High seroconversion rate but low antibody titers after two injections of BNT162b2 (Pfizer-BioNTech) vaccine in patients treated by chemotherapy for solid cancers Authors

Romain Palich, M. Veyri, A. Vozy, S. Marot, J. Gligorov, M.-A. Benderra, P. Maingon, L. Morand-Joubert, Z. Adjoutah, A.-G. Marcelin, et al.

ARTICLE TYPE

Letter

TITLE

High seroconversion rate but low antibody titers after two injections of BNT162b2 (Pfizer-BioNTech) vaccine in patients treated by chemotherapy for solid cancers

Authors

R. Palich[1*], M. Veyri[2*], A. Vozy[2], S. Marot[3], J. Gligorov[4], M.-A. Benderra[4], P. Maingon[5], L. Morand-Joubert[6], Z. Adjoutah[7], A.-G. Marcelin[3], J.-P. Spano[2], J. Barrière[8]

* These two authors have equally contributed to this work.

Affiliations

1. Sorbonne Université, INSERM, Institut Pierre Louis d'Epidémiologie et de Santé Publique (iPLESP), Assistance Publique-Hôpitaux de Paris (AP-HP), Pitié Salpêtrière Hospital, Departments of Medical Oncology and Infectious Diseases, Paris, France
2. Sorbonne Université, INSERM, Institut Pierre Louis d'Epidémiologie et de Santé Publique (iPLESP), Assistance Publique-Hôpitaux de Paris (AP-HP), Pitié Salpêtrière Hospital, Department of Medical Oncology, Institut Universitaire de Cancérologie (IUC), CLIP² Galilée, Paris, France
3. Sorbonne Université, INSERM, Institut Pierre Louis d'Epidémiologie et de Santé Publique (iPLESP), Assistance Publique-Hôpitaux de Paris (AP-HP), Pitié Salpêtrière Hospital, Department of Virology, Paris, France

4. Institut Universitaire de Cancérologie AP-HP. Sorbonne Université, Department of Medical Oncology Tenon Hospital, Inserm U938, , CLIP² Galilée, Paris, France
5. Sorbonne Université, INSERM, Institut Pierre Louis d'Epidémiologie et de Santé Publique (iPLESP), Assistance Publique-Hôpitaux de Paris (AP-HP), Pitié Salpêtrière Hospital, Department of Oncology Radiotherapy, Institut Universitaire de Cancérologie (IUC), CLIP² Galilée, Paris, France
6. Sorbonne Université, INSERM, Institut Pierre Louis d'Epidémiologie et de Santé Publique (iPLESP), Assistance Publique-Hôpitaux de Paris (AP-HP), Saint Antoine Hospital, Department of Virology, Paris, France
7. Department of Biology, Cerballiance, Cagnes-sur-Mer, France
8. Department of Medical Oncology, Polyclinique Saint Jean, Cagnes-sur-Mer, France

Corresponding author

Dr Romain Palich

Medical Oncology department, Pitié-Salpêtrière hospital, 47-83 boulevard de l'hôpital, F-75013 Paris

Tel: +33.1.42.16.01.71, fax: +33.1.42.16.04.45, email: romain.palich@aphp.fr

Words count

561

Key words

Cancer; SARS-CoV-2; COVID-19; mRNA vaccine; Vaccination; Serology

BODY TEXT

Recent data, including ours, showed that patients treated for solid cancers (SCs) had low anti-spike antibody response after a first dose of mRNA SARS-CoV-2 vaccine, with seroconversion rates ranging from 38% to 55%, in comparison with healthy controls having seroconversion rates ranging from 94% to 100% [1–3]. This humoral response was more impaired in elderly and treated by chemotherapy patients. Herein, we aimed to compare the proportion and the level of antibody response 3-4 weeks after the second injection of the BNT162b2 (Pfizer-BioNTech) vaccine in patients with SCs and health volunteers (HVs), as control population.

Patients with SCs on active treatment or with treatment in the two last years and HVs who underwent SARS-CoV-2 vaccination between 05/01/2021 and 02/04/2021 at the Pitié-Salpêtrière et Tenon hospitals, Paris, France, and at the Saint Jean Polyclinic, Nice, France, were selected for analysis. The titration of anti-SARS-CoV-2 antibodies was proposed 3-4 weeks after the second injection of BNT162b2 (Pfizer/BioNTech) vaccine. Anti-spike antibodies were detected using different assays (Supplementary Table). For quantitative analysis, only titrations using the Abbott Elity SARS-CoV-2 immunoglobulin (Ig) G chemiluminescent microparticle immunoassay (CMIA) (detection threshold: 50 UA/mL), and the Roche Elecsys SARS-CoV-2 total Ig electrochemiluminescent immunoassay (ECLIA) (detection threshold: 0.8 U/mL) were retained. Median titers of anti-spike antibodies were compared between patients with SCs and HVs, and between different subpopulations of patients, using Kruskall-Wallis' tests. This study was approved by the "Commission Nationale de l'Informatique et des Libertés" (MR004, registration number: 2221945).

No patients had prior exposition to COVID-19 as none of them had IgG anti-nucleoprotein before vaccination. SARS-CoV-2 antibodies were measured in 223 patients and 49 HVs (Supplementary Table). The median age of patients was 67 years (interquartile range [IQR] 60-

75) years, with 142 women (64%) and 81 men (36%), and 129 (58%) were treated by chemotherapy at time of vaccination. The seroconversion rate was 94% in patients, and 100% in HVs. The 13/223 (6%) non-seroconverters patients were 8 women and 5 men, with age ranging from 45 to 90 years, mostly metastatic (*n*=8), including 10/13 treated by chemotherapy. Titers of anti-spike antibodies were significantly lower in patients with SCs in comparison with HVs, and significantly lower in those receiving chemotherapy (in combination or not with other treatments as targeted therapies), regardless of the assay used (Figure). Titers of anti-spike antibodies did not differ depending on age, gender, cancer location and metastatic status. Only one mild case of COVID-19 occurred after the first injection of vaccine, in a patient with colon cancer.

In summary, the mRNA vaccine boost led to a high seroconversion rate, reinforcing the need not to delay the second dose. However, anti-spike antibody titers were 3-10 times lower in patients with SCs than in healthy controls, raising concerns about impaired humoral immunity, especially in patients treated by chemotherapy. At the same time, the seroconversion data are rather reassuring among patients on anti-HER2, anti PD-1/PD-L1, antiangiogenic treatment or hormone therapy without associated chemotherapy. Nevertheless, correlates of immunity to the SARS-CoV-2 are not still defined, and further studies are required to determine the SARS-CoV-2 correlates of vaccine-induced protection based on neutralizing antibodies and cellular immunity [4]. We still lack hindsight to determine when a third dose (second booster) should be offered in patients with SCs. Pending additional data, we would highly recommend again vaccination for family and friendship circles, to provide an indirect protection against COVID-19 to this population.

TRANSPARENCY DECLARATION

JPS declares he has received advisory fees and meeting invitations from Roche, BMS, MSD, Pfizer, Lilly, PFO, Leo Pharma, Myriads, Biogaran, AZ and Gilead. JG declares he has received advisory fees and meeting invitations from AZ, Exact Science, Lilly, Novartis, Pierre Fabre, Pfizer, Roche and Seagen. All other authors have no conflicts of interest to declare.

Figure. Anti-spike antibody titers in health care workers (HCWs) and cancer patients (CPs), using Roche Elecsys assay (A) and Abbott Alinity assay (B).

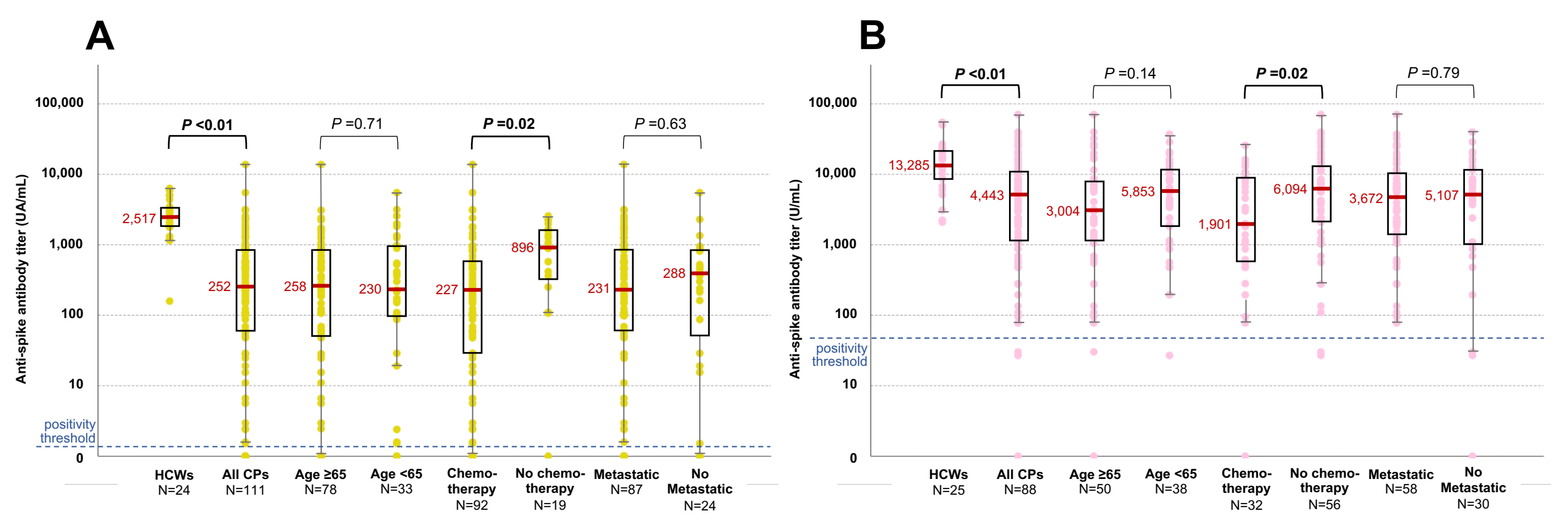
REFERENCES

1. Monin L, Laing AG, Muñoz-Ruiz M et al. Safety and immunogenicity of one versus two doses of the COVID-19 vaccine BNT162b2 for patients with cancer: interim analysis of a prospective observational study. *Lancet Oncol*. 2021;S1470-2045(21)00213-8.

2. Palich R, Veyri M, Marot S et al. Weak immunogenicity after a single dose of SARS-CoV-2 mRNA vaccine in treated cancer patients. *Ann Oncol*. 2021;S0923-7534(21)01184-4.

3. Barrière J, Chamorey E, Adjtoutah Z et al. Impaired immunogenicity of BNT162b2 anti-SARS-CoV-2 vaccine in patients treated for solid tumors. *Ann. Oncol*. 2021;S0923-7534(21)01183-2.

4. Poland GA, Ovsyannikova IG, Kennedy RB. SARS-CoV-2 immunity: review and applications to phase 3 vaccine candidates. *The Lancet*. 2020;396(10262):1595–1606.


A
Anti-spike antibody titer (UA/mL)
100,000
10,000
1,000
100
10
0
positivity threshold
P <0.01
P =0.71
P =0.02
P =0.63
2,517
252
258
230
227
896
231
288
HCWs N=24
All CPs N=111
Age ≥65 N=78
Age <65 N=33
Chemo-therapy N=92
No chemo-therapy N=19
Metastatic N=87
No Metastatic N=24
B
Anti-spike antibody titer (U/mL)
100,000
10,000
1,000
100
10
0
positivity threshold
P <0.01
P =0.14
P =0.02
P =0.79
13,285
4,443
3,004
5,853
1,901
6,094
3,672
5,107
HCWs N=25
All CPs N=88
Age ≥65 N=50
Age <65 N=38
Chemo-therapy N=32
No chemo-therapy N=56
Metastatic N=58
No Metastatic N=30

Supplementary Table. Characteristics of cancer patients and health care workers, with SARS-CoV-2 serological outcomes.

Patients with solid cancers (*N*=223)	
Treatment location, *n*(%)	
- Paris, France	115 (52)
- Nice, France	108 (48)
Gender, *n*(%)	
- Women	142 (64)
- Men	81 (36)
Age, years, median (IQR)	67 (60-75)
Cancer location, *n*(%)	
- Breast	88 (40)
- Digestive	36 (16)
- Lung	31 (14)
- Gynecological	24 (11)
- Prostate	9 (4.0)
- Bladder	8 (3.6)
- Pancreas	8 (3.6)
- Kidney	6 (2.7)
- Upper aero-digestive tract	6 (2.7)
- Others	7 (3.1)
Cancer staging, *n*(%)	
- Local	71 (32)
- Metastatic	152 (68)
Cancer treatment, *n*(%)[1]	
- Chemotherapy	129 (58)
- Targeted therapy[2]	77 (35)
- Immunotherapy[3]	29 (13)
- Hormone therapy	26 (12)
- Radiotherapy	5 (2.2)
- Clinical surveillance	23 (10)
Time between second vaccine injection and SARS-CoV-2 serology, days, median (IQR)	25 (21-29)
Serological assay, *n*(%)	
- Roche[4]	111 (50)
- Abbott[5]	88 (39)
- Other[6]	24 (11)
Negative anti-S IgG, *n*(%)	13 (6)
Healthy volunteers (*N*=49)	
Gender, *n*(%)	
- Women	32 (65)
- Men	17 (35)
Age, years, median (IQR)	53 (47-60)
Time between second vaccine injection and SARS-CoV-2 serology, days, median (IQR)	8 (7-14)
Serological assay, *n*(%)	
- Roche	24 (49)
- Abbott	25 (51)
Negative anti-S IgG, *n*(%)	0 (0)

NOTES. IQR, interquartile range. 1. Non-exclusive categories. 2. Including anti-HER-2, bevacizumab and anti-CDK-4/6 treatments. 3. Including anti-PD-1 and anti-PD-L1 treatments. 4. Roche Elecsys SARS-CoV-2 total Ig electrochemiluminescent immunoassay (ECLIA), with detection threshold: 0.8 U/mL for anti-S Ig. 5. Abbott Alinity SARS-CoV-2 IgG chemiluminescent microparticle immunoassay (CMIA), with detection threshold: 50 UA/mL for anti-S IgG. 6. Including Siemens Atellica SARS-CoV-2 total Ig, Diasorin Liaison SARS-CoV-2 IgG, Beckman SARS-CoV-2 IgG, Biomerieux Vidas SARS-CoV-2 IgG and Ortho Clinical Diagnostics Vitros SARS-CoV-2 IgG assays, with detection threshold according to manufacturers' instructions.