# Biases and Reluctances Causing Cancer Patients in Dilemma for COVID-19 Vaccination

Ferhat Ekinci<sup>1</sup>, Atike Pınar Erdoğan<sup>2</sup>, Gamze Göksel<sup>3</sup>

# ABSTRACT

#### **Background**

We have planned this study to determine opinions of this patient group, who are affected negatively both in physical aspect during the treatment process of cancer and who are fragile and sensitive for psycho-social aspects, their opposition level and misimpressions related to vaccine and for eliminating these reluctances if possible.

#### Methods

Between February 2021 and 15 April 2021, all cancer patients applying to our oncology clinic have been first asked to fill in the questionnaire, which includes three articles where suggestions expressing their attitude towards vaccination were asked and subsequently nine articles expressing suggestions about vaccine opposition

#### Results

According to responses to a decision for vaccination, we have learned that 446 (79,6%) patients thought to have the Covid-19 vaccine, 62 (11.1%) were hesitant, and 52 (9.3%) did not think to have a vaccine.

# **Conclusions**

The most critical data obtained from this study is that there were severe biases related to adverse effects due to vaccines, although patients have a positive attitude about vaccination. The most important task of health authorities should be to eliminate reluctance without waiting for patients to take a more negative attitude on this subject.

# **Keywords**

Vaccine opposition; cancer patients; coronavirus disease; COVID-19; vaccine hesitancy;

### INTRODUCTION

The COVID-19 outbreak that began with pneumonia cases of unknown origin in Wuhan province of China in December 2019 has led to the infection of millions of people and hundreds of thousands of losses of lives throughout the world. The disease shows its influence more, especially in the geriatric population and people with comorbid diseases. Therefore, 'not being infected' may currently be considered the best solution for not being affected by the disease. Nevertheless, any effective treatment that may change the course of the disease has not been found yet.

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For this reason, the most critical steps recommended to be obeyed to be protected from infection can be summarized as; triad of a mask, distance, and hygiene.<sup>3,4</sup> Additionally, social isolation methods, including strict quarantine applications, are sometimes introduced globally. All these precautions lead to psycho-social destruction in patients who are highly fragile, especially cancer patients. It appears that all eyes were focused on vaccine studies with great expectations in order to overcome all these dilemmas.<sup>4,5</sup>

Of course, we owe the first vaccination studies to eradicate a contagious disease to a scientist named Edward Jenner with his studies on the variola (smallpox) virus in 1796. In fact, he is accounted as the architecture of a complete and challenging process leading to eradicating the contagious disease from the history of humanity in 1979.5 Albeit modern medicine determines an attitude in favor of vaccination in the light of proof-based data, it should also fight vaccine opposition that occurred in the community. Again, if we return to the private issue of smallpox vaccine; it caused that vaccination had become compulsory in 1853 with the first vaccination law in England in 1840 and that anti-vaccination front has reached an exploding point as a result of restrictions and punishments to parents who have not wanted vaccination in 1867. The person who is a symbolic leader of that front was a researcher named Alfred Russel Wallace, known for his research on 'natural selection'. He insisted that the vaccine was useless and dangerous, although the opposite proves.<sup>5</sup> Fortunately, eradication of smallpox disease with the help of vaccines after about one hundred years from those discussions is the most significant evidence showing that he is unfair, isn't it? Of course, we cannot ignore some arguments for which this community part is suitable as a pioneer in socio-political meaning. First of these causes comes vaccine obligation by disregarding ethical, religious, social, and traditional values of people, forcing them for such an obligation without convincing them sufficiently with scientific evidence give health authorities a conscientious and legal load.<sup>5,6</sup> If we describe the masses participating in this discussion as irrational, radical, and religiously motivated masses, we cannot access them at all, and we could not enlighten today about vaccination with the light we obtained from history.

Although vaccination studies tracked a positive course in the first year of the COVID-19 pandemic, the existence of false information (disinformation) related to 'a volunteer lost life due to vaccination just at the clinical experimental phase' has led to biased approaches towards vaccination studies.7 Again, it is observed that falsified news is difficult to believe, such that vaccines would gain functionality in line with the benefit of big drug companies or that a microchip is wanted to be inserted to people via vaccine have partially found reaction in the community.8 It is an important cause for people to be wary that vaccines would be applied to vast community environments for the first time. Possibly many people would not be in those first vaccinated. Also, development of possible side effects associated with the vaccine, perception of intervening towards freedom in case vaccine would be compulsory, and suspicions related to a fair distribution of vaccine are not among subjects that we can provide development from Wallace until COVID-19 vaccination.9

A comprehensive community-based questionnaire study conducted by the IPSOS research company globally shows the dominance of reluctance towards vaccine rather than anti-vaccination. 10 These data shed light on the points that we should focus on in order to make vaccines widespread. However, adequate research has not been done yet specifically for cancer patients. We think that opinions of this patient group who were negatively affected physically during the treatment process of disease and who are more fragile and sensitive in psycho-social meaning, their level of opposition and misimpressions need to be determined. This reluctance should be eliminated if possible. For this purpose, after we revised the questionnaires present in the literature and made them suitable for COVID-19 vaccination, we applied them to obtain our patients' opinions. A scientific-based analysis would be provided, which shed light on the literature under the light of obtained data.

#### **MATERIALS AND METHODS**

#### **Design and Application Method of Questionnaire**

Three choices were placed after a suggestion of 'mark the proper choice from A, B, and C choices about Covid-19 vaccination that is suitable for you' at the beginning paragraph of the anti-vaccine scale of abbreviated nine articles to categorize patients. A request was made as 'please mark one of the indicated situations from A, B, C choices suitable for you.' As it is also seen in a



translated version of the questionnaire (Supplementary materials—questionnaire), these choices are:

- A) I think to have COVID-19 Vaccine
- B) I am hesitant about having COVID-19 Vaccine
- C) I do not think to have COVID-19 Vaccine

After marking one of the A, B, and C choices above, the agreement degree for suggestions of nine articles were enumerated from 1 (definitely disagree) to 5 (definitely agree) according to agreement degree, and they were asked to mark the proper one of them. Because only the first three articles contain positive opinions related to the vaccine, these were subjected to inverse calculation (5 points was given for the suggestion of 'definitely disagree' and gradually decreasing until 'definitely agree' that was given 1 point) differently from the other six articles while calculating scores. Afterward, the average score of anti-vaccine (ASAV) was analyzed according to patient characteristics.

#### **Patient Characteristics and Data Collection**

Questionnaires were given to all patients applying to our oncology clinic between 1 February 2021 and 15 April 2021 after verbal information and written consent. Because questionnaire results of patients would be evaluated by considering disease characteristics, age, gender, history of treatment (chemotherapy (CT) and radiotherapy (RT), currently received a type of treatment (CT, hormonotherapy, immunotherapy, tyrosine kinase inhibitors, and monoclonal antibodies), the aim of treatment (adjuvant, neoadjuvant and palliative), disease status at the time of application (no distribution, local or metastatic invasion) were recorded. Besides, patients were collected under six categories for the aspect of diagnosis types. These were breast, gastrointestinal system, thorax, urogenital, head and neck, and other cancers. At the same time, it was reported that if patients were control patients, their diagnoses, metastases, and application dates.

#### **Statistical Method**

Data were analyzed by IBM SPSS V23. Compliance to normal distribution was examined by the Kolmogorov-Smirnov test. The chi-square test was used for comparing categorical variables according to groups. One-way variance analysis was used to compare normally distributed quantitative data according to groups, and multiple comparisons were conducted

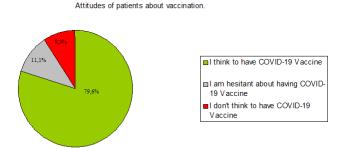
using the Duncan test. Analysis results were taken as average  $\pm$  standard deviation and median (minimum-maximum) for quantitative data, and categorical data were presented as frequency (percent). The significance level was taken as p<0,05.

**Ethical Clearance:** The ethics committee's approval numbered E-20478486-050.04.04-38992 was obtained by the Health Sciences Ethics Committee of Manisa Celal Bayar University.

#### **RESULTS:**

# Correlation of Average of Anti-Vaccine Score with Patient Characteristics

The average score of vaccine opposition (ASAV) of 560 patients who participated in the COVID-19 anti-vaccine scale was  $2.5\pm0.7$  (Table 1). The average application age of patients was  $57.0 \pm 12.1$ , and there is a statistically significant weak negative correlation with ASAV (r=-0,122; p=0,004) (Table 2). A small decrease of ASAV is obtained with the increase of age. ASAV shows a rise in one thinking to have vaccine compared to not thinking to have a vaccine, and this increase has been determined as statistically significant (p<0,001) (Table 3). According to responses for a decision of vaccination; we have learned that 446 (79,6%) patients thought to have COVID-19 vaccine (group A), 62 (11.1%) were hesitant about vaccination (group B), 52 (9.3%) did not think to have the vaccine (group C) (Figure 1 and see Table 4 for differences between groups).



**Figure 1:** Attitudes of patients about vaccination.

When we categorized patients according to age, it was observed that ASAV was highest under 50 years of age  $(2,63 \pm 0,72)$  and lowest above 65 years of age, and this difference has not been statistically significant (p. 0,647). The vast majority of patients of 71,4% (n:400) consisted of females, and it is seen that ASAV is higher



compared to males  $(2.59 \pm 0.69 \text{ vs. } 2.37 \pm 0.71)$ . Again, this difference is also statistically significant (p: 0.001). When patients were examined according to diagnostic groups, it is seen that almost half of them consisted of patients with breast cancer (n: 268, 47,9%). No significant difference has been found for the aspect of ASAV with other diagnostic groups (p: 0,067). On the analysis made according to disease status at the time of application, it has been determined that half of as patients were in the noninvasive group (n: 281, 50,2%), and any significant difference has not been determined between ones with local-regional invasion from other groups (n: 49, 8,8%) and ones having a metastatic disease (n: 230, 41.1%) (p:0.136). It is observed that 462 (82.5%) patients had CT previously and 98 (17.5%) patients have not received CT at all, and any significant difference has not been reported between those two groups for the aspect of ASAV (p:0.760). Again, whether patients currently having CT or not does not create any statistical difference for the aspect of ASAV (p:0.132). When patients are grouped for the aspect of the history of RT, it has been seen that patients without a history of

RT had higher ASAV (n: 229, 40.9%) compared to ones with RT history (n: 331, 59.1%)  $(2.61 \pm 0.68 \text{ vs. } 2.48)$  $\pm$  0,71) and it has been determined to be statistically significant (p.0.026). When patients were categorized according to treatment purpose, it has been seen that the majority were metastatic (n:219, 52.3%) and that any significant difference for the aspect of ASAV has not been determined compared to people applying for the purpose of adjuvant (n:170, 40,6%) and neoadjuvant (n:30,7,2%) (p.0.408). No significant difference has been determined for the aspect of ASAV whether patients had target-oriented treatment (p:0.717) or not and according to types of hormonotherapy, immunotherapy, tyrosine kinase inhibitor, and monoclonal antibody among those having these treatments (p: 0.528). Finally, the vast majority of patients applying to the questionnaire process consisted of people applying for any treatment (n: 451, 80.5%), and it is seen that ASAV was close to each other  $(2,56 \pm 0,71 \text{ vs. } 2,41 \pm 0,66)$  between them and people coming for control purpose (n:103, 19.5%) and ASAV was statistically non-significant (p:0.051)

**Table 1.** Descriptive statistics belonging to quantitative data

|                        | Average | Std. deviation | Median | Minimum | Maximum |
|------------------------|---------|----------------|--------|---------|---------|
| Age of application     | 57,0    | 12,1           | 58,0   | 21,0    | 83,0    |
| Duration of diagnosis  | 908,1   | 892,0          | 591,0  | 0,0     | 4535,0  |
| Duration of metastasis | 651,9   | 642,8          | 482,0  | 0,0     | 3481,0  |
| Anti-vaccine score     | 2,5     | 0,7            | 2,6    | 1,0     | 4,7     |

**Table 2.** Examining correlation between vaccine opposition and age of application, duration of diagnosis and duration of metastasis

|                 | Anti-vaccination score |       |  |
|-----------------|------------------------|-------|--|
|                 | r                      | p     |  |
| Application Age | -0,122                 | 0,004 |  |
| Diagnosis time  | -0,045                 | 0,292 |  |
| Metastasis Time | -0,052                 | 0,428 |  |

r: Spearman's rho correlation coefficient



**Table 3.** Comparison of anti-vaccine score according to patient characteristics

| Prequency (n)   Average study   Average (min max.)   Test statistics   p   | •   |               |                     |                     |                 |       |
|--|---|---------------|---------------------|---------------------|-----------------|-------|
| Under 50 years old   156 (27.9)   2.63 ± 0.72   2.67 (1.00 - 4.22)   Between 50-65 years old   227 (40.5)   2.52 ± 0.69   2.56 (1.00 - 4.67)   F=2.824   0.647   |   | Frequency (n) |                     | Average. (min max.) | Test statistics | p     |
| Between 50-65 years old   227 (40.5)   2.52 ± 0.69   2.56 (1.00 - 4.67)   F=2.824   0.647  | Age categorized                           |               |                     |                     |                 |       |
| Over 65 years old  | Under 50 years old                        | 156 (27,9)    | $2,63 \pm 0,72$     | 2,67 (1,00 - 4,22)  |                 |       |
| Gender         Male         160 (28,6)         2.37 ± 0.71         2.33 (1.00 · 4.67)         t=-3.386         0.001           Female         400 (71,4)         2.59 ± 0.69         2.67 (1.00 · 4.67)         t=-3.386         0.001           Diagnosis categorized         32 (8.7)         2.60 ± 0.70         2.56 (1.00 · 4.67)         Thorax         32 (5.7)         2.32 ± 0.77         2.17 (1.11 · 4.11)         Gis         114 (20.4)         2.50 ± 0.66         2.56 (1.00 · 4.67)         F=2.077         0.067           Gis         114 (20.4)         2.50 ± 0.66         2.56 (1.00 · 4.67)         F=2.077         0.067           Head Neck         19 (3.4)         2.60 ± 0.73         2.56 (1.00 · 4.67)         F=2.007         0.067           Head Neck         19 (3.4)         2.60 ± 0.73         2.56 (1.00 · 4.67)         F=2.007         0.067           Rare tumor and other         34 (6.1)         2.28 ± 0.81         2.33 (1.00 · 3.89)         F=2.007         0.067           Disease status         No invasion         281 (50.2)         2.55 ± 0.69         2.56 (1.00 · 4.67)         F=2.001         0.136           Metastatic         230 (41.1)         2.47 ± 0.72         2.44 (1.00 · 4.67)         F=2.001         0.136           CT history         Absent   | Between 50-65 years old                   | 227 (40,5)    | $2,52 \pm 0,69$     | 2,56 (1,00 - 4,67)  | F=2,824         | 0,647 |
| Male       160 (28.6)       2,37 ± 0,71       2,33 (1,00 - 4,67)       t=-3,386       0,001         Female       400 (71,4)       2,59 ± 0,69       2,67 (1,00 - 4,67)       t=-3,386       0,001         Diagnosis categorized       32 (847.9)       2,60 ± 0,70       2,56 (1,00 - 4,67)       Thorax       32 (5.7)       2,32 ± 0,77       2,17 (1,11 - 4,11)       7.7 (1,11 - 4,11)       7.7 (1,11 - 4,11)       7.7 (1,11 - 4,11)       7.7 (1,11 - 4,11)       7.7 (1,11 - 4,11)       7.7 (1,11 - 4,11)       7.7 (1,11 - 4,11)       7.7 (1,11 - 4,11)       7.7 (1,11 - 4,11)       7.7 (1,11 - 4,11)       7.7 (1,11 - 4,11)       7.7 (1,11 - 4,11)       7.7 (1,11 - 4,11)       7.7 (1,11 - 4,11)       7.7 (1,11 - 4,11)       7.7 (1,11 - 4,01)       7.7 (1,11 - 4,01)       7.7 (1,11 - 4,01)       7.7 (1,11 - 4,01)       7.7 (1,11 - 4,01)       7.7 (1,01 - 4,67) <td>Over 65 years old</td> <td>177 (31,6)</td> <td><math>2,45 \pm 0,69</math></td> <td>2,44 (1,00 - 4,67)</td> <td></td> <td></td>  | Over 65 years old                         | 177 (31,6)    | $2,45 \pm 0,69$     | 2,44 (1,00 - 4,67)  |                 |       |
| Female   | Gender                                    |               |                     |                     |                 |       |
| Female 400 (71,4) 2,59 ± 0,69 2,67 (1,00 - 4,67)  Diagnosis categorized  Breast 268 (47.9) 2,60 ± 0,70 2,56 (1,00 - 4,67)  Thorax 32 (5,7) 2,32 ± 0,77 2,17 (1,11 - 4,11)  Gis 114 (20.4) 2,50 ± 0,66 2,56 (1,00 - 4,01)  Urogenital 93 (16,6) 2,52 ± 0,64 2,44 (1,00 - 4,00)  Head Neck 19 (3,4) 2,60 ± 0,73 2,56 (1,44 - 4,67)  Rare tumor and other 34 (6,1) 2,28 ± 0,81 2,33 (1,00 - 3,89)  Disease status  No invasion 281 (50,2) 2,55 ± 0,69 2,56 (1,00 - 4,67)  Local-regional 49 (8,8) 2,68 ± 0,64 2,67 (1,11 - 4,00) F=2,001 0,136  Metastatic 230 (41,1) 2,47 ± 0,72 2,44 (1,00 - 4,67)  The sent 462 (82,5) 2,54 ± 0,69 2,56 (1,00 - 4,67)  Present 462 (82,5) 2,54 ± 0,69 2,56 (1,00 - 4,67)  Thorax 32 (4,10 - 4,67) 10,132  Present 331 (59,1) 2,48 ± 0,71 2,44 (1,00 - 4,67) 10,132  Purpose if receiving treatment Adjuvant 170 (40,6) 2,61 ± 0,71 2,56 (1,00 - 4,67)  No 370 (66,1) 2,59 ± 0,69 2,56 (1,00 - 4,67)  Purpose if receiving treatment Adjuvant 170 (40,6) 2,61 ± 0,71 2,56 (1,00 - 4,67)  No 268 (48,6) 2,54 ± 0,69 2,56 (1,00 - 4,67)  Is he/she receiving target-oriented agent No 268 (48,6) 2,54 ± 0,69 2,56 (1,00 - 4,67)  Yes 284 (51,4) 2,52 ± 0,71 2,56 (1,00 - 4,67)  Its category if he/she is receiving target-oriented Homonotherapy 32 (11,3) 2,41 ± 0,75 2,44 (1,00 - 4,33)  Immunotherapy 32 (11,3) 2,41 ± 0,75 2,44 (1,00 - 4,33)  Immunotherapy 32 (11,3) 2,41 ± 0,75 2,44 (1,00 - 3,78)  | Male                                      | 160 (28,6)    | $2,37 \pm 0,71$     | 2,33 (1,00 - 4,67)  | 2.206           | 0.004 |
| Breast 268 (47,9) 2,60 ± 0,70 2,56 (1,00 - 4,67)  Thorax 32 (5,7) 2,32 ± 0,77 2,17 (1,11 - 4,11)  Gis 114 (20,4) 2,50 ± 0,66 2,56 (1,00 - 4,11)  Urogenital 93 (16,6) 2,52 ± 0,64 2,44 (1,00 - 4,00)  Head Neck 19 (3,4) 2,60 ± 0,73 2,56 (1,44 - 4,67)  Rare tumor and other 34 (6,1) 2,28 ± 0,81 2,33 (1,00 - 3,89)  Disease status  No invasion 281 (50,2) 2,55 ± 0,69 2,56 (1,00 - 4,67)  Local-regional 49 (8,8) 2,68 ± 0,64 2,67 (1,11 - 4,00) F=2,001 0,136  Metastatic 230 (41,1) 2,47 ± 0,72 2,44 (1,00 - 4,67)  Thistory  Absent 98 (17,5) 2,51 ± 0,75 2,44 (1,00 - 4,67)  Present 462 (82,5) 2,54 ± 0,69 2,56 (1,00 - 4,67)  Fersent 331 (59,1) 2,48 ± 0,71 2,44 (1,00 - 4,67)  Is he/she currently having CT  No 370 (66,1) 2,50 ± 0,70 2,50 (1,00 - 4,67)  Neoadjuvant 170 (40,6) 2,61 ± 0,71 2,67 (1,00 - 4,67)  Neoadjuvant 170 (40,6) 2,61 ± 0,71 2,56 (1,00 - 4,67)  Neoadjuvant 30 (7,2) 2,54 ± 0,68 2,56 (1,00 - 4,67)  No 268 (48,6) 2,54 ± 0,69 2,56 (1,00 - 4,67)  Yes 284 (51,4) 2,52 ± 0,71 2,56 (1,00 - 4,67)  Feo.898 0,408  Metastatic-pulliative 219 (52,3) 2,51 ± 0,71 2,56 (1,00 - 4,67)  No 268 (48,6) 2,54 ± 0,69 2,56 (1,00 - 4,67)  Yes 284 (51,4) 2,52 ± 0,71 2,56 (1,00 - 4,67)  Thomasurer and the static-pulliative 219 (52,3) 2,51 ± 0,71 2,56 (1,00 - 4,67)  Homonotherapy 140 (49,3) 2,50 ± 0,70 2,44 (1,00 - 4,33)  Immunotherapy 32 (11,3) 2,41 ± 0,75 2,44 (1,00 - 4,33)  Immunotherapy 32 (11,3) 2,41 ± 0,75 2,44 (1,00 - 3,78)   | Female                                    | 400 (71,4)    | $2,59 \pm 0,69$     | 2,67 (1,00 - 4,67)  | t=-3,386        | 0,001 |
| Thorax 32 (5.7) 2.32 ± 0.77 2.17 (1.11 - 4.11) Gis 114 (20.4) 2.50 ± 0.66 2.56 (1.00 - 4.11) F=2.077 0.067  Urogenital 93 (16.6) 2.52 ± 0.64 2.44 (1.00 - 4.00) Head Neck 19 (3.4) 2.60 ± 0.73 2.56 (1.44 - 4.67) Rare tumor and other 34 (6.1) 2.28 ± 0.81 2.33 (1.00 - 3.89)  Disease status  No invasion 281 (50.2) 2.55 ± 0.69 2.56 (1.00 - 4.67) Local-regional 49 (8.8) 2.68 ± 0.64 2.67 (1.11 - 4.00) F=2.001 0.136  Metastatic 230 (41.1) 2.47 ± 0.72 2.44 (1.00 - 4.67)  CT history  Absent 98 (17.5) 2.54 ± 0.69 2.56 (1.00 - 4.67) Present 462 (82.5) 2.54 ± 0.69 2.56 (1.00 - 4.67)  En Absent 229 (40.9) 2.61 ± 0.68 2.67 (1.00 - 4.67)  F=2.0306 0.760  RT history  Absent 229 (40.9) 2.61 ± 0.68 2.67 (1.00 - 4.67) Present 331 (59.1) 2.48 ± 0.71 2.44 (1.00 - 4.67)  F=2.232 0.026  Is he/she currently having CT  No 370 (66.1) 2.50 ± 0.70 2.50 (1.00 - 4.67) Yes 190 (33.9) 2.59 ± 0.69 2.56 (1.00 - 4.67)  Purpose if receiving treatment  Adjuvant 170 (40.6) 2.61 ± 0.71 2.67 (1.00 - 4.67) No 268 (48.6) 2.54 ± 0.68 2.56 (1.11 - 4.00) F=0.898 0.408  Metastatic-palliative 219 (52.3) 2.51 ± 0.71 2.56 (1.00 - 4.67) Yes 284 (51.4) 2.55 ± 0.69 2.56 (1.00 - 4.67)  Tis he/she receiving target-oriented agent No 268 (48.6) 2.54 ± 0.69 2.56 (1.00 - 4.67) Yes 284 (51.4) 2.55 ± 0.71 2.56 (1.00 - 4.67)  Its category if he/she is receiving target-oriented agent Homonotherapy 140 (49.3) 2.50 ± 0.70 2.44 (1.00 - 3.78)   | Diagnosis categorized                     |               |                     |                     |                 |       |
| Gis 114 (20,4) 2,50 ± 0,66 2,56 (1,00 - 4,11) F=2,077 0,067  Urogenital 93 (16,6) 2,52 ± 0,64 2,44 (1,00 - 4,00) F=2,077 0,067  Head Neck 19 (3,4) 2,60 ± 0,73 2,56 (1,44 - 4,67) 2,33 (1,00 - 3,89)  Disease status  No invasion 281 (50,2) 2,55 ± 0,69 2,56 (1,00 - 4,67)  | Breast                                    | 268 (47,9)    | $2,60 \pm 0,70$     | 2,56 (1,00 - 4,67)  |                 |       |
| Urogenital 93 (16.6) 2,52 ± 0,64 2,44 (1,00 - 4,00)  Head Neck 19 (3,4) 2,60 ± 0,73 2,56 (1,44 - 4,67)  Rare tumor and other 34 (6.1) 2,28 ± 0,81 2,33 (1,00 - 3,89)  Disease status  No invasion 281 (50,2) 2,55 ± 0,69 2,56 (1,00 - 4,67)  Local-regional 49 (8,8) 2,68 ± 0,64 2,67 (1,11 - 4,00) F=2,001 0,136  Metastatic 230 (41,1) 2,47 ± 0,72 2,44 (1,00 - 4,67)  Thistory  Absent 98 (17,5) 2,51 ± 0,75 2,44 (1,00 - 4,67)  Present 462 (82,5) 2,54 ± 0,69 2,56 (1,00 - 4,67) t=-0,306 0,760  RT history  Absent 229 (40,9) 2,61 ± 0,68 2,67 (1,00 - 4,67) t=-2,232 0,026  Is he/she currently having CT  No 370 (66,1) 2,50 ± 0,70 2,50 (1,00 - 4,67) t=-1,508 0,132  Yes 190 (33,9) 2,59 ± 0,69 2,56 (1,00 - 4,67)  Prosent 30 (7,2) 2,54 ± 0,68 2,56 (1,11 - 4,00) F=0,898 0,408  Metastatic-palliative 219 (52,3) 2,51 ± 0,71 2,56 (1,00 - 4,67)  Is he/she receiving treatment  No 268 (48,6) 2,54 ± 0,69 2,56 (1,00 - 4,67)  Yes 284 (51,4) 2,52 ± 0,71 2,56 (1,00 - 4,67)  Its category if he/she is receiving target-oriented agent  No 268 (48,6) 2,54 ± 0,69 2,56 (1,00 - 4,67)  Yes 284 (51,4) 2,52 ± 0,71 2,56 (1,00 - 4,33) t=0,363  0,717  Its category if he/she is receiving target-oriented  Homonotherapy 140 (49,3) 2,50 ± 0,70 2,44 (1,00 - 4,33) t=0,363  Immunotherapy 32 (11,3) 2,41 ± 0,75 2,44 (1,00 - 3,78)  | Thorax                                    | 32 (5,7)      | $2,32 \pm 0,77$     | 2,17 (1,11 - 4,11)  |                 |       |
| Urogenital 93 (16.6) 2.52 ± 0.64 2.44 (1.00 - 4.00)  Head Neck 19 (3.4) 2.60 ± 0.73 2.56 (1.44 - 4.67)  Rare tumor and other 34 (6.1) 2.28 ± 0.81 2.33 (1.00 - 3.89)  Disease status  No invasion 281 (50.2) 2.55 ± 0.69 2.56 (1.00 - 4.67)  Local-regional 49 (8.8) 2.68 ± 0.64 2.67 (1.11 - 4.00) F=2.001 0.136  Metastatic 230 (41.1) 2.47 ± 0.72 2.44 (1.00 - 4.67)  Thistory  Absent 98 (17.5) 2.51 ± 0.75 2.44 (1.00 - 4.67)  Present 462 (82.5) 2.54 ± 0.69 2.56 (1.00 - 4.67)  Present 331 (59.1) 2.48 ± 0.71 2.44 (1.00 - 4.67)  Is he/she currently having CT  No 370 (66.1) 2.50 ± 0.70 2.50 (1.00 - 4.67)  Yes 190 (33.9) 2.59 ± 0.69 2.56 (1.00 - 4.67)  Neoadjuvant 170 (40.6) 2.61 ± 0.71 2.67 (1.00 - 4.67)  Neoadjuvant 30 (7.2) 2.54 ± 0.68 2.56 (1.11 - 4.00) F=0.898 0.408  Metastatic-palliative 219 (52.3) 2.51 ± 0.71 2.56 (1.00 - 4.67)  Is he/she receiving treatment  No 268 (48.6) 2.54 ± 0.69 2.56 (1.00 - 4.67)  Yes 284 (51.4) 2.52 ± 0.71 2.56 (1.00 - 4.67)  Its category if he/she is receiving target-oriented agent  Homonotherapy 140 (49.3) 2.50 ± 0.70 2.44 (1.00 - 4.33)  Immunotherapy 32 (11.3) 2.41 ± 0.75 2.44 (1.00 - 3.78)  | Gis                                       | 114 (20,4)    | $2,50 \pm 0,66$     | 2,56 (1,00 - 4,11)  | F 2.077         | 0.067 |
| Rare tumor and other       34 (6,1)       2,28 ± 0,81       2,33 (1,00 - 3,89)         Disease status       281 (50,2)       2,55 ± 0,69       2,56 (1,00 - 4,67)         Local-regional       49 (8,8)       2,68 ± 0,64       2,67 (1,11 - 4,00)       F=2,001       0,136         Metastatic       230 (41,1)       2,47 ± 0,72       2,44 (1,00 - 4,67)       F=2,001       0,136         CT history       Absent       98 (17,5)       2,51 ± 0,75       2,44 (1,00 - 4,67)       F=2,001       0,760         RT history       Absent       229 (40,9)       2,51 ± 0,75       2,44 (1,00 - 4,67)       F=0,306       0,760         RT history       Absent       229 (40,9)       2,61 ± 0,68       2,67 (1,00 - 4,67)       F=2,232       0,026         Is he/she currently having CT       No       370 (66,1)       2,50 ± 0,70       2,50 (1,00 - 4,67)       F=2,232       0,026         Purpose if receiving treatment       Adjuvant       170 (40,6)       2,61 ± 0,71       2,67 (1,00 - 4,67)       F=1,508       0,132         Perpose if receiving treatment       Adjuvant       170 (40,6)       2,61 ± 0,71       2,67 (1,00 - 4,67)       F=0,898       0,408         Metastatic-palliative       219 (52,3)       2,51 ± 0,71       2,56 (1,00 - 4,67)       F=0,898  | Urogenital                                | 93 (16,6)     | $2,52 \pm 0,64$     | 2,44 (1,00 - 4,00)  | F=2,077         | 0,067 |
| Disease status  No invasion  281 (50,2)  2,55 ± 0,69  2,56 (1,00 - 4,67)  Local-regional  49 (8,8)  2,68 ± 0,64  2,67 (1,11 - 4,00)  F=2,001  0,136  Metastatic  230 (41,1)  2,47 ± 0,72  2,44 (1,00 - 4,67)  Thistory  Absent  98 (17,5)  2,51 ± 0,75  2,54 ± 0,69  2,56 (1,00 - 4,67)  Present  462 (82,5)  2,54 ± 0,69  2,56 (1,00 - 4,67)  Thistory  Absent  229 (40,9)  2,61 ± 0,68  2,67 (1,00 - 4,67)  Present  331 (59,1)  370 (66,1)  2,50 ± 0,70  2,50 (1,00 - 4,67)  Yes  190 (33,9)  2,59 ± 0,69  2,56 (1,00 - 4,67)  Purpose if receiving treatment  Adjuvant  170 (40,6)  2,61 ± 0,71  2,67 (1,00 - 4,67)  Neoadjuvant  30 (7,2)  2,54 ± 0,68  2,56 (1,11 - 4,00)  F=0,898  0,408  Metastatic-palliative  219 (52,3)  2,51 ± 0,71  2,56 (1,00 - 4,67)  Yes  284 (51,4)  2,52 ± 0,71  2,56 (1,00 - 4,67)  Thistory  1 = 0,363  0,717  Its category if he/she is receiving target-oriented agent  Homonotherapy  140 (49,3)  2,50 ± 0,70  2,44 (1,00 - 4,33)  1 = 0,363  0,717   | Head Neck                                 | 19 (3,4)      | $2,60 \pm 0,73$     | 2,56 (1,44 - 4,67)  |                 |       |
| No invasion 281 (50,2) 2,55 ± 0,69 2,56 (1,00 - 4,67)   Local-regional 49 (8,8) 2,68 ± 0,64 2,67 (1,11 - 4,00) F=2,001 0,136   Metastatic 230 (41,1) 2,47 ± 0,72 2,44 (1,00 - 4,67)    CT history    Absent 98 (17,5) 2,51 ± 0,75 2,44 (1,00 - 4,11) t=-0,306 0,760    RT history    Absent 229 (40,9) 2,61 ± 0,68 2,67 (1,00 - 4,67) t=2,232 0,026    Is he/she currently having CT    No 370 (66,1) 2,50 ± 0,70 2,50 (1,00 - 4,67) t=2,232 0,132    Yes 190 (33,9) 2,59 ± 0,69 2,56 (1,00 - 4,67) t=-1,508 0,132    Purpose if receiving treatment   Adjuvant 170 (40,6) 2,61 ± 0,71 2,67 (1,00 - 4,67)   Neoadjuvant 30 (7,2) 2,54 ± 0,68 2,56 (1,11 - 4,00) F=0,898 0,408    Metastatic-palliative 219 (52,3) 2,51 ± 0,71 2,56 (1,00 - 4,67)   Yes 284 (51,4) 2,52 ± 0,71 2,56 (1,00 - 4,67)   The control of the control of  | Rare tumor and other                      | 34 (6,1)      | $2,\!28 \pm 0,\!81$ | 2,33 (1,00 - 3,89)  |                 |       |
| Local-regional 49 (8,8) 2,68 ± 0,64 2,67 (1,11 - 4,00) F=2,001 0,136  Metastatic 230 (41,1) 2,47 ± 0,72 2,44 (1,00 - 4,67)  CT history  Absent 98 (17,5) 2,51 ± 0,75 2,44 (1,00 - 4,11) t=-0,306 0,760  Present 462 (82,5) 2,54 ± 0,69 2,56 (1,00 - 4,67) t=-2,232 0,026  RT history  Absent 229 (40,9) 2,61 ± 0,68 2,67 (1,00 - 4,67) t=2,232 0,026  Present 331 (59,1) 2,48 ± 0,71 2,44 (1,00 - 4,67) t=2,232 0,026  Is he/she currently having CT  No 370 (66,1) 2,50 ± 0,70 2,50 (1,00 - 4,67) t=-1,508 0,132  Yes 190 (33,9) 2,59 ± 0,69 2,56 (1,00 - 4,67) t=-1,508 0,132  Purpose if receiving treatment  Adjuvant 170 (40,6) 2,61 ± 0,71 2,67 (1,00 - 4,67) t=-1,508 0,408  Metastatic-palliative 219 (52,3) 2,51 ± 0,71 2,56 (1,00 - 4,67)  Is he/she receiving target-oriented agent No 268 (48,6) 2,54 ± 0,69 2,56 (1,00 - 4,67)  Yes 284 (51,4) 2,52 ± 0,71 2,56 (1,00 - 4,67)  Its category if he/she is receiving target-oriented formula for the she is the she of the she is the she of the she is the she of the she of the she of the s   | Disease status                            |               |                     |                     |                 |       |
| Metastatic         230 (41,1) $2,47 \pm 0,72$ $2,44 (1,00 - 4,67)$ CT history         Absent $98 (17,5)$ $2,51 \pm 0,75$ $2,44 (1,00 - 4,11)$ $t=0,306$ $0,760$ Present $462 (82,5)$ $2,54 \pm 0,69$ $2,56 (1,00 - 4,67)$ $t=0,306$ $0,760$ RT history         Absent $229 (40,9)$ $2,61 \pm 0,68$ $2,67 (1,00 - 4,67)$ $t=2,232$ $0,026$ Present $331 (59,1)$ $2,48 \pm 0,71$ $2,44 (1,00 - 4,67)$ $t=2,232$ $0,026$ Is he/she currently having CT $0,00000000000000000000000000000000000$  | No invasion                               | 281 (50,2)    | $2,55 \pm 0,69$     | 2,56 (1,00 - 4,67)  |                 |       |
| CT history  Absent  Present $462 (82,5)$ $2,51 \pm 0,75$ $2,44 (1,00 - 4,11)$ Present $462 (82,5)$ $2,54 \pm 0,69$ $2,56 (1,00 - 4,67)$ RT history  Absent $229 (40,9)$ $2,61 \pm 0,68$ $2,67 (1,00 - 4,67)$ Present $331 (59,1)$ $2,48 \pm 0,71$ $2,44 (1,00 - 4,67)$ $2,44 (1,00 - 4,67)$ $2,232$ $0,026$ RT history  Absent $229 (40,9)$ $2,61 \pm 0,68$ $2,67 (1,00 - 4,67)$ $2,50 \pm 0,70$ | Local-regional                            | 49 (8,8)      | $2,68 \pm 0,64$     | 2,67 (1,11 - 4,00)  | F=2,001         | 0,136 |
| Absent 98 (17,5) 2,51 ± 0,75 2,44 (1,00 - 4,11) $\pm -0,306$ 0,760 Present 462 (82,5) 2,54 ± 0,69 2,56 (1,00 - 4,67) $\pm -0,306$ 0,760 RT history  Absent 229 (40,9) 2,61 ± 0,68 2,67 (1,00 - 4,67) $\pm -2,232$ 0,026 Present 331 (59,1) 2,48 ± 0,71 2,44 (1,00 - 4,67) $\pm -2,232$ 0,026 She currently having CT  No 370 (66,1) 2,50 ± 0,70 2,50 (1,00 - 4,33) $\pm -1,508$ 0,132 Yes 190 (33,9) 2,59 ± 0,69 2,56 (1,00 - 4,67) $\pm -1,508$ 0,132 Purpose if receiving treatment Adjuvant 170 (40,6) 2,61 ± 0,71 2,67 (1,00 - 4,67) $\pm -1,508$ 0,408 Metastatic-palliative 219 (52,3) 2,51 ± 0,71 2,56 (1,00 - 4,67) Is he/she receiving target-oriented agent No 268 (48,6) 2,54 ± 0,69 2,56 (1,00 - 4,67) $\pm -0,363$ 0,717 Yes 284 (51,4) 2,52 ± 0,71 2,56 (1,00 - 4,33) $\pm -0,363$ 0,717 Its category if he/she is receiving target-oriented Homonotherapy 140 (49,3) 2,50 ± 0,70 2,44 (1,00 - 4,33) $\pm -0,363$ 1mmunotherapy 32 (11,3) 2,41 ± 0,75 2,44 (1,00 - 3,78)   | Metastatic                                | 230 (41,1)    | $2,47 \pm 0,72$     | 2,44 (1,00 - 4,67)  |                 |       |
| Present $462 (82,5)$ $2,54 \pm 0,69$ $2,56 (1,00 - 4,67)$ $\leftarrow 0,306$ $0,760$ RT history  Absent $229 (40,9)$ $2,61 \pm 0,68$ $2,67 (1,00 - 4,67)$ $\leftarrow 2,232$ $0,026$ Present $331 (59,1)$ $2,48 \pm 0,71$ $2,44 (1,00 - 4,67)$ $\leftarrow 2,232$ $0,026$ Is he/she currently having CT  No $370 (66,1)$ $2,50 \pm 0,70$ $2,50 (1,00 - 4,33)$ $\leftarrow 1,508$ $0,132$ Purpose if receiving treatment  Adjuvant $170 (40,6)$ $2,61 \pm 0,71$ $2,67 (1,00 - 4,67)$ Neoadjuvant $30 (7,2)$ $2,54 \pm 0,68$ $2,56 (1,11 - 4,00)$ F=0,898 $0,408$ Metastatic-palliative $219 (52,3)$ $2,51 \pm 0,71$ $2,56 (1,00 - 4,67)$ Is he/she receiving target-oriented agent  No $268 (48,6)$ $2,54 \pm 0,69$ $2,56 (1,00 - 4,67)$ Yes $284 (51,4)$ $2,52 \pm 0,71$ $2,56 (1,00 - 4,33)$ Its category if he/she is receiving target-oriented  Homonotherapy $140 (49,3)$ $2,50 \pm 0,70$ $2,44 (1,00 - 4,33)$ Immunotherapy $32 (11,3)$ $2,41 \pm 0,75$ $2,44 (1,00 - 3,78)$  | CT history                                |               |                     |                     |                 |       |
| Present 462 (82,5) 2,54 ± 0,69 2,56 (1,00 - 4,67)  RT history  Absent 229 (40,9) 2,61 ± 0,68 2,67 (1,00 - 4,67)  Present 331 (59,1) 2,48 ± 0,71 2,44 (1,00 - 4,67)  Is he/she currently having CT  No 370 (66,1) 2,50 ± 0,70 2,50 (1,00 - 4,33)  Yes 190 (33,9) 2,59 ± 0,69 2,56 (1,00 - 4,67)  Purpose if receiving treatment  Adjuvant 170 (40,6) 2,61 ± 0,71 2,67 (1,00 - 4,67)  Neoadjuvant 30 (7,2) 2,54 ± 0,68 2,56 (1,11 - 4,00) F=0,898 0,408  Metastatic-palliative 219 (52,3) 2,51 ± 0,71 2,56 (1,00 - 4,67)  Is he/she receiving target-oriented agent  No 268 (48,6) 2,54 ± 0,69 2,56 (1,00 - 4,67)  Yes 284 (51,4) 2,52 ± 0,71 2,56 (1,00 - 4,33)  Its category if he/she is receiving target-oriented  Homonotherapy 140 (49,3) 2,50 ± 0,70 2,44 (1,00 - 4,33)  Immunotherapy 32 (11,3) 2,41 ± 0,75 2,44 (1,00 - 3,78)   | Absent                                    | 98 (17,5)     | $2,51 \pm 0,75$     | 2,44 (1,00 - 4,11)  |                 |       |
| Absent 229 (40,9) 2,61 ± 0,68 2,67 (1,00 - 4,67) $t=2,232$ 0,026 Present 331 (59,1) 2,48 ± 0,71 2,44 (1,00 - 4,67) $t=2,232$ 0,026 Is he/she currently having CT  No 370 (66,1) 2,50 ± 0,70 2,50 (1,00 - 4,33) $t=-1,508$ 0,132 Yes 190 (33,9) 2,59 ± 0,69 2,56 (1,00 - 4,67) $t=-1,508$ 0,132 Purpose if receiving treatment Adjuvant 170 (40,6) 2,61 ± 0,71 2,67 (1,00 - 4,67) $t=-1,508$ 0,408 Metastatic-palliative 219 (52,3) 2,51 ± 0,71 2,56 (1,00 - 4,67) $t=-1,508$ 1s he/she receiving target-oriented agent No 268 (48,6) 2,54 ± 0,69 2,56 (1,00 - 4,67) $t=-1,508$ 1ts category if he/she is receiving target-oriented 49,30 2,50 ± 0,70 2,44 (1,00 - 4,33) $t=-1,508$ 1mmunotherapy 140 (49,3) 2,50 ± 0,70 2,44 (1,00 - 4,33) $t=-1,508$ 1mmunotherapy 32 (11,3) 2,41 ± 0,75 2,44 (1,00 - 3,78)   | Present                                   | 462 (82,5)    | $2,54 \pm 0,69$     | 2,56 (1,00 - 4,67)  | t=-0,306        | 0,760 |
| Present 331 (59,1) 2,48 ± 0,71 2,44 (1,00 - 4,67) $\leftarrow$ 2,232 0,026 Is he/she currently having CT  No 370 (66,1) 2,50 ± 0,70 2,50 (1,00 - 4,33) $\leftarrow$ 1,508 0,132 Yes 190 (33,9) 2,59 ± 0,69 2,56 (1,00 - 4,67) Purpose if receiving treatment  Adjuvant 170 (40,6) 2,61 ± 0,71 2,67 (1,00 - 4,67) Neoadjuvant 30 (7,2) 2,54 ± 0,68 2,56 (1,11 - 4,00) F=0,898 0,408 Metastatic-palliative 219 (52,3) 2,51 ± 0,71 2,56 (1,00 - 4,67) Is he/she receiving target-oriented agent No 268 (48,6) 2,54 ± 0,69 2,56 (1,00 - 4,67) $\leftarrow$ 2,56 (1,00 - 4,67) Its category if he/she is receiving target-oriented Homonotherapy 140 (49,3) 2,50 ± 0,70 2,44 (1,00 - 4,33) Immunotherapy 32 (11,3) 2,41 ± 0,75 2,44 (1,00 - 3,78)   | RT history                                |               |                     |                     |                 |       |
| Present 331 (59,1) 2,48 ± 0,71 2,44 (1,00 - 4,67)  Is he/she currently having CT  No 370 (66,1) 2,50 ± 0,70 2,50 (1,00 - 4,33)  Yes 190 (33,9) 2,59 ± 0,69 2,56 (1,00 - 4,67)  Purpose if receiving treatment  Adjuvant 170 (40,6) 2,61 ± 0,71 2,67 (1,00 - 4,67)  Neoadjuvant 30 (7,2) 2,54 ± 0,68 2,56 (1,11 - 4,00) F=0,898 0,408  Metastatic-palliative 219 (52,3) 2,51 ± 0,71 2,56 (1,00 - 4,67)  Is he/she receiving target-oriented agent  No 268 (48,6) 2,54 ± 0,69 2,56 (1,00 - 4,67)  Yes 284 (51,4) 2,52 ± 0,71 2,56 (1,00 - 4,33)  Its category if he/she is receiving target-oriented  Homonotherapy 140 (49,3) 2,50 ± 0,70 2,44 (1,00 - 4,33)  Immunotherapy 32 (11,3) 2,41 ± 0,75 2,44 (1,00 - 3,78)  | Absent                                    | 229 (40,9)    | $2,61 \pm 0,68$     | 2,67 (1,00 - 4,67)  |                 | 0.006 |
| No $370 (66,1)$ $2.50 \pm 0.70$ $2.50 (1.00 - 4.33)$ $t=-1.508$ $0.132$ Yes $190 (33.9)$ $2.59 \pm 0.69$ $2.56 (1.00 - 4.67)$ $t=-1.508$ $0.132$ Purpose if receiving treatment $Adjuvant$ $170 (40.6)$ $2.61 \pm 0.71$ $2.67 (1.00 - 4.67)$ $0.408$ Neoadjuvant $30 (7.2)$ $2.54 \pm 0.68$ $2.56 (1.11 - 4.00)$ $0.408$ Metastatic-palliative $219 (52.3)$ $2.51 \pm 0.71$ $2.56 (1.00 - 4.67)$ Is he/she receiving target-oriented agent $0.408$ $0.408$ $0.408$ No $0.408$ $0.408$ $0.408$ $0.408$ Yes $0.408$ $0.408$ $0.408$ $0.408$ Yes $0.408$ $0.408$ $0.408$ $0.408$ $0.408$ Yes $0.408$ $0.408$ $0.408$ $0.408$ $0.408$ Its category if he/she is receiving target-oriented $0.408$ $0.408$ $0.408$ $0.408$ $0.408$ $0.408$ $0.408$ $0.408$ $0.408$ $0.408$ $0.408$  | Present                                   | 331 (59,1)    | $2,\!48 \pm 0,\!71$ | 2,44 (1,00 - 4,67)  | t=2,232         | 0,026 |
| Yes 190 (33,9) 2,59 ± 0,69 2,56 (1,00 - 4,67) $= -1,508$ 0,132 Purpose if receiving treatment  Adjuvant 170 (40,6) 2,61 ± 0,71 2,67 (1,00 - 4,67) Neoadjuvant 30 (7,2) 2,54 ± 0,68 2,56 (1,11 - 4,00) $= -1,508$ 0,408 Metastatic-palliative 219 (52,3) 2,51 ± 0,71 2,56 (1,00 - 4,67) Is he/she receiving target-oriented agent No 268 (48,6) 2,54 ± 0,69 2,56 (1,00 - 4,67) $= -1,508$ 1 $= -1,508$ 0,408   | Is he/she currently having CT             |               |                     |                     |                 |       |
| Yes $190 (33.9)$ $2.59 \pm 0.69$ $2.56 (1.00 - 4.67)$ Purpose if receiving treatment       170 (40.6) $2.61 \pm 0.71$ $2.67 (1.00 - 4.67)$ Neoadjuvant $30 (7.2)$ $2.54 \pm 0.68$ $2.56 (1.11 - 4.00)$ $F=0.898$ $0.408$ Metastatic-palliative $219 (52.3)$ $2.51 \pm 0.71$ $2.56 (1.00 - 4.67)$ $1.00 - 4.67$ Is he/she receiving target-oriented agent $0.00 - 4.67$ $0$   | No  | 370 (66,1)    | $2,50 \pm 0,70$     | 2,50 (1,00 - 4,33)  | 1.500           | 0.122 |
| Adjuvant 170 (40,6) 2,61 ± 0,71 2,67 (1,00 - 4,67)  Neoadjuvant 30 (7,2) 2,54 ± 0,68 2,56 (1,11 - 4,00) F=0,898 0,408  Metastatic-palliative 219 (52,3) 2,51 ± 0,71 2,56 (1,00 - 4,67)  Is he/she receiving target-oriented agent No 268 (48,6) 2,54 ± 0,69 2,56 (1,00 - 4,67)  Yes 284 (51,4) 2,52 ± 0,71 2,56 (1,00 - 4,33)  Its category if he/she is receiving target-oriented Homonotherapy 140 (49,3) 2,50 ± 0,70 2,44 (1,00 - 4,33)  Immunotherapy 32 (11,3) 2,41 ± 0,75 2,44 (1,00 - 3,78)   | Yes                                       | 190 (33,9)    | $2,59 \pm 0,69$     | 2,56 (1,00 - 4,67)  | t=-1,508        | 0,132 |
| Neoadjuvant $30 (7,2)$ $2,54 \pm 0,68$ $2,56 (1,11 - 4,00)$ $F=0,898$ $0,408$ Metastatic-palliative $219 (52,3)$ $2,51 \pm 0,71$ $2,56 (1,00 - 4,67)$ Is he/she receiving target-oriented agent $0,00000000000000000000000000000000000$  | Purpose if receiving treatment            |               |                     |                     |                 |       |
| Metastatic-palliative $219 (52,3)$ $2,51 \pm 0,71$ $2,56 (1,00 - 4,67)$ Is he/she receiving target-oriented agent       No $268 (48,6)$ $2,54 \pm 0,69$ $2,56 (1,00 - 4,67)$ $t=0,363$ $0,717$ Yes $284 (51,4)$ $2,52 \pm 0,71$ $2,56 (1,00 - 4,33)$ $t=0,363$ $0,717$ Its category if he/she is receiving target-oriented $t=0,363$   | Adjuvant                                  | 170 (40,6)    | $2,61 \pm 0,71$     | 2,67 (1,00 - 4,67)  |                 |       |
| Is he/she receiving target-oriented agent  No  268 (48,6)  2,54 ± 0,69  2,56 (1,00 - 4,67)  Yes  284 (51,4)  2,52 ± 0,71  2,56 (1,00 - 4,33)  Its category if he/she is receiving target-oriented  Homonotherapy  140 (49,3)  2,50 ± 0,70  2,44 (1,00 - 4,33)  Immunotherapy  32 (11,3)  2,41 ± 0,75  2,44 (1,00 - 3,78)   | Neoadjuvant                               | 30 (7,2)      | $2,54 \pm 0,68$     | 2,56 (1,11 - 4,00)  | F=0,898         | 0,408 |
| No 268 (48,6) 2,54 ± 0,69 2,56 (1,00 - 4,67) $\pm 0,363$ 0,717 Yes 284 (51,4) 2,52 ± 0,71 2,56 (1,00 - 4,33) $\pm 0,363$ 0,717 Its category if he/she is receiving target-oriented Homonotherapy 140 (49,3) 2,50 ± 0,70 2,44 (1,00 - 4,33) $\pm 0,363$ Immunotherapy 32 (11,3) 2,41 ± 0,75 2,44 (1,00 - 3,78)  | Metastatic-palliative                     | 219 (52,3)    | $2,51 \pm 0,71$     | 2,56 (1,00 - 4,67)  |                 |       |
| Yes $284 (51,4)$ $2,52 \pm 0,71$ $2,56 (1,00 - 4,33)$ $t=0,363$ 0,717  Its category if he/she is receiving target- oriented Homonotherapy $140 (49,3)$ $2,50 \pm 0,70$ $2,44 (1,00 - 4,33)$ Immunotherapy $32 (11,3)$ $2,41 \pm 0,75$ $2,44 (1,00 - 3,78)$   | Is he/she receiving target-oriented agent |               |                     |                     |                 |       |
| Yes $284 (51,4)$ $2,52 \pm 0,71$ $2,56 (1,00 - 4,33)$ Its category if he/she is receiving target- oriented  Homonotherapy $140 (49,3)$ $2,50 \pm 0,70$ $2,44 (1,00 - 4,33)$ Immunotherapy $32 (11,3)$ $2,41 \pm 0,75$ $2,44 (1,00 - 3,78)$   | No  | 268 (48,6)    | $2,54 \pm 0,69$     | 2,56 (1,00 - 4,67)  | . 0.252         | 0.515 |
| oriented   | Yes                                       | 284 (51,4)    | $2,52 \pm 0,71$     | 2,56 (1,00 - 4,33)  | t=0,363         | 0,717 |
| Immunotherapy $32 (11,3)$ $2.41 \pm 0.75$ $2.44 (1.00 - 3.78)$   |   |               |                     |                     |                 |       |
| Immunotherapy $32 (11,3)$ $2,41 \pm 0,75$ $2,44 (1,00 - 3,78)$ F=0.742 0.528   | Homonotherapy                             | 140 (49,3)    | $2,50 \pm 0,70$     | 2,44 (1,00 - 4,33)  |                 |       |
| F=0.742 0.528  | Immunotherapy                             | 32 (11,3)     | $2,41 \pm 0,75$     | 2,44 (1,00 - 3,78)  | E 0.512         | 0,528 |
| Thyrosine kinase inh $36 (12,7)$ $2,48 \pm 0,76$ $2,56 (1,00 - 4,11)$  | Thyrosine kinase inh                      | 36 (12,7)     | $2,\!48 \pm 0,\!76$ | 2,56 (1,00 - 4,11)  | F=0,742         |       |
| Monoclonal antibody $76 (26.8)$ $2.61 \pm 0.70$ $2.72 (1.00 - 4.11)$   | Monoclonal antibody                       | 76 (26,8)     | $2,61 \pm 0,70$     | 2,72 (1,00 - 4,11)  |                 |       |
| Is he/she control patient  | Is he/she control patient                 |               |                     |                     |                 |       |



|  | Frequency (n) | Average ± std.<br>Deviation | Average. (min max.) | Test statistics | p      |
|--|---------------|-----------------------------|---------------------|-----------------|--------|
| No   | 451 (80,5)    | $2,56 \pm 0,71$             | 2,56 (1,00 - 4,67)  | t=1,954         | 0.051  |
| Yes  | 109 (19,5)    | $2,41 \pm 0,66$             | 2,44 (1,00 - 4,11)  | 1-1,934         | 0,051  |
| Decision of vaccination                        |               |                             |                     |                 |        |
| I think to have Covid-19 vaccine               | 446 (79,6)    | $2,\!37\pm0,\!64^a$         | 2,33 (1,00 - 4,11)  |                 |        |
| I am hesitant about having<br>Covid-19 Vaccine | 62 (11,1)     | $2,99\pm0,51^{\mathrm{b}}$  | 3,00 (1,89 - 4,11)  | F=76,063        | <0,001 |
| I don't think to have Covid-19<br>Vaccine      | 52 (9,3)      | $3,34\pm0,61^{\rm c}$       | 3,33 (2,00 - 4,67)  |                 |        |

t: t test statistics of independent two samples, F: One-way variance analysis test statistics, a-c: There isn't any difference between groups having the same letter. GIS: Gastrointestinal System, CT: Chemotherapy, RT: Radiotherapy

**Table 4.** Comparison of patient characteristics according to decision of vaccination

|                            | I think to have vaccine | I am reluctant about vaccination | I don't think to have vaccine | Test statistics   | p      |
|----------------------------|-------------------------|----------------------------------|-------------------------------|-------------------|--------|
| Age categorized            |                         |                                  |                               |                   |        |
| Below 50 years old         | 109 (24,4)a             | 29 (46,8)b                       | 18 (34,6)ab                   |                   |        |
| 50-65 years old            | 177 (39,7)              | 30 (48,4)                        | 20 (38,5)                     | $\chi^2 = 28,751$ | <0,001 |
| Over 65 years old          | 160 (35,9)a             | 3 (4,8)b                         | 14 (26,9)a                    |                   |        |
| Gender                     |                         |                                  |                               |                   |        |
| Male                       | 133 (29,8)              | 13 (21)                          | 14 (26,9)                     | 2                 | 0,338  |
| Female                     | 313 (70,2)              | 49 (79)                          | 38 (73,1)                     | $\chi^2 = 2,167$  | 0,338  |
| Diagnosis categorized      |                         |                                  |                               |                   |        |
| Breast                     | 202 (45,3)a             | 40 (64,5)b                       | 26 (50)ab                     |                   |        |
| Thorax                     | 26 (5,8)                | 4 (6,5)                          | 2 (3,8)                       |                   |        |
| Gis                        | 98 (22)                 | 7 (11,3)                         | 9 (17,3)                      | 2                 | <0,001 |
| Urogenital                 | 82 (18,4)               | 7 (11,3)                         | 4 (7,7)                       | $\chi^2 = 37,647$ | <0,001 |
| Head neck                  | 11 (2,5)a               | 0 (0)a                           | 8 (15,4)b                     |                   |        |
| Rare tumor and other       | 27 (6,1)                | 4 (6,5)                          | 3 (5,8)                       |                   |        |
| Disease status             |                         |                                  |                               |                   |        |
| No distribution            | 226 (50,7)              | 33 (53,2)                        | 22 (42,3)                     |                   |        |
| Local-regional             | 34 (7,6)                | 10 (16,1)                        | 5 (9,6)                       | $\chi^2 = 7,634$  | 0,106  |
| Metastatic                 | 186 (41,7)              | 19 (30,6)                        | 25 (48,1)                     |                   |        |
| History of CT              |                         |                                  |                               |                   |        |
| Absent                     | 80 (17,9)               | 14 (22,6)                        | 4 (7,7)                       | $\chi^2 = 4.632$  | 0.099  |
| Present                    | 366 (82,1)              | 48 (77,4)                        | 48 (92,3)                     | X =4,632          | 0,099  |
| History of RT              |                         |                                  |                               |                   |        |
| Absent                     | 179 (40,1)              | 29 (46,8)                        | 21 (40,4)                     | v.2               | 0.607  |
| Present                    | 267 (59,9)              | 33 (53,2)                        | 31 (59,6)                     | $\chi^2 = 0.999$  | 0,007  |
| Is he/she receiving CT now |                         |                                  |                               |                   |        |
| No                         | 300 (67,3)a             | 45 (72,6)a                       | 25 (48,1)b                    | 2                 | 0,011  |
| Yes                        | 146 (32,7)              | 17 (27,4)                        | 27 (51,9)                     | $\chi^2 = 8,966$  | 0,011  |



|   | I think to have vaccine | I am reluctant about vaccination | I don't think to have vaccine | Test statistics  | p     |
|---|-------------------------|----------------------------------|-------------------------------|------------------|-------|
| Purpose if she/he receives treatment        |                         |                                  |                               |                  |       |
| Adjuvant                                    | 134 (40,6)              | 24 (51,1)                        | 12 (28,6)                     |                  |       |
| Neoadjuvant                                 | 21 (6,4)                | 5 (10,6)                         | 4 (9,5)                       | $\chi^2 = 6,718$ | 0,152 |
| Metastatic-palliative                       | 175 (53)                | 18 (38,3)                        | 26 (61,9)                     |                  |       |
| Does she/he receive a Target-oriented Agent |                         |                                  |                               |                  |       |
| No  | 217 (49,2)              | 25 (41,7)                        | 26 (51)                       | 2                | 0.512 |
| Yes   | 224 (50,8)              | 35 (58,3)                        | 25 (49)                       | $\chi^2 = 1,335$ | 0,513 |
| Category if she/he receives target-oriented |                         |                                  |                               |                  |       |
| Hormonotherapy                              | 109 (48,7)              | 21 (60)                          | 10 (40)                       |                  |       |
| Immunotherapy                               | 29 (12,9)               | 3 (8,6)                          | 0 (0)                         | 2                | 0.120 |
| Thyrosine kinase inhibitor                  | 29 (12,9)               | 4 (11,4)                         | 3 (12)                        | $\chi^2 = 9,895$ | 0,129 |
| Monoclonal antibody                         | 57 (25,4)               | 7 (20)                           | 12 (48)                       |                  |       |
| Is he/she a control patient                 |                         |                                  |                               |                  |       |
| No  | 350 (78,5)a             | 56 (90,3)b                       | 45 (86,5)ab                   | 2                | 0.045 |
| Yes   | 96 (21,5)               | 6 (9,7)                          | 7 (13,5)                      | $\chi^2 = 6,191$ | 0,045 |

 $\chi^2$ : Qui-square test, a-b: There isn't any difference between times having same letter. GIS: Gastrointestinal System, CT: Chemotherapy, RT: Radiotherapy

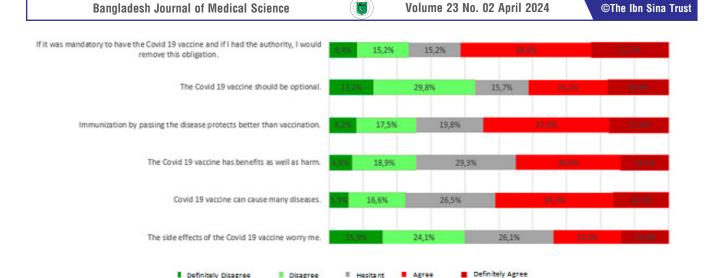
#### **General Attitude of Patients about COVID-19 Vaccine**

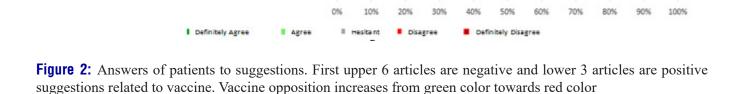
Primarily, there are three positive suggestions in our questionnaire related to COVID-19 (see figure 2 for all answers to suggestions). The first one of them, 'the most powerful prevention against COVID-19 outbreak is vaccine', is a suggestion where hesitant ones (21,1%) and non-agreed ones (totally 12,1%) were some higher than other positive ones. This might have demonstrated to us that patients still look for an alternative except for the vaccine. Ratios of hesitant people to suggestions of 'Disease reduces if everybody vaccinated' and 'COVID-19 Vaccine is an effective method for protecting our health' (15%, 19,5%, respectively) and non-agreed ones (total 10,1%, 10%, respectively) were both at a low level and were with similar ratios. It has been reported that opposition was at the lowest level in the suggestion of' side effects of COVID-19 vaccine make me anxious' compared to other articles (total 33,9%). However, the most interesting one is that more than half of patients have declared an agreement for the suggestion of 'Covid-19 vaccine may cause many diseases' (total 51,0%). It is seen that he sitant population was most intense in the suggestion of 'COVID-19 vaccine has harms as much as its benefits' (29,3%). The ratio of people agreeing with the suggestion of 'Immunization by catching disease protects better than vaccine' has been determined as 54,5%.

Disagreed people to the most discussed article of vaccine opposition, the suggestion of 'COVID-19 vaccine should be optional', is in a pretty high ratio (43,0%). Ones saying agreement to this suggestion remains at 41,2%. That means it appears that an attitude towards vaccine obligation gains weight. Finally, the suggestion of 'If having COVID-19 vaccine becomes compulsory and if I have any authority at hand, I will release this obligation' may be interpreted as an expression of vaccine opposition in a solid base. This suggestion has taken place as the article for which the highest opposition has been reported in the scale (total 61,3%).

#### DISCUSSION

As seen in the example of the smallpox vaccine, the history of vaccination proceeded in parallel with antivaccination. Therefore, if scientists want to obtain success in vaccination, they must eliminate people's reluctance and biases about vaccination. Way of rescuing from COVID-19 pandemic we are inside in the best way passes from an effective vaccination. Because especially cancer patients experience quite sensitive processes from diagnosis up to all stages of treatment, it leads eyes onto this subject. Our aim in this study is to handle the opinions of this patient group about the vaccine and determine an attitude on eliminating biases.





We have learned from the questionnaire that 79,6% of patients thought to have COVID-19 vaccine, 11.1% were hesitant to have a vaccination, and only 9.3% did not think about having a vaccine. Even based on this data, it can be concluded that a more significant majority of patients have a favorable opinion on the vaccine decision.

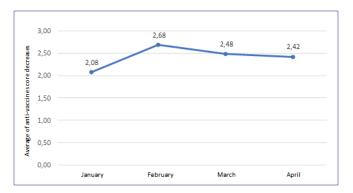
The most powerful measure against the Covid 19 epidemic is vaccination.

If everyone is vaccinated, the disease will decrease.

Covid 19 Vaccine is an effective method to protect our health.

The research made by the Ipsos research company with 19519 persons in a total of 22 countries between 24 July and 7 August 2020 is the source from where we obtained the first data on this subject. 10 Albeit vaccine has not been discovered at that time, a more significant majority of the general population, such as 74%, have indicated that they want to have the vaccination if discovered, and 26% have pointed out that they do not want it to be vaccinated. However, ones not having vaccines represent a minor part, such as 9.3% among cancer patients, according to the result we obtained from our study. However, more profound gaps about this subject when looked at according to countries should also be considered. For example, it

has been reported that while people who do not want to have vaccine was %3 in China, it was reported to be highest as 47% in Russia. 10 The thing that drives people not to want to have a vaccine is possible side effects about the vaccine, while another cause was the belief that the vaccine would not be effective. 10 In our study, patients' reluctance about side effects remains at the backplane compared with other articles. Possibly, the fact that vaccination studies have started and that cases with severe side effects were not reported may provide relief on this subject. As a matter of fact –in a way supporting this hypothesis- we see in our study that ASAV had raised when vaccination studies were newly started in our country, but it decreased with time (Figure 3). One of the suggestions taking most opposition score in our study, 'immunization by catching disease protects better than vaccine' has a meaning superposing with the opinion that vaccine may be ineffective. In fact, catching disease may also result in death at the same time. The result we reached with this suggestion is putting the fact in front of us how much road should be taken in vaccination.



**Figure 3.** Line graph of anti-vaccine score according to admission month. It appears that average of anti-vaccine score decreases with time as vaccination increased.

A study by Brodziak et al. conducted with 635 cancer patients between 26 January 2021 and 18 February 2021 stands close to our study both with the questionnaire design and results obtained apart from being online.11 While 60.1% of patients enrolled in the study have reported positive opinions about vaccination, this ratio has resulted in a pretty high value of 79.6% in our study. In this study, the suggestion that vaccine developed very fast (46,3 %), fear against side effects of vaccine (44,7%), and anxiety about the effectiveness of the vaccine (44,4%) is the suggestion taking highest antivaccine scores. Again, another exciting result obtained is that those reporting they are adequately informed about the possibilities and safety of vaccines remained at a low rate with 38.3% among cancer patients. This data also shows that the health system should spend more effort with patients about the vaccine. Many deficiencies sourced from much information such as this and alike under reluctance of vaccination give us hope towards a solution.

We have obtained information deficiency of cancer patients on vaccination and data underlining the power of informing by oncologists from studies of Kelkar et al. published in March 2021.<sup>12</sup> That study is a design conducted by giving a questionnaire measuring knowledge and attitude of 264 cancer patients before and informing online seminars and after the seminar. The most striking result obtained here is that while the ratio of people who did not want to have COVID-19 was 71% before the seminar, this ratio has raised to 82,5% after the seminar. Ratios of indecisive people about vaccination and vaccine opponents showed a decrease after informing seminar consistently (from

24% to 15,4% and from 5% to 2%, respectively). 12 It is an established truth that evidence-based approaches and convincing attitudes may bring success in vaccination as long as each authority can observe the public's psychological, social, political, and cultural factors and acquire behavior that can eliminate reluctance.<sup>13</sup> Being insistent on vaccine opposition though enlightened adequately about the vaccine can be thought of as a belief system set in a frame and based on consistent reasons in itself.14 Our arguments should be firm, evidence-based, and understandable to solve vaccine opposition in such a situation and a historical background. In addition, religious motivations and negative experiences about vaccination that drive people to this behavior also need to be considered in vaccine opposition.<sup>14,15</sup> Therefore, we have to move by knowing that vaccine opposition can never be zeroed.12

Being the source of knowledge of cancer patients about COVID-19 vaccines were doctors, clinics, or hospitals at the first rank makes it possible for cancer patients to reach the correct source of information and provide an initiative to health authorities. <sup>12,16</sup> A patient may expect the same attitude from his/her doctor also about vaccination as the same he/she is in an expectation from the doctor for benefits and possible harms of treatment during the decision of chemotherapy. Suspects of patients should be eliminated similarly by establishing correct communication channels on this subject. Otherwise, we may indirectly cause that they provide access to different information channels where differentiating accurate information from unreal ones. <sup>7,8,12</sup>

The most powerful aspects of our study are that number of participants was high and that questionnaires were given at the time of application to an outpatient clinic, not online. Our principle restriction is that especially demographic data (living place, income level, education status, etc.) and sources of obtaining knowledge have not been questioned.

#### CONCLUSIONS

This study is one of at least two researches that determined behaviors and attitudes of cancer patients about vaccination. The most critical data obtained is the appearance of severe biases about adverse effects created by the vaccine, although patients have a positive



attitude about vaccination. The most important task of health authorities should be to eliminate reluctance without delay before patients take a more negative attitude on this subject.

**Author Contributions:** Concept –F.E; Design – G.G.; Supervision – A.P.E.; Materials –F.E; Data collection & processing – F.E; Analysis and/or interpretation –A.P.E; Literature search – F.E; Writing – F.E; Critical review – A.P.E.

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**Availability of Data and Materials:** Readers can access all data used in this article.

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