Barriers and Facilitators to the Use of Genomic-Based Targeted Lung Cancer Therapies in the VA: Qualitative Findings

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Reflexive testing, standardization of the mutation test ordering procedure and results reporting, and elimination of the preauthorization requirements could facilitate the utilization of targeted therapies.

Lung cancer is the most frequent cause of cancer-related mortality worldwide.[1] The most prevalent type of lung cancer is non-small cell lung cancer (NSCLC), which comprises about 85% of lung cancer cases.[2] As there are no cost-effective approaches to screening for lung cancer, most lung cancers are identified at an advanced stage (stage IIIB or IV).

New approaches to managing advanced lung cancer have emerged in recent years, including drugs designed to target specific genetic mutations in some tumors.[3] The National Comprehensive Cancer Network (NCCN) recommends erlotinib, a receptor tyrosine kinase inhibitor of the epidermal growth factor receptor (EGFR) for first-line treatment of advanced NSCLC with EGFR mutation.[4] Crizotinib is recommended to treat cancers that test positive for the anaplastic lymphoma kinase (ALK) mutation.[4] Utilization of targeting agents has been found to extend the survival times for patients with the specified mutations.[5] Both erlotinib and crizotinib are available at the VHA.

Previous research showed that VHA providers expressed overall favorable attitudes about genomic medicine.[6] Providers perceived genomic medicine to have an important and possibly transformative role in medicine. Barriers to utilization of genomic medicine involved concerns about coordination of care, changes in workload, and increased length of patient visits. In addition to these system-level barriers, many providers had concerns about the proficiency of VHA-based practitioners to appropriately use genomic medicine.

Previous research has evaluated utilization of genomic testing and genomic-based targeted therapy (GBTT) in VA and community settings.[5-8] It is unclear whether VHA-based providers are following clinical guidelines regarding genomic testing and utilization of GBTT.[4] The authors set out to identify factors that impede and encourage guideline-consistent care in the management of NSCLC at the VHA. The authors specifically sought information about oncologists' perceptions and experiences with EGFR and ALK mutation testing in patients with advanced NSCLC, as well as use of erlotinib and crizotinib in treating such patients.

METHODS

This study was approved by the institutional review boards at Michael E. DeBakey VAMC in Houston, Texas and Baylor College of Medicine. In-depth qualitative interviews were conducted with VHA oncologists to examine their reported barriers and facilitators to mutation testing and prescribing of genomic-based treatment in patients with advanced NSCLC.

The sample of participants was recruited from a list of VHA medical oncologists, compiled by the study project coordinator. Investigators stratified the list by American College of Surgeons Commission on Cancer (CoC) accreditation status (yes/no) and used a stratified purposive sampling technique to recruit participants from CoC-accredited facilities and nonaccredited facilities. Recruitment and data collection occurred between March 2015 and February 2016. Oncologists were considered for inclusion if they

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TABLE
Providers' Demographic Characteristics

Characteristics	CoC Accredited	Not CoC Accredited	No. (%) (N = 30)
Age, mean, y	44.3	51.8	47.3
Sex			
Male	8	10	18 (60)
Female	10	2	12 (40)
Race/Ethnicity			
White	9	7	16 (53.3)
Asian	8	3	11 (36.7)
Hispanic	1	0	1 (3.3)
No response/other	0	2	2 (6.7)
Years since fellowship			
< 5	7	3	10 (33.3)
5-9	4	0	4 (13.3)
10-14	2	1	3 (10.0)
15-19	2	2	4 (13.3)
> 20	2	5	7(23.3)
No response	1	1	2 (6.7)
Years at VA			
< 5	9	4	13 (43.3)
5-9	4	2	6 (20.0)
10-14	0	2	3 (6.7)
15-19	4	2	6 (20.0)
> 20	0	1	1 (3.3)
No response	1	1	2 (6.7)
Medical school			
Foreign	9	7	16 (53.3)
Domestic	8	4	12 (40.0)
No response	1	1	2 (6.7)
Monthly NSCLC patients, No.			
0-20	9	5	14 (46.6)
21-40	5	3	8 (26.6)
41-60	0	0	0 (0)
61-80	2	0	2 (6.6)
81-100	1	1	2 (6.6)
101-120	0	0	2 (6.6)
No response	1	1	2 (6.6)
Proportion panel NSCLC, %			
0-20	9	4	13 (43.3)
21-40	7	4	11 (36.6)
41-60	0	0	0 (0)
61-80	0	1	1 (3.3)
81-100	1	2	3 (10.0)
No response	1	1	2 (6.6)
Specializes in lung cancer			
Yes	4	4	8 (26.7)
No	14	7	21 (70.0)
No response	0	1	1 (3.3)

Abbreviations: CoC, American College of Surgeons Commission on Cancer; NSCLC, non-small cell lung cancer.

(1) were specialists in oncology; (2) practiced at the VHA during the time of recruitment; and (3) had experience treating lung cancer at a VHA facility. During recruitment, potential participants were told that the investigators were interested in learning about oncologists' experiences and decisions about using GBTT to treat advanced lung cancer in the VHA. Participants were scheduled for telephone-based interviews, and verbal consent was obtained prior to all interviews. Interviews ranged from 19 to 90 minutes (average, 40 min).

Recruitment was stopped at the point of thematic saturation, defined a priori as the point when 2 independent coders agreed that 3 consecutive transcripts for a given interview category (see below) rendered no new thematic concepts.[9,10] Consistent with the theoretical framework developed by Cabana and colleagues, interviews were designed to elicit information about oncologists' knowledge, attitudes, intent to use GBTT, and perceived facilitators and barriers to using GBTT in the VHA.[11] Additional findings are presented elsewhere.[12] The interview guide was pilot tested and revised prior to initiating data collection. All interviews were recorded, transcribed, and analyzed for content.

Analysis

Data were analyzed using framework analysis methodology, which allows for the inclusion of existing concepts as well as emergent themes within an established theoretical framework.[13] Two independent coders with expertise in framework analysis independently created codes and indexed the data using Atlas.ti 6.2 (Scientific Software Development, Berlin, Germany). Disagreements about coding decisions were resolved through group consensus. Coding centered on 2 themes:

- Barriers and facilitators to mutation testing. This includes system or facility factors and testing weaknesses that act as barriers to ordering mutation testing, system or facility factors that facilitate ordering mutation testing, and oncologists' suggestions for ways to encourage more testing in the VHA.
- Barriers and facilitators to prescribing GBTT. This includes system or facility factors that act as barriers to prescribing GBTT, system or facility factors that facilitate prescribing GBTT, and oncologists' suggestions for ways to encourage more prescribing of GBTT in the VHA.

Thirty medical oncologists were interviewed. Participant demographics are presented in the Table.

BARRIERS TO TESTING

The 2 most commonly cited barriers to ordering mutation testing can be considered weaknesses in the testing process: lack of tissue and wait time for results. Almost all providers identified lack of tissue as a barrier to ordering a mutation test. After pathology uses the sample of tissue for an initial histologic diagnosis, often there is not enough specimen remaining for the mutation test. Some providers acknowledge that they can rebiopsy patients to get an adequate sample. This, of course, is associated with its own set of barriers; some patients are unwilling to undergo a repeat biopsy, and in some cases, the providers would not advise rebiopsy due to health risks. However, for others, the repeat biopsy is viewed as a way to mitigate the problem of scant tissue.

Another frequently cited testing weakness involved the wait time for results. Because the mutation analysis is not conducted in the VHA facility, providers often must wait 2 to 4 weeks to receive results. This can present a problem because some providers do not want to wait for the results before recommending a course of treatment.

Several providers cited system and facility factors as barriers to mutation testing. The most common of these involves the ordering process. Oncology providers often remarked that ordering the mutation test is cumbersome or inconvenient because there is no ordering mechanism in the Computerized Patient Record System (CPRS). Many different approaches for ordering a mutation test exist, including e-mailing the pathology department, calling to place the order, or requesting the test in person. As providers can order many, if not most, other tests via CPRS, it is clear that this presents an inconvenient exception.

Budgetary constraints were another frequently cited system or facility-level barrier. Providers sometimes were unable to access the test due to the cost. Several providers informed the interviewers that the cost of the test is deducted from the pathology department's budget, and this could present a major constraint to testing. A less commonly cited system or facility level barrier involves the inability to biopsy at the VHA. This was mentioned by only 2 providers who, due to lack of equipment or lack of personnel, were unable to acquire additional tissue samples at their facilities.

Finally, several providers noted that in some cases patients did not wish to undergo a biopsy. Thus, patient preference can act as a barrier to mutation testing. Some patients wish to forgo treatment, which eliminates the need for a mutation test. Other patients believe that due to their smoking history, they are unlikely to have an ALK or EGFR mutation and instead immediately opt for chemotherapy. Only a small minority of participants identified no barriers to mutation testing.

FACILITATORS FOR TESTING

Many providers complimented the availability of the mutation test. Interestingly, while some providers mentioned that lack of CPRS ordering was a barrier to testing, several also listed access to a CPRS order as a facilitator. These providers commented that ordering a test was streamlined and easy, given the mechanism in CPRS. Some VHA facilities offer CPRS order capabilities, and others do not. Other oncologists commented more generally on the cooperativeness of the pathology department in ordering mutation tests. It seems that facilities may use different ordering procedures, but in most of these facilities, a high degree of cooperation exists between departments to send out for tests that are requested.

Providers offered many ideas for ways to improve mutation testing or to facilitate the testing. By far, the most commonly cited way to improve the testing process was to make mutation testing reflexive for metastatic nonsquamous NSCLC. Some acknowledged that to achieve this would require a change to the budgeting process such that the test would not drain the pathology department's budget. Implementing reflexive testing of patients, as recommended by guidelines, would understandably address several of the barriers that were identified in this study. Other providers recommended standardizing the ordering procedure and location of results. Specifically, providers recommended creating a button in CPRS for ordering and always reporting the results in the same place in CPRS.

BARRIERS TO GBTT PRESCRIBING

The clear majority of providers identified no barriers to prescribing GBTTs. A few mentioned that they were required to submit a

nonformulary consult. A representative quote described this as "more out of a formality, and the pharmacist basically is there with me and he approves it on the spot and provides the prescription on the day, right when I'm seeing the patient." Only a very small minority of providers identified medication cost as a barrier, but even those respondents did not indicate that cost prevented them from offering GBTTs to their patients. Rather, cost consciousness simply made them more mindful and judicious when making decisions about prescribing GBTTs.

FACILITATORS TO GBTT PRESCRIBING

Several providers listed availability of the costly medication in the VHA as a facilitator to prescribing. Veterans can obtain GBTTs with little to no insurance cost or copayment, which is not always the case outside the VHA.

One recommendation for further facilitating prescribing of GBTTs involved eliminating the preauthorization requirement, particularly in first-line use for patients testing positive for ALK or EGFR mutations. Although the preauthorization was not seen as a significant barrier, removal of this formality could make prescribing easier.

DISCUSSION

Although in some cases, testing weaknesses (lack of tissue, wait time to receive results) can interrupt a treatment trajectory, many of the barriers identified in this study are modifiable. Overwhelmingly, oncologists recommended making mutation testing reflexive for metastatic nonsquamous NSCLC. Implementing reflexive testing of patients, as recommended by guidelines, would understandably address issues related to variable utilization of genomic testing in VHA.[12] Additionally, in response to system and facility barriers to mutation testing, other providers recommended standardizing the ordering procedure and location of results. Utilization of GBTT can be facilitated by eliminating the preauthorization requirement, particularly in first-line use for patients with positive mutations. Although the preauthorization was not seen as a significant barrier, removal of this formality could make prescribing easier.

This study extends previous research that identified underuse of genomic testing in community-based practices. The authors sought to interview a broad sample of providers from various facilities (small, large, CoC accredited, nonaccredited) to understand the range of conditions faced by VA providers. Some providers face more barriers than do others, whereas some face few or no barriers. This wide range of experiences can help to better understand the factors that facilitate guideline-adherent care.

Limitations

The authors recognize that availability of resources and testing and prescribing practices are constantly evolving and perhaps have improved since the data were collected. Thus, the age of the study data might be a limitation to the study. Like most qualitative studies, these findings are limited in their generalizability beyond the study population. Additionally, the authors were limited to recruiting oncologists with reliable contact information listed in the VHA directory. Although this could have introduced some degree of sampling bias, the authors are confident that the sample sufficiently represents the population of VHA-based medical oncologists who treat lung cancer. Despite these limitations, these findings provide novel perspectives on barriers and facilitators to genomic testing GBTT prescribing in the VHA. The authors identify modifiable barriers to testing and prescribing that can be addressed to improve and standardize care of advanced lung cancer in the VHA.

CONCLUSION

Efforts should be made to address modifiable barriers to mutation testing and guideline-consistent prescribing of GBTT in the VA setting. Implementation of specific practices like reflexive testing for all metastatic nonsquamous NSCLC, standardization of the mutation test ordering procedure, standardization of results reporting, and elimination of the preauthorization to prescribe GBTT could impact the utilization of GBTT in VHA.

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AUTHOR DISCLOSURES

The authors report no actual or potential conflicts of interest with regard to this article.

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REFERENCES

1. Jemal A, Bray F, Center MM, Ferlay J, Ward E, Forman D. Global cancer statistics. *CA Cancer J Clin.* 2011;61(2):69-90.
2. American Cancer Society. What is non-small cell lung cancer? https://www.cancer.org/cancer/non-small-cell-lung-cancer/about/what-is-non-small-cell-lung-cancer.html. Updated May 16, 2016. Accessed January 19, 2018.
3. Oxnard GR, Binder A, Jänne PA. New targetable oncogenes in non-small-cell lung cancer. *J Clin Oncol*. 2013;31(8):1097-1104.
4. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines). non-small cell lung cancer 2. 2018. https://www.nccn.org/professionals/physician_gls/pdf/nscl.pdf. Updated December 19, 2017. Accessed January 31, 2018.
5. Rosell R, Moran T, Queralt C, et al; Spanish Lung Cancer Group. Screening for epidermal growth factor receptor mutations in lung cancer. *N Engl J Med.* 2009;361(10):958-967.
6. Arar N, Seo J, Abboud HE, Parchman M, Noel P. Providers' behavioral beliefs regarding the delivery of genomic medicine at the Veterans Health Administration. *Per Med.* 2010;7(5):485-494.
7. Lynch JA, Berse B, Dotson D, Khoury MJ, Coomer N, Kautter J. Utilization of genetic tests: analysis of gene-specific billing in Medicare claims data. *Genet Med.* 2017;19(8):890-899.
8. Gutierrez ME, Choi K, Lanman RB, et al. Genomic profiling of advanced non-small cell lung cancer in community settings: gaps and opportunities. *Clin Lung Cancer,* 2017;18(6):651-659.
9. Morse JM. The significance of saturation. *Qual Health Res.*1995;5(2):147-149.
10. Aita VA, McIlvain HE. An armchair adventure in case study research. In: Crabtree BF, Miller WF, eds. *Doing Qualitative Research.* Thousand Oaks, CA: Sage; 1999:253-268.
11. Cabana MD, Rand CS, Powe NR, et al. Why don't physicians follow clinical practice guidelines? A framework for improvement. *JAMA.* 1999;282(15):1458-1465.
12. Arney JB, Helm A, Crook T, Braun U, Chen GJ, Hayes TG. Utilization of genomic testing in advanced non-small cell lung cancer among oncologists in the Veterans Health Administration. *Lung Cancer,* 2018;116:25-29.
13. Ritchie J, Spencer L. Qualitative data analysis for applied policy research. In: Bryman A, Burgess RG, eds. *Analyzing Qualitative Data.* New York, NY: Routledge; 1994:173-194.