Patterns of Biomarker Use in Cancer Treatment Among Medical Oncologists in the Philippines

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PURPOSE Several factors affect how medical oncologists in the Philippines use biomarkers in real-world practice. This study describes patterns of biomarker testing for the management of breast, colorectal, and lung cancers among medical oncologists in the Philippines.

METHODS A cross-sectional survey was performed among practicing medical oncologists in the Philippines from November to December 2019. The questionnaire determined the ideal and practical use of biomarkers as perceived by the respondents. Responses were summarized. Associations between biomarker use across select conditions were determined.

RESULTS A total of 127 respondents (38% of medical oncologists in the Philippines) participated in this study. In actual practice, 97% of the respondents requested estrogen receptor/progesterone receptor testing, and 93% requested human epidermal growth factor receptor 2 testing. For colorectal cancer, the respondents would use *KRAS* and mismatch repair/microsatellite instability, but 59.84% had never used *BRAF*. For lung cancer, 97.64% of respondents would test for epidermal growth factor receptor (*EGFR*), 88.19% would test for PD-L1, 80.31% for anaplastic lymphoma kinase, 58.27% for *ROS1*, and 33.07% for *BRAF*. In actual practice, *EGFR* was the most frequently ordered test (67.72%), while 44.80% of medical oncologists had never used *ROS1*. The most common reason for testing was adherence to international guidelines (96%). The most commonly cited barrier to biomarker use was patients' financial constraints (94.49%). Overall, the respondents' use of biomarkers was not significantly associated with institutional affiliation, the number of patients they saw monthly, and the availability of biomarker tests in their areas of practice.

CONCLUSION Medical oncologists in the Philippines would use biomarkers in treating breast, colorectal, and lung cancers if these were clinically indicated and if cost were not a factor. Financial difficulty experienced by patients was the most commonly cited barrier to biomarker use.

INTRODUCTION

Cancer management is shifting toward an era of precision oncology, with personalized cancer treatment as the ultimate goal. The ongoing development of targeted small molecules and immuno-oncology biopharmaceuticals largely drives this paradigm shift. Precision oncology relies on validated biomarkers and their companion diagnostics. The presence or absence of a biomarker determines whether a treatment strategy is appropriate. Biomarkers can classify patients according to their disease risk and prognosis.[1]

Personalized treatment strategies lead to improved clinical outcomes in many cancers. For instance, superior clinical outcomes were demonstrated for human epidermal growth factor receptor 2 (HER2)–directed therapy in HER2-positive metastatic breast cancer,[2] epidermal growth factor receptor (*EGFR*)–directed therapy in metastatic colorectal cancer with wild-type *RAS*,[3,4] and *EGFR*-directed therapy in non–small-cell lung cancer (NSCLC) with actionable *EGFR* driver mutations.[5,6] As a result, many clinical practice guidelines now recommend biomarker-driven approaches. Table 1 lists the key biomarkers recommended by the National Comprehensive Cancer Network (NCCN), ASCO, and the European Society for Medical Oncology (ESMO) in breast, colorectal, and lung cancers.

Although precision oncology holds promise in improving clinical outcomes, there are many regions in the world where its use remains limited. In such places, the potential of biomarker-driven treatment strategies may be hindered by several factors, including the countries' health policies and care delivery

CONTEXT

Key Objective

The study described real-world biomarker testing practices among medical oncologists in the Philippines in the management of breast, colorectal, and lung cancers, the top three malignancies in the country.

Knowledge Generated

Medical oncologists in the Philippines would use biomarkers if these were clinically indicated and if cost were not a factor. Testing was driven most frequently by guideline recommendations. Patients' limited finances and refusal to undergo testing, and the unavailability of biomarkers, were the most commonly cited barriers to testing.

Relevance

Filipino medical oncologists treat patients in a resource-limited context where health expenditures are generally out-of-pocket and where biomarker tests are not readily accessible. Improved access to biomarker testing may be accomplished through programs that lower the cost of the tests, provide financial assistance, and increase the number of capable laboratories.

systems.[20] For example, in the Philippines, a low- and middle-income country (LMIC) in Southeast Asia, patients often have to pay out-of-pocket for the tests. Laboratories are concentrated in highly urbanized cities, which limits access to testing for patients residing in remote areas. Because medical oncologists need to discuss the costs of biomarker tests and subsequent therapeutic options with their patients before treatment, the use of biomarkers as the lynchpin of treatment planning may prove difficult in the setting of LMICs. This is an important consideration in the effort to harmonize treatment guidelines on molecular diagnostics and patient-tailored treatment options between more progressive and developing regions of the world.[21]

The practice of medical oncology in the Philippines is governed by the Philippine Society of Medical Oncology (PSMO). In 2019, PSMO had 332 members (275 board-certified members and 57 fellows-in-training). The aim of this study was to describe the patterns of biomarker testing among medical oncologists in the Philippines for the management of breast, colorectal, and lung cancers, the country's top three malignancies.[22] In addition, we aimed to identify the driving factors and barriers to biomarker use in the country.

TABLE 1. Guideline Recommendations for Biomarker Use in Specific Cancers by NCCN, ASCO, and ESMO, and Cost of Test in the Philippines

Biomarker	Key Indications	Cost of Biomarker Test (USD)
Breast cancer[7-12]		
ER	All stages	80-100
PR	All stages	80-100
HER2	All stages	70-80
Oncotype DX, MammaPrint[a]	Early, hormone receptor positive, HER2 negative	4,000
Colorectal cancer[13-16]		
RAS (KRAS/NRAS)	Metastatic	560-820
BRAF	Metastatic	400-600
MSI and/or MMR	All stages, for those with personal history of colorectal cancer	280-300
Lung cancer[17-19]		
EGFR (exon 19, exon21 L858R, other less common mutations)	Advanced/metastatic NSCLC	360-480
ALK	Advanced/metastatic NSCLC	40-120
ROS1	Advanced/metastatic NSCLC	370
BRAF	Advanced/metastatic NSCLC	550
PD-L1	Advanced/metastatic NSCLC	360

Abbreviations. ALK, anaplastic lymphoma kinase; EGFR, epidermal growth factor receptor; ER/PR, estrogen receptor/progesterone receptor; ESMO, European Society for Medical Oncology; HER2, human epidermal growth factor receptor 2; MMR, mismatch repair; MSI, microsatellite instability; NCCN, National Comprehensive Cancer Network; NSCLC, non–small-cell lung cancer; USD, US dollars.

[a]Oncotype Dx (Genomic Health Inc., Redwood City, CA); MammaPrint (Agendia, Amsterdam, the Netherlands).

METHODS

Study Design and Participant Eligibility

From November to December 2019, a cross-sectional survey among medical oncologists was conducted. All members of PSMO were eligible to participate. Nonconsent for participation was the only exclusion criterion. This study received ethical approval from the University of the Philippines Manila Research Ethics Board (UPM REB code 2019-414-01).

Survey Questionnaire

Before the survey, the authors developed a 15-item instrument, formatted as an online Google form (Google, Mountain View, CA) and printed questionnaire (Data Supplement). Of the 15 questions, four were devoted to demographics, nine to biomarker use for each cancer type, and two to factors that drive or hinder biomarker testing. On a Likert scale of always, sometimes, often, and never, respondents were asked to indicate how often they used these tests in actual practice. These categorizations were subjective. Several questions allowed multiple responses to be given, including (1) the respondent's institutional affiliation, (2) tests used in actual clinical practice and those that would be ordered if cost did not play a role, and (3) factors that drive or hinder biomarker testing from the respondents' perspective.

The instruments were pretested among eight medical oncologists for cultural acceptability, ease of use, and overall appeal. These oncologists were staff consultants and trainees from a government hospital and academic medical center in Manila who were preselected because of their knowledge and experience in cancer treatment.

E-mail invitations to participate in the study were sent to all society members and fellows-in-training through the PSMO secretariat. Printed questionnaires were also distributed during the 2019 PSMO Annual Convention held in November for which 91.3% of the members were registered. The printed questionnaires were distributed in the convention's registration booth. Invitations to participate in the study were announced before the plenary sessions. Participants could choose between printed or online instruments. Follow-up e-mails were sent by the PSMO secretariat to all members, including nonresponders.

Data Analysis

The responses were summarized using descriptive statistics using Stata 13.0 software (StataCorp, College Station, TX). A series of χ^2 tests of association and Fisher's exact tests were performed to determine the presence of association between the frequency of physicians' use of biomarkers across select conditions, such as public/private institutions, number of patients they saw monthly, availability of the said biomarkers in their areas of practice, and whether their patients experienced financial constraints. The level of significance for all sets of analysis was set at $P < .05$, using two-tailed comparisons.

RESULTS

A total of 127 unique responses were collected. These comprised 38% of the 332 medical oncologists affiliated with PSMO. Eighty-two (65%) of respondents completed the printed questionnaire, and 45 (35%) answered the online form.

Sixty-three percent of respondents were staff consultants. Two thirds of the medical oncologists were affiliated with private hospitals or clinics, and 56.8% were in their first 3 years of practice. More than half of the medical oncologists practiced in Metro Manila (Table 2). Table 3 lists the average number of patients seen monthly by the respondents for each cancer type.

Biomarker Testing for Breast Cancer

If cost were not an issue, almost all respondents would order estrogen receptor (ER)/progesterone receptor (PR) and HER2 testing (Fig 1). Twenty-five percent would include protein encoded by the *MKI67* gene (Ki-67). Other volunteered responses for testing were *BRCA* mutations (four respondents), Oncotype Dx (Genomic Health, Redwood City, CA; two respondents), and androgen receptor (one respondent). In actual practice, ER/PR and HER2 testing were almost always used (Fig 2).

Biomarker Testing for Colorectal Cancer

Approximately half of the respondents saw three to 10 patients with colorectal cancer monthly (Table 2). If cost

TABLE 2. Respondent Demographic Characteristics (N = 127)

Demographic Characteristic	No. (%)
Type of physician	
Consultant	80 (62.99)
Fellow-in-training	47 (37.01)
Affiliation	
Private hospital/clinic	79 (62.20)
Academic medical center	52 (40.94)
Government hospital	46 (36.22)
Pharmaceutical industry	2 (1.57)
Time in practice/training, years	
≤ 3	71 (56.8)
4-10	26 (20.8)
11-20	22 (17.6)
> 20	6 (4.8)
Place of practice	
Metro Manila	68 (54.4)
Northern Luzon	14 (11.2)
Southern Luzon	13 (10.4)
Visayas	17 (13.6)
Mindanao	13 (10.4)

TABLE 3. Number of Patients Seen in a Month According to Cancer Diagnosis

Type of Malignancy	No. (%)
Breast cancer	
0	1 (0.79)
1-2	15 (11.81)
3-10	44 (34.65)
11-30	42 (33.07)
> 30	25 (19.69)
Colorectal cancer	
0	3 (2.36)
1-2	29 (22.83)
3-10	60 (47.24)
11-30	33 (25.98)
> 30	2 (1.57)
Lung cancer	
0	3 (2.36)
1-2	49 (38.58)
3-10	62 (48.82)
11-30	13 (10.24)
> 30	0 (0.00)

FIG 1. Biomarker use in breast cancer if cost were not an issue. ER/PR, estrogen receptor/progesterone receptor; FISH, fluorescence in situ hybridization; HER2, human epidermal growth factor receptor 2.

were not an issue and if the tests were clinically indicated, almost all respondents would test for *KRAS* mutation. Only 63.78% would test for *BRAF* mutations (Fig 3). In actual practice, < 50% of respondents routinely requested *KRAS/NRAS*, *BRAF*, and microsatellite instability (MSI)/mismatch repair (MMR) tests (Fig 4). Sixty percent of the respondents never tested for *BRAF* mutations.

Biomarker Testing for Lung Cancer

Almost all respondents would request *EGFR* mutation testing if cost were not an issue and if clinically indicated. PD-L1 and anaplastic lymphoma kinase (*ALK*) were also common responses (Fig 5), and 54.33% of respondents
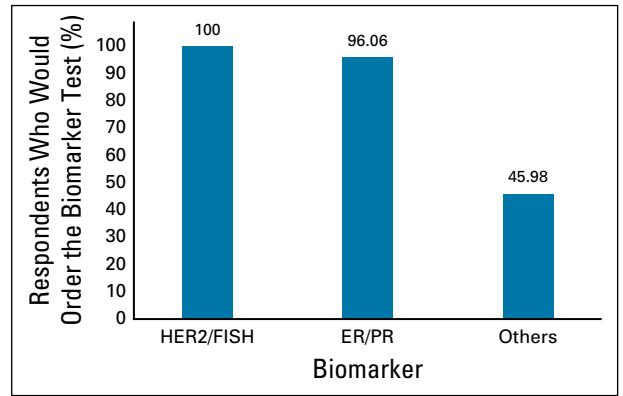
would test for *T790M* mutation. In actual clinical practice, 67.72% of the respondents always ordered *EGFR* testing (Fig 6).

Driving Factors for and Barriers to Biomarker Testing

The most frequent reason cited by respondents for why they would pursue biomarker testing was that the tests are recommended by clinical practice guidelines (Table 4). The guidelines used by the respondents were NCCN (32.28%), ASCO (4.72%), ESMO (1.57%), and all three of these (61.47%). Other factors that drove them to use biomarkers were their patients' advanced or metastatic stage (76.38%) and their patients' inclusion in clinical trials that made use of such biomarkers (49.61%; Table 4).

The respondents reported several barriers that hindered them from pursuing biomarker testing for their patients (Table 4). They would not pursue testing if their patients reported financial difficulties (94.49%), if their patients stated that they did not wish to be tested (60%), if the tests were not available in their areas of practice (58.27%), and if there was insufficient tissue sample for the tests to be reliably performed (47.24%).

FIG 2. Biomarker testing practices in breast cancer in actual practice. ER/PR, estrogen receptor/progesterone receptor; FISH, fluorescence in situ hybridization; HER2, human epidermal growth factor receptor 2.
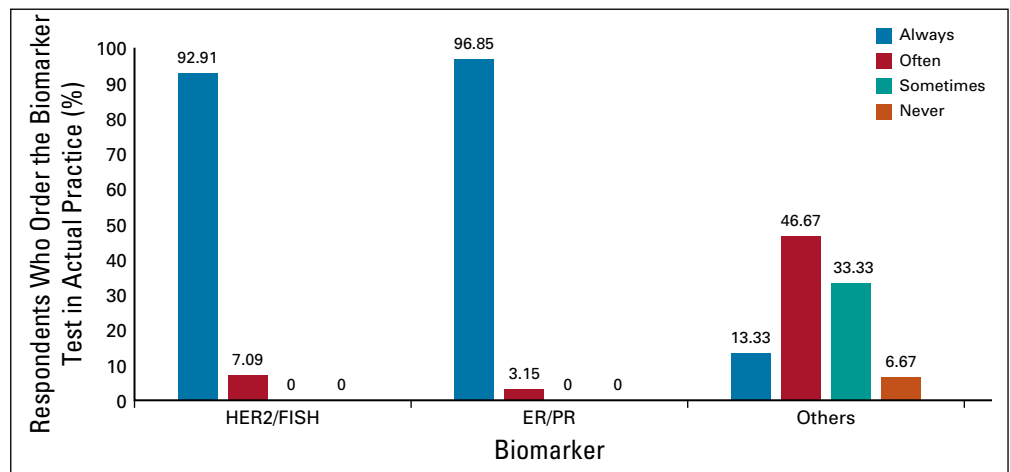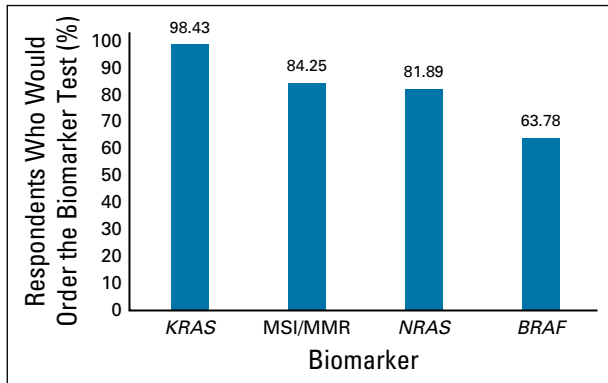
FIG 3. Biomarker use in colorectal cancer if cost were not an issue. MMR, mismatch repair; MSI, microsatellite instability.

FIG 5. Biomarker use in lung cancer if cost were not an issue.

Factors Associated With Biomarker Use

The respondents' use of biomarkers was not significantly associated with their institutional affiliation (Appendix Table A1), their patients' financial difficulties (Appendix Table A2), the availability of biomarkers in their areas of practice (Appendix Table A3), and the number of patients they saw monthly (Appendix Table A4). However, there were several exceptions. Respondents affiliated with academic institutions tested for *EGFR T790M* for lung cancer ($P = .02$) and *NRAS* ($P = .01$) for colorectal cancer more frequently than respondents who were not affiliated with academia (Appendix Table A5). There was a nonsignificant trend for an association between the use of *EGFR* for lung cancer among respondents affiliated with private hospitals compared with those affiliated with government-run hospitals ($P = .08$).

A significant association between the respondents' use of biomarkers and the number of patients seen monthly was observed only in *ROS1* for lung cancer ($P = .04$). It seemed that respondents who saw more patients with lung cancer monthly ordered *EGFR* ($P = .08$), PD-L1 ($P = .11$), and *EGFR T790M* ($P = .08$) tests, although the associations
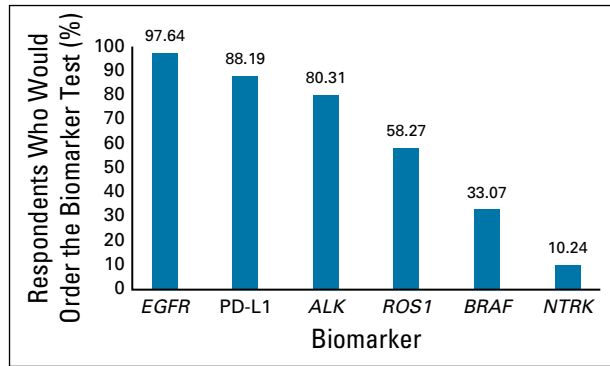
were not significant. Regardless of the number of patients seen, the medical oncologists tended to prescribe *NTRK* testing for patients with lung cancer less frequently ($P = .07$). The association between biomarker use and its availability in the area of practice was only significant for *KRAS/NRAS* in colorectal cancer ($P < .01$).

DISCUSSION

To our knowledge, this study is the first to describe real-world practices of medical oncologists in the Philippines with regard to precision medicine in cancer management. In actual practice, patterns of biomarker use seemed heterogenous. Testing was driven most frequently by guideline recommendations. Patients' limited finances and refusal to undergo testing, as well as the unavailability of biomarkers in oncologists' areas of practice, were the most common barriers that hindered the respondents from pursuing the recommended tests.

This study was important to carry out for three reasons:

1. Filipino medical oncologists treat patients in a setting where health expenditures are generally out-of-pocket.
2. Filipino patients may opt to defer treatment to spare their families from economic and emotional hardships.[23]

FIG 4. Biomarker testing practices in colorectal cancer in actual practice. MMR, mismatch repair; MSI, microsatellite instability.
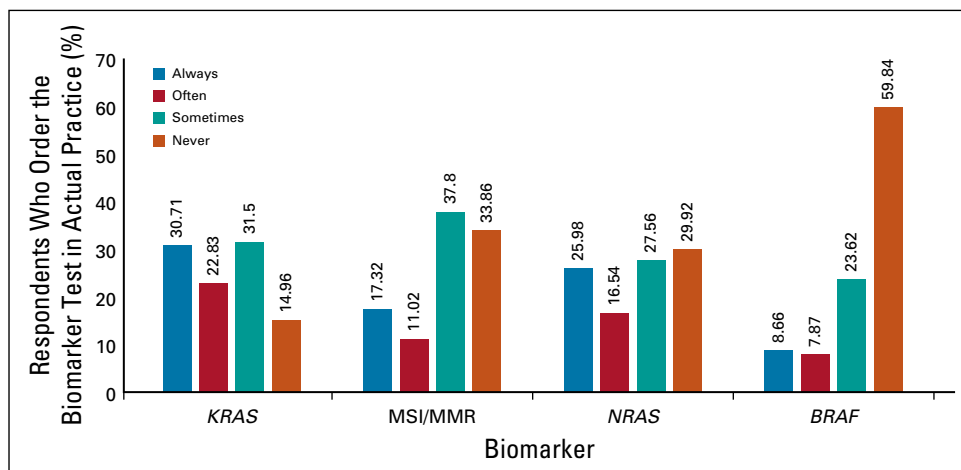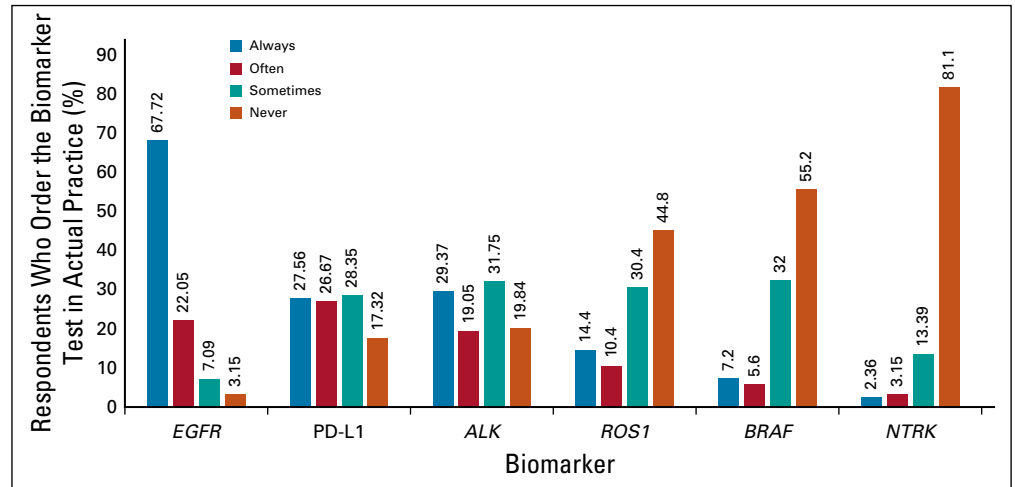
FIG 6. Biomarker testing practices in lung cancer in actual practice.

3. Some medical oncologists practice in areas where biomarker tests may not be readily available. In this study, particular focus was given to breast, colorectal, and lung cancers because these were the most common malignancies in the Philippines.[22]

In breast cancer, we showed that the respondents used ER/PR and HER2 testing routinely. A quarter of respondents would test for Ki-67, despite the controversy about its value because of a lack of standardized assessments.[24] It seemed that the respondents did not rely exclusively on guideline recommendations.

In colorectal cancer, the respondents would use KRAS, NRAS, BRAF, and MSI/MMR status testing if these were

TABLE 4. Driving Factors for and Barriers to Biomarker Use

Variable	No. (%)
Driving factors	
Tests are based on clinical practice guidelines	122 (96.06)
Patient has advanced or metastatic disease	97 (76.38)
Patient is included in clinical trial	63 (49.61)
No other treatment options exist; biomarkers may lead to more options	54 (42.52)
Test is based on the institution's oncology pathway/protocol	46 (36.22)
Barriers	
Patients experience financial constraints	120 (94.49)
Patients do not want to be tested	75 (59.06)
Test is not available in area of practice	74 (58.27)
There is insufficient tissue sample	60 (47.24)
Test results come out late	9 (7.09)
Tests do not change clinical decision and management	7 (5.51)
Medical oncologist is not familiar with test	4 (3.15)
Medical oncologist is familiar with test but believes that there are not enough study data to support testing	3 (2.36)

indicated and if cost were not an issue (Table 4). Approximately 40% of respondents, however, answered that they would not order BRAF testing despite guideline recommendations for its use in metastatic disease. In actual clinical practice, < 30% of respondents requested all four tests routinely. A prominent finding was that 59.84% of respondents had never used BRAF. It seemed that on top of cost, other issues serve as barriers to biomarker use.

In lung cancer, almost all respondents (97.64%) would test for EGFR mutations. In actual practice, however, only 67.72% tested for EGFR routinely. Of note, 55.2% and 44.8% of respondents had never used BRAF and ROS1, respectively, in real-world practice.

Guideline recommendation was the most frequent motivation for biomarker testing. This mirrored the results of a similar survey of oncologists from other countries.[25] In the absence of local guidelines, medical oncologists in the Philippines refer to guidelines developed by NCCN, ASCO, and ESMO. Updated regularly, these reflect the standards of care in developed regions with ready access to cutting-edge molecular tests and targeted treatments that may not be available in the Philippines. Recently, regional guidelines have emerged to adapt western guidelines, taking into account ethnic differences associated with the treatment of metastatic NSCLC cancer in Asian patients. PSMO was not part of the consensus panel for these guidelines. Even these Pan-Asian guidelines might not be directly applicable in the Philippine setting.[26]

For the three cancers, evidence shows that biomarkers can guide treatment planning for the first and subsequent lines. Related to this, our results showed that medical oncologists used biomarker testing to explore alternative treatment options.

Of note, almost half reported using biomarker tests because their patients were included in clinical trials (Table 4). Testing was likely required before enrollment. Oncologists who practiced in academic medical centers would have more exposure to clinical trials. We showed a significant

association between the use of *EGFR T790M* and *NRAS* with affiliation to academia.

Almost all the respondents indicated that they would not pursue biomarker testing if their patients reported financial difficulties (Table 4). Biomarker tests are expensive (Table 1). Given that the average monthly income of Filipino households is 26,000 Philippine pesos (US $500),[27] the cost of cancer diagnosis and treatment would be prohibitive for many. According to one study, 40.6% of Filipinos with cancer will experience financial catastrophe that arises from their illness.[23] The costs of cancer care consist of expenditures for medications and diagnostics, including biomarkers. This issue is not limited to LMICs.[25]

Sixty percent of the respondents would not pursue testing if their patients refused to be tested. Patients might not comprehend the benefits of testing,[25] they might want to proceed with best supportive care instead, or they might be daunted by the cost of treatment.

Approximately 60% of respondents reported that the unavailability of tests in their areas of practice hindered testing (Table 4), similar to the findings of a multinational study.[25] As of 2019, the tests for *BRCA* mutation, Oncotype Dx, *KRAS*, *NRAS*, *BRAF*, MSI, *EGFR*, *ALK*, *BRAF*, PD-L1, *T790M*, and *ROS1* were only available in six centers in Metro Manila (Fig 7).

Insufficient tissue sample was another barrier. This reason should merit clarification from respondents because in at least some instances, it would seem remediable. Certainly, the quantity and quality of the tumor material is a limiting factor for adequate biomarker analysis.[24]

We determined the presence of an association between the physician's use of biomarkers and select conditions. In general, we noted no statistically significant associations, likely because of our study's sample size. Nevertheless, there were several key exceptions for which the association was significant—*EGFR T790M* and *NRAS* with academic center affiliation, *ROS1* with more patients with lung cancer seen monthly, and *KRAS/NRAS* with its availability in the area of practice. Several points might explain these findings: (1) physicians from academic and private institutions would have greater access to the biomarker tests, (2) physicians from private hospitals would have more contact with patients who could afford treatment, and (3) physicians who saw more patients monthly would have more opportunities to pursue testing.

Our study had several limitations. First, there was a risk of social desirability bias; respondents might have felt pressured to give more acceptable answers. While the effect of this bias could not be eliminated completely, maintaining respondent anonymity would mitigate it.[28] In this study, we used anonymized questionnaires. Online submissions could not be traced back to the sender, and paper submissions were through a third party (PSMO secretariat). Another concern was nonresponse bias possibly as a result

FIG 7. Tests for *BRCA* mutation, Oncotype Dx, *KRAS*, *NRAS*, *BRAF*, microsatellite instability, epidermal growth factor receptor, anaplastic lymphoma kinase, *BRAF*, PD-L1, *T790M*, and *ROS1* are only available in the National Capital Region (Metro Manila, Philippines), which is highlighted in red.

of indifference or busyness. Furthermore, studies have reported that physician response rates to surveys tend to be low.[29,30] Regardless of the reasons, interventions that could improve response rates include personalizing cover letters, incentivizing survey response, and implementing a thorough follow-up system for nonresponders.[29-32] In our study, we aggressively pursued an advertising campaign through e-mail sent to the entire PSMO and supplemented by frequent announcements during plenary sessions. In addition, we made electronic and paper formats of the survey available to make participation more convenient. Despite these interventions, the response rate was only 38%, and respondents tended to be younger members of the society. Second, although we attempted to include all medical oncologists, our study had a response rate of < 40%, which is comparable to other similarly conducted studies.[9,30,33,34] A strength of the study is the participation of medical oncologists from various institutions, including oncology trainees and attending physicians (Table 2). Because all medical oncologists affiliated with PSMO were invited, the probability of a differential response bias could have been

lessened. Nevertheless, there was a higher response rate among respondents who were from Metro Manila and were in private practice. On the basis of the PSMO membership data, 43% of consultants practice in Metro Manila. The concentration of medical oncologists affiliated with private hospitals/clinics in urbanized areas was reflected in the distribution of respondents of this study. Third, we did not perform qualitative analysis (interviews or focus group discussions) to probe the underlying reasons. The study relied solely on a printed instrument to elicit responses. Nevertheless, the questionnaire provided the respondents an opportunity to volunteer other reasons if they saw fit to do so. Fourth, by leaving some questions open to interpretation due to the vagueness of the statement (ie, "as clinically indicated"), the survey might have assumed that the respondents were fully aware of the indications for each of the tests. Fifth, the survey did not attempt to measure the baseline knowledge of the respondents with respect to biomarker testing guidelines. This would have allowed better contextualization of the study's results. Finally, the driving factors and barriers to testing were not analyzed separately for each cancer type; the responses could certainly vary depending on the cancer. In the end, the study described the general factors affecting physicians' biomarker use in the Philippines.

In summary, medical oncologists in the Philippines would use biomarkers in the management of breast, colorectal, and lung cancers if these were clinically indicated and if cost were not an issue. Almost all the respondents indicated that they would not pursue testing if their patients reported financial difficulties.

Given our findings, we have the following recommendations. First, additional patient access programs may need to be developed and existing ones strengthened. These programs may involve lowering the costs of the tests through government regulations, increasing the number of certified and capable laboratories throughout the Philippines, and giving patients financial subsidies. Second, patient-centered education on the value of the tests in cancer treatment may need to be implemented in the clinics. Third, medical societies may provide avenues for continuing medical education on precision medicine. Finally, hospitals ought to engage in clinical trials whenever possible because these may allow free access to molecular diagnostics.

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APPENDIX

TABLE A1. Frequency Distribution of Responses Across Type of Institution

Biomarker Test Used	Public/Government No. (%)	Private No. (%)	P
No. of respondents	48 (37.80)	79 (62.20)	—
Breast cancer			
ER/PR			
Always	46 (95.83)	77 (97.47)	.61
Often	2 (4.17)	2 (2.53)	
HER2/FISH for HER2			
Always	46 (95.83)	72 (91.14)	.32
Often	2 (4.17)	7 (8.86)	
Others			
Always	2 (4.17)	—	
Often	2 (4.17)	5 (6.33)	.34
Sometimes	2 (4.17)	3 (3.80)	
Never	—	1 (1.27)	
Lung cancer			
EGFR			
Always	28 (58.33)	58 (73.42)	
Often	16 (33.33)	12 (15.19)	.08
Sometimes	2 (4.17)	7 (8.86)	
Never	2 (4.17)	2 (2.53)	
ROS1			
Always	8 (17.02)	10 (12.82)	
Often	5 (10.64)	8 (10.26)	.28
Sometimes	18 (38.30)	20 (25.64)	
Never	16 (34.04)	40 (51.28)	
BRAF			
Always	4 (8.51)	5 (6.41)	
Often	2 (4.26)	5 (6.41)	.38
Sometimes	16 (40.43)	21 (26.92)	
Never	22 (46.81)	47 (60.26)	
PD-L1			
Always	13 (27.08)	22 (27.85)	
Often	11 (22.92)	23 (29.11)	.55
Sometimes	17 (35.42)	19 (24.05)	
Never	7 (14.58)	15 (18.99)	
EGFR T790M			
Always	14 (29.17)	16 (20.25)	
Often	9 (18.75)	13 (16.46)	.54
Sometimes	14 (29.17)	32 (40.51)	
Never	11 (22.92)	18 (22.78)	

(Continued in next column)

TABLE A1. Frequency Distribution of Responses Across Type of Institution (Continued)

Biomarker Test Used	Public/Government No. (%)	Private No. (%)	P
NTRK			
Always	2 (4.17)	1 (1.27)	
Often	1 (2.08)	3 (3.80)	.71
Sometimes	6 (12.50)	11 (13.92)	
Never	39 (81.25)	64 (81.01)	
Colorectal cancer			
KRAS			
Always	13 (27.08)	26 (32.91)	
Often	12 (25)	17 (21.52)	.89
Sometimes	15 (31.25)	25 (31.65)	
Never	8 (16.67)	11 (13.92)	
NRAS			
Always	12 (25)	21 (26.58)	
Often	9 (18.75)	12 (15.19)	.74
Sometimes	15 (31.25)	20 (25.32)	
Never	12 (25)	26 (32.91)	
BRAF			
Always	6 (12.50)	5 (6.33)	
Often	2 (4.17)	8 (10.13)	.36
Sometimes	13 (27.08)	17 (21.52)	
Never	27 (56.25)	49 (62.03)	
MSI/MMR			
Always	8 (16.67)	14 (17.72)	
Often	5 (10.42)	9 (11.39)	.74
Sometimes	21 (43.75)	27 (34.18)	
Never	14 (29.17)	29 (36.71)	

Abbreviations: EGFR, epidermal growth factor receptor; ER/PR, estrogen receptor/progesterone receptor; FISH, fluorescence in situ; HER2, human epidermal growth factor receptor; MMR, mismatch repair; MSI, microsatellite instability.

TABLE A2. Frequency Distribution of Responses Across Presence of Financial Constraints

Biomarker Test Used	Financial Constraints, No. (%) Without	With	P
No. of respondents	7 (5.51)	120 (94.49)	—
Breast cancer			
ER/PR			
Always	7 (100)	116 (96.67)	.80
Often	—	4 (3.33)	
HER2/FISH for HER2			
Always	7 (100)	111 (92.50)	.60
Often	—	9 (7.50)	
Others			
Always	—	2 (1.67)	
Often	1 (14.29)	6 (5.00)	.75
Sometimes	—	5 (4.17)	
Never	—	1 (0.83)	
Lung cancer			
EGFR			
Always	6 (85.71)	80 (66.67)	
Often	1 (14.29)	27 (22.50)	.73
Sometimes	—	9 (7.50)	
Never	—	4 (3.33)	
ROS1			
Always	4 (57.14)	14 (11.67)	
Often	—	13 (10.83)	.01*
Sometimes	1 (14.29)	37 (30.83)	
Never	1 (14.29)	55 (45.83)	
BRAF			
Always	2 (28.57)	7 (5.83)	
Often	2 (28.57)	5 (4.17)	.01*
Sometimes	—	40 (33.33)	
Never	2 (28.57)	67 (55.83)	
PD-L1			
Always	4 (57.14)	31 (25.83)	
Often	1 (14.29)	33 (27.50)	.46
Sometimes	1 (14.29)	35 (29.17)	
Never	1 (14.29)	21 (17.50)	
EGFR T790M			
Always	4 (57.14)	26 (21.67)	
Often	—	22 (18.33)	.12
Sometimes	1 (14.29)	45 (37.50)	
Never	2 (28.57)	27 (22.50)	
NTRK			
Always	1 (14.29)	2 (1.67)	
Often	1 (14.29)	3 (2.50)	.06

(Continued in next column)

TABLE A2. Frequency Distribution of Responses Across Presence of Financial Constraints (Continued)

Biomarker Test Used	Financial Constraints, No. (%) Without	With	P
Sometimes	—	17 (14.17)	
Never	5 (71.43)	98 (81.67)	
Colorectal cancer			
KRAS			
Always	4 (57.14)	35 (29.17)	
Often	1 (14.29)	28 (23.33)	.45
Sometimes	1 (14.29)	39 (32.50)	
Never	1 (14.29)	18 (15.00)	
NRAS			
Always	3 (42.86)	30 (25.00)	
Often	1 (14.29)	20 (16.67)	.70
Sometimes	2 (28.57)	33 (27.50)	
Never	1 (14.29)	37 (30.83)	
BRAF			
Always	2 (28.57)	9 (7.50)	
Often	—	10 (8.33)	.22
Sometimes	2 (28.57)	28 (23.33)	
Never	3 (42.86)	73 (60.83)	
MSI/MMR			
Always	3 (42.86)	19 (15.83)	
Often	—	14 (11.67)	.25
Sometimes	3 (42.86)	45 (37.50)	
Never	1 (14.29)	42 (35.00)	

Abbreviations: EGFR, epidermal growth factor receptor; ER/PR, estrogen receptor/progesterone receptor; FISH, fluorescence in situ; HER2, human epidermal growth factor receptor; MMR, mismatch repair; MSI, microsatellite instability.
*Significant at P < .05.

TABLE A3. Frequency Distribution of Responses Across Availability of Biomarker Tests

Biomarker Test Used	With Readily Available Biomarkers Tests, No. (%)		
	Yes	No	P
No. of respondents	53 (41.73)	74 (58.27)	—
Breast cancer			
ER/PR			
Always	52 (98.11)	71 (95.95)	.49
Often	1 (1.89)	3 (4.05)	
HER2/FISH for HER2			
Always	51 (96.23)	67 (90.54)	.22
Often	2 (3.77)	7 (9.46)	
Others			
Always	2 (25)	—	
Often	4 (50)	3 (42.86)	.18
Sometimes	1 (12.50)	4 (57.14)	
Never	1 (12.50)	—	
Lung cancer			
EGFR			
Always	39 (73.58)	47 (63.51)	
Often	12 (22.64)	16 (21.62)	.24
Sometimes	2 (3.77)	7 (9.46)	
Never	—	4 (5.41)	
ROS1			
Always	12 (22.64)	6 (8.11)	
Often	4 (7.55)	9 (12.16)	.10
Sometimes	17 (32.08)	21 (28.38)	
Never	20 (37.74)	36 (48.65)	
BRAF			
Always	6 (11.32)	3 (4.05)	
Often	3 (5.66)	4 (5.41)	.19
Sometimes	20 (37.74)	20 (27.03)	
Never	24 (45.28)	45 (60.81)	
PD-L1			
Always	21 (39.62)	14 (18.92)	
Often	12 (22.64)	22 (29.73)	.08
Sometimes	13 (24.53)	23 (31.08)	
Never	7 (13.21)	15 (20.27)	
EGFR T790M			
Always	14 (26.42)	16 (21.62)	
Often	11 (20.75)	11 (14.86)	.61
Sometimes	16 (30.19)	30 (40.54)	
Never	12 (22.64)	17 (22.97)	
NTRK			
Always	2 (3.77)	1 (1.35)	

(Continued in next column)

TABLE A3. Frequency Distribution of Responses Across Availability of Biomarker Tests (Continued)

Biomarker Test Used	With Readily Available Biomarkers Tests, No. (%)		
	Yes	No	P
Often	2 (3.77)	2 (2.70)	.82
Sometimes	7 (13.21)	10 (13.51)	
Never	42 (79.25)	61 (82.43)	
Colorectal cancer			
KRAS			
Always	24 (45.28)	15 (20.27)	
Often	10 (18.87)	19 (25.68)	< .01*
Sometimes	17 (32.08)	23 (31.08)	
Never	2 (3.77)	17 (22.97)	
NRAS			
Always	20 (37.74)	13 (17.57)	
Often	7 (13.21)	14 (18.92)	< .01*
Sometimes	18 (33.96)	17 (22.97)	
Never	8 (15.09)	30 (40.54)	
BRAF			
Always	8 (15.09)	3 (4.05)	
Often	4 (7.55)	6 (8.11)	.12
Sometimes	14 (26.42)	16 (21.62)	
Never	27 (50.94)	49 (66.22)	
MSI/MMR			
Always	16 (30.19)	6 (8.11)	
Often	4 (7.55)	10 (13.51)	.01*
Sometimes	20 (37.74)	28 (37.84)	
Never	13 (24.53)	30 (40.54)	

Abbreviations: EGFR, epidermal growth factor receptor; ER/PR, estrogen receptor/progesterone receptor; FISH, fluorescence in situ; HER2, human epidermal growth factor receptor; MMR, mismatch repair; MSI, microsatellite instability.
*Significant at $P < .05$.

TABLE A4. Frequency Distribution of Responses Across Number of Patients Seen

Biomarker Test Used	Patients Seen in a Month, No. (%)				
	1-2	3-10	11-30	> 30	*P*
Breast cancer	16 (12.60)	44 (34.65)	42 (33.07)	25 (19.69)	—
ER/PR					
Always	16 (100)	43 (97.73)	40 (95.24)	24 (96)	.90
Often	—	1 (2.27)	2 (4.76)	1 (4)	
HER2/FISH for HER2					
Always	16 (100)	41 (93.18)	37 (88.10)	24 (96)	.53
Often	—	3 (6.82)	5 (11.90)	1 (4)	
Others					
Always	—	—	2 (4.76)	—	
Often	—	5 (11.36)	2 (4.76)	—	.03*
Sometimes	—	—	2 (4.76)	3 (12)	
Never	—	1 (2.27)	—	—	
Lung cancer	3 (2.36)	49 (38.58)	62 (48.82)	13 (10.24)	—
EGFR					
Always	2 (66.67)	29 (59.18)	43 (69.35)	12 (92.31)	
Often	—	11 (22.45)	16 (25.81)	1 (7.69)	.08
Sometimes	—	6 (12.24)	3 (4.84)	—	
Never	1 (33.33)	3 (6.12)	—	—	
ROS1					
Always	—	2 (4.26)	13 (20.97)	3 (23.08)	
Often	—	4 (8.51)	6 (9.68)	3 (23.08)	.04*
Sometimes	—	17 (36.17)	16 (25.81)	5 (38.46)	
Never	3 (100)	24 (51.06)	27 (43.55)	2 (15.38)	
BRAF					
Always	—	1 (2.13)	6 (9.68)	2 (15.38)	
Often	—	1 (2.13)	4 (6.45)	2 (15.38)	.25
Sometimes	—	17 (36.17)	18 (29.03)	5 (38.46)	
Never	3 (100)	28 (59.57)	34 (54.84)	4 (30.77)	
PD-L1					
Always	2 (66.67)	7 (14.29)	19 (30.65)	7 (53.85)	
Often	—	14 (28.57)	17 (27.42)	3 (23.08)	.11
Sometimes	—	16 (32.65)	18 (29.03)	2 (15.38)	
Never	1 (33.33)	12 (24.49)	8 (12.90)	1 (7.69)	
EGFR T790M					
Always	2 (66.67)	9 (18.37)	15 (24.19)	4 (30.77)	
Often	—	9 (18.37)	12 (19.35)	1 (7.69)	.08
Sometimes	—	21 (42.86)	17 (27.42)	8 (61.54)	
Never	1 (33.33)	10 (20.41)	18 (29.03)	—	

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TABLE A4. Frequency Distribution of Responses Across Number of Patients Seen (Continued)

Biomarker Test Used	Patients Seen in a Month, No. (%)				
	1-2	3-10	11-30	> 30	P
NTRK					
Always	—	1 (2.04)	2 (3.23)	—	
Often	—	—	1 (1.61)	3 (23.08)	.07
Sometimes	—	9 (18.37)	6 (9.68)	2 (15.38)	
Never	3 (100)	39 (79.59)	53 (85.48)	8 (61.54)	
Colorectal cancer	3 (2.36)	29 (22.83)	60 (47.24)	35 (27.56)	—
KRAS					
Always	—	6 (20.69)	19 (31.67)	14 (40)	
Often	—	5 (17.24)	17 (28.33)	7 (20)	.21
Sometimes	1 (33.33)	11 (37.93)	17 (28.33)	11 (31.43)	
Never	2 (66.67)	7 (24.14)	7 (11.67)	3 (8.57)	
NRAS					
Always	—	6 (20.69)	17 (28.33)	10 (28.57)	
Often	—	5 (17.24)	10 (16.67)	6 (17.14)	.32
Sometimes	—	6 (20.69)	16 (26.67)	13 (37.14)	
Never	3 (100)	12 (41.38)	17 (28.33)	6 (17.14)	
BRAF					
Always	—	3 (10.34)	5 (8.33)	3 (8.57)	
Often	—	1 (3.45)	5 (8.33)	4 (11.43)	.75
Sometimes	—	4 (13.79)	16 (26.67)	10 (28.57)	
Never	3 (100)	21 (72.41)	34 (56.67)	18 (51.43)	
MSI/MMR					
Always	—	4 (13.79)	9 (15)	9 (25.71)	
Often	—	1 (3.45)	10 (16.67)	3 (8.57)	.26
Sometimes	—	11 (37.93)	24 (40)	13 (37.14)	
Never	3 (100)	13 (44.83)	17 (28.33)	10 (28.57)	

Abbreviations: *EGFR*, epidermal growth factor receptor; ER/PR, estrogen receptor/progesterone receptor; FISH, fluorescence in situ; HER2, human epidermal growth factor receptor; MMR, mismatch repair; MSI, microsatellite instability.

*Significant at *P* < .05.

TABLE A5. Frequency Distribution of Responses Across Type of Institution

Biomarker Test Used	Nonacademic No. (%)	Academic Center No. (%)	P
No. of respondents	75 (59.06)	52 (40.94)	—
Breast cancer			
ER/PR			
Always	73 (97.33)	50 (96.15)	.71
Often	2 (2.67)	2 (3.85)	
HER2/FISH for HER2			
Always	70 (93.33)	48 (92.31)	.83
Often	5 (6.67)	4 (7.69)	
Others			
Always	—	2 (3.85)	
Often	4 (5.33)	3 (5.77)	.61
Sometimes	3 (4)	2 (3.85)	
Never	1 (1.33)	—	
Lung cancer			
EGFR			
Always	46 (61.33)	40 (76.92)	
Often	21 (28)	7 (13.46)	.06
Sometimes	7 (9.33)	2 (3.85)	
Never	1 (1.33)	3 (5.77)	
ROS1			
Always	8 (10.67)	10 (19.23)	
Often	8 (10.67)	5 (9.62)	.59
Sometimes	23 (30.67)	15 (28.85)	
Never	35 (46.67)	21 (40.38)	
BRAF			
Always	3 (4)	6 (11.54)	
Often	5 (6.67)	2 (3.85)	.38
Sometimes	25 (33.33)	15 (28.85)	
Never	41 (54.67)	28(53.85)	
PD-L1			
Always	17 (22.67)	18 (34.62)	
Often	21 (28)	13 (25.00)	.32
Sometimes	25 (33.33)	11 (21.15)	
Never	12 (16)	10 (19.23)	
EGFR T790M			
Always	11 (14.67)	19 (35.64)	
Often	13 (17.33)	9 (17.31)	.02*
Sometimes	29 (38.67)	17 (32.69)	
Never	22 (29.33)	7 (13.46)	
NTRK			
Always	1 (1.33)	2 (3.85)	
Often	3 (4)	1 (1.92)	.74
Sometimes	11 (14.67)	6 (11.54)	
Never	60 (80)	43 (82.69)	

TABLE A5. Frequency Distribution of Responses Across Type of Institution (Continued)

Biomarker Test Used	Nonacademic No. (%)	Academic Center No. (%)	P
Colorectal cancer			
KRAS			
Always	17 (22.67)	22 (42.31)	
Often	17 (22.67)	12 (23.08)	.10
Sometimes	28 (37.33)	12 (23.08)	
Never	13 (17.33)	6 (11.54)	
NRAS			
Always	12 (16)	21 (40.38)	
Often	11 (14.67)	10 (19.23)	.01*
Sometimes	23 (30.67)	12 (23.08)	
Never	29 (38.67)	9 (17.31)	
BRAF			
Always	4 (5.33)	7 (13.46)	
Often	8 (18.67)	2 (3.85)	.23
Sometimes	17 (22.67)	13 (25)	
Never	46 (61.33)	30 (57.69)	
MSI/MMR			
Always	11 (14.67)	11 (21.15)	
Often	9 (12)	5 (9.62)	.27
Sometimes	25 (33.33)	23 (44.23)	
Never	30 (40)	13 (25)	

Abbreviations: EGFR, epidermal growth factor receptor; ER/PR, estrogen receptor/progesterone receptor; FISH, fluorescence in situ; HER2, human epidermal growth factor receptor; MMR, mismatch repair; MSI, microsatellite instability.

*Significant at $P < .05$.