DR230330 – ANRS0514s (MUCOBOOST) – Information for research participants

Title: Randomised, controlled, multicentre phase I/II trial comparing the safety and immunogenicity of a booster dose of an intranasal COVID-19 vaccine expressing recombinant SARS-CoV-2 N/S proteins with a booster dose of an mRNA COVID-19 vaccine in healthy adult volunteers

In brief	Coordinating investigator: Dr Zoha Maakaroun-Vermesse (Vaccinology Unit/CIC 1415, Tours University Hospital), F CRIN I REIVAC national vaccinology network Co-coordinating investigator: Prof. Odile Launay (Cochin-Pasteur Vaccinology CIC/CIC1417, APHP, Paris Cité University), F CRIN I REIVAC national vaccinology network Scientific advisor: Prof. Isabelle Dimier-Poisson (BioMAP, University of Tours - INRAe)
	Structure/teams: Data management: CIC 1415 biometrics (Tours University Hospital) Methodology and statistical analysis: UMS 54 MART (Inserm – University of Bordeaux) Central laboratories: - BioMAP (University of Tours – INRAe) - U1259 MAVIVHe (University of Tours – Inserm) - Bacteriology, Virology and Hospital Hygiene Department CNR-VIH (Tours University Hospital) Provision of the LVT-001 vaccine: LOVALTECH
	Start date: May 2025 Research end date: Quarter 2 2028 (provisional)
	Expected number of participants: 238 participants Phase I: 36 participants Phase II: 202 participants
	Trial status: Ongoing
	Pathology: COVID-19
	Joint promotion: Inserm - ANRS MIE and CHRU de Tours
	Funded under the RECH MIE 2022 call for projects
The project	This is a randomised, comparative, multicentre, open-label, phase I/II trial conducted in France, which evaluates the safety and immunogenicity of a booster dose of an intranasal vaccine against COVID-19 (LVT-001) compared to a booster dose of an mRNA vaccine against COVID-19 (Pfizer-BioNTech) in healthy adult volunteers. Study population: A total of 36 and 202 healthy volunteers will be recruited for phase I and phase II, respectively, and followed up for 12 months. Interventions: Phase I: The experimental drug is the intranasal recombinant protein vaccine LVT-001 administered on day 0 in each nostril: - Cohort A (12 participants): low dose - Cohort B (12 participants): medium dose - Cohort C (12 participants): high dose Phase II: Two investigational drugs will be compared:

	- The selected dose of the intranasal recombinant protein vaccine LVT-001, administered on day 0 into each nostril. - The intramuscular mRNA vaccine against COVID-19 (Pfizer-BioNTech), administered as a standard booster. What are the expected results? In this Phase I trial involving healthy participants, no direct benefit is expected from participating in the trial, other than the theoretical benefit of eliciting a mucosal immune response against SARS-CoV-2. There are currently no data from clinical trials on the use of a nasal protein vaccine in humans. Expected risks include local nasal reactions and systemic reactions similar to those seen with other vaccines. The expected adverse effects following vaccination should be manageable with standard care as determined by the investigators. The safety profile of this vaccine candidate therefore justifies the launch of this Phase I/II clinical trial. Although this is the first time a nasal protein vaccine has been used in a clinical trial in humans, it will be administered in increasing doses, with built-in safety margins to ensure that progression to the next group of participants at the same dose is justified.
Latest news (if applicable)	The first vaccination in Cohort A was carried out at the Tours University Hospital on 21/05/2025. A cumulative review of safety data conducted on day 14 of the sixth participant in Cohort A confirmed good tolerability conditions, allowing Cohort B to be opened at the CIC 1415 at the Tours University Hospital and recruitment to continue in Cohort A at the Cochin-Pasteur Vaccinology CIC on 8 August 2025. The next cumulative safety data review for the opening of Cohort C is scheduled for October 2025, with Phase II set to begin in the^{third}quarter^{of} 2026.
References Publications (if applicable)	None to date
Type of study	Drug trial and multicentre
Primary objectives	Phase I: To evaluate the safety of three different booster doses of an intranasal COVID-19 vaccine (LVT-001) expressing recombinant SARS-CoV-2 N/S proteins in healthy volunteers. Phase II: Evaluate, based on nasal swabs, the superiority in terms of mucosal humoral immune response of a booster dose of an intranasal COVID-19 vaccine (LVT-001) expressing recombinant SARS-CoV-2 N/S proteins compared to a booster dose of an intramuscular mRNA COVID-19 vaccine (Pfizer-BioNTech) in healthy adult volunteers at D28.
Secondary objectives	1) To evaluate, based on nasal swabs, the mucosal humoral immune response by measuring the concentrations of anti-S and anti-N IgA specific to the recombinant N/S proteins of the intranasal vaccine by ELISA at D0, D7 (Phase I), D14, D28 (Phase I), M3, M6 and M12, respectively in each arm. 2) To evaluate, using nasal swabs, the mucosal neutralising immune response specific to the recombinant N/S proteins of the intranasal vaccine using

	PRNT and VLP tests on D0, D7 (Phase I), D14, D28, M3, M6 and M12, respectively, in each arm. 3) Evaluate, using serum samples, the systemic humoral immune response by measuring the concentrations of anti-S and anti-N IgG specific to the recombinant N/S proteins of the intranasal vaccine by ELISA on D0, D7 (Phase I), D14, D28, M3, M6 and M12 respectively in each arm. 4) Evaluate, using serum samples, the systemic neutralising humoral immune response specific to the recombinant N/S proteins of the intranasal vaccine by PRNT and VLP tests on D0, D7 (Phase I), D14, D28, M3, M6 and M12 respectively, in each arm. 5) Evaluate, from blood samples, the systemic cellular immune response against N and S antigens by measuring the number of specific IFN-γ-secreting T lymphocytes using the ELISpot technique on D0, D7 (Phase I), and D14. D28, M3, M6 and M12 in each arm (subset of trial participants recruited at the Tours centre only). 6) Assess the proportion of participants with confirmed COVID-19 infections in each arm between D0 and M12. 7) Identify SARS-CoV-2 variants that escape vaccination. 8) Assess the proportion of participants with severe COVID-19 infections in each arm between Day 0 and Month 12. 9) For Phase II only: Assess the safety and tolerability of the LVT-001 vaccine.