original contributions

Accessing Targeted Therapies: A Potential Roadblock to Implementing Precision Oncology?

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QUESTION ASKED: How is next-generation sequencing (NGS) testing guiding clinical management of oncologists providing clinical care to patients?

SUMMARY ANSWER: NGS testing is used frequently and affects clinical management to varying degrees. However, a substantial proportion of oncologists face difficulties obtaining US Food and Drug Administration (FDA)–approved therapies on the basis of NGS testing results for their patients.

WHAT WE DID: We developed and administered a 32-question questionnaire evaluating NGS testing use and outcomes to a survey pool of American Society of Clinical Oncology members.

WHAT WE FOUND: Most oncologists reported that NGS testing provided actionable information to a moderate or great extent, although approximately one third of respondents reported that patients were sometimes or often unable to access the relevant FDA-approved therapy. When no actionable results were found, those reporting great or moderate guidance from NGS testing were more likely to request the compassionate use of an unapproved drug, enroll in a clinical trial, and treat off-label with a drug approved for another indication.

BIAS, CONFOUNDING FACTOR(S), REAL-LIFE IMPLICATIONS: Survey respondents were younger, more likely to work in academic settings, and more interested in clinical research than the average US oncologist. Genomic testing is increasingly informing management decisions in clinical oncology. Improving access to FDA-approved therapies when testing indicates their use remains an important goal to ensure equitable treatment and outcomes.

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ASSOCIATED CONTENT

Appendix

Data Supplement

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CARE DELIVERY

original contributions

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abstract

PURPOSE Advances in genomic techniques have led to increased use of next-generation sequencing (NGS). We evaluated the extent to which these tests guide treatment decisions.

METHODS We developed and distributed a survey assessing NGS use and outcomes to a survey pool of ASCO members. Comparisons between groups were performed with Wilcoxon two-sample, chi-square, and Fisher's exact tests.

RESULTS Among 178 respondents, 62% were male, 54% White, and 67% affiliated with academic centers. More than half (56%) indicated that NGS provided actionable information to a moderate or great extent. Use was highest (median $\geq$ 70% of cases) for lung and gastric cancer, and lowest (median $<$ 25% of cases) in head and neck and genitourinary cancers. Approximately one third of respondents reported that, despite identification of an actionable molecular variant, patients were sometimes or often unable to access the relevant US Food and Drug Administration–approved therapy. When NGS did not provide actionable results, individuals reporting great or moderate guidance overall from NGS in treatment recommendations were more likely to request the compassionate use of an unapproved drug ($P < .001$), enroll on a clinical trial ($P < .01$), or treat off-label with a drug approved for another indication ($P = .02$).

CONCLUSION When NGS identifies an actionable result, a substantial proportion of clinicians reported encountering challenges obtaining approved therapies on the basis of these results. Perceived overall impact of NGS appears associated with clinical behavior unrelated to actionable NGS test results, including pursuing off-label or compassionate use of unapproved therapies or referring to a clinical trial.

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The widespread uptake of next-generation sequencing (NGS) in recent years has advanced the implementation of precision oncology in routine clinical practice.[1,2] Ideally, NGS identification of actionable cancer genomic variants permits the selection of potentially effective and well-tolerated targeted therapies.[1] Advances in tumor genomics have led to the elucidation of a growing number of targetable molecular alterations, which in turn results in a growing number of targeted therapies.[3,4] Additionally, NGS results such as tumor mutational burden and microsatellite instability have emerged as biomarkers for the selection of patients for immune checkpoint inhibitors.[5,6]

In recent years, an increasing number of cancer types have US Food and Drug Administration (FDA)–approved molecular targeted therapy options. Indeed, drugs targeting molecular variants in lung cancer, melanoma, hepatocellular carcinoma, ovarian cancer, breast cancer, renal cancer, chronic myelogenous leukemia, multiple myeloma, mantle cell lymphoma, chronic lymphocytic leukemia, and GI stromal tumors are currently available.[7] Recently, the FDA granted accelerated approval to entrectinib and larotrectinib for all solid tumors harboring *NTRK* fusions, regardless of tissue of origin.[8]

A growing proportion of US oncologists incorporate NGS into their clinical practice, with one third applying the NGS results to therapeutic decision making.[9] Indeed, it has been argued that NGS should be performed on all patients with advanced cancer.[10] Additionally, Medicare and Medicaid expanded access to NGS testing for all patients with advanced cancer (recurrent, metastatic, relapsed, refractory, or

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stage III or IV cancer) in 2018.[11] However, the optimal application of NGS and other advanced diagnostics in oncology requires clear understanding of results and reliable access to relevant therapies. We therefore studied these considerations among practicing medical oncologists.

METHODS

Survey Design

The survey was designed by the Research Advocacy Network, with input from personnel from the National Institutes of Health and the ASCO's Center for Research and Analytics. Rainforest Action Network is a nonprofit organization dedicated to advancing cancer research through advocacy.[12] This study was granted an exemption by the Advarra Institutional Review Board. The survey instrument with questions is included in the Data Supplement (online only). A version of the survey was cognitively tested with six oncologists from a variety of settings. Each physician was interviewed by telephone with questions focused on clarity, relevance, ease, and importance, with this feedback incorporated into edits. The survey had 32 questions and was programmed by ASCO staff (using RedCAP)[13] for online administration.

The primary objective of the survey was to understand when practicing oncologists in the United States use NGS testing and how they use the NGS test results in the care of patients with advanced cancer. Secondary objectives included (1) defining what patient population (cancer type and line of therapy) is currently being tested and (2) examining whether and how the test results are currently being used in treatment of patients' cancer.

Respondent Selection

We distributed the survey to a random selection of 600 members of the ASCO Research Survey Pool via e-mail hyperlink on May 13, 2019. These individuals received up to four notifications, including the initial invitation and three reminders. Within ASCO's Center for Research and Analytics, the ASCO Research Survey Pool provides a mechanism for surveying oncology professionals, with the pool consisting of ASCO members who have opted in to participate in research survey projects conducted by other members.[14]

Providers were eligible for the survey if they reported (1) treating or evaluating patients with advanced solid tumors and (2) ordered, reviewed, or used the results of NGS testing in evaluating and treating patients with advanced cancer within the previous 3 months.

Survey Analysis

Respondents were included in the analysis if they completed the survey. Descriptive statistics were generated, including proportions for categorical variables and means and medians for continuous variables. Wilcoxon rank sum test, chi-squared test, and Fisher's exact test were used to compare groups with statistical significance defined at an α level of .05. Statistical analyses were performed on SAS for Windows version 9.4 (SAS Institute, Cary, NC).

RESULTS

Among the 600 individuals to whom a survey invitation was sent, 212 (35%) responded, of whom 182 (30%) were eligible for analysis. Among the 30 ineligible responses, 18 reported treating patients with hematologic malignancies only and 12 reported not ordering or using the results of NGS testing within the prior 3 months. Four individuals (1%) did not complete the survey after starting it, and their results were not included in the analysis. Most respondents were male (62%), White (54%), associated with academic centers (67%) (Table 1). In general, respondents associated with academic medical centers treated fewer cancer types than other respondents (mean 1 *v* 6.5; $P < .001$). Seventy percent of respondents spent at least half of their professional time engaged in patient care, whereas only 12% and 2% spent at least half of their time in research and administration, respectively.

Respondents who had access to a molecular tumor board were significantly more likely to perceive that the NGS results guide treatment recommendations to a great-moderate extent ($P = .03$). There was a near-significant trend toward respondents with formal training in the use of NGS testing perceiving that the NGS results guide treatment recommendations to a great-moderate extent ($P = .06$).

NGS was used more frequently in cases without standard treatment options or after disease progression. Nevertheless, more than 40% of respondents reported ordering NGS often or always at the time diagnosis of an advanced cancer with available standard treatment options. Appendix Table A1 (online only) shows NGS use patterns stratified by perceived utility of NGS testing.

More than half of respondents reported that the NGS test results guided their treatment recommendations to a great (19%) or moderate (37%) extent, with 43% selecting small extent and 1% not at all. Respondents reported NGS yielding actionable information as follows: never or rarely 32%, often or always 12%, and sometimes 56%. Lack of actionable information on a completed test (reported as occurring often or always by 67%) was viewed as a far more frequent event than insufficient specimen for testing (reported as occurring often or always by 10%). In cases where testing fails to provide actionable information, the most commonly reported therapeutic decisions were treatment on a clinical trial within my practice (28% chose often or always) or supportive or palliative care (28% chose often or always). Table 2 displays the clinical scenarios encountered when the NGS results provided actionable information. Most commonly, patients were treated with an FDA-indicated therapy (47% often or always) or enrolled in

TABLE 1. Baseline Characteristics of Respondents

Characteristic	Total, No. (%)	To What Extent Did NGS Testing Results Guide You in Your Treatment Recommendations		*P*
		Some or Not At All, No. (%)	Great or Moderate, No. (%)	
Sex				
Female	65 (37)	27 (34)	38 (38)	.31
Male	111 (62)	50 (63)	61 (62)	
Not answered	2 (1)	2 (3)	0 (0)	
Race or ethnicity				
Non-Hispanic White	94 (53)	41 (52)	53 (54)	.97
Asian	55 (31)	25 (32)	30 (30)	
Others	17 (10)	7 (9)	10 (10)	
Not answered	12 (7)	6 (8)	6 (6)	
Years since graduated medical school				
0-5	8 (4)	3 (4)	5 (5)	.90
6-10	36 (20)	16 (20)	20 (20)	
11-20	89 (50)	38 (48)	51 (52)	
> 20	45 (25)	22 (28)	23 (23)	
Region				
West	29 (16)	12 (15)	17 (17)	.87
Midwest	39 (22)	17 (22)	22 (22)	
Northeast	53 (30)	26 (33)	27 (27)	
South	57 (32)	24 (30)	33 (33)	
No. of patients seen for evaluation or treatment per month				
1-25	14 (8)	5 (6)	9 (9)	.48
26-50	31 (17)	13 (16)	18 (18)	
51-100	61 (34)	34 (43)	27 (27)	
101-150	25 (14)	8 (10)	17 (17)	
151-200	22 (12)	9 (11)	13 (13)	
201-250	10 (6)	4 (4)	6 (6)	
> 250	15 (8)	6 (8)	9 (9)	
Type of cancer treated (multiple types permitted)				
Breast cancer	77 (43)	43 (54)	34 (34)	[a]
Colorectal cancer	88 (49)	36 (46)	52 (53)	
CNS tumors	38 (21)	17 (22)	21 (21)	
Gynecologic cancer	54 (30)	24 (30)	30 (30)	
Genitourinary cancer	69 (39)	35 (44)	34 (34)	
Head and neck cancer	60 (34)	28 (35)	32 (32)	
Lung and bronchus cancers	75 (42)	29 (37)	46 (46)	
Melanoma	54 (30)	24 (30)	30 (30)	
Stomach (gastric) cancer	79 (44)	32 (41)	47 (47)	
Other solid tumor	76 (43)	37 (47)	39 (39)	

(continued on following page)

TABLE 1. Baseline Characteristics of Respondents (continued)

Characteristic	Total, No. (%)	To What Extent Did NGS Testing Results Guide You in Your Treatment Recommendations: Some or Not At All, No. (%)	To What Extent Did NGS Testing Results Guide You in Your Treatment Recommendations: Great or Moderate, No. (%)	*P*
Primary practice setting				
AMC or affiliated clinic	120 (67)	52 (66)	68 (68)	.44
Medical center not affiliated with a medical school	8 (5)	1 (1)	7 (7)	
Community hospital (nonacademic)	30 (17)	15 (19)	15 (15)	
Office-based (private practice)	9 (5)	5 (6)	4 (4)	
VA or other military facility or other government, clinical care entity	5 (3)	3 (4)	2 (2)	
Integrated health care delivery system	6 (3)	3 (4)	3 (3)	
Access to a MTB				
Practice or institution convenes MTB	103 (58)	37 (47)	66 (67)	.03
Practice or institution uses an outside MTB	9 (5)	5 (6)	4 (4)	
Practice or institution has no MTB access	66 (37)	37 (47)	29 (29)	
Formal training in the use of NGS testing				
Yes	95 (53)	36 (46)	59 (60)	.06
No	83 (47)	43 (54)	40 (40)	
Enrolled patients in cancer clinical trials in the past 12 months				
Yes	172 (97)	77 (97)	95 (96)	.69
No	6 (3)	2 (3)	4 (4)	
To what extend did NGS testing results guide your treatment recommendations?				
Great or moderate	99 (56)	0 (0)	99 (100)	< .0001
Some or not at all	79 (44)	79 (100)	0 (0)	

Abbreviations: AMC, academic medical center; MTB, molecular tumor board; NGS, next-generation sequencing; VA, Veterans Affairs.
[a]Not calculated as respondents could list multiple cancer types and percentages therefore add up to > 100%.

a clinical trial (27% often or always). One third of respondents reported prescribing but not being able to obtain FDA-indicated therapies sometimes or often (31%), with a similar proportion (32% sometimes or often) encountering challenges when requesting an off-label therapy approved for another cancer type.

Rate of NGS use varied according to cancer type (Fig 1). Use was highest (median ≥ 70% of cases) for lung and gastric cancers and was lowest (median < 25% of cases) in head and neck and genitourinary cancers. These patterns were largely consistent with respondents' cancer-specific experience with prescribing based on the NGS results and observing responses with NGS-directed therapies (Appendix Table A2, online only). For instance, the largest percentage of respondents indicated that they prescribed lung cancer therapy on the basis of the NGS results (88%). Respondents also reported the greatest percentage of cases responding to NGS-based treatment in patients with lung cancer (median 64% of cases).

Practice patterns differed according to the extent to which respondents reported that the NGS test results guided their clinical management (categorized as great or moderate versus some or not at all) (Appendix Table A1). We found that individuals who reported overall being guided to a great or moderate extent by the NGS results were more likely to always order NGS for patients with advanced cancer in the following scenarios: to have information that may inform subsequent or future treatment options (27% *v* 14%) at time of diagnosis of advanced cancer with standard options available (13% *v* 1%), at time of diagnosis of advanced cancer without standard options available (39% *v* 17%), and during treatment of advanced cancer progressed on current treatment (39% *v* 18%). Individuals reporting overall great or moderate guidance from the NGS test results had differing treatment approaches compared with respondents reporting generally less guidance from the NGS test results, even when the NGS test results provided no actionable information. Those reporting generally more guidance from the NGS test results were more likely to treat off-label by using an FDA-approved drug ($P = .02$), treat on a clinical trial within their practice ($P < .01$), and request the compassionate use of an unapproved drug ($P < .001$). In scenarios where the NGS test results did provide

TABLE 2. Outcomes of Next-Generation Sequencing Testing After Identification of Actionable Molecular Variant (n = 175)

Frequency	Treated With FDA-Approved Drug for Use in the Indicated Population, No. (%)	Tried But Could Not Obtain FDA-Approved Drug for Use in the Indicated Population, No. (%)	Treated With Off-Label Drug That Is FDA-Approved for Another Cancer Type, No. (%)	Tried But Could Not Obtain Off-Label Drug That Is FDA-Approved for Another Cancer Type, No. (%)	Patient Enrolled in Clinical Trial, No. (%)	Patient Died Before Test Results Could Inform Treatment, No. (%)
Never or rarely	37 (21)	120 (69)	87 (50)	119 (68)	41 (23)	127 (73)
Sometimes	56 (32)	44 (25)	72 (41)	43 (25)	88 (50)	36 (21)
Often or always	82 (47)	11 (6)	16 (9)	13 (7)	46 (26)	12 (7)

Abbreviation: FDA, US Food and Drug Administration.

actionable information, respondents who reported taking more guidance from the NGS test results were more likely to treat with an FDA-approved drug in the indicated population ($P < .001$), treat with an drug FDA-approved for another cancer type, ie, off-label (including situations where the drug could not be obtained) ($P = .002$), or enroll a patient in a clinical trial ($P = .004$).

Finally, we investigated clinician approaches to rendering treatment decisions on the basis of the actionable NGS test results. Although most respondents (63%, Table 1) had access to a molecular tumor board, most respondents never (34%) accessed the board or did so < 10% (16%) or < 20% (18%) of the time (Appendix Table A3, online only). The tumor board use appeared to reflect experience with these meetings. For instance, among frequent molecular tumor board users, only 1% felt that the discussion guided treatment only to some or no extent. Conversely, 17% of rare users of molecular tumor boards felt this way.

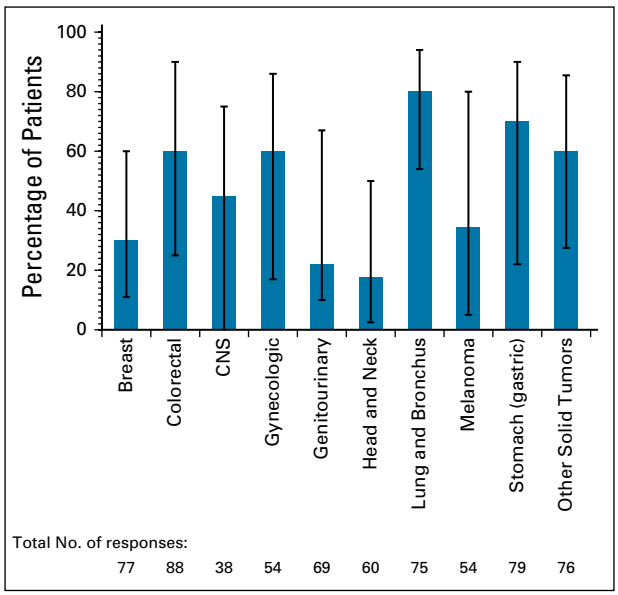

FIG 1. Usage of next-generation sequencing by cancer type. Column heights indicate median percentage, with error bars representing Q1 and Q3 quartiles.

Notably, 50% of respondents reported reviewing the scientific literature 80% or more of the time, and 30% reported discussing cases with individual colleagues 80% or more of the time.

Areas in which additional educational materials or training about NGS were considered useful included using the results to guide decisions about patient treatment (55%), interpreting NGS test reports (47%), managing integration of NGS testing into clinical practice (42%), training for clinic staff to support the use of tumor profiling (39%), determining whether NGS testing is clinically appropriate for a patient (37%), explaining the test results to a patient (37%), explaining tumor profiling–based treatment options to a patient (35%), and explaining the purpose and concepts underlying NGS testing to a patient (25%). Only 7% of respondents felt that additional material or training would not be useful.

DISCUSSION

Oncologists throughout the United States and worldwide are increasingly using NGS to guide treatment of advanced cancer in routine clinical practice.[9] In the present study, we sought to place this use in clinical context by evaluating the perceptions and experiences associated with NGS use and the strategies employed and barriers encountered to implementing the NGS test results in patient management.

Individuals with access to a molecular tumor board and those who had received formal training in the use of NGS testing were more likely to perceive the NGS results as therapeutically useful. In turn, perceived therapeutic impact of NGS appears to be associated with both overall and disease-specific use. Individuals who felt that the NGS test results were likely to guide management were more likely to order NGS in multiple clinical scenarios, including planning for future treatment whether or not standard treatment was available. These respondents also perceived specimen inadequacy to occur less frequently compared with respondents who felt that the NGS test results were less likely to guide management. In general, clinicians reported ordering NGS more frequently for those cancer types with

available targeted therapies associated with higher response rates.

Notably, perceived overall impact of NGS also appears associated with clinical behavior unrelated to the NGS test results. Specifically, in situations where NGS provided no actionable information, respondents who generally believed that the NGS test results were likely to guide management were more likely to seek off-label use of a drug FDA-approved for another indication, treat on a clinical trial, or request the compassionate use of an unapproved drug. These observations suggest that NGS perceptions may serve as a general metric of willingness and ability to explore nonstandard treatment options. It might also reflect whether the respondent treated patients with cancers that are more likely to have NGS-actionable variants. Alternatively, they could reflect access to infrastructure to support both clinical trials and off-label use.

The clear majority of respondents reported enrolling patients in clinical trials. This practice pattern may not be broadly representative of oncologists in the United States, where fewer than 5% of adults with cancer are enrolled in clinical trials.[15] This may be a reflection of respondent selection bias, with 97% of respondents reporting having enrolled patients in a clinical trial in the past 12 months and 67% associated with academic medical centers. Furthermore, NGS ordering (and subsequent identification of a specified result) is often a prerequisite for enrollment in clinical trials.[16]

This study identifies a number of potential barriers between NGS ordering and therapeutic application. Almost half of respondents reported having cases with insufficient tissue for analysis, and 10% encountered this scenario frequently. Furthermore, almost one third of our survey cohort experienced difficulty on a regular basis in obtaining FDA-approved therapies that target the results reported by NGS tests—both in FDA-approved indicated populations and for non-FDA–approved cancer types (ie, off-label). Although challenges in obtaining investigational therapy on the basis of NGS findings through clinical trials or off-label use have been reported previously,[17-19] our current findings suggest that these difficulties apply as well to approved treatments for indicated populations and the same target in other cancer types.

Participation in molecular tumor boards has been shown to increase the prescribing of targeted therapy to patients.[20] In the present study, although molecular tumor boards were perceived as valuable, few respondents routinely accessed them. More frequently, they sought information from the NGS test report, individual colleagues, and the medical literature. Potential reasons for the relatively low use of molecular tumor boards include unfamiliarity with the format, limits on the number of cases reviewed, lack of standardization, and difficulty in perceiving applicability to one's own clinical practice.[21,22] Traditional tumor boards provide a setting to coordinate multidisciplinary care (eg, surgery, radiation, and medical) and also to interpret complex primary clinical data (eg, radiology and pathology images). Given the inclusion of standard treatment recommendations and clinical trial options in contemporary NGS result reports, clinicians may not see a clear role for molecular tumor boards. Yet it has been shown that NGS report recommendations are not always reliable,[23] suggesting that molecular tumor boards play a potential role in confirming or challenging their content, especially for less frequently encountered genomic alterations, for identifying potentially relevant clinical trials, and for clinicians who are less familiar with NGS use.

Access to standard-of-care treatment options remains an ongoing concern for patients and oncologists in the United States. We found that almost one third of respondents tried but could not obtain FDA-approved drug for use after relevant NGS testing relatively frequently. Although the present study did not identify specific obstacles, it seems likely that cost of targeted therapies and lack of insurance likely contribute to these experiences.[20] Among US adults age 18-64 years, 11% overall and 34% without health insurance report not taking medications as prescribed because of cost.[21] This concern may be heightened for oncology targeted therapies, which, despite proven and approved indications, may not be covered by insurance.[20,22,23] These agents are typically administered orally, which under a prescription benefit may be subject to higher co-pays than infusional treatments,[24] which are typically covered under a medical benefit that may be more generous in coverage. In recent years, costs of oral cancer therapies have increased more than 10% annually, compared with 3% annually for prescription drugs generally.[25] Because a 1-month supply of an oral targeted therapy may cost more than $10,000, even a 20% co-pay can be cost prohibitive for many patients.[5] Although it has already been recommended that patients receive counseling on the implications and limitations of test results,[5] our results suggest that such guidance should also address availability of treatment on the basis of NGS results.

Additional limitations of this analysis include a cohort that may not broadly represent practicing oncologists. The sampled population—provided by the ASCO Research Survey Pool—reflects individuals who self-identify as interested in regularly participating in surveys conducted by ASCO members. Given that fewer than 5% of US adults with cancer are enrolled to clinical trials, approximately one fourth of US oncologists work at an academic medical center, and the median age of US oncologists is 52 years, our study sample is younger, more academically focused, and more engaged in clinical research than US oncologists in general.[24,25] Further studies in a more generalized clinical oncology setting are warranted. Additionally, the results of this cross-sectional survey do not imply causation. Finally, although our response rate of 30% is quite low, it is substantially higher than most physician-directed surveys.[26,27]

In conclusion, NGS testing is used frequently in the care of patients with advanced cancer. Regardless of whether the results are actionable, NGS use correlates with willingness to pursue nonstandard treatments, including clinical trials and off-label or compassionate use of targeted therapies. Difficulties in accessing treatment on the basis of the actionable NGS test results—including FDA-approved treatments—occur relatively frequently. To optimize NGS use and impact, ensuring equitable access to the growing number of targeted therapies will be critical.

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AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

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AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

Accessing Targeted Therapies: A Potential Roadblock to Implementing Precision Oncology?

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APPENDIX

TABLE A1. NGS Use Patterns According to Perceived Utility of NGS Test Results

How Often Was NGS Testing Ordered for Each Purpose Below (For Your Patients With Advanced Cancer in the Last 3 Months)?

Frequency	Total Sample, No. (%)	Overall Extent Guided by NGS		P
		Great or Moderate, No. (%)	Some or Not At All, No. (%)	
To have information that may inform subsequent or future treatment options (ie, patient currently has available therapeutic options that do not depend on NGS results) (N = 178)				
Never or rarely	10 (6)	4 (4)	6 (8)	.07
Sometimes	46 (26)	20 (20)	26 (33)	
Often or always	122 (69)	75 (76)	47 (59)	
To identify FDA-approved therapy (N = 178)				
Never or rarely	28 (16)	10 (10)	18 (23)	< .01
Sometimes	40 (22)	18 (18)	22 (28)	
Often or always	110 (62)	71 (72)	39 (49)	
To identify off-label use (N = 178)				
Never or rarely	29 (16)	15 (15)	14 (18)	.29
Sometimes	54 (30)	26 (26)	28 (35)	
Often or always	95 (53)	58 (59)	37 (47)	
To determine clinical trial eligibility (N = 178)				
Never or rarely	15 (8)	6 (6)	9 (11)	.43
Sometimes	44 (25)	24 (24)	20 (25)	
Often or always	119 (67)	69 (70)	50 (63)	
At the time of diagnosis of patients with advanced cancer who have standard treatment options available (N = 178)				
Never or rarely	46 (26)	20 (20)	26 (33)	.07
Sometimes	56 (31)	30 (30)	26 (33)	
Often or always	76 (43)	49 (49)	27 (34)	
At the time of diagnosis of patients with advanced cancer who do not have standard treatment options available (N = 178)				
Never or rarely	14 (8)	6 (6)	8 (10)	.08
Sometimes	32 (18)	13 (13)	19 (24)	
Often or always	132 (74)	80 (80)	52 (66)	
During treatment of patients with advanced cancer whose cancers have progressed on current treatment (N = 178)				
Never or rarely	3 (2)	1 (1)	2 (3)	.03
Sometimes	32 (18)	12 (12)	20 (25)	
Often or always	143 (80)	86 (87)	57 (72)	

How Often Did the Following Situations Occur for These Patients?

Frequency	Total Sample, No. (%)	Overall Extent Guided by NGS		P
		Great or Moderate, No. (%)	Some or Not At All, No. (%)	
Specimen was insufficient for NGS testing (N = 178)				
Never or rarely	77 (43)	43 (43)	34 (43)	.31
Sometimes	83 (47)	49 (50)	34 (43)	
Often or always	18 (10)	7 (7)	11 (14)	
Test provided no actionable information (N = 178)				
Never or rarely	5 (3)	3 (3)	2 (3)	< .001
Sometimes	54 (30)	42 (42)	12 (15)	
Often or always	119 (67)	54 (55)	65 (82)	

(continued on following page)

TABLE A1. NGS Use Patterns According to Perceived Utility of NGS Test Results (continued)

How Often Did the Following Situations Occur for These Patients?				
		Overall Extent Guided by NGS		
Frequency	**Total Sample, No. (%)**	**Great or Moderate, No. (%)**	**Some or Not At All, No. (%)**	***P***
Test provided actionable information (N = 178)				
Never or rarely	57 (32)	14 (14)	43 (54)	< .001
Sometimes	100 (56)	67 (68)	33 (42)	
Often or always	21 (12)	18 (18)	3 (4)	

Thinking About All Your Patients With Advanced Cancer Whose NGS Testing Provided No Actionable Information and When There Is NO Standard of Care, How Often Did the Following Situations Occur (in the Last 3 Months)?				
		Overall Extent Guided by NGS		
Frequency	**Total Sample, No. (%)**	**Great or Moderate, No. (%)**	**Some or Not At All, No. (%)**	***P***
Treated off-label by using an FDA-approved drug (eg, approved for another cancer type) (n = 175)				
Never or rarely	96 (55)	44 (46)	52 (66)	.02
Sometimes	59 (34)	41 (43)	18 (23)	
Often or always	20 (11)	11 (11)	9 (11)	
Treated on a clinical trial within my practice (n = 175)				
Never or rarely	67 (38)	29 (30)	38 (48)	< .01
Sometimes	59 (34)	31 (32)	28 (35)	
Often or always	49 (28)	36 (38)	13 (16)	
Referred to a clinical trial outside my practice (n = 175)				
Never or rarely	87 (50)	44 (46)	43 (54)	.31
Sometimes	66 (38)	37 (39)	29 (37)	
Often or always	22 (13)	15 (16)	7 (9)	
Requested compassionate use of unapproved drug (n = 175)				
Never or rarely	133 (76)	63 (66)	70 (89)	< .001
Sometimes	36 (21)	29 (30)	7 (9)	
Often or always	6 (3)	4 (4)	2 (3)	
Referred to another practice, not necessarily for clinical trial reasons (n = 175)				
Never or rarely	150 (86)	79 (82)	71 (90)	.30
Sometimes	23 (13)	15 (16)	8 (10)	
Often or always	2 (1)	2 (2)	0 (0)	
Used only supportive or palliative care (n = 175)				
Never or rarely	50 (29)	31 (32)	19 (24)	.13
Sometimes	76 (43)	44 (46)	32 (41)	
Often or always	49 (28)	21 (22)	28 (35)	

Thinking About All Your Patients With Advanced Cancer Whose NGS Testing Provided Actionable Information and How Often Did the Following Situations Occur (in the Last 3 Months)?				
		Overall Extent Guided by NGS		
Frequency	**Total Sample, No. (%)**	**Great or Moderate, No. (%)**	**Some or Not At All, No. (%)**	***P***
Treated with FDA-approved drug for use in the indicated population (n = 175)				
Never or rarely	37 (21)	9 (9)	28 (37)	< .001
Sometimes	56 (32)	26 (26)	30 (39)	
Often or always	82 (47)	64 (65)	18 (24)	

(continued on following page)

TABLE A1. NGS Use Patterns According to Perceived Utility of NGS Test Results (continued)

Thinking About All Your Patients With Advanced Cancer Whose NGS Testing Provided Actionable Information and How Often Did the Following Situations Occur (in the Last 3 Months)?

		Overall Extent Guided by NGS		
Frequency	**Total Sample, No. (%)**	**Great or Moderate, No. (%)**	**Some or Not At All, No. (%)**	***P***
Tried but could not obtain FDA-approved drug for use in the indicated population (n = 175)				
Never or rarely	120 (69)	65 (66)	55 (72)	.54
Sometimes	44 (25)	28 (28)	16 (21)	
Often or always	11 (6)	6 (6)	5 (7)	
Treated with off-label drug that is FDA-approved for another cancer type (n = 175)				
Never or rarely	87 (50)	38 (38)	49 (64)	.002
Sometimes	72 (41)	48 (49)	24 (32)	
Often or always	16 (9)	13 (13)	3 (4)	
Tried but could not obtain off-label drug that is FDA-approved for another cancer type (n = 175)				
Never or rarely	119 (68)	59 (60)	60 (79)	.02
Sometimes	43 (25)	32 (32)	11 (14)	
Often or always	13 (7)	8 (8)	5 (7)	
Patient enrolled in clinical trial (n = 175)				
Never or rarely	41 (23)	15 (15)	26 (34)	.004
Sometimes	88 (50)	51 (52)	37 (49)	
Often or always	46 (26)	33 (33)	13 (17)	
Patient died before test results could inform treatment (n = 175)				
Never or rarely	127 (73)	73 (74)	54 (71)	.06
Sometimes	36 (21)	16 (16)	20 (26)	
Often or always	12 (7)	10 (10)	2 (3)	

NOTE. *P* values are based on Fisher's exact test.

Abbreviations: FDA, US Food and Drug Administration; NGS, next-generation sequencing.

TABLE A2. Use and Outcomes of Treatment on the Basis of the NGS Results

Prescribe Therapy on the Basis of the NGS Results, No. (%)										
Outcome	Breast Cancer (n = 72)	Colorectal Cancer (n = 83)	CNS Tumors (n = 27)	Gynecologic Cancer (n = 52)	Genitourinary Cancer (n = 61)	Head and Neck Cancer (n = 48)	Lung and Bronchus Cancer (n = 73)	Melanoma (n = 44)	Gastric Cancer (n = 72)	Other Solid Tumors (n = 68)
No	30 (42)	30 (36)	12 (44)	20 (39)	32 (53)	35 (73)	9 (12)	18 (41)	35 (49)	22 (32)
Yes	42 (58)	53 (64)	15 (56)	32 (62)	29 (48)	13 (27)	64 (88)	26 (59)	37 (51)	46 (68)

Among Those Who Prescribe on the Basis of the NGS Results, the Proportion of Cases Responding to Therapy on the Basis of the NGS Results, No. (%)										
Frequency, %	Breast Cancer (n = 42)	Colorectal Cancer (n = 53)	CNS Tumors (n = 15)	Gynecologic Cancer (n = 32)	Genitourinary Cancer (n = 29)	Head and Neck Cancer (n = 13)	Lung and Bronchus Cancer (n = 64)	Melanoma (n = 26)	Gastric Cancer (n = 37)	Other Solid Tumors (n = 46)
0	1 (2)	1 (2)	0 (0)	0 (0)	1 (4)	1 (8)	2 (3)	0 (0)	1 (3)	0 (0)
1-24	16 (38)	14 (26)	10 (67)	6 (19)	9 (31)	6 (46)	8 (13)	4 (15)	6 (16)	17 (37)
25-49	13 (31)	14 (26)	2 (13)	11 (34)	9 (31)	2 (15)	6 (9)	3 (12)	16 (43)	14 (30)
50-74	10 (24)	15 (28)	3 (20)	12 (38)	8 (28)	3 (23)	26 (41)	14 (54)	12 (32)	12 (26)
75-99	1 (2)	7 (13)	0 (0)	2 (6)	1 (4)	1 (8)	19 (30)	4 (15)	1 (3)	3 (7)
100	1 (2)	2 (4)	0 (0)	1 (3)	1 (4)	0 (0)	3 (5)	1 (4)	1 (3)	0 (0)
Median	30	40	20	43	35	22	64	60	34	28

NOTE. (3a) Frequency of prescribing therapy on the basis of the NGS results according to cancer type. (3b) Proportion of cases responding to therapy on the basis of the NGS results according to cancer type.

Abbreviation: NGS, next-generation sequencing.

TABLE A3. Frequency of Approaches Used to Decide Patient Management When the NGS Test Results Provide Actionable Information (n = 175)

Frequency	Used the NGS Report Recommendations	Accessed Molecular Tumor Board	Talked With Colleague (At My Institution or Elsewhere)	Reviewed Scientific Literature	Explored Feasibility of Offering the FDA-Indicated Drug (eg, Because of Availability, Coverage, Cost, etc)	Explored Eligibility and Access to Clinical Trials
Never	5 (3)	59 (34)	8 (5)	3 (2)	8 (5)	0 (0)
< 10% of the time	27 (15)	28 (16)	18 (10)	10 (6)	15 (9)	4 (2)
About 20% of the time	26 (15)	31 (18)	38 (22)	23 (13)	23 (13)	13 (7)
About 40% of the time	26 (15)	16 (9)	29 (17)	20 (11)	17 (10)	13 (7)
About 60% of the time	25 (14)	12 (7)	29 (17)	33 (19)	39 (22)	27 (15)
About 80% of the time	36 (21)	11 (6)	25 (14)	35 (20)	41 (23)	43 (25)
> 90% of the time	21 (12)	12 (7)	18 (10)	36 (21)	18 (10)	48 (27)
Always	9 (5)	6 (3)	10 (6)	15 (9)	14 (8)	27 (15)

NOTE. Values in table indicate No. (%).

Abbreviations: FDA, US Food and Drug Administration; NGS, next-generation sequencing.