Weak immunogenicity after a single dose of SARS-CoV-2 mRNA vaccine in treated cancer patients

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BODY TEXT

Active cancer and ongoing antineoplastic treatments are major factors for severe COVID-19 and death, reason why the SARS-CoV-2 vaccination remains a priority in cancer patients (CPs) [1]. However, immunocompromised patients were excluded from main studies on mRNA vaccines [2,3], and could have a decreased response to vaccination, as recently demonstrated in solid organ transplant recipients [4]. Herein, we aimed to assess the proportion of antibody response 4 weeks after the first injection of the BNT162b2 (Pfizer-BioNTech) vaccine in CPs and health care workers (HCWs), as control population.

All consecutive patients with cancer on active treatment or with treatment in the two last years and HCWs who underwent SARS-CoV-2 vaccination between 17/02/2021 and 18/03/2021 at the Pitié-Salpêtrière hospital, Paris, France, were selected for analysis. The titration of SARS-CoV-2 antibodies was proposed just before the second injection of BNT162b2 vaccine. Serum anti-nucleoprotein (N) IgG and anti-spike protein (S) IgG against the receptor binding domain (RBD) of the S1 domain were detected usingthe Abbott SARS-CoV-2 IgG chemiluminescent microparticle immunoassay (CMIA), according to the manufacturer's instructions. The presence of anti-N IgG was used as a surrogate marker of prior COVID-19.

Statistical analysis consisted in univariable analysis (Khi-2 tests) and then multivariable analysis (binary logistic regression, including all variables with p-value<0.1 in univariable analysis) in order to determine the factors associated with the lack of seroconversion in CPs. Median titers of anti-S IgG were compared between CPs and HCWs, using a Mood's test. This study was approved by the "Commission Nationale de l'Informatique et des Libertés" (MR004, registration number: 2221945).

SARS-CoV-2 antibodies were measured in 110 CPs and 25 HCWs (Table). In CPs who did not have COVID-19 before vaccination, the seroconversion rate was only 55%, while it reached

100% in HCWs. Titers of anti-S IgG were significantly higher in HCWs in comparison with seropositive CPs (680 *versus* 315 UA/mL, p=0.04). Gender, cancer locations and metastatic status were similar in seroconverters and non-seroconverters CPs (Supplementary Table). After adjustment for potential confounders, two factors were strongly associated with no seroconversion: age over 65 (odds-ratio 3.58, 95%CI 1.40-9.15, p=0.008) and treatment by chemotherapy (odds-ratio 4.34, 95%CI 1.67-11.30, p=0.003).

No symptomatic COVID-19 occurred between the two injections of vaccine in CPs and HCWs.

In summary, almost half CPs showed no anti-spike antibody response after a first injection of BNT162b2 vaccine, and this low seroconversion rate could be much worse in elderly patients and in patients under chemotherapy. In comparison, 100% of the HCWs had anti-spike seroconversion. Moreover, even in CPs with seroconversion, the level of antibody response could be lower than expected.

In conclusion, our findings argue for not extending the 21-day period between the two SARS-CoV-2 vaccine injections in CPs, and for performing serological monitoring to assess antibody response in this particular population, that could lead to adapt the vaccine strategy. We would also recommend vaccination for family and friendship circles.

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. All other authors have no conflicts of interest to declare.

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

Cancer patients (*N*=110)	
Gender, *n*(%)	
- Women	66 (60)
- Men	44 (40)
Age, years, median (IQR)	66 (54-74)
Cancer location, *n*(%)[1]	
- Breast	37 (34)
- Lung	15 (14)
- Gynecological	15 (14)
- Prostate	11 (10)
- Digestive	8 (7.3)
- Kidney	7 (6.4)
- Bladder	5 (4.5)
- Upper aero-digestive tract	6 (5.5)
- Thyroid	5 (4.5)
- Others	3 (2.7)
Cancer staging, *n*(%)	
- Local	47 (43)
- Metastatic	63 (57)
Cancer treatment, *n*(%)[2]	
- Chemotherapy	38 (35)
- Targeted therapy	26 (24)
- Immunotherapy	17 (16)
- Hormonotherapy	16 (15)
- Radiotherapy	6 (5.5)
- Clinical surveillance	18 (16)
Time between first vaccine injection and SARS-CoV-2 serology, days, median (IQR)	27 (26-28)
Positive anti-N IgG, *n*(%)[3]	15 (14)
Positive anti-S IgG, *n*(%)[3]	
- In all patients	64 (58)
- Among patients with positive anti-N IgG (*N*=15)	12 (80)
- Among patients with negative anti-N IgG (*N*=95)	52 (55)
Titer of anti-S IgG, UA/mL, median (IQR)	
- In all anti-S positive patients (*N*=64)	359 (178-998)
- Among patients with positive anti-N IgG (*N*=12)	657 (366-14,112)
- Among patients with negative anti-N IgG (*N*=52)	315 (140-748)
Health care workers (*N*=25)	
Gender, *n*(%)	
- Women	18 (72)
- Men	7 (28)
Age, years, median (IQR)	55 (38-62)
Time between first vaccine injection and SARS-CoV-2 serology, days, median (IQR)	23 (21-27)
Positive anti-N IgG, *n*(%)[3]	0 (0)
Positive anti-S IgG, *n*(%)[3]	25 (100)
Titer of anti-S IgG, UA/mL, median (IQR)	680 (360-930)

NOTES. IQR, interquartile range. 1. Two patients had synchronous cancers (prostate + lung and prostate + colon). 2. Non-exclusive categories. 3. Abbott SARS-CoV-2 IgG chemiluminescent microparticle immunoassay (CMIA), with detection threshold: 0.8 UA/mL for anti-N IgG, and detection threshold: 50 UA/mL for anti-S IgG.

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Supplementary Table. Uni- and multivariable logistic regression of cancer patients' characteristics in relation with the non-seroconversion after the first injection of BNT162b2 vaccine.

	Univariable analysis		Multivariable analysis	
	Odd-ratio (95%CI)	*p*-value	Odd-ratio (95%CI)	*p*-value
Gender				
- Women	Ref.			
- Men	0.96 (0.56-1.64)	0.87		
Age				
- <65 years	Ref.			
- ≥65 years	**1.56 (1.04-2.33)**	**0.03**	**3.58 (1.40-9.15)[1]**	**0.008**
Cancer location				
- Breast	0.91 (0.53-1.55)	0.72		
- Lung	1.21 (0.46-3.18)	0.70		
- Gynecological	0.67 (0.24-1.86)	0.44		
- Prostate	1.21 (0.32-4.55)	0.78		
Cancer staging				
- Local	Ref.			
- Metastatic	0.89 (0.61-1.29)	0.53		
Cancer treatment				
- Chemotherapy	**1.99 (1.17-3.34)**	**0.008**	**4.34 (1.67-11.30)[2]**	**0.003**
- Targeted therapy	0.84 (0.40-1.77)	0.64		
- Immunotherapy	1.21 (0.42-3.48)	0.72		
- Hormonotherapy	0.54 (0.18-1.63)	0.26		
- Radiotherapy	2.42 (0.47-12.58)	0.28		
- Clinical surveillance	0.48 (0.16-1.43)	0.17		

NOTES. 1. After adjustment for cancer treatment. 2. After adjustment for age.