

Check for updates

Biomarker Testing, Targeted Therapy and Clinical Trial Participation by Race Among Patients With Lung Cancer: A Real-World Medicaid Database Study

Debora S. Bruno, MD, MS,^{a,*} Xiaohong Li, MPH,^b Lisa M. Hess, PhD^b

^aUniversity Hospitals Cleveland Medical Center, Case Comprehensive Cancer Center, Cleveland, Ohio ^bEli Lilly and Company, Indianapolis, Indiana

Received 10 March 2023; revised 3 November 2023; accepted 23 January 2024 Available online - 1 February 2024

ABSTRACT

Introduction: Biomarker testing in oncology is fundamental for targeted therapy use and clinical trial participation. Factors contributing to previously identified racial disparities in biomarker testing remain unclear. This study investigated biomarker testing, clinical trial participation, and targeted therapy by race among patients with metastatic lung cancer with Medicaid coverage in the United States.

Methods: The Merative MarketScan Medicaid claims database was used for this study to identify patients diagnosed with having metastatic lung cancer between 2017 and 2019 with at least 121 days of follow-up. Racial differences in biomarker testing, clinical trial enrollment, and targeted therapy use were analyzed using chi-square/*t* tests followed by logistic regression for confounding covariates.

Results: A total of 3845 patients were eligible. A total of 970 (25.2%) patients included in this study were Black. Biomarker testing was observed among 57.0%, targeted therapy among 4.6%, and 2.6% of the study cohort had evidence of clinical trial participation. No significant disparities between Black and White races were identified. Younger age and metastatic disease at initial diagnosis were the strongest independent factors associated with increased biomarker testing. Biomarker testing was positively associated with targeted therapy use (OR = 1.69, p = 0.005).

Conclusions: Patients with metastatic lung cancer with Medicaid coverage were found to have exceedingly low biomarker testing rates; only 57% had evidence of any biomarker testing. Although no consistent differences between Black and White races were identified, this study calls attention to care experienced by socioeconomically disadvantaged patients with metastatic lung cancer in the United States.

© 2024 The Authors. Published by Elsevier Inc. on behalf of the International Association for the Study of Lung Cancer. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/ 4.0/).

Keywords: Biomarker testing; Real-world data; Health care disparities; Targeted therapy; Clinical trials

Introduction

Precision medicine has remarkably shifted the paradigm of oncologic treatment in the past decade. Biomarker testing allows practitioners to select the most effective therapies for patients, while avoiding the use of drugs with less favorable toxicity profile. Currently available precision drugs have provided a survival advantage to patients.^{1,2}

Certainly, the introduction of targeted therapies has substantially affected the care of patients with NSCLC.³ Patients with advanced NSCLC harboring no actionable

ISSN: 2666-3643

https://doi.org/10.1016/j.jtocrr.2024.100643

^{*}Corresponding author.

Address for correspondence: Debora S. Bruno, MD, MS, University Hospitals Cleveland Medical Center, Case Comprehensive Cancer Center, Cleveland, OH. E-mail: Debora.Bruno@UHhospitals.org

Cite this article as: Bruno DS, Li X, Hess LM. Biomarker testing, targeted therapy, and clinical trial participation by race among patients with lung cancer: a real-world Medicaid database study. *JTO Clin Res Rep.* 2024;5:100643.

^{© 2024} The Authors. Published by Elsevier Inc. on behalf of the International Association for the Study of Lung Cancer. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

genomic alterations and treated with chemoimmunotherapy in clinical trials experienced median overall survival (OS) outcomes of 17 to 22 months.^{4,5} In comparison, patients with tumors driven by ALK rearrangements experienced a 5-year OS rate as high as 62% when treated with appropriate targeted agents.⁶ Such findings are corroborated by real-world data, where considerable improvements in OS are identified among patients with NSCLC harboring actionable genomic alterations if exposed to appropriate precision therapies.^{7,8}

As a result, national guidelines endorse the use of systematic, broad-based biomarker testing (with nextgeneration sequencing [NGS]-based methods) for patients with metastatic NSCLC and the subsequent use of targeted therapies for those whose tumors harbor actionable alterations.9 Nevertheless, the benefits of precision medicine may not be available to every patient. Analysis of a contemporaneous cohort of approximately 15,000 patients with NSCLC treated mostly in community practices within the United States encountered very low rates of NGS-based biomarker testing.¹⁰ Furthermore, the use of broad genomic testing panels was significantly lower (p < 0.0001) for patients of Black race compared with their White counterparts.¹¹ The reasons for such disparities could not be determined based on the available data from these studies; potential contributing factors such as socioeconomic status (SES) and accurate insurance plan data were not available for this study.

To address the limitations of prior work evaluating these health care disparities, this study was designed to evaluate outcomes in a cohort of patients of low SES with Medicaid insurance plan coverage. Therefore, this study used a Medicaid claims database to remove the role of various payer types to investigate utilization of biomarker testing, clinical trial participation, and receipt of Food and Drug Administration–approved molecularly driven therapies by race among patients with lung cancer who receive public health insurance coverage owing to low-income status.

Materials and Methods

Database

The Merative MarketScan Research Multi-State Medicaid Database was used for this study. These data reflect real-world treatment patterns and costs by collecting integrated claims data from all providers of care, maintaining health care utilization and cost record connections at the patient level. These databases are fully compliant with U.S. privacy laws and regulations (Health Insurance Portability and Accountability Act) for the use of deidentified data, which are not considered human subjects research in accordance with the U.S. Code of Federal Regulations (CFR Section 45), and are therefore exempt from ethics board review.¹² These administrative claims data contain billable codes for health care delivery and as such do not contain clinical outcome data such as tumor response, progression, biomarker or blood test results, or survival outcomes.

The study cohort was derived during the identification period of January 1, 2017, to December 31, 2019. All enrollment records and inpatient, outpatient, ancillary, and drug claims were included among patients with Medicaid coverage meeting eligibility criteria.

Cohort Eligibility Criteria

Patients who had evidence of at least two International Classification of Disease (ICD) codes for lung cancer (ICD-9: 169.2-162.9 or ICD-10: C34.x-C34.92) recorded in the database at least 30 days apart during between January 1, 2017, and December 31, 2019, were identified.¹³ Patients were further required to have evidence of metastatic disease (ICD-9: 196.0-198.9, 199.0 or ICD-10: C77.x-C79.x, C80.0).¹⁴ The first observation of the metastatic disease code was defined as the index date for this study. It was required that patients have at least 121 days of follow-up after the index date for inclusion in this study to ensure sufficient time was available to observe the study outcomes. For patients with evidence of cancer codes 90 days or more before the metastatic code, the patient was assumed to have been diagnosed with having earlier stage disease and later progressed to metastatic stage. Patients with history of other non-lung cancers before the index date were excluded. Last, eligible patients were required to receive systemic anticancer therapy on or after the index date with at least one drug listed in the National Comprehensive Cancer Network Treatment Guidelines for Oncology for NSCLC during the study period.¹⁵ In claims data, it is not possible to differentiate lung cancer subtypes owing to nonspecific ICD codes. As a result, the cohort for this study reflects a broader patient population of those with a lung cancer diagnosis, despite limiting drugs to those used for the care of patients with NSCLC.

Cohort Characteristics and Outcome Assessment

The Medicaid databases collect a single combined race/ethnicity variable where values include White, Black, Hispanic, or Other. Owing to overlapping racial and ethnic categories, only race was included for statistical comparisons. Hispanic ethnicity was reported descriptively. "Other" race is not defined in this data set and may have included multiple races or ethnic groups. All available demographic variables recorded in the claims data set (e.g., age, sex, race) and clinical factors (e.g., year of diagnosis, metastatic disease status) were used to describe the characteristics of the study cohort at the time of diagnosis.

Biomarker test codes included procedure codes 81235, 81288, 81311, 81301, 81210, 81275, 81276, 81479, 88342, 88341, 88344, 88364, 88360, 88366, 88365, 81402, 81403, 81404, 81519, 81228, or 81229. NGS-based comprehensive genomic testing was identified by procedure codes 81445, 81450, 81455, 0022U, 0037U, 0048U, or 0047U recorded on or after the index cancer diagnosis date (details are provided in Supplementary Table 1). It was understood a priori that NGS-based coding is imprecise owing to the use of other biomarker testing codes for these procedures and any interpretation of specific NGS-based testing would likely be underestimated owing to known billing practices in the U.S. health care system.¹⁶

Clinical trial enrollment was defined by evidence of codes that reflect participation or services provided as part of a clinical trial (ICD-9-V70.7; ICD-10-Z00.6; HCPC S9988, S9990, S9991, S9996, S9992, S9994, G0294, G0293, G9537, or G9057) on or after the index cancer diagnosis date. There are no clinical trial-related billing codes specific to oncology trials. Molecularly targeted therapies were broadly defined as any drug that was U.S. Food and Drug Administration approved during the study period that was associated with an actionable genomic biomarker in any cancer type (selpercatinib, pralsetinib, entrectinib, larotrectinib, crizotinib, afatinib, erlotinib, dacomitinib, osimertinib, ceritinib, dabrafenib + trametinib, alectinib, brigatinib, lorlatinib, cabozantinib, vandetanib, gefitinib, vemurafenib, capmatinib, cetuximab, panitumumab, encorafenib, lapatinib, pertuzumab, olaparib, talazoparib, trastuzumab, or alpelisib). This broad definition allowed for capture of any on- or offlabel use of targeted therapies.

Statistical Analysis

Three logistic regression models were evaluated for each of the outcomes included in this study. Model 1 evaluated cohort characteristics associated with receipt of biomarker testing, model 2 evaluated the association of cohort characteristics and biomarker testing and NGSbased testing with clinical trial participation (yes/no), and model 3 evaluated the association of cohort characteristics and biomarker testing and NGS-based testing with receipt of targeted therapy. Black and White races and Black, White, and Other races were compared using chi-square tests for binary variables and t tests for continuous variables to evaluate the study hypotheses of differences in biomarker testing, receipt of targeted therapy, and clinical trial enrollment by race. Patients of Hispanic ethnicity were excluded from all analyses due to overlapping race/ethnicity variables; as reported in the data, race is unknown for these individuals. Missing or unknown categories were also excluded from all statistical analyses. No imputation was made for missing values. In addition, step-wise logistic regression analyses were conducted to account for a potential confounding effect of covariates. Baseline factors entered as covariates in the model included age, sex, year of metastatic diagnosis (index year), and initially diagnosed with metastatic disease versus progressed from an earlier stage of disease to metastatic. Missing data were included as a group for categorical covariates but excluded for continuous covariates where imputation would have been required. To be retained in the regression model, the threshold was set at alpha less than or equal to 0.10 other than race, which was retained in the model regardless of statistical significance. For the comparative analyses by White and Black race, significance was set at alpha less than 0.05. All analyses were conducted using SAS 9.4.

Results

After applying eligibility criteria, a total of 3845 patients with metastatic lung cancer were included in this study (Fig. 1 and Table 1). Black patients represented 25.2% of the study cohort.

Biomarker Testing (Model 1)

At least one biomarker test claim was observed among 57.0% of patients with metastatic lung cancer. Codes reflecting NGS-based testing were observed among 4.3% of eligible patients (Table 2). There were no differences in receipt of biomarker testing by race (p = 0.52 comparing Black, White, and Other races and p = 0.56 comparing Black versus White race). In logistic regression, age, year of index diagnosis, and stage at initial diagnosis were each significant factors associated with biomarker testing (Table 3). This analysis was not conducted for NGS-specific testing owing to low numbers.

Clinical Trial Participation (Model 2)

Codes reflective of clinical trial participation were observed among 2.6% of patients with metastatic lung cancer (Table 4). In unadjusted analyses, there were no differences in clinical trial participation between Black and White races (p = 0.18), but there were differences between Black, White, and Other races (p = 0.04). In logistic regression analysis, factors associated with clinical trial participation included age, race (Other versus White races), and the presence of NGS-based testing codes (Table 3).



Figure 1. Patient cohort identification.

Targeted Therapy (Model 3)

Targeted therapy was received by 4.6% of patients after metastatic diagnosis (Table 5). There were statistically significant differences in receipt of targeted therapy by race (p < 0.0001), but no differences were observed specifically between Black and White races (p = 0.39). In logistic regression models, factors positively associated with receipt of targeted therapy included younger age, NGS testing codes, biomarker testing codes, Other versus White races, and female sex (Table 3).

Relationship of Biomarker Testing With Clinical Trial Participation and Targeted Therapy

Biomarker testing was not associated with clinical trial participation (p = 0.19). Nevertheless, patients who had evidence of NGS-based testing were significantly more likely to participate in a clinical trial (p = 0.02). Biomarker testing at any time was significantly associated with receiving molecularly targeted therapy

Table 1. Metastatic Lung Cancer Cohort	t Characteristics
Variable	Metastatic Lung Cancer (N = 3845)
Age, mean (SD), y	59.5 (8.9)
Sex, n (%)	
Female	1817 (47.3)
Male	2028 (52.7)
Race and Ethnicity, n (%)	070 (25.2)
Black	970 (25.2)
white	22/1 (59.1)
Uther	122 (3.2)
Missing or unknown	<i>J</i> 7 (1. <i>J</i>) <i>J</i> 25 (11 1)
Medicaid plan n (%)	425 (11.1)
Comprehensive	2773 (72-1)
НМО	974 (74.0)
Missing/unknown	148 (3.8)
Initial diagnosis, n (%)	
Diagnosed early stage, later progressed to metastatic	506 (13.2)
Among those diagnosed early stage, time to metastatic diagnosis, mean (SD), mo	7.9 (5.0)
Diagnosed metastatic	3339 (86.8)
Year of metastatic diagnosis, n (%)	
2017	1280 (33.3)
2018	1370 (35.6)
2019	1195 (31.1)
Mean (SD) number of comorbidities ^a Biomarker testing, ^b n (%)	1.4 (1.7)
No	1655 (43.0)
Yes	2190 (57.0)
NGS-based testing, ^b n (%)	
No	3679 (95.7)
Yes	166 (4.3)
Clinical trial participation, ^{<i>b</i>} n (%)	
No	3744 (97.4)
Yes	101 (2.6)
Receipt of targeted therapy," n (%)	2670 (OF 4)
NU	175 (4 6)
103	175 (4.0)

 a Measured by the Charlson Comorbidity Index during the 6-month period before metastatic diagnosis, excluding cancer codes.

 $^b {\rm Codes}$ are present in the database at any time in the database after index date (first metastatic diagnosis).

HMO, health maintenance organization.

(p < 0.0001), and evidence of NGS-based testing was associated with receipt of targeted therapy (p = 0.0003) (data not found).

Discussion

Although biomarker testing is a fundamental step in determining a patient's eligibility for targeted therapies, this large contemporaneous cohort of low SES Medicaidinsured patients diagnosed with having metastatic lung cancer was found to have exceedingly low rates of biomarker testing (only 57%). Moreover, NGS-based n (% within row)

Table 2. Comparison of	[•] Biomarker Test	Codes by Race
------------------------	-----------------------------	---------------

· · · ·				
Race or Ethnicity	Biomarker Test at Any Time	No Biomarker Test at Any Time	<i>p</i> Value (Black vs. White vs. Other) ^a	p Value (Black vs. White) ^a
All patients (n $=$ 3845)	2190 (57.0)	1655 (43.0)		
Black (n = 970)	560 (57.7)	410 (42.3)	0.52	0.56
White (n = 2271)	1286 (56.6)	985 (43.4)		
Other (n = 122)	64 (52.5)	58 (47.5)		
Hispanic (n = 57) ^b	33 (57.9)	24 (42.1)		
Unknown (n = 425) ^b	247 (58.1)	178 (41.9)		
	NGS Test at	No NGS Test	p Value (Black vs.	p Value
Race/Ethnicity	Any Time	at Any Time	White vs. $Other)^a$	(Black vs. White) a
All patients (n $=$ 3845)	166 (4.3)	3679 (95.7)		
Black (n = 970)	34 (3.5)	936 (96.5)	0.28	0.20
White (n = 2271)	102 (4.5)	2169 (95.5)		
Other (n = 122)	3 (2.5)	119 (97.5)		
Hispanic (n = 57) ^b	3 (5.3)	54 (94.7)		
Unknown (n = $425)^{b}$	24 (5.6)	401 (94.4)		

²Chi-square test.

^bUnknown and Hispanic were not included in any statistical comparison.

NGS, next-generation sequencing.

testing rates were only captured for 4.4% of the study cohort. Such findings are unexpected for patients with metastatic NSCLC, where decisions regarding systemic therapy currently rely fundamentally on molecular test results. In previous work addressing similarly contemporaneous cohorts, biomarker testing rates (at least one biomarker test at any time after diagnosis) for patients with advanced or metastatic NSCLC ranged from 76.5% to 90%.^{10,11,17} This study of patients enrolled to Medicaid differs from those prior studies in that patients in the Medicaid system tend to be younger than the typical patient with lung cancer (patients at age 65 y would generally enroll in Medicare) and are limited to those with low SES.¹⁸ Prior research reveals that younger age may be associated with increased rates of biomarker testing in these diseases,¹⁰ which if anything should have resulted in higher rather than lower rates of biomarker testing in this cohort.

After adjusting for confounding covariates, only younger age, stage of disease at diagnosis, and index year at diagnosis were independently associated with biomarker testing. Of note, all relationships reported in this study are associations, as no causal inference can be made from this retrospective analysis. These covariates are consistent with prior work that has revealed these to be important predictors of biomarker testing.¹⁰ In this data set where all patients with Medicaid coverage are of lower SES, no comparison can be made to groups of higher SES, as these groups are not included in this data set and may differ in terms of other baseline covariates. In this study, there were no differences by race observed, whereas the previously found racial gaps in biomarker test delivery may be largely driven by SES. Nevertheless, this hypothesis must be tested in a future study using a database that records more than a singular stratum of SES in the patient cohort.^{10,11}

Having the opportunity to participate in a clinical trial may translate into survival benefit, particularly for patients with poor prognosis.¹⁹ Previous work has revealed in a real-world analysis that single-gene and comprehensive NGS-based biomarker testing are associated with increased odds of clinical trial participation.¹¹ In this Medicaid cohort, the rates of clinical trial participation were less than 5%, unfortunately consistent with the low national average rates.²⁰ Younger age was independently associated with clinical trial participation, albeit with a very small OR. This reflects the fact that patients were fundamentally young across all groups in this Medicaid cohort. Not surprisingly, increased rates of clinical trial participation were associated with observed NGS-based testing as reflected in the claims data.

Clinical trial participation codes may be underrepresented in this database and may not reflect oncology trials. Patients who participated in trials but did not have corresponding clinical trial reimbursement codes submitted to Medicaid could not be captured. The relationships observed between biomarker testing and both clinical trial enrollment and receipt of molecularly targeted therapy were not consistent and did not hold strong associations across the analyses conducted, and as such, they should not be overinterpreted, but hypotheses of the relationships between these variables should be pursued in future research.

lable 3. Factors Signification of the label	intly Associated Wit Vith $p \leq 0.10)$	h Biomarker	lesting, Clinical Irial Pa	rticipation, and Keo	ceipt of Mole	cularly largeted Iherap	oy" (Black vs. White	kace and
Model 1: Factors Associa	ted With Biomarker	Testing	Model 2: Factors Asso Participation	ociated With Clinica	ıl Trial	Model 3: Factors Asso Molecularly Targeted	ociated With Receipt Therapy	of
Variable	OR (95% CI)	<i>p</i> Value	Variable	OR (95% CI)	p Value	Variable	OR (95% CI)	p Value
Age	0.98 (0.97-0.99)	<0.0001	Age	0.97 (0.95-0.99)	0.005	Age	0.94 (0.92-0.95)	<0.0001
Early stage vs. metastatic	0.34 (0.27-0.42)	<0.0001	NGS-based testing	2.36 (1.11-5.00)	0.03	NGS-based testing	2.72 (1.53-4.83)	0.0006
Index 2018 vs. 2019	1.32 (1.12-1.57)	0.01	Other vs. White race	2.81 (1.24-6.36)	0.04	Biomarker testing	1.69 (1.17-2.45)	0.005
Black vs. White race	1.08 (0.92-1.26)	0.29	Black vs. White race	1.45 (0.92-2.29)	0.60	Black vs. White race	1.33 (0.90-1.96)	0.02
						Other vs. White race	5.07 (2.82-9.11)	<0.0001
						Male vs. Female	0.54 (0.38-0.76)	0.0005
Note. Characteristics in logistic	regression models include	d the following: a variables	ge, sex, year of metastatic dia	gnosis (index year), and i	nitial metastatic	diagnosis vs. progressed to me	etastatic. Additional factor	s in models 2

For categorical variables, the p values for the effect of the parameter does not compare the effect of the two predictor levels. Instead, it compares the effect of the associated predictor level with the average כסאו מווש resung 3 Included promar

effect of all the levels. As a result, the 95% confidence interval of the OR comparing two levels of a factor may not agree with the p value. Of note, patients whose race was unknown or reported as Hispanic were not to unknown race categories race owing included in any statistical comparisons by VGS, next-generation sequencing JTO Clinical and Research Reports Vol. 5 No. 3

Other limitations of this database include the method of collection of race and ethnicity variables. Dissimilar to the standard collection of these two variables, there is a singular race variable with "Hispanic" as an option. Therefore, race and ethnicity cannot be separately evaluated as the Merative Medicaid databases include only the singular variable for study.

Utilization rates of targeted therapies for advanced cancer in this contemporaneous Medicaid cohort, at any given line of therapy, were very low. It is important to note that given the lack of clinical outcomes data in claims databases, the clinical outcomes of these patients could not be evaluated. In addition, there is the possibility that targeted therapies were received under some other voucher or other support program and never billed to Medicaid. This could not be evaluated with the available data.

As would be expected, biomarker testing was independently associated with targeted therapy use for patients with metastatic lung cancer (OR: 1.69, p = 0.005). Although being of any race other than White was also positively associated with targeted therapy use in patients with metastatic lung cancer (OR: 5.07, p < 0.0001), no differences were observed between Black and White patients. Future research may wish to explore not only the rates of testing but also timing of biomarker testing and results obtained. If barriers exist, there may be delays in the receipt of testing even among those tested and the subsequent receipt of targeted therapy for those with biomarker-positive disease.

The Affordable Care Act led to an expansion of Medicaid coverage to include U.S. adult citizens with income at or below 138% the poverty line. As of 2020, 14.8 million newly eligible Americans had enrolled in Medicaid coverage under the Affordable Care Act expansion law as of December 2020.²¹ As expected, Medicaid expansion had a beneficial impact on racial and socioeconomic disparities for patients with cancer.²² Nevertheless, the type, amount, length, and extent of such benefits vary largely by State. Prescription drugs and "other diagnostic tests," for example, are considered optional benefits in Medicaid.^{23,24} Hence, single-gene and NGS-based testing for patients with metastatic lung cancer is not mandatory for patients covered by Medicaid and may not be covered in many States²⁵ and may lead to institutions and patients needing to identify alternative resources to receive standard-of-care testing to avoid receipt of suboptimal care.

After Medicaid expansion took effect, an increase in rates of early detected cancers was revealed in a retrospective Surveillance, Epidemiology and End Results analysis, in part owing to coverage of screening tests in most States.²⁶ Nevertheless, the rates of advanced disease remained disproportionately high when compared with patients treated under private insurance,

Table 4. Comparison of	Table 4. Comparison of Clinical Trial Participation by Race Category					
n (% Within Race)						
Race and Ethnicity	Evidence of Clinical Trial Participation	No Evidence of Clinical Trial Participation	p Value (Black vs. White vs. Other) ^a	p Value (Black vs. White) ^a		
All patients (n = 3845)	101 (2.6)	3744 (97.4)				
Black (n = 970)	30 (3.1)	940 (96.9)	0.04	0.18		
White $(n = 2271)$	52 (2.3)	2219 (97.7)				
Other (n $=$ 122)	7 (5.7)	115 (94.3)				
Hispanic (n = 57) ^b	0 (0.0)	57 (100.0)				
Unknown (n = $425)^{b}$	12 (2.8)	413 (97.2)				
^a Chi-square test.						

^bUnknown and Hispanic were not included in any statistical comparison.

highlighting other potential hurdles leading to health inequity. As such, the implementation of life-saving technologies may prove a challenge, despite insurance coverage. Patient access to clinics and the required time off work for routine clinic, testing, and treatment visits may constitute important contributing factors. Furthermore, the systematic efficiency of ordering tests and addressing their results may prove a challenge to health care providers who are already overwhelmed with ensuring the most basic care needs of patients with multiple comorbidities, and many socioeconomic stressors are met. Care management is, in fact, an optional benefit for Medicaid patients.²³

One of the limitations of this study is the inability to identify and distinguish patients treated in expansion versus non-expansion States due to lack of geographic location data in the database and the lack of data of other resources that could have been identified to cover testing. In addition, the role of histological classification in lung cancer is important for biomarker testing, as currently this is not recommended for patients with SCLC, who account for up to 15% of all lung cancers in the United States. Histological subtype data are not available in the Merative databases, and NSCLC cannot be differentiated from small cell tumors using ICD coding systems alone. Despite the inability to differentiate NSCLC in claims data, the testing rates observed in this study are far lower even considering the proportion that may not be NSCLC. There is also no information regarding type of biomarker being evaluated, and differentiation between single and comprehensive biomarker testing could not be achieved. Hence, the use of comprehensive genomic sequencing was not captured unless a specific NGS coding was used, and findings regarding NGS utilization rates should be interpreted with caution. There are also limitations with the type of clinical trial in which the patient was enrolled. There is no way to confirm that the clinical trial was for an oncology drug; however, given that the time period in which the codes were observed was limited to the postdiagnosis period, this was the assumption in the interpretation of these data. Finally, a major limitation of this analysis is the inability to discriminate the setting where care was primarily delivered (community versus academic and rural versus urban). Therefore, the potential impact of such variables offsetting previously identified racial disparities cannot be assessed.

Despite such constraints, this study provides novel and important insight into the real-world care received by patients with the most prevalent metastatic lung cancer treated under Medicaid in the United States. As the utilization of precision medicine to improve and

Table 5. Comparison of Receipt of Targeted Therapy by Race					
n (% Within Row)					
Race/Ethnicity	Evidence of Targeted Therapy	No Evidence of Targeted Therapy	<i>p</i> Value (Black vs. White vs. Other) ^a	p Value (Black vs. White) ^a	
All patients ($n = 3845$)	175 (4.6)	3670 (95.4)			
Black (n = 970)	42 (4.3)	928 (95.7)	<0.0001	0.39	
White $(n = 2271)$	84 (3.7)	2187 (96.3)			
Other $(n = 122)$	17 (13.9)	105 (86.1)			
Hispanic $(n = 57)^{b}$	8 (14.0)	49 (86.0)			
Unknown (n = $425)^{b}$	24 (5.6)	401 (94.4)			

^aChi-square test.

^bUnknown and Hispanic were not included in any statistical comparison.

extend the lives of patients with cancer becomes standard of care, this study suggests that major disparities may exist for segments of the American population with known socioeconomic disadvantages.²⁷⁻²⁹ It is imperative that scientists, health care providers, and legislators address this matter with urgency and intent. Having identified health equity as a major problematic to tackle, leadership groups such as the American Cancer Society, the American Association for Cancer Research, and the American Society of Clinical Oncology have, in the past few years, decisively shed light into work intended to investigate gaps in cancer therapy delivery and outcomes. Substantial work and research initiatives supported by the National Cancer Institute currently address institutional racism and health equity. Certainly, only by sustained and relentless engagement will the scientific community continue to serve all segments of the society at large with equipoise.

CRediT Authorship Contribution Statement

Debora S. Bruno: Conceptualized and designed the work; Interpreted the data; Provided critical revisions for important intellectual content; Accountable for the content of the work; and Have approved the final version to be submitted.

Xiaohong Li: Analyzed the data; Interpreted the data; Provided critical revisions for important intellectual content; Accountable for the content of the work; and Have approved the final version to be submitted.

Lisa M. Hess: Conceptualized and designed the work; Interpreted the data; Drafted the manuscript; Provided critical revisions for important intellectual content; Accountable for the content of the work; and Have approved the final version to be submitted.

Disclosure

Dr. Bruno receives consulting fees from Novartis, Bristol-Myers Squibb, Mirati Therapeutics, Eli Lilly, AstraZeneca, Syneos Health, Amgen, and Daiichi Sankyo; and independent research funding from AstraZeneca. Dr. Hess and Ms. Li are employees of Eli Lilly and Company.

Acknowledgments

This was an unfunded research project supported by employee time and database access provided by Eli Lilly and Company.

Supplementary Data

Note: To access the supplementary material accompanying this article, visit the online version of the *JTO* *Clinical and Research Reports* at www.jtocrr.org and at https://doi.org/10.1016/j.jtocrr.2024.100643.

References

- Soria JC, Ohe Y, Vansteenkiste J, et al. Osimertinib in untreated EGFR-mutated advanced non-small-cell lung cancer. N Engl J Med. 2018;378:113-125.
- 2. Peters S, Camidge DR, Shaw AT, et al. Alectinib versus crizotinib in untreated ALK-positive non-small-cell lung cancer. *N Engl J Med*. 2017;377:829-838.
- 3. Tan AC, Tan DS. Targeted therapies for lung cancer patients with oncogenic driver molecular alterations. *J Clin Oncol*. 2022;40:611-625.
- Gadgeel S, Rodríguez-Abreu D, Speranza G, et al. Updated analysis from KEYNOTE-189: pembrolizumab or placebo plus pemetrexed and platinum for previously untreated metastatic nonsquamous non-small-cell lung cancer. J Clin Oncol. 2020;38:1505-1517.
- Paz-Ares L, Vicente D, Tafreshi A, et al. A randomized, placebo-controlled trial of pembrolizumab plus chemotherapy in patients with metastatic squamous NSCLC: protocol-specified final analysis of KEYNOTE-407. *J Thorac Oncol.* 2020;15:1657-1669.
- 6. Mok T, Camidge D, Gadgeel S, et al. Updated overall survival and final progression-free survival data for patients with treatment-naive advanced ALK-positive non-small-cell lung cancer in the ALEX study. *Ann Oncol.* 2020;31:1056-1064.
- Singal G, Miller PG, Agarwala V, et al. Association of patient characteristics and tumor genomics with clinical outcomes among patients with non-small cell lung cancer using a clinicogenomic database. JAMA. 2019;321:1391-1399.
- Zhu Y, Han Y, Bhandari NR, Hess L. CGE21-031: genomic biomarker testing, treatments, and survival outcomes among patients with advanced or metastatic NSCLC in the US: a retrospective cohort study. J Natl Compr Canc Netw. 2021;19:CGE21-CGE031.
- NCCN Clinical Practice Guidelines in Oncology: Non-Small Cell Lung Cancer. Version 2.2024; 2024. https:// www.nccn.org/professionals/physician_gls/pdf/nscl.pdf. Accessed February 13, 2024.
- Bruno DS, Hess LM, Li X, Su EW. Disparities in biomarker testing and clinical trial enrollment among patients with lung, breast or colorectal cancers in the United States. *J Precis Oncol*. 2022;6:e2100427.
- Bruno DS, Hess LM, Li X, Su EW, Zhu YE, Patel M. Racial disparities in biomarker testing and clinical trial enrollment in non-small cell lung cancer (NSCLC). *J Clin Oncol*. 2021;39(suppl 15):9005-9005.
- HHS. Human Subject Regulations Decision Charts: 2018 Requirements; 2020. https://www.hhs.gov/ohrp/ regulations-and-policy/decision-charts-2018/index.html. Accessed February 13, 2024.
- Whyte JL, Engel-Nitz NM, Teitelbaum A, Gomez Rey G, Kallich JD. An evaluation of algorithms for identifying metastatic breast, lung, or colorectal cancer in administrative claims data. *Med Care*. 2015;53:e49-e57.
- Nordstrom BL, Simeone JC, Malley KG, et al. Validation of claims algorithms for progression to metastatic cancer

in patients with breast, non-small cell lung, and colorectal cancer. *Front Oncol.* 2016;6:18.

- Ettinger DS, Wood DE, Ainser DL, et al. Non-small cell lung cancer, version 2.2021. J Natl Compr Canc Netw. 2021;19:254-266.
- Hess LM, Michael D, Krein PM, Marquart T, Sireci AN. Costs of biomarker testing among patients with metastatic lung or thyroid cancer in the USA: a real-world commercial claims database study. J Med Econ. 2023;26:43-50.
- Robert NJ, Espirito JL, Chen L, et al. Biomarker testing and tissue journey among patients with metastatic nonsmall cell lung cancer receiving first-line therapy in The US Oncology Network. *Lung Cancer*. 2022;166:197-204.
- SEER. Cancer Stat Facts. Vol. 2022. 2022. https://www. cancer.org/content/dam/cancer-org/research/cancerfacts-and-statistics/annual-cancer-facts-and-figures/2022/ 2022-cancer-facts-and-figures.pdf. Accessed February 13, 2024.
- Unger JM, Barlow WE, Martin DP, et al. Comparison of survival outcomes among cancer patients treated in and out of clinical trials. JNCI J Natl Cancer Inst. 2014;106:dju002.
- 20. Unger JM, Cook E, Tai E, Bleyer A. The role of clinical trial participation in cancer research: barriers, evidence, and strategies. *Am Soc Clin Oncol Educ Book*. 2016;35:185-198.
- CMS. Gov: New HHS Data Show More Americans Than Ever Have Health Coverage Through the Affordable Care Act; 2021. https://www.cms.gov/newsroom/pressreleases/new-hhs-data-show-more-americans-ever-havehealth-coverage-through-affordable-care-act. Accessed February 13, 2024.

- 22. Moss HA, Wu J, Kaplan SJ, Zafar SY. The Affordable Care Act's Medicaid expansion and impact along the cancercare continuum: a systematic review. JNCI J Natl Cancer Inst. 2020;112:779-791.
- 23. Medicaid.org. Mandatory & Optional Medicaid Benefits; 2024. https://www.medicaid.gov/medicaid/ benefits/mandatory-optional-medicaid-benefits/index. html. Accessed February 13, 2024.
- 24. Lin GA, Trosman JR, Douglas MP, et al. Influence of payer coverage and out-of-pocket costs on ordering of NGS panel tests for hereditary cancer in diverse settings. *J Genet Couns*. 2022;31:130-139.
- 25. Lungevity. State Scorecard: State Medicaid Coverage Policy and Impact on Lung Cancer Outcomes; 2020. https://www.lungevity.org/sites/default/files/statescorecards/LUNGevity-scorecard-030920.pdf. Accessed February 13, 2024.
- 26. Soni A, Simon K, Cawley J, Sabik L. Effect of Medicaid expansions of 2014 on overall and earlystage cancer diagnoses. Am J Public Health. 2018;108:216-218.
- 27. Ayanian JZ, Kohler BA, Abe T, Epstein AM. The relation between health insurance coverage and clinical out-comes among women with breast cancer. *N Engl J Med*. 1993;329:326-331.
- 28. Halpern MT, Bian J, Ward EM, Schrag NM, Chen AY. Insurance status and stage of cancer at diagnosis among women with breast cancer. *Cancer*. 2007;110:403-411.
- 29. Greenberg ER, Chute CG, Stukel T, et al. Social and economic factors in the choice of lung cancer treatment. A population-based study in two rural states. *N Engl J Med.* 1988;318:612-617.