ANRS0002S CoviCompare-P

A phase II trial assessing immunogenicity and safety of COVID-19 mRNA Vaccine BNT162b2 in adult volunteers with no history of SARS-CoV-2 infection administered with two doses of vaccine (D1-D29) and in adult volunteers with documented history of SARS-CoV-2 infection (of more than 5 months) administered with only one dose of vaccine.

Sponsor Inserm-

ANRS **Start of inclusions** **08/03/2021**

Inclusion status Completed

End of study **02/12/2023**

Number of participants **280**

Objectives

Main: To assess the humoral immune response to the COVID-19 mRNA Vaccine BNT162b2 in adult volunteers with or without documented history of SARS CoV-2 infection, 28 days after the first or second injection respectively

Secondary(s) :

1. To characterize humoral immune response induced by BNT162b2 at D29 (group 1); at MX (participants to receive the additional dose), at MX+3d* and MX+15d* (*50% of the participants having received the additional vaccination), at MX+28d (participants having received the additional vaccination) and the durability of the immune response at M6, MX+6months and M24 in the 2 groups (with and without documented history of SARS-CoV-2 infection)
2. To assess and characterise the antigen-specific T cell response
3. To evaluate mucosal immunity
4. To determine the repertoire and polyclonality of the humoral response
5. To compare the different post-vaccination immune responses between groups of young and elderly people and, more generally, to assess the effect of age on markers of immune response.
6. To identify biomarkers predictive of the absence or non-persistence of the humoral response
7. To evaluate clinical safety
8. To collect occurrence of SARS-CoV-2 infection and characterise the parameters of immunity at the time of infection
9. Collecting cases of SARS-CoV-2 infection
10. To biobank biological materials (plasma, serum, PBMC…) to address to other secondary ancillary projects

Exploratory objectives

11. To characterize the memory B and T cell response
12. To characterize the Mucosal immunity (functional study) and evaluate the value of Ultrasensitive IgA in saliva by Photoring assay

Information for researchers

A - Methodologies

Methodology

This is a national open phase II trial, assessing the immunogenicity and safety of COVID-19 mRNA Vaccine BNT162b2 in volunteers:
- with no history of SARS-CoV-2 infection and receiving two doses of vaccine (D1-D29) and an additional dose* (MX) according to French recommendations
**: the additional vaccination will be performed according to the schedule and population defined by the French recommendations*
- with history of SARS-CoV-2 infection of more than 5 months and receiving only one dose of vaccine and an additional dose* (MX) according to French recommendations.

Main inclusion criteria

1. 18 to 45 years old or at least 65 years old,
2. Healthy adults or stable medical condition for adults with pre-existing medical conditions. A stable medical condition is defined as disease not requiring significant change in therapy or hospitalization for worsening disease during 3 months before enrolment, nor expected to require any significant change in therapy or hospitalization for worsening disease in foreseeable future.
3. Group 1: Healthy adults with no previous history of SARS COV2 infection (PCR-, antigenic test- or chest TDM- or negative SARS-CoV-2 serology)

Group 2: Healthy adults with history of infection with SARS COV 2 (PCR+, antigenic test+ or chest TDM+ or serology SARS-CoV-2 of more than 5 months) OR have been a household contact subject (who had a positive PCR test/ Ag test/TDM more than 5 months ago) and have presented COVID-19 symptoms [Experienced at least TWO of the following systemic symptoms: Fever (≥ 38ºC), chills, myalgia, headache, sorethroat, new olfactory and taste disorder(s), gastrointestinal symptoms (diarrhea and/or vomiting) or at least ONE of the following respiratory signs/symptoms: cough, shortness of breath or difficulty breathing, OR clinical or radiographical evidence of pneumonia] since at least 5 months ago and have had a positive SARS-CoV-2 serology between this episode and pre-inclusion.

4. A female participant is eligible to participate if she is not pregnant or breastfeeding and one of the following conditions applies:

- Is of non-childbearing potential. To be considered of non-childbearing potential, a female must be post-menopausal for at least 1 year or surgically sterile.
- OR Is of childbearing potential and agrees to use an effective contraceptive method from at least 4 weeks prior to vaccination until at least 4 weeks after the last vaccination. A participant of childbearing potential must have a negative blood pregnancy test at enrolment visit.

5. Understands and agrees to comply with the study procedures (visits, phone calls) based on Investigator judgement
6. Written and informed consent signed by the person and the investigator (no later than the day of pre-inclusion and prior to any examination realized in the frame of the trial) (article L1122-1-1 of the Public Health Code)
7. affiliated or beneficiary of a social security scheme (article L1121-11 of the Public Health Code) (AME is not a social security scheme)
8. A person who agrees to be registered in the national file of persons who lend themselves to biomedical research (article L1121-16 of the Public Health Code).

Main non-inclusion criteria Specific to Research

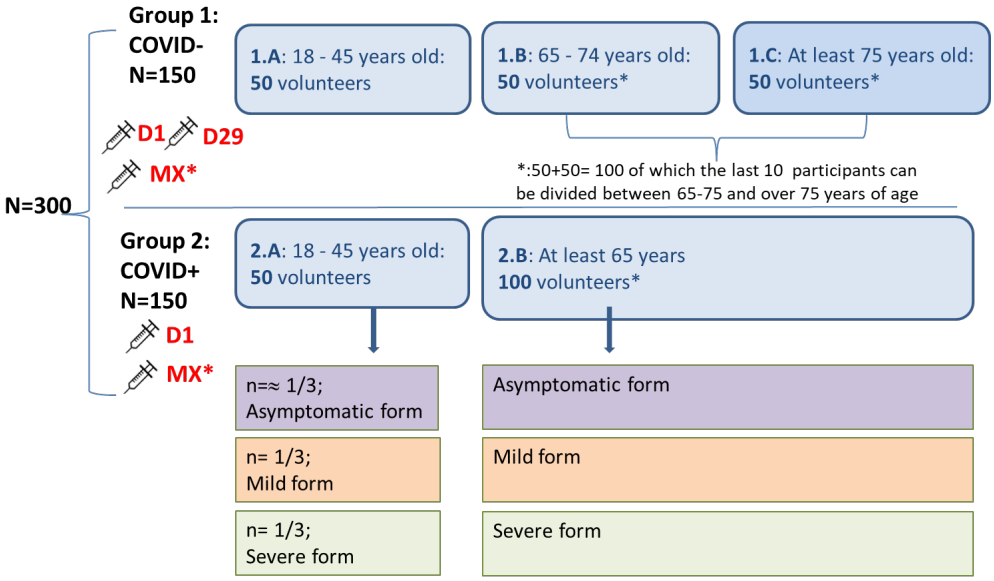
1. Participant is ill or febrile (body temperature ≥ 38.0°C) within 72 prior hours; symptoms suggestive of COVID-19 or being contact subject within the past 14 days at enrolment visit.

(Ill or febrile participants may be re-scheduled within the inclusion period when no longer presenting symptoms, except if condition is COVID19)

2. Participants with positive serology SARS-CoV-2 at the enrolment visit (**only for the group 1)**
3. Participants who already received another anti-SARS-CoV-2-vaccine
4. Participants who received BCG within the last year.
5. Use of immunosuppressive drugs like e.g. corticosteroids at a dosage > 10mg equivalent prednisone /day (excluding topical preparations and inhalers) within 3 months prior to enrolment or 6 months for chemotherapies
6. Received immunoglobulin or other blood product within 3 months prior to enrolment or planned receipt of immunoglobulin or a blood product through study completion.
7. Received any vaccination within 4 weeks prior to first injection or plan to receive a licensed vaccine within 4 weeks after the last injection.
8. History of severe adverse reactions to vaccine administration, including anaphylaxis and related symptoms, such as rash, respiratory difficulty, laryngeal oedema and abdominal pain to vaccines, or history of allergic reaction likely to be exacerbated by any component of the anti-SARS-CoV-2-vaccine.
9. History of severe allergic event

Research diagram :

The recruitment will occur in Clinical Investigational Centers from the COVIREIVAC French Covid-19 Innovative Clinical Research Network in vaccinology.
Participants will mainly be recruited using the file from the COVIREIVAC volunteer platform.
Stratification according to age groups will be carried out and a system will be put in place in order to distribute the forms of COVID (asymptomatic/mild/ severe) for the subgroup A of the group 2.



Schedule of assessments

	Pré-inclusion	Inclusion	Visit	Visit	Follow-up	Visit	Visit	Visit	Visit	Follow-up	End of follow-up visit	SARS-CoV-2 infection visit
	V0 D-6 à D0	**V1 D1**	**V2 D29**	**V3 D57**	**V4 M6**	**Vb MX[2]**	**VB+3d MX+3d[3]**	**Vb+15d M+15d[3]**	**Vb+28d MX+28d[2]**	**V5 MX+6months[5]**	**V6 M24[6]**	**VI Within 24 hours of confirmation of SARS-CoV-2 infection**
Intervalle autorisé des visites (jours)			*+ / -3 d*	*+/-3 d*	*+/- 15 d*	*+/-30 d*	*+2d*	*+/-2d*	*+/-3 d*	*+/-15 d*	*+/-15 d*	
Informed consent	x					X						
Verification of eligibility criteria	x	x										
Clinical examination	x	x	x	x	x	X			x	x	x	x
Medical History	x											
Concomitant therapy	x	x	x	x	x	X	x	x	x	x	x	x
NFS (3mL)	x		x		x	X						
Serology to SARS-CoV-2 (6mL)	x (group1)											
Nasopharyngeal swab for RT-PCR to SARS-CoV-2		x										
Saliva (3mL)		x	x	x	x	X			x	x	x	
Blood drawn for immuno-monitoring and biobanking (~45mL)	x*	x*	x	x	x	X	x (11mL)	x (11mL)	x (25,5mL)	x	x	x
Urinary (U) blood (B, 5mL) pregnancy test	S		U			U						
Administration of Vaccine			 (group1)									

	Pré-inclusion	Inclusion	Visit	Visit	Follow-up	Visit	Visit	Visit	Visit	Follow-up	End of follow-up visit	SARS-CoV-2 infection visit
	V0 D-6 à D0	**V1 D1**	**V2 D29**	**V3 D57**	**V4 M6**	**Vb MX[2]**	**VB+3d MX+3d[3]**	**Vb+15d M+15d[3]**	**Vb+28d MX+28d[2]**	**V5 MX+6months[5]**	**V6 M24[6]**	**VI Within 24 hours of confirmation of SARS-CoV-2 infection**
Interval visit authorized (day)			*+/ -3 d*	*+/-3 d*	*+/-15 d*	*+/-30 d*	*+2 d*	*+/-2 d*	*+/-3 d*	*+/-15 d*	*+/-15 d*	
post-vaccination surveillance (30 minutes)		x	x (group1)			X						
Self-surveillance diary (D)/ memory aid (M) provided		x (C)	x (D,G1) (M, G2)	x (M, G1)		x (D)						
Self-surveillance diary/memory aid reviewed			x	x (D,G1) (M, G2)	x (M)	x (M)	x (D)	x (D)	x (D)	x (M)	x (M)	x
Phone call by the investigator team		48-72H post-injection and once a week			For participants not receiving the additional dose: once a month (from D57 to M11) For participants receiving the additional dose: 48-72H[4] post-MX injection, once a week[4] (from MX to MX+28d) then once a month (from MX+28d to M11)							
Adverse events	x	x	x	x	x	x	x	x	x	x	x	
Nasopharyngeal swab <u>in case of clinical signs throughout the study</u> for RT-PCR to SARS-CoV-2			X (suppl.[1])									
Volume of blood drawn (mL) (Woman)	53,5 (58,5)	46	46,5	43,5	44	28,5	***11***	***11***	25,5	41	41	
Cumulative volume of blood drawn (mL) (Woman) WITHOUT additional vaccine dose	53,5 (58,5)	99,5 (104,5)	146 (151)	189,5 (194,5)	233,5 (238,5)					274,5 (279,5)	315,5 (320,5)	
Cumulative volume of blood drawn (mL) (Woman) WITH additional vaccine dose / ***italic and bold if MX+3d and MX+15d performed***	53,5 (58,5)	99,5 (104,5)	146 (151)	189,5 (194,5)	233,5 (238,5)	262 (267)	***273 (278)***	***284 (289)***	287,5 ***/309,5*** (292,5)/ ***(314,5)***	328,5***/350,5*** *(333,5)/(**355,5**)*	369,5/ ***391,5*** *(374,5)/* ***(396,5)***	

B - Description of data and samples collected

BiolibrariesPlasma	**, serum, saliva, DNA and RNA**
Data	Clinical, biological, pharmacovigilance

C - How to access the collection

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

2- project assessment: **scientific advisory board**

3- Making the collection available**: Scientific Advisory Board**

Contact e-mail address for submitting your project: **biobanque@anrs.fr**