DR230330 – ANRS0514s (MUCOBOOST) – Information for researchers

Title: Randomized, controlled, multicenter Phase I/II study comparing the safety and immunogenicity of a booster dose of an intranasal COVID-19 vaccine expressing SARS-CoV-2 N/S recombinant proteins with a booster dose of COVID-19 mRNA vaccine in healthy adults

In brief	Coordinating investigator: Dr. Zoha Maakaroun-Vermesse (Vaccinology Unit/CIC 1415, Tours University Hospital), F CRIN I REIVAC national vaccinology network Coordinating co-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
	Cosponsorship: Inserm - ANRS MIE and CHRU de Tours
	Funded as part of the RECH MIE 2022 call for projects
The project	This is a randomized, comparative, multicentric, open-label, dose-escalating phase I/II trial in France evaluating safety, efficacy, and immunogenicity of a booster dose of an intranasal COVID-19 vaccine expressing SARS-CoV-2 N/S recombinant proteins versus a booster dose of COVID-19 mRNA vaccine (Pfizer-BioNTech) in healthy adult volunteers. Trial population: A total of 36 and 202 healthy volunteers will be enrolled in Phase I and Phase II, respectively and followed 12 months. Interventions: Phase I: The investigational product is the LVT-001 intranasal recombinant protein vaccine 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 medicinal products will be compared: - The selected dose of the LVT-001 intranasal recombinant protein vaccine, administered on day 0 in 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 trial participation, apart from the theoretical benefit of eliciting 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. The expected risks include local nasal reactions as well as systemic reactions similar to those observed with other vaccines. Anticipated adverse events following vaccination should be manageable using standard routine care, as determined by the investigators. Therefore, the safety profile of this candidate vaccine supports the initiation of this Phase I/II clinical trial. Although this is the first time a nasal protein vaccine has been used in a human clinical trial, it will be administered in increasing doses, with built-in safety margins ensuring that progression to the next group of participants at the same dose is justified.
Latest news	The first vaccination in Cohort A was carried out at Tours University Hospital on 21/05/2025. A cumulative safety data review conducted on day 14 of the sixth participant in Cohort A confirmed good tolerance conditions, allowing Cohort B to be opened at Tours University Hospital and recruitment to continue in Cohort A at the Cochin-Pasteur Vaccinology Centre on 8/08/2025. 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.
Publication references	None to date
Type of study	Drug trial and multicentre
Primary objectives	Phase I: To evaluate the safety of three different doses of a booster of an intranasal COVID-19 vaccine (LVT-001) expressing SARS-CoV-2 N/S recombinant protein in healthy volunteers. Phase II: To evaluate, from nose swabs, the superiority of a booster dose of an intranasal COVID-19 vaccine (LVT-001) expressing SARS-CoV-2 N/S recombinant protein versus a booster dose of intramuscular COVID-19 mRNA vaccine (Pfizer-BioNTech) in healthy adult volunteers in terms of mucosal humoral immune response at D28.
Secondary objectives	1) To evaluate, from nose swabs, the mucosal humoral immune response by measuring anti-S and anti-N IgA concentrations specific to the intranasal vaccine N/S recombinant proteins by ELISA at D0, D7 (Phase I), D14, D28 (Phase I), M3, M6 and M12, respectively in each arm. 2) To evaluate, from nose swabs, the mucosal neutralizing immune response specific to the intranasal vaccine N/S recombinant proteins by PRNT and VLP assays at D0, D7 (Phase I), D14, D28, M3, M6 and M12, respectively in each arm. 3) To evaluate, from serum samples, the systemic humoral immune response by measuring anti-S and anti-N IgG concentrations specific to the intranasal vaccine N/S recombinant proteins by ELISA at D0, D7 (Phase I), D14, D28, M3, M6 and M12, respectively in each arm.

	4) To evaluate, from serum samples, the systemic humoral neutralizing immune response specific to the intranasal vaccine N/S recombinant proteins by PRNT and VLP assays at D0, D7 (phase I), D14, D28, M3, M6 and M12, respectively in each arm. 5) To evaluate, from blood samples, the systemic cellular immune response against N and S antigens by measuring the number of specific IFN-□-secreting T lymphocytes using the ELISpot technique at D0, D7 (Phase I), D14, D28, M3, M6 and M12 in each arm (subset of trial participants recruited in Tours center only). 6) To evaluate the proportion of participants with confirmed COVID-19 infections in each arm between D0 and M12. 7) To identify the variants of the SARS-CoV-2 virus that escape vaccination. 8) To evaluate the proportion of participants with serious COVID-19 infections in each arm between D0 and M12. 9) For Phase II only: To evaluate the safety and tolerability of the LVT-001 vaccine.
Inclusion criteria	1) Written informed consent obtained from the participant. 2) Be male or female between the ages of: a. ≥ 18 and ≤ 55 years for phase I b. ≥ 18 and ≤ 60 years for phase II. 3) Good general health as determined at the discretion of the investigator (vital signs, medical history, and physical examination). 4) BMI: 18,5 kg/m² ≤ BMI <30 kg/m². 5) Received at least 3 doses of a COVID-19 mRNA vaccine, last booster dose received at least 6 months prior to trial vaccine administration OR 2 doses of a COVID-19 mRNA vaccine and confirmed SARS-CoV-2 infection at least 6 months prior to inclusion in the trial. 6) Has expressed interest and availability to meet the trial requirements. 7) For a woman of childbearing potential, plan to be non-pregnant AND use of highly effective contraception from screening until the end of the trial. 8) Agree to abstain from donating blood/plasma or any other bodily fluids from the time of vaccination until 1 year after vaccination (only for LVT-001 vaccine). 9) Agree to stay in the geographical area of one of the clinical sites for the duration of the trial. 10) Agree to implement barrier measures as much as possible (washing hands and wearing a mask) against COVID-19 and respiratory infections between D0 and D28. 11) Agree to be registered in the computerized file of the Ministry of Health (VRB). 12) Be affiliated to French social security system.
Exclusion criteria	1) Temperature ≥38.0°C or symptoms of acute self-limiting illness such as upper respiratory tract infection or gastroenteritis within three days prior to vaccine dose. 2) Any form of contraindication to the trial vaccines tested.

	3) History of chronic rhinitis, nasal septal defect, cleft palate, nasal polyps, or other nasal abnormality that might alter nasal mucosa and affect vaccine response. 4) A piercing or obstruction in the nostrils that could impede vaccine administration. 5) Previous nasal surgery or nasal cauterization. 6) History of frequent epistaxis. 7) Virologically documented (PCR or antigenic test) history of COVID-19 in the past 6 months. 8) Positive COVID-19 PCR test at screening visit. 9) Medical problems due to alcohol. 10) Illicit drug use within the past 12 months. 11) Participation in another trial within 60 days prior to the enrolment visit or planned participation during the present trial period in another clinical study investigating a vaccine, drug, medical device, or medical procedure. Note: Participation in an observational study is allowed. 12) Received influenza vaccination within 14 days prior to trial vaccination, or any other licensed vaccine within 4 weeks prior to study vaccination. 13) Vaccination with a COVID-19 vaccine other than mRNA vaccine. 14) Known sensitivity to any of the ingredients of the trial vaccines. 15) Known allergic reaction to plastic. 16) Positive serology for hepatitis B (HBsAg), C (anti-HCV antibodies) and HIV 1-2. 17) History of severe adverse events following vaccine administration including anaphylactic reaction and associated symptoms such as rash, breathing problems, angioedema, and abdominal pain, or a history of allergic reaction that could be triggered by a component of the SARS-CoV-2 vaccine at the time of the first vaccine administration. 18) Pregnancy positive test (βHCG test) or pregnancy or breastfeeding. 19) Received immunoglobulin or other blood products within three months prior to inclusion or planned administration before the trial completion. 20) Received an immunosuppressive therapy for underlying disease or a treatment with immunosuppressive or cytotoxic drugs or a cancer chemotherapy or radiation therapy within the previous 36 months. 21) Received drugs such as corticosteroids at a dosage > 10 mg prednisone equivalent/day or inhalers corticosteroids, within 3 months prior to inclusion (excluding corticosteroid topical preparations for cutaneous application). 22) Abnormal and deemed clinically significant result by the investigator following the routine analyzes carried out at the time of the screening visit (any grade 4 biological result, even if deemed not clinically significant by the investigator, constitutes an exclusion criterion). 23) History of severe psychiatric disorders that may affect participation in the trial. 24) Any other serious chronic illness requiring immediate monitoring by a hospital specialist.

	25) Any other condition that, in the opinion of the investigator, would compromise the safety or rights of a volunteer participating in the trial or render the subject unable to comply with the protocol. 26) Phase II only: Participants included in phase I will not be included in phase II. 27) Participants under legal protection (e.g., guardianship, tutorship).
Primary endpoint	Phase I 1) Proportion of participants experiencing an immediate AE within an hour and half following vaccine administration. 2) Proportion of participants experiencing solicited local reactogenicity and systemic signs and symptoms for 7 days and 14 days respectively following vaccination. 3) Proportion of participants experiencing an unsolicited AE up to 28 days post administration. 4) Proportion of participants experiencing serious adverse events (SAEs), serious adverse reactions (SARs), suspected unexpected serious adverse reactions (SUSARs) and adverse events of special interest (AESI) respectively throughout the trial period. Phase II Crude variation of the mucosal humoral immune response specific to the vaccine N/S recombinant protein measured by ELISA (Geometric Mean Titers (±SD)) in each arm: IgA from nose swabs between D0 and D28.
Secondary endpoints	1) Crude variation of the mucosal humoral immune response specific to the vaccine N/S recombinant protein measured by ELISA (Geometric Mean Titers (±SD)): IgA from nose swabs between D0 and D7 (Phase I), D14, D28 (Phase I), M3, M6 and M12, respectively. 2) Neutralizing capacity of the mucosal humoral immune response specific to the vaccine N/S recombinant protein measured by PRNT and VLP assays at D0, D7 (Phase I), D14, D28, M3, M6, M12, respectively: Neutralizing Ig from nose swabs. 3) Crude variation of the systemic humoral immune response specific to the vaccine N/S recombinant protein measured by ELISA (Geometric Mean Titers (±SD)): Serum anti-S and anti-N IgG at D0, D7 (Phase I), D14, D28, M3, M6, M12, respectively. 4) Neutralizing capacity of the systemic humoral immune response specific to the vaccine N/S recombinant protein measured by PRNT and VLP assays at D0, D7 (Phase I), D14, D28, M3, M6, M12: Neutralizing serum IgG. 5) Percentage of responders against N and S antigens, respectively, measured by ELISpot SARS-CoV-2 assay at D0, D7 (Phase I) and D14, D28, M3, M6, M12: The quantification of IFN-γ specifically secreted by T lymphocytes following exposure to N and S antigens will be performed on a subset of participants recruited only at the Tours site for feasibility reasons. Phase I: 6 participants in each dose group. Phase II: 40 participants. 6) Proportion of participants with COVID-19 infections confirmed by a positive PCR test or a positive antigen test between D0 and M12 in each arm.

	7) Description of variant types identified on participants with a positive PCR test after vaccination. 8) Proportion of participants with serious COVID-19 infections defined as a hospitalization and/or death due to the COVID-19 between D0 and M12 in each arm 9) Proportion of participants experiencing: • An immediate AE within one hour following vaccine administration. • Solicited local reactogenicity and systemic signs and symptoms for 7 days and 14 days respectively following vaccination. • An unsolicited AE up to 28 days post administration. • Serious adverse events (SAEs), serious adverse reactions (SARs), suspected unexpected serious adverse reactions (SUSARs) and adverse events of special interest (AESI) respectively throughout the study period.

Summary

A – Study methodology and type of data and/or samples collected

Data and samples collected	**Biobanks**	At visits D0, D7 (Phase I), D14, D28, M3, M6 and M12: • Nasopharyngeal swab • Saliva • Serum • PBMC
	Data	Clinical, biological

PHASE I		Vaccination Visit V1	Visit V2	Visit V3	Visit V4	Visit V5	Visit V6	Visit V7	Premature termination
		D0	D7 post-V1	D14 post-V1	D28 post-V1	D90 post-V1=M3	D180 post-V1=M6	D360 post-V1=M12	
Permitted window			+/- 1 day	+/- 1 day	+/- 2 days	+/-10 days	+/-14 days	+/-14 days	
Samples	Blood sample for ELISPOT (7mL, heparin tube)	X	X	X	X	X	X	X	X
	Blood sample (2x5 mL, SST tube)	X	X	X	X	X	X	X	X
	Nasal swabs collection	X	X	X	X	X	X	X	X
	Saliva collection	X	X	X	X	X	X	X	X

PHASE II		Vaccination Visit V1	Visit V2	Visit V3	Visit V4	Visit V5	Visit V6	Premature termination
		D0	D14 post-V1	D28 post-V1	D90 post-V1=M3	D180 post-V1=M6	D360 post-V1=M12	
Permitted window			+/- 1 day	+/- 2 days	+/-10 days	+/-14 days	+/-14 days	
Samples	Blood sample for ELISPOT (7ml, heparin tube)	X	X	X	X	X	X	X
	Blood sample (2x 5ml, SST tube)	X	X	X	X	X	X	X
	Nasal swabs collection	X	X	X	X	X	X	X
	Saliva collection	X	X	X	X	X	X	X

B – Terms and conditions for accessing the collection

1- Project submission: **via the sample request form on the website**

2- Project evaluation: **scientific committee**

3- Provision of the collection**: final decision by the scientific committee or ANRS MIE management if the scientific committee is no longer active**

Contact email address for submitting your project: **biobanque@anrs.fr**