**New Study Results Highlight Efficacy of ARCT-154 sa-mRNA Vaccine Against COVID-19**

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*News*

*Article*

*Nature Communications published the results of a study on ARCT-154, CSL’s sa-mRNA COVID-19 vaccine. The study showed that it is well-tolerated, immunogenic, and effective against multiple strains.*



*COVID-19*

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Nature Communications recently published the results of a phase 1/2/3a/3b study evaluating the safety, immunogenicity, and efficacy of CSL's self-amplifying mRNA (sa-mRNA) vaccine, ARCT-154. The study demonstrated that ARCT-154 was well-tolerated, immunogenic, and provided significant protection against multiple COVID-19 strains. Notably, Japan approved ARCT-154 last November, marking it as the world’s first sa-mRNA vaccine.

While approved mRNA vaccines have been revolutionary in controlling the global pandemic, the continuous emergence of new variants highlights the necessity for a diverse range of vaccine options to ensure public protection.

To learn more about the study, “Safety, immunogenicity, and efficacy of the self-amplifying mRNA ARCT-154 COVID-19 vaccine: pooled phase 1, 2, 3a and 3b randomized, controlled trials” and its results, *Infection Control Today*® (*ICT*®) interviewed Jon Edelman, MD, senior vice president of Vaccines Innovation Unit, CSL.

***ICT*:** **The**[**results**](https://www.prnewswire.com/news-releases/nature-communications-publishes-pivotal-data-demonstrating-efficacy-and-tolerability-of-csl-and-arcturus-therapeutics-covid-19-vaccine-302149979.html)**published in**[***Nature Communications***](https://www.nature.com/articles/s41467-024-47905-1)**demonstrate promising efficacy and tolerability of ARCT-154. Could you provide insights into the key findings of the integrated phase 1/2/3a/3b study and its implications for COVID-19 vaccine development?**

**Jon Edelman, MD:** The study results demonstrate the efficacy and tolerability of CSL’s sa-mRNA COVID-19 vaccine. The results add to [previously](https://www.thelancet.com/journals/laninf/article/PIIS1473-3099%2824%2900060-4/fulltext) [published data](https://www.thelancet.com/journals/laninf/article/PIIS1473-3099%2823%2900650-3/abstract) on ARCT-154 demonstrating superior immunogenicity to Omicron BA 4/5 compared to conventional mRNA COVID-19 vaccine booster and follow-up data demonstrating longer duration of immunity compared to traditional COVID-19 mRNA vaccine booster.

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The study showed in several phases of development that the ARCT-154 vaccine proves to be safe, tolerable, immunogenic, and efficacious. Most adverse events reported in the study were mild or moderate and transient in nature; after two doses being provided as a primary series, more than 94% of participants had an immune response that is considered protective, and efficacy data showed that the vaccine protected more than half of the study population against any COVID-19 symptoms. It protected 95% of the study population against severe COVID-19. Particularly, the protection against severe disease is in line with what was seen in other mRNA SARS-CoV-2 vaccines, and the side effects appear to be less frequent.

***ICT*:** **ARCT-154 has shown significant protection against multiple strains of COVID-19, including the Delta variant. Can you elaborate on the vaccine's effectiveness against different strains and how this could impact global vaccination strategies?**

**JE:**The Phase 3b part of the study was conducted during a time when the Delta variant was dominant in Vietnam, whereas the vaccine contained the ancestral strain. Later in the study, a Phase 3c efficacy part was conducted, and the cases for that phase were collected during a period of Omicron BA.2 and BA.5 dominance. Results from that study show that the ARCT-154 ancestral strain vaccine was approximately 19% more efficacious than ChAdOx.

***ICT*:** **The study highlights high efficacy rates of ARCT-154 against severe COVID-19, particularly in certain demographic groups. What factors contribute to these varying efficacy rates, and how might they inform targeted vaccination efforts?**

**JE:**We found the efficacy against severe COVID-19 was similar across the 3 groups (healthy young adults 100%, at-risk young adults 92%, and older adults 94%).

***ICT*:** **With a neutralizing antibody seroconversion rate of 94.1% after two doses, ARCT-154 has demonstrated robust immunogenicity. How does this level of immune response compare to other COVID-19 vaccines, and what implications does it have for long-term protection against the virus?**

**JE:**Other mRNA vaccines were licensed based on efficacy results, not based on immunogenicity results. The seroconversion rate found with ARCT-154 was demonstrated in a COVID-19 vaccine and SARS-CoV-2 infection naïve population and is therefore very specific to this group. We did compare the immune response of an ARCT-154 booster directly with a booster of original Comirnaty and found the titers of antibodies were 1.44 times higher in ARCT-154 than in Comirnaty.

***ICT*:** **The study involved a diverse participant pool across different age groups and risk categories. How were these demographic factors considered in the design and interpretation of the study results, and what insights were gained regarding vaccine safety and efficacy in these populations?**

**JE:**The study enrolled adults (18 years and older), but by the time the Phase 3 portion of the study started recruiting, it was already clear that certain groups were at higher risk of severe disease due to a SARS-CoV-2 infection. The study population was stratified based on this risk for severe disease (either due to age or due to comorbidities). The protection level appeared to be similar across these groups.

***ICT*:** **Collaboration, including cofounding by Vinbiocare Biotechnology Joint Stock Company, played a significant role in funding and conducting this research. How did these partnerships contribute to the study's success, and what are the implications for future collaborations in vaccine development and research?**

**JE:**Arcturus Therapeutics has an ongoing relationship with Vinbiocore Biotechnology. Vinbiocare is based in Vietnam and, in addition to providing funding, enrolled adult subjects in the study.

Reference:

<https://www.infectioncontroltoday.com/view/new-study-results-highlight-efficacy-arct-154-sa-mrna-vaccine-against-covid-19?utm_source=www.infectioncontroltoday.com&utm_medium=relatedContent>