Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Impaired immunogenicity of BNT162b2 anti-SARS-CoV-2 vaccine in patients treated for solid tumors

Patients in the active phase of treatment for cancer are a population at risk of coronavirus disease-19 (COVID-19) with poor prognosis.[1] While a majority of patients treated for cancer expressed their will to be vaccinated as early as December 2020 in a French survey,[2] no data were available in terms of vaccine efficacy and tolerance, because they were excluded from initial registration trials.

From the beginning of French vaccination campaign, we set up a BNT162b2 (Pfizer/BioNtech) vaccine monitoring observatory (VMO) for vaccinated patients under active treatment in the Department of Oncology of the Saint Jean Polyclinic, Nice, France (∼9000 annual treatment sessions). All participants signed a written consent after receiving an information letter and the VMO was registered with the French authorities, according to ethical and legal policies. A control group of healthy volunteers (HVs), i.e. without known ongoing cancer, was also formed and vaccinated during the same period. Serological assays were realized at week (w) 0 during the first vaccination, during the booster (w3-w4) and 3-4 weeks after the booster (w6-w8). Immunogenicity was measured with Elecsys® Anti-SARS-CoV-2 immunoassay (Roche Diagnostics, Mélan, France) with detection of antibodies directed to total antibodies against the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) spike (S) protein receptor-binding domain (quantitative detection). Serum showing a result $\geq$0.8 UI/ml was declared positive.

We report the results of the first 122 assessable patients with solid tumors included since 18 January 2021 having carried out at least two serologies by 15 March 2021 out of 194 vaccinated patients during this period (64.4%). Three patients were excluded from the final analysis because they had pre-vaccine anti-SARS-CoV-2 immunity. The median age of the 122 patients was 69.5 years (44-90 years), with 64 men (52.5%) and 58 women (47.5%). We analyzed 31 HVs; 2 were excluded from the analysis because they had pre-vaccine immunity against SARS-CoV-2. Among the remaining 29 HVs with a median age of 53 years (range: 21-81 years), 13 carried out the intermediate assessment at w3-w4 and 24 carried out their final w6-w8 assessment.

Among the 122 patients, 105 (86.0%) were treated with chemotherapy (CT) ± targeted therapy. One patient developed COVID-19 with a positive PCR at day 12 from vaccine dose 1. The outcome was quickly favorable and the patient had his booster dose at w3. During the first

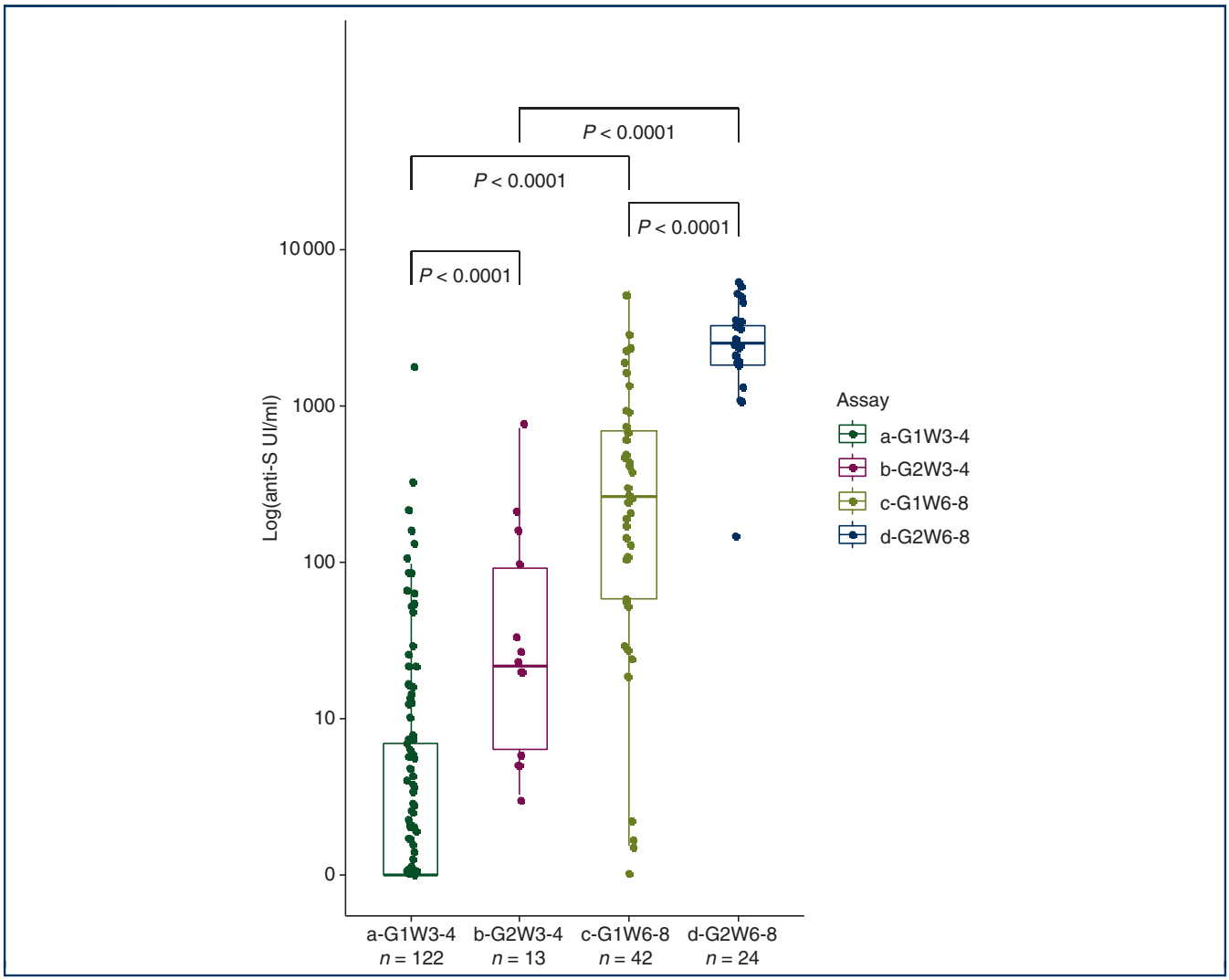

Figure 1. Humoral quantitative anti-spike (S) antibody (logarithmic scale) response at week (w) 3-w4 and w6-w8 from dose 1 of BNT162b2 (Pfizer/BioNtech) messenger RNA (mRNA) vaccine in patients with active treatment for cancer (G1; $n = 122$) and in a healthy volunteer (HV) group (G2; $n = 24$).
a-G1W3-4: cohort of patients with active treatment for cancer at w3-w4/from dose 1 of BNT162b2 (Pfizer/BioNtech) mRNA vaccine (date of booster dose); b-G2W3-4: HV group at w3-w4; c-G1W6-8: cohort of patients at w6-w8 from dose 1 of vaccine; d-G2W6-8: HV group at w6-w8.

serological analysis at w3-w4, 58 [47.5%, 95% confidence interval (CI) 38.4-56.8] patients had an anti-S seroconversion. After recall at w6-w8, 40 (95.2%, 95% CI 83.8-99.4) of the analyzable patients presented an anti-S seroconversion; 2 patients kept an anti-S level <0.8 IU/ml. In comparison with the control group, 13 (100.0%, 95% CI 75.3-100.0) patients had an anti-S seroconversion at w3-w4 and 24 (100.0%, 95% CI 85.7-99.4) at w6-w8. Fewer patients under CT had an anti-S seroconversion at w3-w4 than patients without CT, and with targeted therapy alone (42.9% versus 76.5%; $P = 0.016$).

Median anti-S antibody levels were significantly lower than the levels observed in the HV group at w3-w4 (0.52 UI/ml, range: 0-1962 UI/ml, respectively, versus 21.6 UI/ml, range: 3.26-723.2 UI/ml, $P < 0.001$) and at w6-w8 (245.2 UI/ml, range: 0-5467 UI/ml, respectively, versus 2517 UI/ml, range: 157.6-6318.0 UI/ml, $P < 0.001$) (Figure 1). After the booster dose, the median anti-S antibody levels increased significantly for both patients and HVs ($P < 0.001$).

No serious adverse event was reported.

Impaired immunogenicity of BNT162b2 anti-SARS-CoV-2 vaccine in immunocompromised patients was reported among solid organ transplant recipients.[3] Among patients under cancer therapy, influenza vaccine was less efficient compared to the whole population.[4] Considering the high proportion of weakly responsive or unresponsive patients in this setting after a single dose, patients should be informed of the need to maintain strict social protection measures for at least 6-8 weeks after the first dose of the vaccine and we strongly recommend not to shift the booster dose schedule in patients under CT. The duration of immunity acquired under CT as well as the level of protection against the different SARS-CoV-2 variants are unknown. As already shown for influenza vaccine,[5] efficacy of a second booster dose (third dose) has to be studied.

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Checkpoint inhibition: protecting against or predisposing for second primary tumors? Reply to the Letter to the Editor 'Checkpoint inhibition: protecting against or predisposing for second primary tumors?' by K. P. M. Suijkerbuijk, A. M. May and M. J. M. van Eijs

We thank Dr Suijkerbuijk and collaborators for their comments on our letter 'Reduced risk of second primary cancer (SPC) in patients treated with immune checkpoint inhibitors (ICIs) for a first cancer' and for this opportunity to clarify several aspects of this work.[1,2] More data of this analysis are now reported.[3] We agree with the points they raise.

Indeed, the analysis by an automatic language processing tool may introduce biases. Of note, the majority of data (patient characteristics, treatments) extracted from the electronic patient records were structured data. For the diagnosis of SPC, we secured the extraction by confirming manually the presence or absence of a diagnosis of SPC: (i) in all patients treated with ICIs, and (ii) for all 1830 SPCs identified with ConSoRe.[4]

There was indeed no manual screening of SPC in other patients, which may have underestimated the number of SPC in patients not treated with ICIs in this series, and therefore underestimated the 'protective' impact of ICIs on the risk of SPC. ConSoRe uses more stringent criteria for the identification of SPC for patients with metastasis. We ran a novel analysis with less stringent criteria on the set of patients with metastasis to explore whether more SPC would be identified. Eighty new SPCs were thus identified in the metastatic group and confirmed manually. All were in the non-immunotherapy group. The immunotherapy group had been screened manually before as mentioned. Forty-two were diagnosed in the first 6 months after the first primary cancer (FPC), i.e. in the landmark period, leaving 38 patients with SPC in the metastatic group untreated with ICIs in the observation period (Figure 1).

No significant reduction of the number of SPCs is observed in patients treated with immunotherapy for their FPC in the metastatic phase (Figure 1). The reduction of SPC is significant only for patients for whom ICIs were given for localized disease, possibly because of the metastatic