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.

European Journal of Cancer 165 (2022) 25–26

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.ejcancer.com

Letter to the Editor

Omicron variant: A clear and present danger for patients with cancer

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Received 13 January 2022; accepted 18 January 2022
Available online 18 February 2022

Dear Editor,

Protection of patients with cancer against SARS-CoV-2 infection has been a priority for oncologists since early 2020. Recently, we have recommended to prioritise patients under active treatment to receive an early third vaccine dose if anti-Spike (S) antibody titers <260 binding antibody units (BAU) per millilitre [1]. The adoption of a complete accelerated vaccine scheme for these patients sought to enable them to face the Delta variant of concern (VOC).

The emergence by late November 2021 of the Omicron VOC [2] with partial or major immune escape properties [3], potentially resulting in reinfection of previously infected or vaccinated patients, has prompted us to formulate new recommendations as to what the reactive answer to this major threat should be with respect to patients with cancer.

We would like to draw the oncologic community's attention to the supplementary risk of Omicron-related severe COVID-19 for patients with cancer or haematologic malignancies. Anticipating increased infections, transmissibility, and immune escape, we propose five recommendations for health authorities and healthcare workers:

Proposition 1: Considering the lower median anti-S titer after two vaccine doses in cancer patients, versus general population [4], **a third vaccine dose should be given to all cancer patients as soon as 3–4 months post-second dose (Dose 2), including residual serum anti-S antibody controls, 3 months later**. The available data indicate faster waning immunity toward Omicron VOC versus Delta strain yet increased protection after booster dosing (Dose 3) [5]. Anti-S antibody levels after the third vaccine jab were increased nine-fold versus anti-S serum titers measured after Dose 2 in general population [6]. Some cancer patients show clear benefits from booster dosing,

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https://doi.org/10.1016/j.ejca.2022.01.010

reflected by increased anti-S antibody levels, even when still undergoing chemotherapy, such levels exceeding the concentrations reached after two vaccine doses [7].

Proposition 2: **Set the threshold of serum anti-SARS-CoV-2 S (anti-S) titers at 1000 BAU/mL, this being the level below which an additional vaccine shot (dose 4) should be indicated**. Such cut-off corresponds to titers obtained at 3–4 months after Dose 2 in a population without comorbidities [8] to whom Dose 3 administration is currently proposed in most developed countries to ensure optimal protection against Omicron. Such cut-off could be retained for administering an additional vaccine jab to immune-compromised patients with cancer, regardless of the timing and even earlier than 4 months post-last dose. This would then be Dose 4. Although a high rate of lymphoid malignancy patients under anti-CD20 treatment fail to respond to vaccination, even after a third jab [9], administrating a Dose 4 could display a low (but not null) probability of being efficient in this subgroup.

Proposition 3: **Support pre-exposition prophylaxis using the monoclonal antibody (mAB) combination** tixagevimab/cilgavimab (EVUSHELD, AstraZeneca) for patients with cancer without seroconversion after Dose 3 or 4. Such combination of long-acting anti-S mAbs proves highly efficient *in vitro* on Delta VOC whilst being less affected in terms of *in vitro* neutralisation by numerous Omicron S mutations [4]. Depending on clinical results concerning Omicron resistance, we may need to promptly prioritise sotrovimab mAb (XEVUDY, GSK), which retains *in vitro* neutralisation potency versus Omicron [4].

Proposition 4: **A three-dose complete vaccination for patients' relatives** should be proposed as early as 4 months post-Dose 2. In addition, we recommend vaccination of children aged 5–11 years, when in close, usual contact, with immune-compromised parents, in accordance with most Scientific Pediatric Societies, and US (Food and Drug Administration) and European Medecines Agency (EMA) Health agencies.

Proposition 5: **A high-protection mask, such as Filtering Face Piece Type 2 (FFP2)/mask not resistant to oil filtering at least 95% of particles (N95)**, should be used by patients. Wearing such a mask should be mandatory in audience-receiving sites and public or private transportation (when shared with other people). Recent comparative data support superior individual protection with such masks versus surgical ones [10]. Such superior protection is likely interesting considering Omicron infectiousness. This recommendation is based on a precautionary principle justified by expert consensus because of the very high circulation of a highly infectious viral pathogen such as Omicron to provide optimal protection of the most immune-compromised patients.

Implementing such propositions will help better protect patients with cancer, especially those receiving systemic treatments. We strongly believe that in no time, the Omicron virus will invade the whole planet, being especially threatening to the more fragile immunocompromised patients who possibly are incompletely protected by COVID-19 vaccines. We cannot wait any longer for large-scale prospective studies to disclose their results, as the threat is immediate, as close as January 2022.

Funding/support

None.

Conflict of interest statement

Authors have nothing to disclose.

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