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Efficacy of the mRNA SARS-CoV-2 vaccine in cancer patients during systemic therapy. A single-centre experience

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Introduction. A novel coronavirus, causing severe acute respiratory syndrome 2 (SARS-CoV-2) has spread globally since its emergence in December 2019. The mRNA SARS-CoV-2 vaccines have been proven to be an efficient and safe disease control means among adult patients without immunocompromising conditions. However, cancer patients were among the group of people that was initially excluded from the registration trials.

Material and methods. 60 patients, enrolled to this study, had been voluntarily vaccinated either with the BNT162b2 or mRNA-1273 SARS-CoV-2 vaccine between March and June 2021 and have been undergoing systemic treatment in the Clinical Oncology Unit of the University Clinical Center of the Medical University of Silesia in Katowice, Poland. Patients received 2 injections of vaccine 21 days apart and were tested with Elecsys® Anti-SARS-CoV-2 immunoassay (Roche Diagnostics, France) for the presence of anti-S-protein antibodies in the patients' serum. The serum samples were collected 2 to 8 weeks after receiving the second dose of vaccine.

Results. The BNT162b2 vaccine was administered to 57 patients, while the mRNA-1273 vaccine – to 3 patients. Seroconversion was achieved in 83.33% of patients. The median amount of anti-S-protein antibodies was 75,9 U/ml.There were no statistically significant differences in terms of age between the group with seroconversion and the group without seroconversion (Mann-Whitney U-test p = 0.762). There was no statistically significant correlation between neither the BMI (Spearman test, p = 0.079) norage (Spearman test, p = 0.762) and anti-S-protein antibody levels. Just as the diagnosis (primary tumor localization), clinical stage, type of modality (chemotherapy, chemoradiotherapy, immunotherapy) and the goal of treatment (radical, palliative) were not statistically significant in terms of anti-S-protein antibody levels.

Conclusions. Due to the high number of unresponsive or poorly responsive results, patients undergoing systemic therapy should be advised to maintain other measures of disease control such as distancing, usage of masks. Nevertheless, implementing mRNA SARS-CoV-2 vaccinesinimmunocompromised patientsduring systemic therapyis reasoned, valuable and safe.

Key words: cancer patients, systemic therapy, SARS-CoV-2, COVID-19, SARS-CoV-2 vaccine

Introduction

A novel coronavirus, causing severe acute respiratory syndrome 2 (SARS-CoV-2) has spread globally since its emergence in December 2019, affecting our lives dramatically [1]. Until now it has infected 650 million people worldwide [2]. Since then, governments have applied several control measures such as distancing, usage of masks, testing of exposed or symptomatic patients, isolation of symptomatic patients and vaccination programs.

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The mRNA SARS-CoV-2 vaccines have been proven to be an efficient and safe disease control means among adult patients without immunocompromising conditions. Their effectiveness has been reported to oscillate around 95%. However, cancer patients were among the group of people that was initially excluded from the registration trials [3, 4]. Therefore, vaccine efficacy among patients in this group remains unclear.

What is more, cancer patients are also at greater risk of COVID-19 infection and worse outcomes of treatment [5, 6]. Therefore, it is implied that SARS-CoV-2 vaccination of patients treated with antineoplastic drugs should be prioritized [7, 8]. That is why the Ministry of Health in Poland in 05.03.2021 implemented guidelines encouraging cancer patients to be the first group of patients vaccinated in Poland, beside elderly citizens and health care workers [9].

Material and methods

There were 60 patients who were enrolled in this study. We have included the patients who were voluntarily vaccinated either with BNT162b2 or mRNA-1273 SARS-CoV-2 vaccine between March and June 2021, according to the Polish SARS-CoV-2 vaccination program conducted by the Polish Ministry of Health and were currently undergoing systemic treatment in the Clinical Oncology Unit of the University Clinical Center of the Medical University of Silesia in Katowice, Poland [9]. According to the vaccination program, patients undergoing chemotherapy were vaccinated between the third and seventh day from the last received chemotherapy infusion. Patients undergoing immunotherapy could be vaccinated at any time during their treatment.

Patients received 2 vaccine injections 21 days apart and were tested with Elecsys® Anti-SARS-CoV-2 immunoassay (Roche Diagnostics, France) for the presence of anti-S-protein antibodies in their serum. The serum samples were collected 2 to 8 weeks after receiving the second dose of the vaccine. The test used to determine levels of anti-S-protein antibodies was an electrochemiluminescent immunoassay. Its positive cutoff value was set at 0.80 U/mL, according to procedures guidelines.

We have collected demographic data such as the patients' sex, age, height, weight. Data concerning the oncologic treatment included the diagnosis, clinical stage, type of therapy carried out (chemotherapy, chemoradiotherapy, immunotherapy) and the goal of treatment (radical, palliative) were included in the analysis. We measured the time of receiving the second injection of the vaccine after the last dose of systemic treatment.

The Mann-Whitney U-test for comparing two groups or the Kruskal-Wallis ANOVA test for multi-group comparisons was used to compare quantitative variables. The relationships between quantitative variables were analyzed using the Spearman's rank correlation coefficient. The Chi^2 test and its variants were used to compare the qualitative data. The analysis was performed using STATISTICA 13.3 software (TIBCO software). The $p < 0.05$ values were considered significant.

Results

There were 60 patients included in the statistical analysis – 36 women and 24 men. Demographic details are presented in table I.

The BNT162b2 vaccine was administered to 57 patients, while the mRNA-1273 vaccine – to 3 patients. Seroconversion, defined as the amount of anti-S-protein antibodies above 0.80 U/ml was achieved in 83.33% of patients. The median amount of anti-S-protein antibodies was 75.9 U/ml, (min. –max. range: 0.4–2500 U/ml). There were no statistically significant differences in terms of age between the group with seroconversion and the group without seroconversion (Mann-Whitney U-test, $p = 0.762$). There was no statistically significant correlation between the body-mass index (BMI) and anti-S-protein antibody levels (Spearman test, $p = 0.079$) or age and anti-S-protein antibody levels (Spearman test, $p = 0.762$). Data concerning differences in anti-S-protein antibody levels among different diagnostic groups are pre-

Table I. Demographic data

Parameter	Total	Females	Males
sex	60	36	24
age (years)	• median: 63 • min.–max.: 33–78 • interquartile range: 54.5–67.5	• median: 62 • min.–max.: 35–78 • interquartile range: 51–67	• median: 63.5 • min.–max.: 33–78 • interquartile range: 59–68
weight (kg)	• median: 71 • min.–max.: 47–137 • interquartile range: 59-81.5	• median: 66 • min.–max.: 47–121 • interquartile range: 58.5–76.5	• median: 74 • min.–max.: 50–137 • interquartile range: 68–86.5
BMI (kg/m^2)	• median: 25.36 • min.–max.: 17.47–54.5 • interquartile range: 22.32–28.84	• median: 25.39 • min.–max.: 17.47–54.5 • interquartile range: 22.02–29.39	• median: 25.04 • min. –max.: 17.96–39.18 • interquartile range: 23.22–27.53

Table II. Antibody levels and vaccination efficacy according to patient diagnosis

Diagnostic group (nr of patients)	Anti-S-protein antibody level [U/ml]	% of levels above 0.8 U/ml
breast cancer (14)	• median: 64.86 • min.–max.: 0.4–1,200	71.4%
lung cancer (9)	• median: 76.08 • min.–max.: 0.25–2,500	77.7%
gastrointestinal cancers (24)	• median: 39.77 • min.–max.: 0.4–2,500	91.67%
gynecologic cancers (7)	• median: 39.77 • min.–max.: 0.4–168.3	71.43%

*There were 2 cases of head and neck cancers, 2 cases of NET, 1 case of seminoma and 1 case of AB type metastatic thymoma that are not shown in the table

sented in table II. The differences were not statistically significant (ANOVA Kruskal-Wallis, p = 0.125). The difference in vaccination efficacy between patients diagnosed with gastrointestinal cancers and other patients is not statistically significant (Fisher's exact test, p = 0.144) (tab. II). There were no statistically significant differences between groups with different clinical stages of the disease in terms of antibody levels. Details of this analysis is presented in table III.

The difference in vaccination efficacy between patients in II stage of the disease and other patients is not statistically significant (Fisher's exact test, p = 0.166). There were no statistically significant differences in terms of anti-S-protein antibody levels between patients with palliative and radical intention of treatment (Mann-Whitney U-test, p = 0.326). Table IV presents data regarding different modalities of treatment. There were no statistically significant differences between those groups (ANOVA Kruskal-Wallis, p = 0.268).

The median time between receiving a second injection of the vaccine and the last course of systemic therapy was 10 days (mean: 10.05, min.–max.: 0–46 days). This parameter was not correlated with any level of detected antibodies (Spearman test, p = 0.09). There were no severe adverse events connected with mRNA SARS-CoV-2 vaccinations reported by patients.

Discussion

According to registration trials, the mRNA SARS-CoV-2 vaccine is an effective and safe mean of disease control. Its efficacy was determined at to be 95% (BNT162b2 vaccine) and 94.1% (mRNA-1,273 vaccine).

Those studies as the primary end points had serologic or virologic evidence of SARS-CoV-2 infection or presence of COVID-19 symptoms [3, 4]. We have based our study on detecting seroconversion after at least 2 weeks of receiving the second dose of the vaccination. It was detected in 83.33% of tested patients and there were no statistically significant

Table III. Antibody levels and vaccination efficacy according to clinical stage of the diseases

Clinical stage (number of patients)	Anti-S-protein antibody level [U/ml]	% of levels above 0.8 U/ml
I (6)	• median: 75.9 • min.–max.: 0.4–2,500	83.33%
II (9)	• median: 47.6 • min.–max.: 0.4–1,200	66.67%
III (18)	• median: 55.3 • min.–max.: 0.5–2,500	88.89%
IV (27)	• median: 96.8 • min.–max.: 0.2–2500	85.18%

Table IV. Antibody levels and vaccination efficacy according to treatment modality

Treatment modality (number of patients)	Anti-S-protein antibody level [U/ml]	% of levels above 0.8 U/ml
chemotherapy (42)	• median: 71.1 • min.–max.: 0.4–2,500	80.92%
chemoradiotherapy (2)	• median: 16.3 • min.–max.: 8.7–23.9	100%
immunotherapy (12)	• median: 79.1 • min.–max.: 0.25–2,500	83.33%
chemotherapy with concurrent immunotherapy (4)	• median: 561.6 • min.–max.: 39.7–2,500	100%

differences within secondary analyses performed in this study. This stands in accordance with other studies conducted on patients with immunocompromised conditions. In Barrière's et al. study, 47.5% of patients had anti-S-seroconversion after 3 to 4 weeks, and 95.2% after 6 to 8 weeks after the second dose of the vaccination. What is more, antibody levels were significantly lower compared to the control group consisting of people with no known immunocompromising condition [10].

In Monin's et al. study, seroconversion after the first dose of the vaccination was observed in 35% of cancer patients and in 95% after the booster – 21 days after the 1st injection [11]. According to Addeo et al., seroconversion was observed in 94% of patients after the receipt of two doses of vaccine [12].

Differences between our study and the cited examples may be caused by used methodology. We did not differentiate between patients tested after 2 or 8 weeks after the 2nd dose of the vaccine. Agbarya et al. provided data suggesting that up to 23.3% of patients were seronegative after the second dose of the vaccination [13]. Those results are also compliant with a systemic review by Tran et al. In their study, there were 21 works included providing data from a total of 2,309 patients with solid cancer. Seroconversion after the second dose of the vaccine was observed in 91–97% of patients [14]. The comparison of study results are presented in table V.

Table V. Comparison of study results

Author	Year	Seroconversion in cancer patients	Seroconversion in the control group	Malignancy
Addeo et al. [12]	2021	94%	–	solid tumor and hematologic malignancies
Ariamanesh et al. [15]	2021	86.9%	–	hematologic malignancies
Barrière et al. [10]	2021	95.2%	–	solid tumor
Cai et al. [16]	2022	83.3%	96.3%	solid tumor
Massarweh et al. [17]	2021	90%	100%	solid tumor
Monin et al. [11]	2021	95%	100%	solid tumor
Schmueli et al. [18]	2021	84.1%	98.9%	solid tumor
Waldhorn [19]	2021	79%	84%	solid tumor
Yasin et al. [20]	2022	85.2%	97.5%	solid tumor
this study	2023	83.33%	–	solid tumor

We did not observe any association between the seroconversion rate and age or chemotherapy in our study, which stands in contrast with a study by Yasim et al. [20]. This may be due to differences in the patient population size enrolled in the studies, which was larger in Yasim's study. Similar effects were also detected in studies by Massarweh et al., Ariamanesh et al. and Buttiron Webber et al. [15, 17, 21]. The results of this study are also similar to studies on the influenza vaccination in patients undergoing chemotherapy [22, 23]. The goal of treatment (radical or palliative) or the patients' age did also not affect the results of the vaccination [23]. In our study there was no correlation between BMI and the amount of anti-S antibodies detected. In the large prospective study by Nilles et al., after adjusted analysis there was no evidence of increased seroprevalence with increasing BMI among tested patients. There was also no statistically significant differences between seropositive obese and non-obese patients in terms of peak SARS-CoV-2 IgG titters [24].

Unfortunately, some patients did not follow the Ministry of Health recommendations and had themselves vaccinated within 2 days of finishing the last dose of systemic treatment. There were seven cases of such practice in our study, but only in one case was anti-S-protein antibodies undetectable (a 68-year-old male patient, treated with chemotherapy due to CS III lung cancer, sequential chemoradiation).

Conclusions

Due to the high number of unresponsive or poorly responsive results, patients undergoing systemic therapy should be advised to maintain other measures of disease control such as social distancing and the use of masks. Swab testing of asymptomatic patients should be considered before admission to the hospital. The duration of immunity after receiving a 2-dose regimen remains unknown and requires further studies.

Conflict of interest: none declared. Elecsys® Anti-SARS-CoV-2 immunoassay tests were provided by Roche.

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