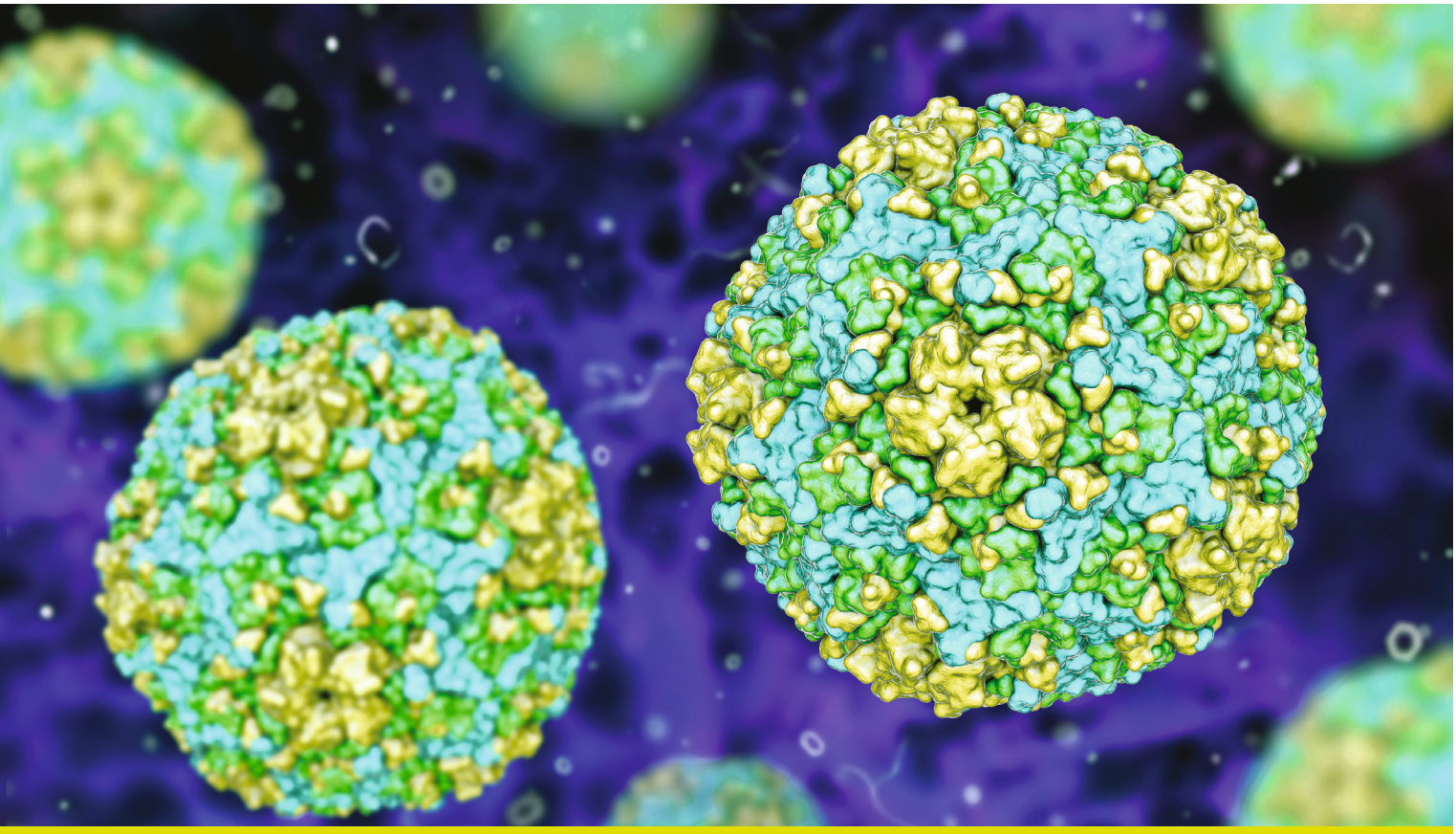
Vaccsheet

Intravacc.
Innovating vaccines

Avacc® 5: A first-in-class inactivated-virus vaccine against enterovirus D68



At a glance

Technology
Inactivated virus produced in a well-established Vero cell system (Cell-Vacc).

Status
Pre-clinical studies in mice and dose-response studies are completed.

Target
Enterovirus D68 (EV D68)

Route of administration & schedule
Intramuscular injection; likely 2 doses.

Unmet need
A 2022 meta-analysis estimated a global EV D68 infection prevalence of 4%. The analysis included studies in 41 countries around the globe (including sick and presumed healthy subjects) showing prevalences ranging from 0 to 74%.[1]

4%
Worldwide infection prevalence

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Enterovirus D68 infection

In 2014, an outbreak of respiratory illness and neurological impairment in North America drew global attention to infections by enterovirus D68.[2] Though the virus was not new – it was first described in 1962[3] – its association with severe illness, mainly in children, led to surveillance programs in many countries.[1] Since then, several countries have reported a biennial cyclical rise in EV D68 infections, which are temporally associated with rises in confirmed cases of acute flaccid myelitis (AFM)[4] and influenza-like illness.[5] EV D68 infection is a global public health concern. The estimated infection prevalence varies widely by region and study, but a 2022 meta-analysis puts the combined prevalence (combined random effect rate) at 4%.[1]

Concept: A first-in-class inactivated-virus vaccine

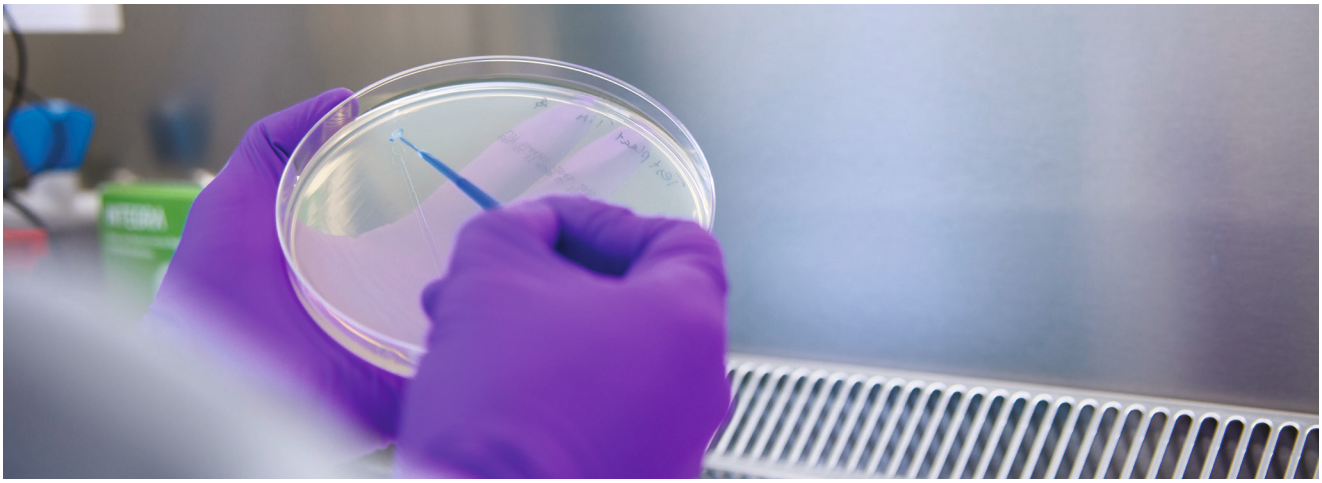
Avacc 5 is a concept vaccine against EV D68 infection. Based on an inactivated virus, the vaccine is designed for intramuscular administration.

Technology: A safe and well-established production platform

The EV D68 vaccine is produced on Intravacc's cell-based platform (Cell-Vacc), cultured on our proprietary, cGMP-grade, regulatory-approved Vero cells. Successfully used in viral vaccine development and large-scale production since 1987, this mature cell-based platform also includes ready-to-use cell banks, downstream purification processes, and full technology transfer. The platform allows fast-track development and generates high-quality, high-yield viral output, which is then purified and inactivated.

Current status: Strong results from immunogenicity studies

Avacc 5 is being developed through to phase I clinical trials under a contract from the U.S. National Institutes of Health (NIH). Vaccine dose, vaccination schedule, and the requirement for an adjuvant have been evaluated in a series of immunogenicity studies. The results showed that Avacc 5 induces high levels of virus-neutralizing antibodies in all vaccinated animals and for all doses tested. The observed protective responses occurred already after two doses (Figure 1). Furthermore, Avacc 5 elicits cross-protection against different clade B2 EV D68 viruses (Figure 2).



Vaccination with Avacc 5 results in high levels of virus-neutralizing antibodies

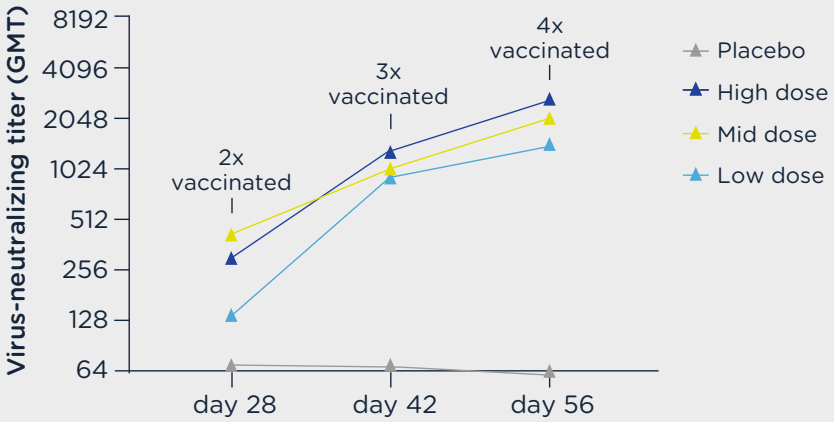


Figure 1. Mice vaccinated with Avacc 5 showed increased levels of virus-neutralizing antibodies already after a second dose compared to a placebo. A third and fourth vaccination further increased the recorded virus-neutralizing titer. A response to vaccination was evident in all subjects and at all dose levels tested.

Vaccination with Avacc 5 induces cross-neutralization against clade B2 of EV D68

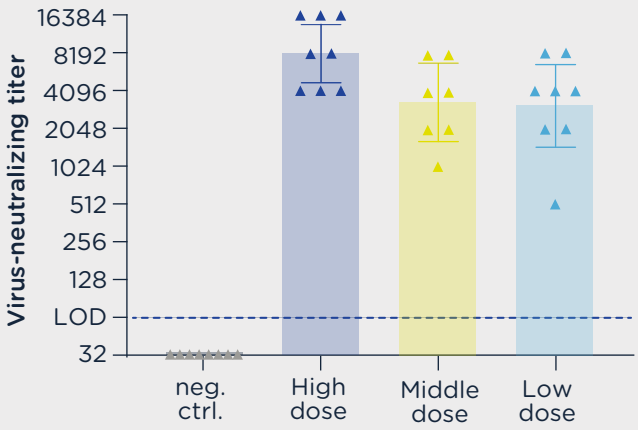


Figure 2. Mice vaccinated with Avacc 5, which is derived from EV D68 clade B1, exhibited high levels of clade B2 cross-neutralizing antibodies. Furthermore cross-neutralization against clade D was also demonstrated (data not shown). This response was consistently observed across high, middle, and low doses.

LOD = limit of detection.

Further clinical stages will advance under other partnerships or licensing. Such agreements include access to GMP master seed lots, a scalable and high-yield production process with a full assay panel, a pre-clinical data package, and a tailored transfer package. Next development steps include:

Manufacturing

A GMP master seed lot has been produced and released.

Characterization

Toxicology studies are planned in 2024.

Regulatory affairs

A phase I clinical trial is planned for end of 2024/beginning of 2025.

Other supportive data and structures for partnership or licensing are available and can be presented in a confidential follow-up meeting.

National Institute of Allergy and Infectious Diseases

www.niaid.nih.gov

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[1] Fall, A. *et al.* (2022) PLOS Neglected Tropical Diseases. doi: 10.1371/journal.pntd.0010073

[2] Brown, B.A. *et al.* (2014) Genome Announc. doi: 10.1128/genomeA.01201-14

[3] Schieble, J.H. *et al.* (1967) J. Virol. doi: 10.1128/jvi.1.3.494-499.1967

[4] Fang, X. and Huda, R. (2020) J. Clin. Neurol. doi: 10.3988/jcn.2020.16.3.376

[5] Fall, A. (2022) J. Clin. Virol. doi: 10.1016/j.jcv.2023.105379

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