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# COVID-19 vaccination in patients with breast cancer and gynecological malignancies: A German perspective



BREAST

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#### ABSTRACT

*Introduction:* The side effects of systemic cancer therapy and the lack of clinical data on safety and efficacy of COVID-19 vaccination in cancer patients cause uncertainty among the patients about whether to get vaccinated or not. Here, we evaluated attitude towards and effects of COVID-19 vaccination in patients with breast and gynecological cancer undergoing systemic cancer therapy.

*Methods:* Since March 15th, 2021, cancer patients who received one of the approved COVID-19 vaccines were routinely interviewed about immediate and late side effects. Clinical parameters such as current therapy, time interval between therapy administration and vaccination, and changes in the therapy schedule due to vaccination were documented. The collected data were analyzed de-identified as a part of routine quality assurance.

*Results:* By July 27th, 2021, 218 patients (74.3% breast cancer patients) had received one of two COVID-19 vaccine doses, and 112 patients had received both doses: 77.5% received Conmirnaty (BioNTech/Pfizer), 16.1% Vaxzevria (Astra Zeneca) and 5.9% COVID-19 Vaccine Moderna. The COVID-19 vaccines had an acceptable safety profile with self-limiting local and systemic adverse events, which rarely lasted >48 h post vaccination. Symptoms occurred predominantly after the second dose of the vaccine and less frequently in older patients >55 years. No vaccine-related serious adverse events were reported, and only limited effects of vaccination on the therapy schedule were observed.

*Conclusions:* Breast and gynecologic cancer patients tolerate the COVID-19 vaccination while undergoing systemic cancer therapy without any additional side effects beyond those reported in the general population.

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#### 1. Introduction

The COVID-19 pandemic has measurable consequences on oncological care as well as the lives of cancer patients [1]. Oncological patients are specifically at risk of developing severe COVID-19 disease due to immunosuppression, caused by either the disease itself or the treatment [2,3]. Additionally, delays in both surgery and systemic therapy in hospitals were reported [4]. Other delays are due to patient concerns of COVID-19 infection during admission to the hospital, causing them to postpone necessary diagnostics,

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treatment, or follow-up visits, which subsequently may affect disease prognosis [5,6]. COVID-19 vaccination is thus an important factor in maintaining and improving cancer care during the COVID-19 pandemic.

As of July 2021, there are four vaccines which gained European Medicines Agency (EMA) approval: Conmirnaty by Pfizer on 12/21/20, COVID-19 vaccine Moderna on 01/06/21, Vaxzevria by Astra Zeneca on 01/29/21, and the Janssen COVID-19 vaccine on 03/11/21 [7].

By March 4th, 2021, vaccination of the second priority group, including cancer patients, was initiated in Germany. While many of the cancer patients receiving treatment were registered to receive the COVID-19 vaccine, a considerable number of patients was still reluctant to obtain it. Although the timing of vaccine



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administration during standard of care for cancer patients has been described by the recommendations of major oncologic societies [8], past and ongoing vaccine safety and efficacy clinical trials have excluded patients undergoing anticancer treatment [9,10]. To emulate the attitude of the patients towards vaccination and subsequently improve our counselling regarding COVID-19 vaccination, we collected parameters such as the willingness to be vaccinated and the side effects of the vaccine during anticancer treatment. As part of a quality assurance project, we aimed to evaluate whether COVID-19 vaccination of patients undergoing systemic oncologic therapy was associated with stronger adverse events than those reported for the general population or with substantial delays in therapy administration.

### 2. Methods

#### 2.1. Study population and data collection

Interviews regarding COVID-19 vaccination were performed as part of routine care and quality assurance in breast and gynecological cancer patients between March 15th, 2021, and July 28th, 2021. All data were collected routinely from patients receiving therapy at the two oncology outpatient clinics of the Department of OB&GYN, Ludwig-Maximilians-University (LMU) Hospital in Munich, Germany (Supplementary Fig.1). Information provided by the patients was documented and saved in the patients' electronic record. The data were de-identified for analysis.

Clinical parameters such as age, cancer type, stage at diagnosis, current therapy, type of vaccine, time between oncological therapy administration and vaccination, as well as changes in the therapy schedule due to vaccination were assessed. Furthermore, the will-ingness of non-vaccinated patients to be vaccinated was determined. Data collection on COVID-19 vaccination was performed in a two-tiered fashion (Fig. 1): First, the attitude of non-vaccinated patients towards vaccination was explicitly addressed and

assessed in routine doctor-patient discussions. Second, patients who had already received vaccination were interviewed about immediate (0-2 days) and late (within two weeks after vaccination) adverse events, as well as the effects of the vaccine on the schedule of oncologic treatment. Patients who had received the vaccine before their start of anti-cancer therapy were included as well. Symptoms were subjectively assessed by the patients themselves.

#### 2.2. Study definitions

In line with the pivotal trials that investigated the safety and efficacy of the above-mentioned vaccines, patients included in our analysis were divided into two age groups, 18–55 years and >55 years. Patients with breast and gynecological cancer were included in the study; types of anti-cancer therapy included neoadjuvant, adjuvant, and maintenance therapy as well as therapy for locally recurrent or metastatic disease.

All major therapies, including chemotherapy, targeted therapy, endocrine-based targeted therapy, immunotherapy, and endocrine plus bisphosphonate were included. Chemotherapy regimens mainly consisted of anthracyclines and taxane and/or carboplatinbased regimens. HER2-targeted therapies, bevacizumab, and PARPinhibitors were included in the targeted therapy group. Endocrine based targeted therapies comprised of CDK-4/6-inhibitors, PIK3CAinhibitors, or mTOR-inhibitors in combination with aromataseinhibitors or Fulvestrant. Immunotherapy included PD-1, PD-L1, and CTRL-4 inhibitors. The endocrine and bisphosphonate therapy group included patients receiving endocrine-based therapy and bisphosphonates in the adjuvant or metastatic setting, and two patients receiving endocrine-based or bisphosphonate therapy.

#### 2.3. Statistical analysis

Patient characteristics and endpoints were summarized.



Fig. 1. Two-tiered assessment of the patients' view on COVID-19 vaccination (structure of the data collection).

Statistical analysis was performed using R Studio, Version 1.4.1103. Pearson's chi-square test and Fisher's exact test were used to test for differences between specific groups. All statistical tests were performed two-sided. P-values of <0.05 were considered statistically significant. Power calculation and sample size justification were performed using G\*Power. For the calculations performed using chi-square, a total sample size of 69 patients was required to achieve an actual power of 0.95, reporting a medium effect size of 0.5 for calculations with up to three degrees of freedom.

#### 3. Results

3.1. Demographic characteristics and clinical presentation of patients assessed for their willingness to receive the COVID-19 vaccine

Initially, we interviewed cancer patients undergoing oncological therapy about their attitude towards COVID-19 vaccination. A total of 120 patients (101 patients with breast cancer and 19 with gynecological malignancies) were interviewed (Fig. 1). Characteristics of the breast cancer patients are shown in Table 1 and those patients with gynecological malignancies in Table 2. Median age among breast cancer and gynecological cancer patients was 57 and 56 years, respectively. Among breast cancer patients, 68.3% had advanced disease, as well as 94.7% (18/19 patients) of the gynecological cancer patients.

The majority of the patients in both the breast and gynecological cohorts were in metastatic or adjuvant therapy. Breast cancer patients received targeted therapy (32.7%), chemotherapy (28.7%), endocrine-based targeted therapy (3%), and bisphosphonate therapy  $\pm$  chemotherapy (3%), and bisphosphonate therapy  $\pm$  endocrine-based maintenance therapy (7.9%) (Table 1). For patients with gynecological malignancies, the most common systemic therapy was chemotherapy (63.2%) followed by targeted therapy (26.3%), and immunotherapy  $\pm$  chemotherapy (10.5%) (Table 2).

3.2. Cancer patients express a strong willingness to receive the COVID-19 vaccine

The majority of the patients included was registered to receive

the vaccine, while 31.9% preferred to postpone, and 5.9% refused the vaccine (Tables 1–3, Supplementary Fig. 2). The reasons for postponing or refusing vaccination were assessed (Table 3). The most common reasons were the belief that vaccine-related adverse events would worsen current anti-cancer therapy side effects (29%) and the lack of information regarding the safety of the COVID-19 vaccine in cancer patients undergoing oncological therapy (27%) (Table 3). Interestingly, patients with gynecological malignancies had a significantly lower willingness to be vaccinated (45.5% registered to receive the vaccine) than those with breast cancer (66.3% registered for vaccination) (p < 0.05).

## 3.3. Demographic characteristics and clinical presentation of vaccinated patients

By July 28th, a total of 218 patients with breast and gynecological cancer had received one dose and 112 patients both doses of the COVID-19 vaccine (Fig. 1, Supplementary Fig. 3). The clinical characteristics of the vaccinated patients are shown in Tables 4 and 5. 38 of the patients initially interviewed for their attitude towards COVID-19 vaccination (Tables 1 and 2) received their vaccination during the survey (Fig. 1) and thus are also included in Tables 4 and 5 The majority of the patients had advanced-stage or metastatic disease. The vaccine-related adverse events in patients who received the vaccine before the start of cancer therapy were assessed separately (Tables 4 and 5).

## 3.4. COVID-19 vaccine-related adverse events in breast and gynecological cancer patients

To profile the vaccination side effects in cancer patients, we next assessed the vaccine-related adverse events within two weeks after vaccination in our breast and gynecological cancer cohort. The most frequent side effects in the first 48 h after vaccination were pain at injection site (45.9% after the first dose, 51.4% after the second dose) as well as fatigue (22.5% after the first dose, 35.1% after the second dose) (Table 6).

The majority of the patients documented no symptoms lasting more than 48 h (84.9% after the first dose, 81.1% after the second dose) (Table 6).

We further analyzed the adverse events profile according to age.

#### Table 1

Clinical characteristics of patients with breast cancer in our patient cohort undergoing assessment of their attitude towards vaccination.

Characteristic	All patients	Registered for vaccination	Postponing vaccination	Refusing vaccination
In total	101	68	27	6
Gender	4 ♂, 97♀	3 ở, 64 º	1 ở, <b>26</b> ♀	6 9
Age median/mean (y) range (y)	57/56.45 23–85	56/55.4 28–85	60/59.93 23–85	50/52.33 29–80
UICC stage of disease I/II (%) III/IV (%)	32 (31.7) 69 (68.3)	23 (71.8) 45 (65.2)	7 (21.9) 20 (29)	2 (6.3) 4 (5.8)
Therapy modality neoadjuvant therapy (%) adjuvant therapy (%) metastatic therapy (%) maintenance therapy (%)	12 (11.9) 30 (29.7) 57 (56.4) 2 (2.0)	11 (91.7) 18 (60.0) 38 (66.7) 1 (50.0)	1 (8.3) 10 (33.3) 15 (26.3) 1 (50.0)	0 2 (6.7) 4 (7.0) 0
Oncological therapy chemotherapy targeted therapy endocrine-based targeted therapy immunotherapy ± chemotherapy endocrine/bisphosphonate	29 (28.7) 33 (32.7) 28 (27.7) 3 (3.0) 8 (7.9)	20 (69.0) 20 (60.6) 18 (64.3) 3 (100) 7 (87.5)	8 (27.6) 8 (24.2) 10 (35.7) 0 1 (12.5)	1 (3.4) 5 (15.2) 0 0 0

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#### Table 2

Clinical characteristics of patients with gynecological malignancies in our patient cohort undergoing assessment of their attitude towards vaccination.

Characteristics	All patients	Registered for vaccination	Postponing vaccination	Refusing vaccination
In total	19	7	11	1
Age				
median/mean (y)	56/56.6	56/58.9	54/54.45	64
range (y)	34-78	52-78	34-78	
Type of carcinoma				
ovarian (%)	13 (68.4)	6 (46.2)	6 (46.2)	1 (5.3)
simulate ovarian + endometrium (%)	2(10.5)	1 (50)	1 (50)	
endometrium (%)	2 (10.5)	0	2 (100)	
cervical (%)	2 (10.5)	0	2 (100)	
FIGO stage of disease				
I/II	1 (5.3)	0	1	0
III/IV (%)	18 (94.7)	7 (38.9)	10 (55.6)	1 (5.6)
Therapy modality				
adjuvant therapy (%)	4 (21.1)	3 (75.0)	1 (25.0)	0
metastatic therapy (%)	7 (36.8)	2 (28.6)	5 (62.5)	1 (12.5)
maintenance therapy (%)	5 (26.3)	2 (40.0)	3 (60.0)	0
recurrent therapy (%)	3 (15.8)	0	2 (100)	0
Oncological therapy				
chemotherapy (%)	12 (63.2)	4 (3.3)	7 (58.3)	1 (8.3)
targeted therapy (%)	5 (26.3)	3 (60.0)	2 (40.0)	0
immunotherapy ± chemotherapy (%)	2 (10.5)	0	2 (100)	0

#### Table 3

Assessment of willingness for vaccination: reasons for postponing or refusing vaccination.

Reasons for postponing vaccination	
current side effects of therapy (%)	11 (29.7)
lack of data on safety in cancer patients (%)	10 (27.0)
prefers vaccine with general practitioner (%)	7 (18.9)
previous COVID-19 infection (%)	6 (16.2)
not sure yet (%)	5 (13.5)
refuses Vaxzevria vaccine (%)	7 (18.9)
other (%)	7 (18.9)
Reasons for refusing vaccination	
generally opposed to vaccine	2
fear of possible side effects	5
belief that vaccine does not work	1
belief that the vaccine is unsafe due to quick	5
development	
other	1

 Table 4

 Clinical characteristics of patients with breast cancer having received the COVID-19 vaccine.

Characteristics	First dose ( $n = 162$ )	Second dose $(n = 80)$
Gender	6 ở, 156 ệ	3ð, 77 ♀
Age	(10, 72)	(0 (51 - 72)
range	30–92	60 (51–73) 31–92
Stage of disease (UICC or FIGO)		
I/II	58	30
III/IV	104	50
Therapy modality		
neoadjuvant therapy (%)	24 (14.3)	13 (16.0)
adjuvant therapy (%)	39 (23.2)	18 (22.2)
metastatic therapy (%)	87 (51.8)	40 (49.3)
maintenance therapy (%)	15 (8.9)	9 (11.1)
recurrent therapy (%)	3 (1.8)	1 (1.2)
Oncological therapy		
Chemotherapy (%)	32 (19.8)	16 (20.0)
Targeted therapy (%)	43 (26.5)	21 (26.2)
endocrine-based targeted therapy (%)	40 (24,7)	20 (25.0)
immunotherapy ± chemotherapy (%)	2 (1.2)	2 (2.5)
endocrine based/bisphosphonate (%)	23 (14.2)	9 (11.3)
none (vaccinated before start of therapy) (%)	22 (13.6)	12 (15.0)

#### Table 5

Clinical characteristics of patients with gynecological malignancies having received the COVID-19 vaccine.

Characteristics	First dose $(n = 58)$	Second dose $(n = 32)$
Age Median (IQR) range	62 (53–71.25) 32–83	59.5 (52.75–68) 32–82
Type of carcinoma Ovarian (%) Endometrium (%) Uterine sarcoma Cervical (%) Vulvar (%) Dysgerminoma (%) Peritoneal (%)	44 (75.9) 3 (5.1) 1 (1.7) 7 (12.2) 1 (1.7) 1 (1.7) 1 (1.7)	22 (68.8) 3 (9.4) 1 (3.1) 4 (12.5) 0 1 (3.1) 1 (3.1)
Stage of disease (UICC or FIGO) I/II III/IV	7 51	5 27
Therapy situation adjuvant therapy (%) metastatic therapy (%) maintenance therapy (%) recurrent therapy (%)	18 (31.0) 15 (25.9) 11 (19.0) 14 (24.1)	9 (28.1) 12 (37.5) 4 (12.5) 7 (21.9)
Oncological therapy Chemotherapy (%) Targeted therapy (%) Immunotherapy ± chemotherapy (%) none (vaccinated before start of therapy) (%)	31 (53.4) 10 (17.2) 7 (12.2) 10 (17.2)	19 (59.4) 6 (18.8) 4 (12.5) 3 (9.4)

#### Table 6

Patient experience with the COVID-19 vaccine.

Characteristics	First dose $(n = 218)$	Second dose ( $n = 112$ )
Sick with COVID-19 in the past year	5	1
Vaccine		
Conmirnaty (%)	169 (77.5)	93 (83.0)
Vaxzevria (%)	35 (16.1)	8 (7.1)
COVID-19 vaccine Moderna (%)	13 (5.9)	9 (8.0)
N/A	1 (0.5)	2 (1.8)
Side effects 0–2 days after vaccination		
none (%)	80 (36.7)	32 (28.8)
local pain (%)	100 (45.9)	57 (51.4)
local swelling (%)	17 (7.8)	13 (11.7)
fever (%)	14 (6.4)	13 (11.7)
chills (%)	21 (9.6)	14 (12.6)
fatigue (%)	49 (22.5)	39 (35.1)
headache (%)	19 (8.7)	14 (12.6)
dizziness (%)	7 (3.2)	7 (6.3)
malaise (%)	18 (8.3)	13 (11.7)
joint pain (%)	15 (6.9)	12 (10.8)
muscle pain (%)	18 (8.3)	14 (12.7)
nausea (%)	7 (3.2)	3 (2.7)
vomiting (%)	1 (0.5)	2 (1.8)
diarrhea (%)	3 (1.4)	2 (1.8)
Side effects >48 h after vaccination		
None (%)	185 (84.9)	90 (81.1)
Local (%)	4 (1.8)	7 (6.3)
Systemic (%)	27 (12.4)	12 (10.8)
local & systemic (%)	2 (0.9)	3 (2.7)
Effects on oncological therapy		
postponement	11	3
pause of oral therapy	6	0
dose reduction	1	1

The vaccinated patients aged 18–55 years experienced significantly more frequent side effects after the first dose of vaccine (Fig. 2A, p < 0.05). In both age groups, patients experienced fewer side effects after the first dose compared to after the second dose (p < 0.05, Fig. 2A–B).

Patients with gynecological malignancies tended to experience more frequent systemic symptoms, such as fever, chills, malaise, and joint pain, than those with breast cancer after the second vaccine dose (Fig. 3A–B: not significant, p > 0.05).



Fig. 2. Side effects after COVID-19 vaccination: 18–55 years vs. >55 years old patients, A: Overview of side effects in the first 48 h after the first dose of the vaccine. B: Overview of side effects in the first 48 h after the second dose of the vaccine.

#### 3.5. Effects of COVID-19 vaccination on cancer therapy

We next evaluated to what extent vaccination affected administration of cancer therapy. Fig. 4 summarizes the most common symptoms after vaccination, which were analyzed by type of oncological therapy received at time of vaccination. Interestingly, patients who were vaccinated before starting cancer therapy tended to have more flu-like symptoms such as fever and chills after the first vaccine dose compared to those patients who got vaccinated while already undergoing chemotherapy (Fig. 4A, not significant, p > 0.05). After both vaccine doses, patients who received the vaccine before the start of anti-cancer therapy reported less adverse events in general than those who received the vaccine while undergoing oncological therapy (Fig. 4 A-B, not significant). Taken together, the timing of vaccination in patients receiving neutropenia-causing therapies did not appear to significantly influence the side effect profile in our patients (Fig. 5).

In total, COVID-19 vaccination cumulatively affected oncological therapy in 15 patients after the first dose, culminating in 11 postponements of therapy for an average of 6.9 days (Table 6). Six patients paused their oral therapy for an average of 1.5 days and one cancer therapy dose reduction before both doses of COVID-19 vaccine was recommended in one patient who had had prior neutropenia episodes. Finally, there were only three other instances of therapy delays after administration of the second vaccine dose (Table 6).

#### 4. Discussion

We first evaluated the willingness to receive vaccine in a cohort of 120 patients with breast or gynecological cancer. Our results show that a high number of patients were concerned about receiving the COVID-19 vaccine while undergoing oncological therapy. Furthermore, we evaluated the safety profile of COVID-19 vaccination, including local and systemic adverse events, in a second cohort of cancer patients. Our data show that COVID-19 vaccination was safe in our cohort of 218 breast and gynecological cancer patients and that it had only limited effects on the schedule of anti-cancer therapies.

In total, 61.2% of our surveyed patients were registered to receive the vaccine. Even though cancer patients are at a high risk of developing severe COVID-19 disease [2,3] and the vaccines were



Side effects

Fig. 3. Side effects after COVID-19 vaccination: patients with breast cancer patients vs. gynecological cancer patients. Side effects in the first 48 h after the second vaccine dose.



Fig. 4. Side effects after COVID-19 vaccination according to type of oncological therapy received at the time of vaccination. A: Side effects in the first 48 h after the first vaccine dose. B: Overview of side effects in the first 48 h after second dose of vaccine.



Fig. 5. Side effects after COVID-19 vaccination according to the time interval between therapy adjustment and date of vaccination in patients receiving chemotherapy. A: Overview of symptoms in the first 48 h after the first vaccine dose B: Overview of symptoms in the first 48 h after second dose of vaccine.

designed to protect the population, the surveyed cancer patients appeared to be rather skeptical towards vaccination. Possible reasons for this attitude are the lack of clinical data on the safety and efficacy of the approved vaccines in oncological patients, and the fear of additional adverse events on top of those caused by their current anti-cancer therapy. The German Robert Koch Institute performed a survey among the German population, enrolling 1005 adults (March 18, 2021 - May 7, 2021) [11]. These results showed that 72.6% of patients expressed a definitive willingness to receive the vaccine. Given the fact that our data indicated only 61.2% patients were willing to get the vaccine, we can state that cancer patients appear to be more skeptical about the COVID-19 vaccine compared to the general population. These results underline the importance of data regarding the safety of COVID-19 vaccine administration in cancer patients.

Furthermore our data indicate that adverse effects are unlikely to last longer than 48 h post vaccination, and symptoms occur predominantly after the second dose. A study was recently published on COVID-19 vaccination of 151 cancer patients, of whom 95 had solid tumors and one third of them were breast or gynecological cancer patients [12]. Injection site pain and fatigue were the most frequent symptoms, similar to our results. However, in contrast to our results, more patients experienced no toxicity after the second dose compared to the first dose (71% after second dose vs. 54% after the first dose). This difference may be due to the inclusion of patients with different types of cancer such as 56 patients with hematologic malignancies in the study by Monin et al. [12] and indicates the need of cancer-type specific analyses.

Another study recently compared COVID-19 vaccine-related side-effects in 170 patients treated with immune checkpoint inhibitors to those in a control group [13]. Their results showed the most common side effects local injection site pain (63%) and fatigue (34%) (similar to our results) and additionally muscle pain (34%). They reported no adverse events requiring hospitalization or medical intervention.

It is well known that immune responses are reduced in the older patients compared to younger patients due to immunosenescence [14]. This statement is in line with our results, which showed fewer vaccine-related symptoms in the older patients (>55 years, Fig. 2A–B). However, recent studies have demonstrated that elderly people in the general population showed immunologic responses to the COVID-19 vaccine one month after the second dose of Conmirnaty, similar to the responses of younger populations [15,16].

Patients who received the vaccine before the start of anti-cancer therapy are expected to show more vaccine-related adverse events compared to those under oncological therapy, since cancer patients experience neutropenia and immune suppression during systemic therapy. Interestingly, our data indicate that this group of patients experienced more flu-like systemic symptoms in the first 48 h after first dose of vaccine compared to patients vaccinated while on treatment (Fig. 4 A).

Previous studies have shown that patients may experience differing immune responses depending on their stage of cancer treatment when they receive a vaccine. A study examined the seroprotection of the influenza vaccine administered to cancer patients undergoing chemotherapy. This study showed a tendency towards increased seroprotection in breast cancer patients vaccinated 11 days after a dose of chemotherapy vs. 1 day after a dose of chemotherapy. Furthermore, there were significantly more adverse events in patients vaccinated 11 days vs. 1 day after chemotherapy [17]. In contrast, our results show that the cancer therapy-vaccination interval does not significantly affect adverse events in cancer patients (Fig. 5A–B).

As already mentioned, therapy schedules were often delayed especially at the beginning of the pandemic. This was mainly due to concerns of COVID-infection during hospital admission [18]. In addition, a decrease of newly diagnosed breast cancer patients was observed ([6,19]) due to a pause of mammography screenings during lockdown in Germany. Therefore, one might expect an increase of number of patients with advanced stages.

Given the conclusion of our study that there were only limited effects of the COVID-19 vaccines on the oncological therapy schedule (Table 6), the vaccination not only did not interfere with the treatment schedule, but rather facilitated timely the oncological therapy and therefore also the clinical management of breast and gynaecological cancer patients. The next purpose is to avert a further lockdown by increasing the vaccination rate in the general population and thus COVID-19 vaccines are essential in order to be able to offer timely diagnostic and screening services on a continuous basis.

Limitations of our routine data collection consist mainly of the small patient number and the fact that no immunogenicity assays after vaccination were performed in clinical routine to truly document the efficacy of the COVID-19 vaccine. The above-mentioned study [12] with 151 cancer patients showed a 95% (18/19 patients) anti-SARS-CoV-2 IgG response and 88% (14/16 patients) T-cell response 14 days after the second dose. Another study reported 94% seropositivity in 131 patients with solid and hematological malignancies (27 patients with breast cancer, 3 with gynecological malignancies) 3–4 weeks after the second dose of vaccine [20].

#### 5. Conclusion

Overall, these findings from a clinical routine setting show that vaccine-related adverse events are self-limiting and mostly of short duration in cancer patients. No direct vaccine-related serious adverse events were observed. Considering the increased risk of fatal outcomes of COVID-19 infection in cancer patients [2,3], benefits of the vaccine likely far outweigh vaccine-related harms. Although further trials are required to confirm benefits and risks of COVID-19 vaccination in cancer patients, our findings may reassure breast and gynecological cancer patients who are to receive the COVID-19 vaccine while undergoing systemic therapy. To this aim, our results regarding the safety of the three COVID-19 vaccines in patients with breast cancer and gynecological malignancies support current guidelines that recommend COVID-19 vaccination of cancer patients under active oncological therapy.

#### **Ethical statement**

The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

#### **Declaration of competing interest**

None.

#### Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.breast.2021.10.012.

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