Associations Between Medicaid Insurance, Biomarker Testing, and Outcomes in Patients With Advanced NSCLC

Cary P. Gross, MD1,2; Craig S. Meyer, PhD, MPH3; Sarika Ogale, PhD3; Matthew Kent, MS4; and William B. Wong, PharmD, MS5

ABSTRACT

Background: Evidence suggests that patients with Medicaid experience lower-quality cancer care than those with commercial insurance. Whether this trend persists in the era of personalized medicine is unclear. This study examined the associations between Medicaid (vs commercial) insurance and receipt of biomarker testing, targeted therapy, and overall survival in patients with advanced non–small cell lung cancer (aNSCLC).

Methods: We conducted a retrospective study of patients who received an aNSCLC diagnosis from January 2011 to September 2019 using a nationwide US healthcare database. Eligible patients were aged 18 to 64 years with Medicaid or commercial insurance at diagnosis. Receipt of biomarker testing (ALK, EGFR, ROS1, BRAF, and PD-L1) was assessed. The likelihood of testing, biomarker-driven therapy (cancer immunotherapy or tyrosine kinase inhibitor treatment), and mortality were compared by insurance type using adjusted Cox regression.

Results: Our sample included 6,145 commercially insured and 865 Medicaid beneficiaries. Medicaid beneficiaries were more likely to be Black or African American (20% vs 9.3%; P < .001) and were less likely to have undergone biomarker testing (57% vs 71%; P < .001). In the adjusted analysis, Medicaid beneficiaries were less likely to have evidence of testing (hazard ratio [HR] 0.81; P < .001), any first-line treatment (HR, 0.72; P < .001), and first-line biomarker-driven therapy (HR, 0.70; P < .001). Medicaid beneficiaries with evidence of biomarker testing had a lower risk of death compared with those without evidence of biomarker testing (HR, 1.27 [95% CI, 1.06–1.52]; P = .010). Higher risk of death was observed in patients with Medicaid versus commercially insured patients (HR, 1.23; P < .001); this result remained unchanged after adjusting for biomarker testing (HR, 1.22; P < .001) but was partially ameliorated after adjustment for testing and treatment type (HR, 1.12; P = .010).

Conclusions: Medicaid beneficiaries with aNSCLC were less likely to receive biomarker testing and biomarker-driven therapies, which may in part contribute to a higher observed risk of mortality compared with commercially insured patients.


Background

Lung cancer is the leading cause of cancer death, representing approximately 25% of all cancer deaths.1 Non–small cell lung cancer (NSCLC) comprises the majority of patients with lung cancer1 and has seen significant improvements in survival over the past decade.2 Advances in personalized therapies for advanced NSCLC (aNSCLC), which allow treatment based on the genetic makeup of a tumor, have significantly contributed to the improved outcomes of patients.2

Despite the therapeutic advancements, the realized benefits of personalized medicine may be hindered by the disparities that exist in the care of patients with NSCLC. Furthermore, insurance has been previously identified as an important factor in dictating the cancer care that patients receive.3–5 Specifically, prior work4,6 suggests that patients with Medicaid experience lower-quality cancer care and worse survival outcomes.6,7 A study examining cancer survival found that those with public insurance (non-Medicare) had a higher risk of mortality across different cancers, ranging from 11% to 25% (increased risk).8

Limited data indicate whether these disparities persist in the era of personalized medicine. An analysis examining ALK biomarker testing in patients with NSCLC found that Medicaid beneficiaries were 40% less likely to be tested compared with commercially insured patients.9 Another study found that Medicaid expansion was associated with an improvement in time to treatment for Black or African American patients.10 Another study found an association with Medicaid expansion and improved survival in states with expanded Medicaid, underscoring the relationship between access to care and cancer outcomes.11 However, it remains unknown whether access to biomarker testing and personalized treatments is driving the differences in outcomes. We examined the associations between Medicaid (vs commercial) insurance and the receipt of biomarker testing.

See JNCCN.org for supplemental online content.
and targeted therapy, and explored the association with overall survival (OS) in a contemporary cohort of patients with aNSCLC.

**Methods**

**Study Design and Data Source**

We conducted a retrospective analysis using the Flatiron Health database, which is derived from nationwide longitudinal electronic health records (EHRs). During the study period, these data originated from approximately 280 cancer clinics representing >2.2 million US patients with cancer. The deidentified patient-level data include structured and unstructured data, curated via technology-enabled abstraction.\(^{12,13}\) Institutional Review Board approval of the study protocol was obtained before study conduct and included a waiver of informed consent. The EHR data are linked with external mortality data, and the quality of the mortality data has been previously evaluated and validated.\(^{14,15}\) Commercially or Medicaid-insured patients with NSCLC and an advanced diagnosis from January 1, 2011, through September 30, 2019, were included in the study. Additional inclusion criteria included requirement of a clinic visit within 120 days of advanced diagnosis and being aged 18 to 64 years at diagnosis of advanced disease. Patients were excluded if they received clinical study drugs or care at academic sites, or if they had biomarker testing before their advanced diagnosis date. To mitigate the risk of missing biomarker or treatment records because of patients seeking care outside the Flatiron Health network, we excluded patients who had their first biomarker test ≥3 months or their first evidence of treatment ≥4 months from their advanced diagnosis date. Patient attrition is shown in supplemental eTable 1 (available with this article at JNCCN.org).

**Construction of Variables**

Clinical characteristics included demographics and clinical factors (Table 1). Patients were assigned to Medicaid or commercially insured cohorts based on the record of insurance before or within 90 days of the advanced diagnosis date. Patients lacking information on start or end dates for their coverage were assigned to the Medicaid or commercial insurance cohorts as long as their insurance type was exclusively one or the other. Patients with overlapping insurance types were excluded.

Biomarker testing was evaluated during the first 3 months after the advanced cancer diagnosis. Biomarkers examined included ALK, EGFR, ROSI, BRAF, and PD-L1. In addition to individual biomarker testing rates, we also assessed receipt of all recommended biomarker tests, which was defined as the time period after a targeted therapy became available (approved by the FDA). Dates when targeted therapies were first approved by the FDA for each biomarker were as follows: ALK: August 26, 2011 (crizotinib); EGFR: May 14, 2013 (erlotinib); ROSI: March 11, 2016 (crizotinib); PD-L1: October 2, 2015 (pembrolizumab); and BRAF: June 27, 2017 (dabrafenib + trametinib).

We identified first-line (1L) therapy occurring within 4 months after advanced cancer diagnosis. Treatment-related outcomes included the proportion of patients receiving 1L therapy and the frequency of receiving 1L therapy. Treatment classifications included tyrosine kinase inhibitor (TKI)-based (afatinib, alectinib, crizotinib, ceritinib, dabrafenib, dacotinib, erlotinib, gefitinib, lorlatinib, osimertinib, trametinib), cancer immunotherapy–based (atezolizumab, durvalumab, nivolumab, pembrolizumab), and other chemotherapy/biologic-based (not including those mentioned).

**Statistical Analysis**

Biomarker testing–related outcomes included testing rates, the proportion of patients receiving recommended biomarker tests (defined earlier, based on the date of availability of a therapy indicated for a given biomarker), and the likelihood of receiving biomarker tests by insurance type. Biomarker testing was assessed via (1) biomarker testing rate by person-time and (2) an overall proportion. The biomarker testing rate by person-time was estimated by dividing the number of patients with a given biomarker test before age 65 years divided by the amount of person-time “at risk,” which included the time from diagnosis until receipt of the test or age 65 years, whichever came first (after age 65 years it was assumed that the patient would be eligible for Medicare and no longer at risk for having Medicaid as the primary insurance). The overall proportion was estimated by dividing the number of patients who received a biomarker test within 3 months of diagnosis by the total number of eligible patients. For biomarker temporal trends analyses, we classified patients by year and quarter (eg, Q2 2012) or semester (eg, S1 2012) of their advanced diagnosis.

Descriptive statistics, including means and percentages for continuous variables and counts and percentages for categorical variables, were used along with the Student t test or chi-square test statistics, respectively, to compare differences in baseline patient characteristics by insurance type. We used a logistic regression model with covariates for insurance (Medicaid vs commercial) and time to assess differences in the receipt of the recommended biomarker tests between insurance cohorts over time by each semester (eg, half/year). Because guideline recommendations for biomarker testing are primarily focused on nonsquamous cell carcinoma histology, we conducted a subgroup analysis assessing receipt of recommended biomarker tests by insurance type among patients with nonsquamous cell carcinoma histology. An interaction term between time and insurance was included.
to assess whether any differences changed over time. We then used a series of sequential models to conduct an exploratory analysis of the relation between insurance type and OS. Patients were followed up from advanced diagnosis to receipt of testing, treatment, death, or last known visit date. We used Cox regression models to estimate the relative hazard of biomarker testing, treatment, and mortality according to insurance type.

Final hazard ratios (HRs) and 95% confidence intervals for all outcomes were adjusted for baseline characteristics, including gender, age, race/ethnicity, region, smoking status, histology, year of advanced diagnosis, liver metastases, brain and central nervous system metastases, and bone metastases. Models for mortality were sequentially adjusted for testing, then treatment (any 1L treatment, then type of 1L treatment) as time-varying covariates to account for potential immortal time bias resulting from potential differences in timing/receipt of testing and treatment between insurance cohorts. Finally, we constructed separate models for patients with each insurance type to evaluate the association of testing and treatment on mortality separately in patients with Medicaid and commercially insured patients.

A sensitivity analysis examining the interaction between histology and insurance was conducted to assess for a differential effect by histology. The Kaplan-Meier method was used to calculate OS distributions, with the log-rank test

### Table 1. Baseline Patient Characteristics by Insurance Type

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Commercial Health Plan</th>
<th>Medicaid</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total, n</td>
<td>6,145</td>
<td>865</td>
<td></td>
</tr>
<tr>
<td>Median age at aNSCLC diagnosis (IQR), y</td>
<td>59.0 (55.0–62.0)</td>
<td>58.0 (54.0–61.0)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td>.011</td>
</tr>
<tr>
<td>Female</td>
<td>2,950 (48)</td>
<td>372 (43)</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>3,194 (52)</td>
<td>493 (57)</td>
<td></td>
</tr>
<tr>
<td>Missing</td>
<td>1 (&lt;0.1)</td>
<td>0 (0)</td>
<td></td>
</tr>
<tr>
<td>Race/Ethnicity</td>
<td></td>
<td>&lt;.001</td>
<td></td>
</tr>
<tr>
<td>Asian</td>
<td>182 (3.0)</td>
<td>12 (1.4)</td>
<td></td>
</tr>
<tr>
<td>Black or African American</td>
<td>571 (9.3)</td>
<td>174 (20)</td>
<td></td>
</tr>
<tr>
<td>Hispanic or Latino</td>
<td>206 (3.4)</td>
<td>21 (2.4)</td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>3,978 (65)</td>
<td>508 (59)</td>
<td></td>
</tr>
<tr>
<td>Other race</td>
<td>514 (8.4)</td>
<td>70 (8.1)</td>
<td></td>
</tr>
<tr>
<td>Missing</td>
<td>694 (11)</td>
<td>80 (9.2)</td>
<td></td>
</tr>
<tr>
<td>Region</td>
<td></td>
<td>&lt;.001</td>
<td></td>
</tr>
<tr>
<td>Midwest</td>
<td>1,185 (19)</td>
<td>199 (23)</td>
<td></td>
</tr>
<tr>
<td>Northeast</td>
<td>1,245 (20)</td>
<td>124 (14)</td>
<td></td>
</tr>
<tr>
<td>South</td>
<td>2,573 (42)</td>
<td>473 (55)</td>
<td></td>
</tr>
<tr>
<td>West</td>
<td>1,056 (17)</td>
<td>47 (5.4)</td>
<td></td>
</tr>
<tr>
<td>Puerto Rico</td>
<td>44 (0.7)</td>
<td>0 (0.0)</td>
<td></td>
</tr>
<tr>
<td>Missing</td>
<td>42 (0.7)</td>
<td>22 (2.5)</td>
<td></td>
</tr>
<tr>
<td>Year of advanced diagnosis</td>
<td></td>
<td>&lt;.001</td>
<td></td>
</tr>
<tr>
<td>2011</td>
<td>310 (5.0)</td>
<td>65 (7.5)</td>
<td></td>
</tr>
<tr>
<td>2012</td>
<td>498 (8.1)</td>
<td>95 (11)</td>
<td></td>
</tr>
<tr>
<td>2013</td>
<td>591 (9.6)</td>
<td>81 (9.4)</td>
<td></td>
</tr>
<tr>
<td>2014</td>
<td>707 (12)</td>
<td>118 (14)</td>
<td></td>
</tr>
<tr>
<td>2015</td>
<td>818 (13)</td>
<td>123 (14)</td>
<td></td>
</tr>
<tr>
<td>2016</td>
<td>809 (13)</td>
<td>108 (12)</td>
<td></td>
</tr>
<tr>
<td>2017</td>
<td>915 (15)</td>
<td>120 (14)</td>
<td></td>
</tr>
<tr>
<td>2018</td>
<td>905 (15)</td>
<td>104 (12)</td>
<td></td>
</tr>
<tr>
<td>2019</td>
<td>592 (9.6)</td>
<td>51 (5.9)</td>
<td></td>
</tr>
</tbody>
</table>

(continued)
used to test differences by insurance type. The statistical significance threshold was set a priori using 2-sided tests at $P<.05$. All analyses were performed using R version 3.5.3 (R Foundation for Statistical Computing).

Results

Baseline Patient Characteristics

A total of 7,010 patients were included in the analysis, of whom 6,145 were in the commercially insured cohort and 865 in the Medicaid cohort. Although most of the demographic and clinical characteristics were similar between the 2 cohorts, race/ethnicity, region, and smoking status were significantly different ($P<.001$), with the Medicaid cohort having a greater proportion of Black or African American patients (20% vs 9.3%), more patients from the South (55% vs 42%), and more patients likely to be smokers (93% vs 85%; Table 1).

Biomarker Testing Patterns

Compared with commercially insured patients, a smaller proportion of Medicaid beneficiaries were observed to be tested for each individual biomarker in terms of the proportion of patients receiving tests (Figure 1) and the frequency of testing (supplemental eFigure 1). For instance, differences in biomarker testing for potential targeted agents (EGFR, ALK, ROS1, and BRAF) ranged from 12% to 15% ($P<.001$), whereas differences in PD-L1 testing to identify candidates for cancer immunotherapy was 9% ($P<.001$). Similar differences were observed when examining the rate of testing, which accounted for variable times of follow-up, although the difference in PD-L1 testing was not statistically significant ($P=15$).

In addition to the fewer tests observed for Medicaid beneficiaries in individual biomarkers, a smaller proportion of Medicaid beneficiaries was observed to have been tested for all recommended biomarkers. This difference was consistent regardless of the number of biomarker tests recommended during the time period ($P<.001$ for insurance and time), and the magnitude of the difference did not change over time ($P=.583$ for interaction between time and insurance; Figure 2). Lower proportions of testing in patients with Medicaid were generally observed over time for EGFR, ALK, ROS1, and BRAF. However, PD-L1 testing seemed to be more similar between the 2 cohorts (supplemental eFigure 2). After controlling for baseline characteristics, including histology, Medicaid beneficiaries were 19% less likely to be tested compared with commercially insured patients (HR, 0.81; 95% CI, 0.74–0.89; $P<.001$; Table 2). A similar pattern was observed when biomarker testing rates were stratified by histology. In addition, testing rates were numerically higher for those with commercial insurance compared with those with Medicaid in both nonsquamous and squamous cell carcinoma histology, although these differences were not tested statistically (supplemental eTable 2).

Treatment Patterns

A lower proportion of Medicaid beneficiaries compared with commercially insured beneficiaries was observed to have any 1L treatment (67% vs 79%; $P<.001$) and any biomarker-driven therapy (TKI- or cancer immunotherapy–based regimens; 14% vs 25%; $P<.001$). After adjustment for baseline characteristics and tumor histology, Medicaid beneficiaries were 28% less likely to receive any 1L treatment (HR, 0.72; 95% CI, 0.66–0.79; $P<.001$) and 30% less likely to be treated using a biomarker-driven therapy (HR, 0.70; 95% CI, 0.58–0.85; $P<.001$; Table 2). Among those tested, Medicaid beneficiaries were 29% less likely to be treated using a biomarker-driven therapy (HR, 0.71; 95% CI, 0.58–0.88; $P<.001$); yet among the subgroup of patients with a positive driver mutation, there was no difference in receipt of targeted therapy (HR, 0.90; 95% CI, 0.60–1.34; $P=.60$; Table 2).

Overall Survival

Median OS in the Medicaid cohort was 7.8 months (95% CI, 7.0–8.7 months) compared with 10.3 months (95% CI, 10.0–10.7 months) in the commercial cohort (log-rank $P<.01$; Figure 3A). After adjustment for baseline clinical factors, Medicaid beneficiaries had a 23% higher risk of mortality (HR, 1.23; 95% CI, 1.13–1.35; Table 3). Adding testing to the model resulted in minimal change to the HR (HR, 1.22; 95% CI, 1.12–1.33); however, after adding testing and type of treatment to the model, the HR approached 1 (HR, 1.12; 95% CI, 1.03–1.22; $P=.010$) but the result remained statistically significant, indicating that other unmeasured factors may be contributing to the difference in OS between Medicaid beneficiaries and commercially insured patients.

Among Medicaid beneficiaries, those who had at least 1 biomarker test had a longer median OS (8.7 months; 95% CI, 7.6–10.3 months) compared with those who had no tests (OS, 6.9 months; 95% CI, 6.2–7.9 months) (log-rank $P<.01$) (Figure 3B). After controlling for clinical factors and histologic type, we found that Medicaid beneficiaries who were not tested had a 27% higher risk of mortality than those who had at least 1 biomarker test (HR, 1.27; 95% CI, 1.06–1.52; $P=.013$; Table 3). After adjusting for type of treatment, the effect was attenuated minimally (HR, 1.23; 95% CI, 1.02–1.48; $P=.026$).

Discussion

This analysis of a large national oncology EHR database found that Medicaid (vs commercial insurance) beneficiaries
with aNSCLC were less likely to receive recomm-ended biomarker testing or targeted therapy. Notably, Medicaid insurance may also be associated with inferior OS, partially mediated by treatment differences between patients with Medicaid and commercially insured patients. Although previous studies have shown poorer outcomes with Medicaid beneﬁciaries, these studies have commonly used older data.6,7 Because precision medicine has brought substantial changes to clinical practice and the promise of longer OS for patients with aNSCLC, our ﬁndings suggest that disparities in both molecular testing and receipt of targeted therapy may be perpetuating socioeconomic disparities.

Our ﬁndings are consistent with earlier studies that found molecular testing to be less likely in Medicaid or Medicare–Medicaid dual-eligible populations9,16; however, neither study examined the magnitude and potential impact of these testing disparities on OS in Medicaid beneﬁciaries versus commercially insured patients. Although determining why testing disparities exist is beyond the scope of this study, there are a number of potential explanations. In our study, a larger proportion of patients with Medicaid had squamous cell carcinoma histology, for which driver mutations may be less prevalent and less likely to be tested. However, our ﬁndings persisted after adjusting for histology. In addition, sensitivity analyses found that a smaller proportion of Medicaid beneﬁciaries was tested for all recommended biomarkers in the nonsquamous cell carcinoma histology subgroup (P<.001; consistent with the overall cohort); a lack of a differential effect on receipt of biomarker-driven therapy between insurance by histology (interaction P>.6) indicates that these results seem to be consistent across histologies.

Inconsistent Medicaid policies may be another potential explanation for testing variation. A recent report found that only approximately 40% of state Medicaid programs provided coverage for comprehensive biomarker testing.17 Lower access to testing may lead to fewer opportunities for biomarker-driven therapies, and among those tested there was a disparity in the receipt of biomarker-driven therapy, indicating other potential access barriers to treatments. Although the drivers behind the lack of treatment utilization among Medicaid beneﬁciaries are unclear, similar to testing, a lack of timely updated coverage policies may play a role. Because the evidence base underlying different genetic tests and associated targeted therapies is evolving rapidly, it is critical to develop an approach for payors to promptly and comprehensively evaluate evidence and incorporate it into coverage deci-
sions, because the disparity in the receipt of biomarker-driven therapies may influence outcomes. In this study, Medicaid beneﬁciaries without biomarker testing had an increased risk of mortality of 27%, indicating the potential impact that updating coverage policies to improve access to biomarker testing, and subsequent treatment, may have in this population.

Figure 1. Biomarker testing patterns by insurance type. All differences between Medicaid and commercial insurance are statistically signiﬁcant (P<.001).
Similar to other studies that have assessed cancer survival,\textsuperscript{5,8,18} OS may be shorter in the Medicaid population compared with a commercially insured population in the era of precision medicine. Our sequential modeling approach provides some mechanistic insights regarding this relationship in the context of a modern aNSCLC practice. Although the increased risk of mortality associated with Medicaid was not ameliorated when molecular testing was added to the model, there was a decrease in the Medicaid-associated hazard when receipt of any treatment was added. Furthermore, the risk of death was further attenuated when accounting for the type of treatment. This result suggests that disparities in biomarker testing itself may not drive OS differences between patients with Medicaid and commercially insured patients but that access to treatment, in particular biomarker-driven therapies, may be of importance in narrowing the survival gap. Nonetheless, these factors can only partially explain the survival differences observed, and thus other factors, such as social determinants of health, may play a role. In light of these findings, programs/policies

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{Figure2}
\caption{Proportion of patients receiving all recommended biomarker tests over time. Arrows indicate the half-year period when each biomarker was first recommended (as determined by FDA approval of targeted therapy indicated for that biomarker).}
\end{figure}

\textbf{Table 2. Risk of Testing and Treatment}

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Comparison</th>
<th>HR (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any biomarker testing</td>
<td>Medicaid (ref: commercial)</td>
<td>0.81 (0.74–0.89)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Any treatment</td>
<td>Medicaid (ref: commercial)</td>
<td>0.72 (0.66–0.79)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Any 1L CIT or TKI</td>
<td>Medicaid (ref: commercial)</td>
<td>0.70 (0.58–0.85)</td>
<td>.001</td>
</tr>
<tr>
<td>Any 1L CIT or TKI among those tested</td>
<td>Medicaid (ref: commercial)</td>
<td>0.71 (0.58–0.88)</td>
<td>.001</td>
</tr>
<tr>
<td>Among driver mutation–positive*</td>
<td>Medicaid (ref: commercial)</td>
<td>0.90 (0.60–1.34)</td>
<td>.60</td>
</tr>
<tr>
<td>Among PD-L1 moderate or high expression</td>
<td>Medicaid (ref: commercial)</td>
<td>0.66 (0.42–1.03)</td>
<td>.07</td>
</tr>
<tr>
<td>Among PD-L1 low expression</td>
<td>Medicaid (ref: commercial)</td>
<td>1.14 (0.56–2.30)</td>
<td>.70</td>
</tr>
</tbody>
</table>

All models adjusted for gender, age at advanced diagnosis, race/ethnicity, region, smoking status, histology, year of advanced diagnosis, liver metastases, brain or central nervous system metastases, bone metastases.

Abbreviations: 1L, first-line; CIT, cancer immunotherapy; HR, hazard ratio; TKI, tyrosine kinase inhibitor.

*Driver mutation–positive includes ALK, BRAF, EGFR, and ROS1.
that address not only testing and treatment access barriers but also other issues specific to Medicaid beneficiaries are needed to improve survival outcomes. A cohort analysis of patients in cancer clinical trials with positive findings provided further evidence supporting this need to address social determinants of health. Unger et al.\(^{19}\) found a much smaller added survival benefit of an experimental drug compared with the standard of care in patients with Medicaid or no insurance versus those with commercial insurance. The authors speculated that this finding reflected the impacts of socioeconomic status and disparities in access to healthcare services, which may result in differential access to support services and postprotocol therapy.

There are a number of areas of future research that may further inform healthcare policies and quality-of-care improvements. First, additional research aimed at identifying the specific drivers of the observed disparities in OS would be helpful to inform the design of programs that specifically address Medicaid beneficiary needs. Our findings strongly suggest that access to biomarker testing and targeted therapy may be necessary but not sufficient as strategies to address disparities. Future work could focus on patient access to oncology care, the impact of non-cancer illnesses on outcomes, Medicaid reimbursement policies, and whether financial toxicity associated with treatment or other health-related social needs is rendering targeted therapies unaffordable for some Medicaid beneficiaries. In addition, further understanding regarding testing, treatment, and outcomes of patients with Medicare compared with commercial and Medicaid beneficiaries may be warranted due to differing coverage policies.

Figure 3. Overall survival by (A) insurance type and (B) receipt of testing among patients with Medicaid.
particularly in light of the Medicare national coverage determination for next-generation sequencing.

This analysis has a number of limitations to consider. First, as with all studies based on real-world data, it is subject to misclassification and missingness with the potential for patients to receive care outside of the Flatiron Health network. We therefore sought to mitigate this risk through our inclusion criteria requiring patients to have an office visit after their advanced diagnosis and excluding those who had their first treatment >120 days after advanced diagnosis and their first test >90 days after advanced diagnosis. In addition, insurance status may change over time and may not be completely captured in the EHRs; however, this risk was mitigated by excluding patients who had evidence of both commercial insurance and Medicaid. Although this analysis focused on community-based care, academic sites also care for Medicaid beneficiaries and may have different testing rates, so our results may not be generalizable across all sites of care. Last, we had limited information on performance status; however, the missingness and distribution of ECOG performance status scores were balanced between the cohorts.

**Conclusions**

Medicaid beneficiaries with aNSCLC had a 19% and 30% higher risk of not receiving biomarker testing and biomarker-driven therapy, respectively. Furthermore, Medicaid beneficiaries had an observed 23% higher risk of mortality than commercially insured patients, which may be partially mediated by disparities in receipt of treatment in general and targeted therapies in particular. Improved access to evidence-based molecular testing and targeted therapies may improve outcomes for Medicaid beneficiaries with lung cancer.

Submitted February 1, 2021; final revision received June 11, 2021; accepted for publication July 13, 2021.


**Disclosures:** Dr. Gross has disclosed receiving research grants from NCCN (funds from Pfizer/AstraZeneca), Genentech, and Johnson & Johnson; and serving as a principal investigator for NCCN/AstraZeneca. Drs. Meyer and Wong have disclosed that they are employed by Genentech, Inc. and participating in research for Genentech, Inc., and hold stock in Roche. Dr. Ogale has disclosed being employed by Genentech, Inc., and holding stock in Roche. Mr. Kent has disclosed being employed by Genesis Research.

**Funding:** This work was supported by funding from Genentech Inc.

**Correspondence:** Cary P. Gross, MD, Department of Internal Medicine, Yale School of Medicine, 367 Cedar Street, New Haven, CT 06510. Email: cary.gross@yale.edu

---

**Table 3. Risk of Mortality**

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Comparison</th>
<th>HR (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>OS</td>
<td>Medicaid (ref: commercial)</td>
<td>1.23 (1.13–1.35)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>OS, adjusted for testing</td>
<td>Medicaid (ref: commercial)</td>
<td>1.22 (1.12–1.33)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>OS, adjusted for testing and any treatment</td>
<td>Medicaid (ref: commercial)</td>
<td>1.15 (1.06–1.26)</td>
<td>.001</td>
</tr>
<tr>
<td>OS, adjusted for testing and treatment type*</td>
<td>Medicaid (ref: commercial)</td>
<td>1.12 (1.03–1.22)</td>
<td>.010</td>
</tr>
<tr>
<td>OS among Medicaid beneficiaries</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>OS</td>
<td>No testing (ref: received at least 1 test)</td>
<td>1.27 (1.06–1.52)</td>
<td>.010</td>
</tr>
<tr>
<td>OS, adjusted for any treatment</td>
<td>No testing (ref: received at least 1 test)</td>
<td>1.26 (1.05–1.52)</td>
<td>.013</td>
</tr>
<tr>
<td>OS, adjusted for treatment type*</td>
<td>No testing (ref: received at least 1 test)</td>
<td>1.23 (1.02–1.48)</td>
<td>.026</td>
</tr>
</tbody>
</table>

All models adjusted for gender, age at advanced diagnosis, race/ethnicity, region, smoking status, histology, year of advanced diagnosis, liver metastases, brain or central nervous system metastases, bone metastases.

Abbreviations: HR, hazard ratio; OS, overall survival.

*No treatment, biomarker-driven therapy, or chemotherapy.


Supplemental online content for:

**Associations Between Medicaid Insurance, Biomarker Testing, and Outcomes in Patients With Advanced NSCLC**

Cary P. Gross, MD; Craig S. Meyer, PhD, MPH; Sarika Ogale, PhD; Matthew Kent, MS; and William B. Wong, PharmD, MS

*J Natl Compr Canc Netw 2022;20(5):479–487.e2*

- **eFigure 1**: Testing Frequency per 1,000 Person-Days
- **eFigure 2**: Biomarker Testing Rates Over Time
- **eTable 1**: Patient Attrition
- **eTable 2**: Testing Rates by Histology
eFigure 1. Testing frequency per 1,000 person-days.

*P < .001.

eFigure 2. Biomarker testing rates over time.
**eTable 1. Patient Attrition**

<table>
<thead>
<tr>
<th>Step</th>
<th>n</th>
<th>Percentage of Previous Step</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients with a diagnosis of advanced NSCLC after 2011</td>
<td>57,637</td>
<td>—</td>
</tr>
<tr>
<td>Patients with any visit within 120 d of advanced diagnosis date</td>
<td>52,768</td>
<td>91.6</td>
</tr>
<tr>
<td>Patients aged 18–64 y (inclusive) at advanced diagnosis date</td>
<td>16,923</td>
<td>32.1</td>
</tr>
<tr>
<td>Patients without a clinical study drug in first-line treatment</td>
<td>16,514</td>
<td>97.6</td>
</tr>
<tr>
<td>Patients from a community practice</td>
<td>15,051</td>
<td>91.1</td>
</tr>
<tr>
<td>Patients with their last visit or administration after advanced diagnosis date</td>
<td>15,051</td>
<td>100</td>
</tr>
<tr>
<td>Patients with no biomarker testing before advanced diagnosis date</td>
<td>14,105</td>
<td>93.7</td>
</tr>
<tr>
<td>Patients with evidence of Medicaid or commercial insurance at advanced diagnosis date</td>
<td>7,843</td>
<td>55.6</td>
</tr>
<tr>
<td>Excluded patients who had their first biomarker test &gt;3 mo from advanced diagnosis date or were treated &gt;4 mo from advanced diagnosis date</td>
<td>7,010</td>
<td>89.4</td>
</tr>
</tbody>
</table>

Abbreviation: NSCLC, non–small cell lung cancer.

**eTable 2. Testing Rates by Histology**

<table>
<thead>
<tr>
<th>Biomarker</th>
<th>Commercial Health Plan</th>
<th>Medicaid</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Tests, n</td>
<td>Tests per 1,000 Person-Days</td>
</tr>
<tr>
<td>Nonsquamous</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ALK</td>
<td>3,322</td>
<td>7.22</td>
</tr>
<tr>
<td>BRAF</td>
<td>1,712</td>
<td>1.55</td>
</tr>
<tr>
<td>EGFR</td>
<td>3,450</td>
<td>8.87</td>
</tr>
<tr>
<td>PD-L1</td>
<td>1,813</td>
<td>1.67</td>
</tr>
<tr>
<td>ROS1</td>
<td>2,262</td>
<td>2.48</td>
</tr>
<tr>
<td>Squamous</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ALK</td>
<td>360</td>
<td>1.26</td>
</tr>
<tr>
<td>BRAF</td>
<td>247</td>
<td>0.77</td>
</tr>
<tr>
<td>EGFR</td>
<td>362</td>
<td>1.28</td>
</tr>
<tr>
<td>PD-L1</td>
<td>360</td>
<td>1.22</td>
</tr>
<tr>
<td>ROS1</td>
<td>282</td>
<td>0.90</td>
</tr>
</tbody>
</table>