A French cohort for assessing COVID-19 vaccine responses in specific populations

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To the Editor—The COVID-19 vaccination campaign started in France on 27 December 2020. It has been rolled out in different priority phases according to the risk of developing a severe form of COVID-19 and the risk of being exposed to the causative coronavirus SARS-CoV-2. By 5 May 2021, four vaccines against COVID-19 were approved by the European Medicines Agency and were available in France: COMIRNATY (the COVID-19 mRNA vaccine BNT162b2; BioNTech–Pfizer); COVID-19 Vaccine Moderna (mRNA-1273; Moderna); VAXZEVRIA (ChAdOx1-nCoV19; AstraZeneca–Oxford University); and COVID-19 Vaccine Janssen (Ad26.COV2.S; Janssen). Specific populations are defined as people at risk of developing severe forms of the disease and in whom the immunogenicity and efficacy of vaccines against that disease may differ from that of the general population (e.g., recipients of solid-organ transplants or patients undergoing hemodialysis). The safety, immunogenicity and efficacy of vaccines in specific populations, which are heterogeneous groups of patients, are affected by the nature and intensity of the underlying disease(s), the age of the patient and any other treatments the patient is taking, and are possibly affected by the vaccine platform used. So far, no or only limited data on specific populations are available from published results of phase 3 trials of authorized vaccines against COVID-19. Initial immunogenicity data available for some of these specific populations showed low antibody responses to the SARS-CoV-2 spike protein in patients who received solid-organ transplantation[1–4], patients undergoing hemodialysis[5,6], patients receiving chemotherapy or immunotherapy for solid cancer or hematologic malignancies[7,8], and patients receiving infliximab for inflammatory bowel disease[9]. Most of these studies reported small sample sizes.

To assess the immune response of COVID-19 vaccines in different specific populations, INSERM (Institut National de la Santé et de la Recherche Médicale) and ANRS-MIE (Agence Nationale de Recherche sur le Sida–Maladies Infectieuses Emergentes), in collaboration with the COVIREIVAC network, ten national disease-specific societies and seven patients' associations (France Rein, Transhépate, ARSEP Foundation, CNAO, FFD, EGMOS and TRT5 CHV), launched, on 25 March 2021, the ANRS0001S COV-POPART study (ClinicalTrials.gov NCT04824651). COV-POPART is a national multi-center prospective multi-cohort study of specific populations vaccinated against COVID-19 that aims to include 10,700 patients.

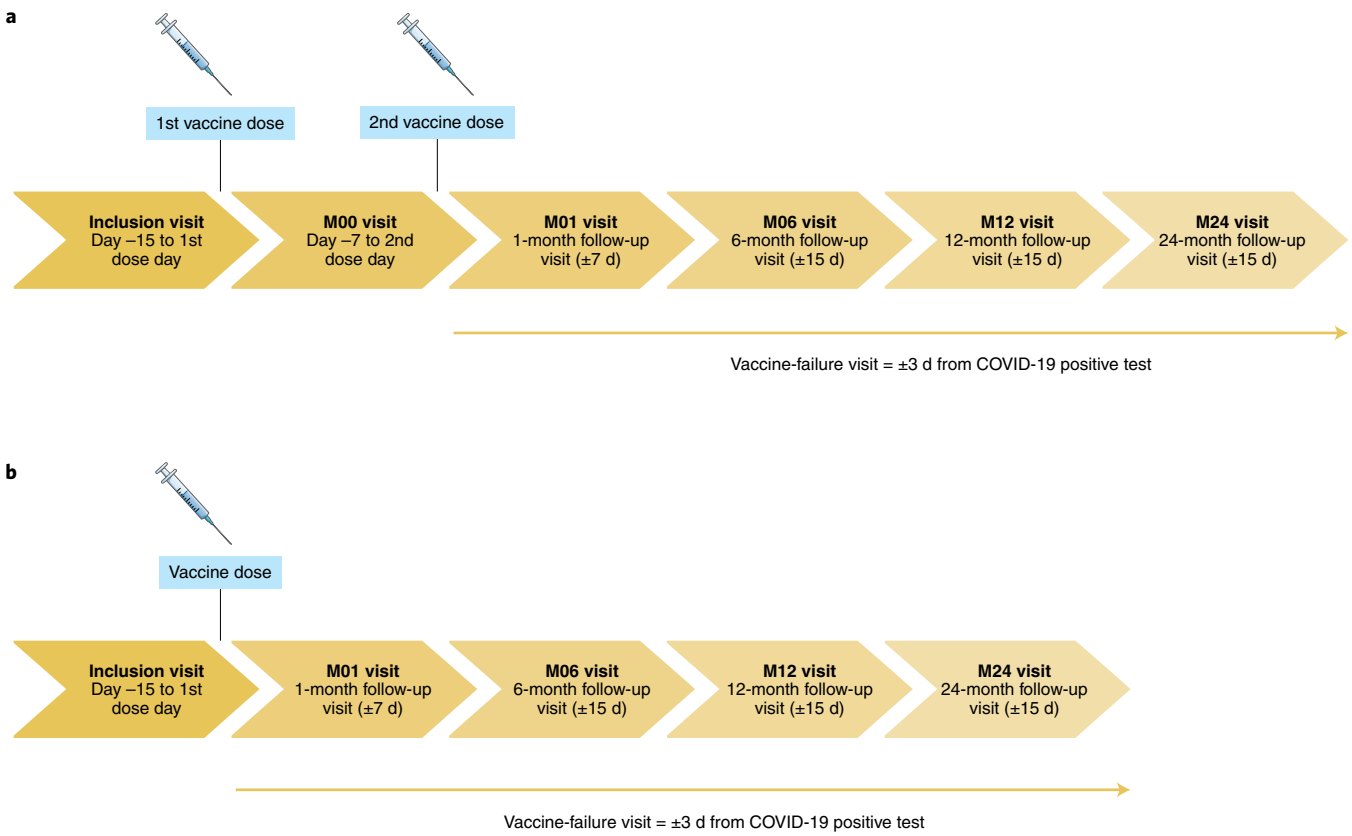

Fig. 1 | COV-POPART study designs. a, Study design for a two-dose vaccine regimen. **b**, Study design for a one-dose vaccine regimen.

Patients with solid cancer ($n = 800$), solid-organ transplantation ($n = 700$), hematopoietic stem cell transplantation ($n = 350$), chronic renal failure with or without dialysis ($n = 350$), multiple sclerosis or neuromyelitis optica spectrum disorders ($n = 600$), autoimmune inflammatory rheumatic diseases ($n = 600$), systemic autoimmune diseases ($n = 600$), hypogammaglobulinemia ($n = 300$), obesity (1,400), diabetes mellitus ($n = 1,400$) and/or infection with human immunodeficiency virus ($n = 1,400$) will be included. All adults affected by at least one of these chronic conditions, without a history of COVID-19 and not yet vaccinated, will be included in one of the 35 participating centers, which represent more than 250 clinical sites. A control group without any of the above-mentioned underlying conditions will also be included ($n = 1,850$; 18–74 years of age ($n = 1,400$) and ≥75 years of age ($n = 450$)).

The main objective will be to analyze the humoral immune response by assessing IgG antibody to the SARS-CoV-2 spike protein (by ELISA), IgG antibody to the SARS-CoV-2 receptor-binding domain (by ELISA) and specific neutralizing antibody to SARS-CoV-2 (by classical in vitro neutralization assay) at 1 month, 6 months, 12 months and 24 months after the first dose (Janssen vaccine) or second dose (all other vaccines) of the vaccine regimen (Fig. 1). Secondary objectives will be to compare the kinetics and strength of the immune responses of each subpopulation (e.g., recipients of solid-organ transplantation) with those of the control group and to make this comparison between specific subpopulations; to assess the factors (such as age, disease stage, treatment, type of vaccine, etc.) associated with the kinetics and strength of the immune responses in each subpopulation; and to characterize the immunology and virology of any vaccination failures, defined as a positive RT-PCR result for SARS-CoV-2 (performed because of clinical symptoms or during routine follow-up) at least 7 days and 15 days after the completion of vaccination (for the two-dose regimen and one-dose regimen, respectively).

In the case of vaccine failure, an additional visit will be required during which specific samples will be collected, including peripheral blood mononuclear cells, blood RNA and DNA, and nasopharyngeal swabs for sequencing of SARS-CoV-2.

In addition, a smaller ancillary study (30–40 participants from each subpopulation) will assess and characterize in-depth antigen-specific T cell responses, and will analyze the gene expression of the immune response through the use of transcriptomics.

Serological and immunological analysis will be centralized to allow standardization of tests and better comparison between patient cohorts of the immunogenicity of vaccines against COVID-19. A new biobank will be implemented to allow future comparisons and assessments. Samples will be made available to other researchers upon request to the scientific committee of the cohort.

Finally, given concerns about the development of thrombotic thrombocytopenia after immunization with ChAdOx1-nCoV19, the French Haute Autorité de Santé advocated, on 8 April 2021, for the use of an mRNA vaccine as a second dose in those below 55 years of age who received a prime dose of ChAdOx1-nCoV19. To assess the immune response of this new heterologous prime–boost COVID-19 vaccine regimen, researchers have added to the COV-POPART study an additional cohort of 200 patients affected by this mixed schedule.

Data collected from participants in the COV-POPART study will be linked to the French Health Data Hub (https://www.health-data-hub.fr/). This will allow the collection of data on cause of death, hospitalizations and monitoring of pre-existing health conditions during the follow-up.

The COV-POPART study will explore responses to vaccines against COVID-19 in a large number of at-risk patients by determining the strength and duration of their immune response and factors associated with this. By sharing the data as quickly as possible, the COV-POPART study will add valuable information that may allow possible adaptations of vaccine recommendations for certain subgroups or may serve as a basis for the implementation of clinical trials on enhanced vaccine regimens, including additional boost with standard or higher doses or adjuvanted vaccines. Finally, the COV-POPART study is intended to be adaptive to include new subpopulations (e.g., pediatric populations) depending on the evolution of the French immunization guidelines or to explore questions that may arise during follow-up, such as the evaluation of added boosting doses, new mixed-vaccine regimens or new authorized vaccines against COVID-19. ❐

Paul Loubet[1,2,24] ✉, Linda Wittkop[3,4,24], Eric Tartour[5], Beatrice Parfait[6], Benoit Barrou[7], Jean-Yves Blay[8], Maryvonne Hourmant[9], Marie Lachâtre[2,10], David-Axel Laplaud[11], Martine Laville[12], Bruno Laviolle[13], Jean-Daniel Lelievre[14], Jacques Morel[15], Stéphanie Nguyen[16], Jean-Philippe Spano[17], Benjamin Terrier[18], Anne Thiebaut[19], Jean-Francois Viallard[20], François Vrtovsnik[21], Xavier de Lamballerie[22] and Odile Launay[2,23]

[1]Department of Infectious and Tropical Diseases, INSERM U1047, Centre Hospitalier Universitaire (CHU) Nîmes, University of Montpellier, Nîmes, France. [2]INSERM, French Clinical Research Infrastructure Network, Réseau Innovative Clinical Research in Vaccinology, Paris, France. [3]Institut de Santé Publique d'Epidémiologie et de Développement, INSERM, Bordeaux Population Health Research Center, UMR 1219, Centre d'Investigation Clinique–Epidémiologie Clinique 1401, University of Bordeaux, Bordeaux, France. [4]Service d'Information Médicale, CHU de Bordeaux, Pôle de Santé Publique, Bordeaux, France. [5]Service Immunologie Biologique, Paris-Centre de Recherche Cardiovasculaire, INSERM U970, Assistance Publique–Hôpitaux de Paris (APHP), Hôpital Européen Georges Pompidou, Université de Paris, Paris, France. [6]Fédération des Centre de Ressources Biologiques–Plateforme de Ressources Biologiques APHP, Centre-Université de Paris, Centre de Ressources Biologique Cochin, Hôpital Cochin, Paris, France. [7]Service de Transplantation Rénale, Pitié Salpêtrière, APHP, Sorbonne Université, Paris, France. [8]Centre Leon Berard UNICANCER et Université Lyon I, Lyon, France. [9]Service de Néphrologie-Immunologie clinique, CHU Nantes, Nantes, France. [10]Centre d'Investigation Clinique (CIC) Cochin Pasteur, APHP, Hôpital Cochin, Paris, France. [11]Centre de Recherche en Transplantation et Immunologie–INSERM U1064, Service de Neurologie, CIC 1413, Université de Nantes, CHU Nantes, Nantes, France. [12]Hospices Civils de Lyon, Université Claude Bernard Lyon 1, Association Française d'Etudes et de Recherche de l'Obésité, French Clinical Research Infrastructure Network–French Obesity Research Centre of Excellence Network, Nantes, France. [13]University of Rennes, CHU Rennes, INSERM, CIC 1414, Rennes, France. [14]Vaccine Research Institute, INSERM and APHP, Hôpital H. Mondor, Créteil, France. [15]Rheumatology Department, CHU and University of Montpellier, Montpellier, France. [16]APHP–Sorbonne Université, INSERM U1135, CNRS ERL 8255, Centre d'Immunologie et des Maladies Infectieuses–Paris, Paris, France. [17]APHP–Sorbonne Université, Institut Pierre Louis d'Epidemiologie et de Santé Publique INSERM 1136, Paris, France. [18]Service de Médecine Interne, Hôpital Cochin, APHP, Paris, France. [19]Département d'Hématologie, CHU Grenoble Alpes, Grenoble, France. [20]Université de Bordeaux, Hôpital Haut-Lévêque, Bordeaux, France. [21]Service de Néphrologie, Hôpital Bichat-Claude Bernard, APHP, Departement Hospitalo-Universitaire Fire, Université de Paris, Paris, France. [22]Unité des Virus Émergents, Aix-Marseille Université, Institut de Recherche pour le Développement 190, INSERM 1207, Institut Hospitalo-Universitaire Méditerranée Infection, Marseille, France. [23]INSERM, CIC Cochin Pasteur, Assistance Publique Hôpitaux de Paris, Hôpital Cochin, Université de Paris, Sorbonne Paris Cité,

Paris, France. [24]*These authors contributed equally: Paul Loubet, Linda Wittkop.*
✉*e-mail: paul.loubet@chu-nimes.fr*

Published online: 12 July 2021
https://doi.org/10.1038/s41591-021-01435-1

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Acknowledgements

We thank the patients of the ANRS0001S COV-POPART Cohort; the scientific committee of the ANRS0001S COV-POPART Study Group (P. Loubet, O. Launay, L. Wittkop, E. Tartour, B. Parfait, B. Barrou, J.-Y. Blay, M. Hourmant, M. Lachâtre, D.-A. Laplaud, M. Laville, B. Laviolle, J.-D. Lelievre, J. Morel, S. Nguyen, J.-P. Spano, B. Terrier, A. Thiebaut, J.-F. Viallard, F. Vrtovsnik, X. de Lamballerie, M. Vialemaringe, L. Esterle, J. Longobardi, A. Levier, S. Le Mestre, S. Lancrey-Javal, I. Ortega-Perez, A. Bouakane, A. Diallo, L. Meyer, P. Vanhems, A. Trouiller, B. Thevenin Lemoine, E. Buleux, E. Plassart, A.-S. Joly, I. Sartori, J.-F. Thebaut, A. Huet, N. André, L. Vallet, A. de Guerra Remi Slama, D. Deplanque and P. Rossignol); the steering committee of the ANRS0001S COV-POPART Study Group (P. Loubet, O. Launay, L. Wittkop, E. Tartour, X. de Lamballerie, L. Esterle, J. Longobardi, S. Kamal, A.Levier, S. Le Mestre, S. Lancrey-Javal, I. Ortega-Perez, A. Bouakane, B. Parfait, S. Circosta, L.-Victorien Vieillard and A. Boston); the Investigation centers of the ANRS0001S COV-POPART study (CHU Saint Etienne, CHU Besançon, Hôpital Foch, CHU Henri Mondor (APHP), CHU La Pitié-Salpétrière (APHP), CHU Angers, CHU Nantes, CH La Roche sur Yon, CHU Nice, CHU Caen, CHU Clermont-Ferrand, Hospices Civiles de Lyon, CHU Cochin (APHP), CHU Nîmes, Centre Léon Bérard, CHU Bichat (APHP), CHU Saint-Louis (APHP), CHU Tours, CHU Strasbourg, CHU Montpellier, CHU Dijon, CHU Saint-Antoine (APHP), CHU Bordeaux, CHU Toulouse, CHU Lille, Marseille (Assistance Publique–Hôpitaux de Marseille), Hôpital Saint Joseph (Marseille), CHU Grenoble, CHU Nancy, CHU Rouen, CHU Brest, CHU Limoges, CHU Rennes, CHU HEGP (APHP), Clinique Bordeaux Nord, Hôpital Européen de Marseille and Institut Gustave Roussy); and the scientific societies (Société Francophone de Sclérose En Plaques, Fondation ARSEP, Société Francophone de Greffe de Moelle et de Thérapie Cellulaire (SFGM-TC), Société Francophone de Transplantation (SFT), Société Française de Rhumatologie (SFR), Société Française de Néphrologie Dialyze et Transplantation (SFNDT), Société Francophone du diabète, de la Société Française d'endocrinologie, de l'AFERO (association Française d'Études et de recherche pour l'Obésité) et de la Société Française de Nutrition (SFN), FORCE, Société Française Oncologie Médicale, Fédération Francophone de Cancérologie, Société Française du Cancer, Société Française d'Immunologie (SFI), Société de Pathologie Infectieuse de Langue Française (SPILF), Unicancer, LYRICAN (INCA-INSERM DGOS), EURACAN (European Commission)). Funding was received from ANRS | Emerging Infectious Diseases, Ministère des Solidarités et de la Santé and Ministère de l'Enseignement Supérieur, de la Recherche et de l'Innovation.

Competing interests

P.L. has received personal fees as a speaker or consultant from Pfizer and Astrazeneca. J.M. has received honoraria as a speaker or consultant of less than €8,000 from Abbvie, Biogen, Bristol Myers Squibb, Boerhinger Ingelheim, Galapagos, GlaxoSmithKline, Fresenius Kabi, Lilly, Mylan, Novartis, Pfizer and Sanofi, and grants (outside the submitted work) from Lilly and Novartis. J.P.S. has received personal fees as a speaker or consultant from Pfizer and Astrazeneca. O.L. has received personal fees from Sanofi Pasteur; grants, personal fees and non-financial support from Pfizer, Janssen and Sanofi Pasteur–Merck Sharp & Dohme; and grants and non-financial support from GlaxoSmithKline.