Table 2. Distribution of Deauville Scores for First and Second Dose of Moderna and Pfizer Vaccines

Activity scale	Moderna 1	Moderna 2	Pfizer 1	Pfizer 2
Deauville 1	6	1	22	13
Deauville 2	3	2	8	4
Deauville 3	0	2	0	0
Deauville 4	0	1	0	0
Deauville 5	1	1	1	3

dose. In this cohort, ipsilateral axillary nodal activity was much less common after the first vaccine dose, and women were more likely to develop reactive nodes, an important implication for breast cancer imaging concordant with the statement issued by the Society of Breast Imaging.[6]

Limitations. This was a single institutional study with limited sample size and follow-up, comparing 2 COVID-19 vaccines available at Yale School of Medicine in early vaccination stage. However, the study was conducted by strict and reproducible PET and CT criteria, and provides a framework for the future studies in this field.

Conclusions | Ipsilateral axillary nodal reactivity is commonly seen after the intramuscular administration of the COVID-19 mRNA vaccines, more so after the second dose than after the first, and more commonly with the Moderna than the Pfizer vaccine.

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1. Gallamini A, Barrington SF, Biggi A, et al. The predictive role of interim positron emission tomography for Hodgkin lymphoma treatment outcome is confirmed using the interpretation criteria of the Deauville five-point scale. *Haematologica*. 2014;99(6):1107-1113. doi:10.3324/haematol.2013.103218

2. Coates EE, Costner PJ, Nason MC, et al; VRC 900 Study Team. Lymph node activation by PET/CT following vaccination with licensed vaccines for human papillomaviruses. *Clin Nucl Med*. 2017;42(5):329-334. doi:10.1097/RLU.0000000000001603

3. Shirone N, Shinkai T, Yamane T, et al. Axillary lymph node accumulation on FDG-PET/CT after influenza vaccination. *Ann Nucl Med*. 2012;26(3):248-252. doi:10.1007/s12149-011-0568-x

4. Özütemiz C, Krystosek LA, Church AL, et al. Lymphadenopathy in COVID-19 vaccine recipients: Diagnostic dilemma in oncology patients. *Radiology*. 2021; 210275. doi:10.1148/radiol.2021210275

5. CDC. Local Reactions, Systemic Reactions, Adverse Events, and Serious Adverse Events: Moderna COVID-19 Vaccine. Accessed April 7, 2021. https://www.cdc.gov/vaccines/covid-19/info-by-product/moderna/reactogenicity.html

6. SBI. Recommendations for the Management of Axillary Adenopathy in Patients with Recent COVID-19 Vaccination. Accessed Aptil 7, 2021. https://www.sbi-online.org/Portals/0/Position%20Statements/2021/SBI-recommendations-for-managing-axillary-adenopathy-post-COVID-vaccination.pdf

Attitudes and Factors Associated With COVID-19 Vaccine Hesitancy Among Patients With Breast Cancer

The COVID-19 pandemic has had a substantial effect on cancer care.[1] The recent widespread availability of vaccines against SARS-CoV-2 is a promising strategy to prevent COVID-19–associated mortality. However, previous reports have shown a high hesitancy rate to receive a COVID-19 vaccine among oncologic patients.[2,3] Because breast cancer is the most commonly diagnosed malignant neoplasm,[4] it is imperative to evaluate the specific concerns regarding COVID-19 vaccination among patients with this disease.

Methods | From March 12 to March 26, 2021, any woman with breast cancer residing in Mexico who visited the social media channels of nongovernmental organizations dedicated to improving breast cancer care were invited to complete a web-based survey. To assess COVID-19 vaccine hesitancy rates, participants were dichotomized into a vaccine-acceptant group (ie, willing to be vaccinated immediately) and a vaccine-hesitant group (ie, prefer to wait, only if vaccine is mandatory, or refuse). Respondents who previously had been vaccinated against COVID-19 were excluded from the statistical analysis.

Data analyses were performed using SPSS, version 27 (IBM Inc). Significance was defined as 2-tailed $P < .05$. The Research Ethics Committee of the School of Medicine of the *Instituto Tecnologico y de Estudios Superiores de Monterrey* approved the study. Informed consent was waived because the research was deemed to be of minimal risk and no identifiable data were collected.

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Results | In all, 619 women with breast cancer residing in Mexico who visited the social media channels dedicated to improving breast cancer care responded to the survey; of these, 79 (13%) were excluded for prior COVID-19 vaccination. The remaining 540 women (median [range], 49 [23-85] years) were included. Of these 540 participants, 357 (66%) were willing to be vaccinated immediately and 183 (34%) were hesitant to be vaccinated—142 (26%) would wait to see the vaccine's adverse effects in others, 23 (4%) would only be vaccinated if it became mandatory, and 18 (3%) would refuse to be vaccinated.

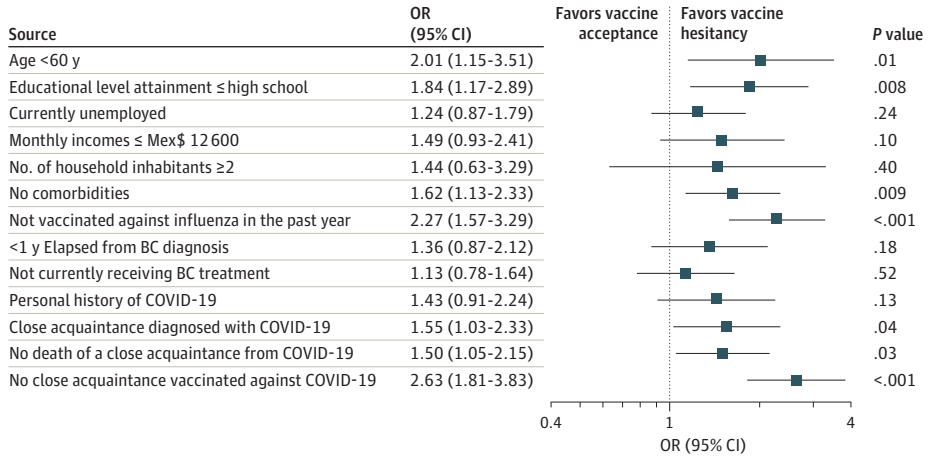
The most common reasons motivating vaccine-acceptant patients were: to prevent COVID-19 (n = 301; 84%), to take care of their relatives (n = 227; 64%), an autoperceived social responsibility (n = 227; 64%), a fear of getting seriously ill (n = 217; 61%), and/or a desire for "getting back to normal" (n = 186; 52%). The reasons motivating vaccine hesitancy and the factors that might influence hesitant patients to accept immunization are shown in the **Table**. Regarding misconceptions, participants believed that the COVID-19 vaccines may contain a virus capable of causing infection (n = 115; 21%), are contraindicated in patients with breast cancer (n = 29; 5%), are not effective (n = 19; 4%), carry a computer chip to surveil the population (n = 10; 2%), and/or could cause infertility (n = 6; 1%).

Univariate analyses showed that factors associated with vaccine hesitancy include mistrust in the health care system (odds ratio [OR], 8.79; 95% CI, 4.26-18.15), misconception that COVID-19 vaccination is contraindicated in patients with breast cancer (OR, 8.41; 95% CI, 3.36-21.05), not having a close acquaintance already vaccinated against COVID-19 (OR, 2.63; 95% CI, 1.81-3.83), noncompliance with prior influenza immunization (OR, 2.27; 95% CI, 1.57-3.29), age younger than 60 years (OR, 2.01; 95% CI, 1.15-3.51), low educational attainment (OR, 1.84; 95% CI, 1.17-2.89), and not having a close acquaintance deceased from COVID-19 (OR, 1.5; 95% CI, 1.05-2.15) (**Figure**). Significant variables were included in a multivariate model and remained independent predictors of vaccine hesitancy, except for being less than 60 years of age (OR, 1.74; 95% CI, 0.87-3.50; P = .12) and not having a close acquaintance who died of COVID-19 (OR, 1.42; 95% CI, 0.89-2.29; P = .14). In comparison with the vaccine-acceptant group, hesitant patients were more likely to state that having a close acquaintance who did not experience a vaccine-related adverse reaction (OR, 5.66; 95% CI, 3.47-9.22), having more information about vaccine effectiveness (OR, 3.82; 95% CI, 2.58-5.68) and safety (OR, 3.10; 95% CI, 2.09-4.60), mandatory vaccination (OR, 3.33; 95% CI, 1.48-7.48), and being recommended by their oncologist to be vaccinated (OR, 3.29; 95% CI, 2.27-4.77) were needed to motivate them to receive a COVID-19 vaccine.

Table. Concerns and Motivations Regarding COVID-19 Vaccination Among Patients With Breast Cancer

Concerns and motivations	No. (%) Acceptant group (n = 357)	No. (%) Hesitant group (n = 183)
What concerns make you not want to receive a COVID-19 vaccine?		
Fear of adverse reactions	39 (10.9)	100 (54.6)
Distrust of the health care system	10 (2.8)	37 (20.2)
Belief that vaccination is not indicated for patients with breast cancer	6 (1.7)	23 (12.6)
Treating physician has not recommended it	8 (2.2)	18 (9.8)
Belief that vaccination is not effective	2 (0.6)	17 (9.3)
Belief that vaccination can cause COVID-19	2 (0.6)	14 (7.7)
Belief that vaccine is not necessary because I already had COVID-19	3 (0.8)	3 (1.6)
What would motivate you to be vaccinated against COVID-19?		
Vaccination being recommended by my oncologist	127 (35.6)	118 (64.5)
More information about its effectiveness	66 (18.5)	85 (46.4)
More information about its safety	69 (19.3)	78 (42.6)
If someone close to me receives it and does not experience adverse reactions	29 (8.1)	61 (33.3)
Vaccination being recommended by my primary care physician	35 (9.8)	32 (17.5)
Vaccination becoming mandatory	10 (2.8)	16 (8.7)
Endorsement of vaccination by national authorities	17 (4.8)	6 (3.3)

Figure. Univariate Logistic Regression Analysis to Identify Factors Associated With COVID-19 Vaccine Hesitancy Among Patients With Breast Cancer



Abbreviations: BC, breast cancer; Mex$, Mexican peso.

Boxes indicate odds ratios; whiskers show 95% CIs.

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Discussion | The suboptimal acceptance of a COVID-19 vaccine is a reason for concern,[5] especially among individuals with a higher risk of severe illness. Strategies that focus on building vaccine literacy and confidence in the health care system are urgently needed to enhance vaccine acceptance. To achieve this, clear and credible communication that addresses patient misinformation and specific concerns must be encouraged.[5] Moreover, the active participation of oncologists is essential to educate cancer patients on the benefits of COVID-19 immunization and to endorse vaccination.

Some limitations of this study include its cross-sectional nature, reliance on self-reported data, limited sample size, and lack of formal survey sampling. However, this study provides much needed data to elucidate the factors associated with vaccine hesitancy in patients with breast cancer.

Immunization remains the leading strategy for reducing the COVID-19 burden. Interventions directed toward raising awareness of the benefits of vaccination, especially among the most vulnerable, are a priority for increasing the uptake of COVID-19 vaccines.

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1. Jazieh AR, Akbulut H, Curigliano G, et al; International Research Network on COVID-19 Impact on Cancer Care. Impact of the COVID-19 pandemic on cancer care: a global collaborative study. *JCO Glob Oncol*. 2020;6:1428-1438. doi:10.1200/GO.20.00351

2. Dutch Federation of Cancer Organizations. Kankerzorg in de anderhalvemeter-samenleving, wat is jouw ervaring? Accessed April 5, 2021. https://nfk.nl/nieuws/kankerzorg-in-de-anderhalvemeter-samenleving-wat-is-jouw-ervaring

3. Barrière J, Gal J, Hoch B, et al. Acceptance of SARS-CoV-2 vaccination among French patients with cancer: a cross-sectional survey. *Ann Oncol*. 2021;32(5):673-674. doi:10.1016/j.annonc.2021.01.066

4. Sung H, Ferlay J, Siegel RL, et al. Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin*. Published online February 4, 2021. doi:10.3322/caac.21660

5. Lazarus JV, Ratzan SC, Palayew A, et al. A global survey of potential acceptance of a COVID-19 vaccine. *Nat Med*. 2021;27(2):225-228. doi:10.1038/s41591-020-1124-9

COMMENT & RESPONSE

Inappropriate Use of the Same Cutoff by Different Sequencing Panels for Tumor Mutation Burden as Immunotherapy Biomarker

To the Editor We read with great interest the article by Valero et al[1] that described response rates, with respect to tumors with 10 or more mutations per megabase, in a cohort of 1678 patients treated with immune checkpoint inhibitors (ICIs). Including this study, the same research group reported 3 related studies recently. The other 2 studies, by Samstein et al[2] and Valero et al,[3] reported the predictive value of tumor mutation burden (TMB) on immunotherapy with the top 20 percentile (20%) as the cutoff and the association of TMB with survival with or without the immunotherapy context in patients with cancer, respectively. Although most of the patients with cancer receiving immunotherapy in these studies overlapped and some of the results were also duplicated, these 3 studies reported real-world data on immunotherapy, provided important clues for the clinical application of TMB as a biomarker, and guided possible ICI trial design. For this research, we have 2 comments.

First, the value of 10 or more tumor mutations per megabase approved by the US Food and Drug Administration for the FoundationOne CDx assay (Foundation Medicine, Inc) cannot be simply used as the TMB cutoff in this study. Previous studies have shown that although there was a high correlation between different sequencing panels and between sequencing panels and whole-exome sequencing,[4] the TMB values varied greatly owing to the differences of genomic regions covered, the sequencing capabilities of distinct regions, and the TMB calculation methods among different sequencing panels. For example, in patients with non-small cell lung cancer, the clinically relevant cutoff for high TMB of 10.0 mutations per megabase by FoundationOne CDx projected to 7.7 (95% CI, 7.1-8.3) mutations per megabase by whole-exome sequencing and 12.3 mutations per megabase by the TruSight Oncology 500 assay (Illumina, Inc).[5]

Second, although 10 mutations per megabase and 20% as the high TMB cutoffs are consistent in predicting better immunotherapy efficacy in most cases, there are exceptions. We used data of 1662 patients treated with ICIs from the Samstein et al[2] cohort and found that 10 mutations per megabase as the high

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