Clinical harm from failure to deploy personalized medicine for patients with metastatic non–small cell lung cancer

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Plain language summary

Doctors recommend broad genomic testing for patients with advanced lung cancer to find the best-matched treatment. But in real life, many patients are not getting tested—and for those that do, many still do not receive matched treatment. These gaps can cut lives short. If all patients were tested, had usable results, and were treated with best-matched therapy, approximately 20,000 people per year in the United States could live longer.

Implications for managed care pharmacy

Most health plans cover multigene panel testing for metastatic non–small cell lung cancer consistent with the National Comprehensive Cancer Network guidelines. Care for patients can be personalized with appropriate testing; inadequate testing can result in harm, both from drug adverse effects and shortened survival. This study quantifies the population impact to inform and guide policy and decision-making. Review of biomarker testing results by managed care pharmacists before drug authorization could improve testing rates, drug appropriateness, and overall survival.

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ABSTRACT

BACKGROUND: Among the estimated 234,580 patients diagnosed with lung or bronchus cancer in 2024, an estimated 66%, or 154,823 patients, were diagnosed with advanced or metastatic non–small cell lung cancer (mNSCLC). More than half of patients have a genomic variant that can be treated with targeted therapy. Despite widespread evidence supporting the survival benefits of biomarker-driven management of patients with mNSCLC, real-world implementation of precision oncology has not kept pace with recommendations.

OBJECTIVE: To quantify the potential survival deficit from underutilization of precision oncology (genomic testing and matched therapy) for patients with newly diagnosed mNSCLC in the United States.

METHODS: We developed a simulation model comparing Observed Practice with Optimal Practice in which all eligible patients receive biomarker testing and appropriate treatment. We assessed a mix of 3 testing pathways assessed: (1) guideline-concordant biomarker testing consistent with National Comprehensive Cancer Network (NCCN) Guideline recommendations, (2) nonguideline biomarker testing, and (3) no biomarker testing. Input values and probabilities for each pathway were obtained from published data. Survival deficit was estimated as life-years lost in Observed Practice vs Optimal Practice.

RESULTS: Among the estimated 92,401 patients with new metastatic adenocarcinoma or large cell carcinoma histology, 49,427 patients were projected to have at least 1 of the 10 NCCN-recommended mutations with a known targeted first-line therapy. Among those harboring actionable mutations, 46,757 were assumed to be identified and treated with precision-matched targeted therapy (PMTT) in Optimal Practice vs 28,177 in Observed Practice. The 46,757 patients receiving PMTT in Optimal Practice realized a total of 113,417 life-years, a gain of 20,901 over the patients treated in Observed Practice.

CONCLUSIONS: Among patients with mNSCLC in the United States, suboptimal use of recommended panel testing and implementation of

ABSTRACT *continued*

precision medicine for newly diagnosed mNSCLC is associated with life-years lost. Investments in effective programs that improve adherence to NCCN guideline recommendations and test-concordant therapy would result in increased life expectancy for up to 20,000 patients annually.

Among the estimated 234,580 patients diagnosed with lung or bronchus cancer in 2024, an estimated 66%, or 154,823 patients, are diagnosed with advanced or metastatic non–small cell lung cancer (mNSCLC).[1] More than half of patients have a genomic variant that can be treated with targeted therapy.[2,3] Identifying these actionable mutations is important: multiple trials have demonstrated improved progression-free survival and overall survival (OS), along with favorable safety profiles for several targeted therapies compared with treatment with traditional chemotherapy in mNSCLC populations.[4–6] In contrast, patients eligible for targeted therapy who do not receive it have a survival deficit of 8-14 months.[2,6–10] As a result of advances in biomarker-guided treatment for mNSCLC there has been a significant improvement in long-term outcomes for these patients, nearly doubling the 3-year relative survival rate from 26% in 2004 to 43% in 2018.[11]

Several consensus panels support implementing a precision oncology approach that includes biomarker profiling and precision-matched targeted therapy (PMTT) as a critical component for the management of patients with mNSCLC.[12–15] For example, National Comprehensive Cancer Network (NCCN) Guidelines strongly recommend multigene panel testing (MGPT) of 19 biomarkers for NSCLC (10 impact first-line and subsequent treatment, and 9 impact second-line or subsequent treatments).[12]

Despite widespread evidence supporting the survival benefits of biomarker-driven management of patients with mNSCLC, real-world implementation of precision oncology has not kept pace with recommendations. Multiple studies report that a substantial proportion fail to receive appropriate testing or matched therapies.[5,6,16–20] For example, a recent analysis demonstrated that 94% of commercially available targeted panels (<50 genes) failed to capture all NCCN-recommend biomarkers.[21] Of all newly diagnosed patients with mNSCLC, nearly half fail to receive biomarker test results to inform their care.[5] Of the remaining patients who do receive results from a biomarker test, approximately 30% do not receive appropriate targeted treatments. Overall, 64.4% of potentially eligible patients with mNSCLC do not benefit from a precision oncology approach.[5] A recent US study further noted reduced biomarker testing in men; Hispanic, Latino, and Black/African American patients compared with White patients; smokers vs nonsmokers; and patients with Medicaid.[20] Racial disparities in patients with NSCLC who received multigene testing were further elucidated in a review that reported broad ranges of testing among Asian (3.8%-54%), Black (6.3%-65%), and White (6.8%-50.1%) patients and a smaller range for Hispanic patients, which trended toward fewer patients being tested (5.7%-14.4%).[22]

This study quantifies the potential survival deficit associated with underutilization of guideline-concordant testing and treatment in patients with newly diagnosed NSCLC. Accordingly, we conducted a pragmatic, targeted review and synthesis of practice-based evidence, encompassing studies that simulate the underutilization of comprehensive genomic tumor testing and PMTT among patients with mNSCLC and comparative outcomes between targeted and nontargeted treatments. This approach allowed us to evaluate the clinical consequences associated with suboptimal implementation of precision oncology in patients with mNSCLC in the United States.

Methods

PRACTICE COMPARISON FRAMEWORK

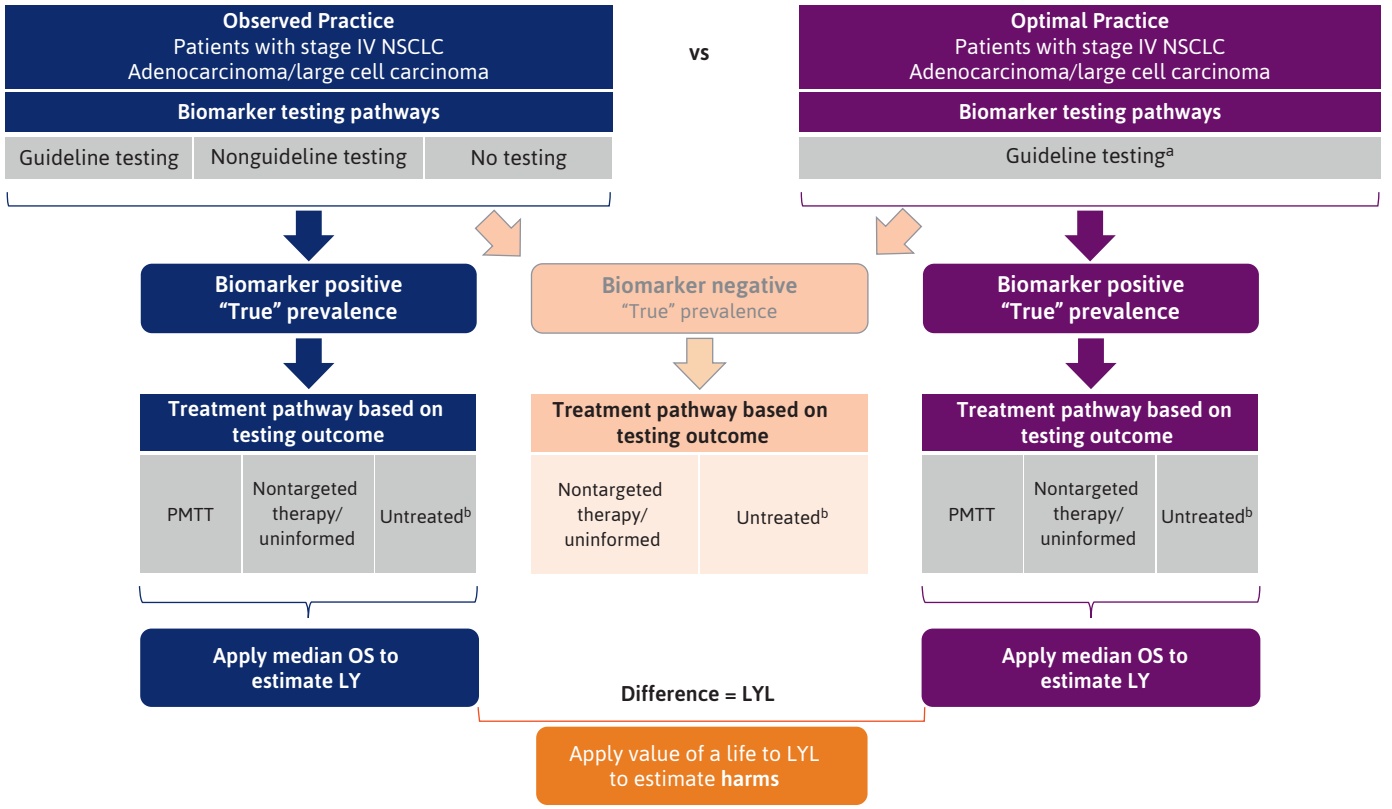
We developed an Excel-based simulation model framework to compare observed precision oncology practice ("Observed Practice") vs an optimal practice ("Optimal Practice") to test the impact of widespread implementation of guideline-concordant MGPT. Optimal Practice reflected a practice environment in which all eligible patients with mNSCLC receive guideline-concordant biomarker testing ("guideline testing"), corresponding to broad genomic profiling that includes the 10 driver mutations recommended by the NCCN Guidelines v3.2026 for first-line therapy selection and appropriate PMTT aligned with guideline recommendations[12] (Figure 1).

In Observed Practice there were 3 testing pathways: (1) optimal, guideline testing (as defined above); (2) suboptimal, guideline-discordant biomarker testing ("nonguideline testing"), defined as testing for fewer than 10 target driver mutations (eg, small-panel testing or single-gene testing); and (3) no biomarker testing ("no testing"). Survival deficit was estimated as the life-years lost with Observed Practice relative to Optimal Practice.

PRAGMATIC LITERATURE REVIEW

A pragmatic literature review was conducted to inform model inputs. Inputs for key clinical parameters included the number of patients with newly diagnosed mNSCLC,[1,22,23] biomarker testing rates (guideline testing, nonguideline testing, or no testing),[16] the underlying prevalence of at least 1

FIGURE 1 Policy Analysis Framework for Metastatic NSCLC



[a]*The assumption is that under optimal practice, 100% of this population would receive optimal testing; however, the framework allows for the inclusion of suboptimal and no testing (not displayed).*
[b]*It was assumed that 5.4% were not treated regardless of mutation status, assuming other factors affecting the decision (eg, mortality, hospice/palliative care, or decision to forego therapy). This estimate was derived from a published study.*[19]
LY = life-years; LYL = life-years lost; NSCLC = non–small cell lung cancer; OS = overall survival; PMTT = precision-matched targeted therapy.

actionable targeted biomarker (present/not present),[3] the probabilities of an actionable biomarker test outcome in each treatment pathway,[5,19] and OS associated with each treatment option (PMTT, nontargeted therapy, or no treatment)[2,6] (Table 1). Authors' consensus was used to select recent estimates that reflected current biomarker testing practices and most closely aligned with the target population of interest, biomarker testing pathways, and related survival outcomes. These input values are described in the sections below.

TARGET POPULATION

To calculate the number of patients with newly diagnosed mNSCLC who were eligible for genomic testing, we developed a patient funnel (Figure 2) starting with the incidence of lung and bronchus cancers in the United States (n = 234,580) obtained from Cancer Statistics from 2024.[1] We estimated the proportion of newly diagnosed lung and bronchus cancers that were nonsquamous NSCLC (57% overall: 56% adenocarcinoma and 1% large cell carcinoma) from the National Cancer Institute Surveillance, Epidemiology, and End Results (SEER) *Explorer, an interactive, web-based tool used to analyze cancer statistics from SEER. To this, the proportion of patients with advanced or metastatic disease (69.2% overall; 69% adenocarcinoma and 75% large cell carcinoma), defined as those identified with regional or distant metastases, was applied to calculate the target population for our model.[23,24]

Among the target population it was necessary to estimate the "true" prevalence of an actionable biomarker to calculate the impact of failing to employ guideline testing. Thus, the prevalence of patients with at least 1 actionable biomarker was assumed to be 53.5%[3] in both Observed and Optimal

TABLE 1 Population and Clinical Inputs

Input	Value	Source
Testing strategy use (Observed Practice), %		
Guideline testing, median (95% CI)	60.0 (45-75)	Wu et al, 2022[16]
Nonguideline testing, median (95% CI)	29.0 (14-44)	Wu et al, 2022[16]
No testing	11.0 (fixed at 11)	Wu et al, 2022[16]
Testing strategy use (Optimal Scenario), %		
Guideline testing	100 (alternate assumption 90)	Assumption
"True" prevalence of mutations, median (95% CI), %		
Positive mutation	53.5 (23-54)	Meng et al, 2024[3]; range from Aggarwal 2023,[2] Meng 2024,[3] and Scott 2024[6]
Negative mutation	46.5 (46-77)	Calculated[a]
Treatment pathway based on testing outcome (Observed Practice), %		
Mutation positive: guideline testing		
Precision-matched targeted therapy, median (95% CI)	70.8 (46-86)	Sadik et al, 2022[5]
Nontargeted therapy (uninformed), median (95% CI)	23.8 (4-49)	Calculated[a]
No treatment	5.4 (fixed at 5.4)	Tsimberidou et al, 2024[19]
Mutation positive: nonguideline testing, %		
Precision-matched targeted therapy, median (95% CI)	50.1 (25-75)	Sadik et al, 2022[5]
Nontargeted therapy (uninformed), median (95% CI)	44.5 (20-70)	Calculated[a]
No treatment	5.4 (fixed at 5.4)	Tsimberidou et al, 2024[19]
Mutation positive: no testing/mutation negative, %		
Nontargeted therapy (uninformed)	94.6	Calculated[a]
No treatment	5.4	Tsimberidou et al, 2024[19]
Treatment pathway based on testing outcome (Optimal Practice), %		
Mutation positive		
Precision-matched targeted therapy	94.6	Calculated[a]
Nontargeted therapy (uninformed)	0	Assumption
No treatment	5.4	Tsimberidou et al, 2024[19]
Mutation negative		
Nontargeted therapy (appropriate)	94.6	Calculated[a]
No treatment	5.4	Tsimberidou et al, 2024[19]

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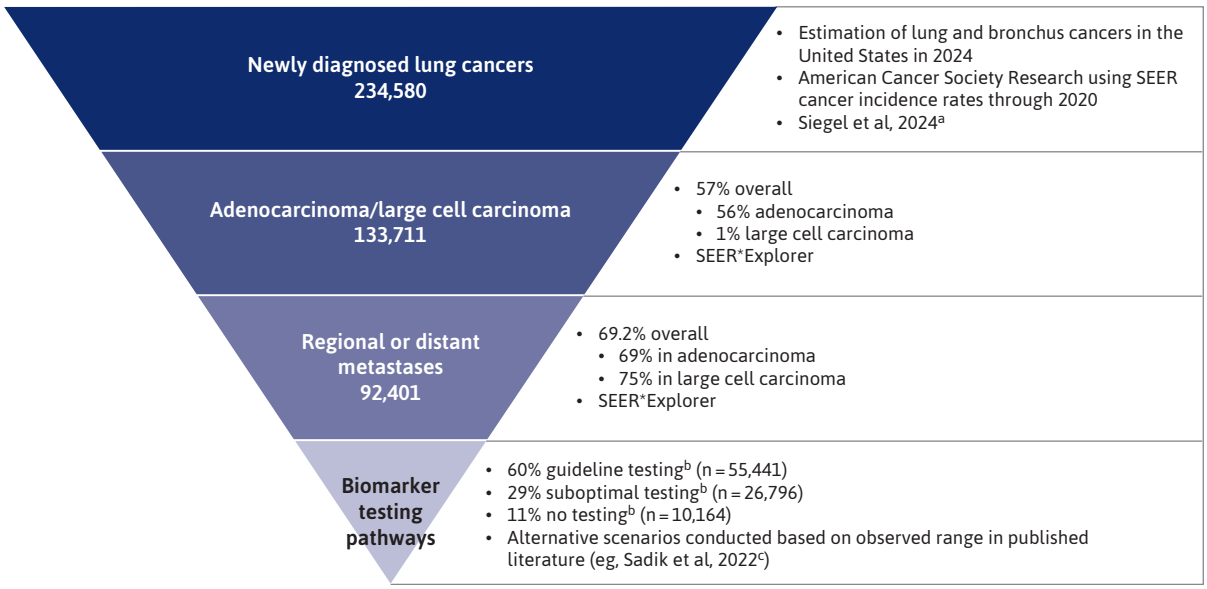
TABLE 1 Population and Clinical Inputs *(continued)*

Input	Value	Source
Overall survival, median (95% CI), months		
Precision-matched targeted therapy	28.8 (23.3-34.6)	Scott et al, 2024[6]
Nontargeted therapy (uninformed and appropriate)	15.3 (11.5-19.7)	Scott et al, 2024[6]
No treatment	5.4 (2.8-9.2)	Aggarwal et al, 2023[2]

[a]*Calculated as 100% minus the known/assumed percentage(s) in the remaining groups within each category (eg, 100%−% with positive mutation = % with negative mutation).*

FIGURE 2 Population Funnel



[a]*Siegel et al, 2024.*[1]
[b]*Wu et al, 2022.*[16]
[c]*Sadik et al, 2022.*[5]

Practice (Table 1). The impact of this assumption was tested in uncertainty analyses, as described below.

PRACTICE AND CLINICAL INPUTS TO ESTIMATE SURVIVAL GAINS

Implementation of guideline testing was defined as 100% in Optimal Practice, assuming that all newly diagnosed patients would receive testing to identify all relevant treatment options and thus inform decision-making. Uptake of guideline testing in Observed Practice was set to 60.0% based on findings from a real-world US study of trends in biomarker testing in patients with advanced NSCLC.[16] This study also informed the inputs for nonguideline testing and no testing.

Each treatment pathway corresponded to a likelihood of PMTT assignment, matched or uninformed nontargeted therapy ("nontargeted therapy"), and no treatment. These inputs were defined to be broadly representative of the uptake of guideline-concordant MGPT to inform policy and decision-making and not to be exact estimates of specific biomarker pathways. Consistent with this, input values were

derived from 2 recent publications assessing the impact of implementing clinical practice gaps in mNSCLC.[5,19] Input values were considered over a range of plausible estimates derived from the literature (Table 1).

OS for biomarker-positive patients receiving PMTT or nontargeted therapy was obtained from a published study of real-world outcomes in patients with advanced (stage IV) NSCLC.[6] Median OS for treatment assignments of PMTT (28.8 months, 95% CI = 23.3-34.6),[6] nontargeted therapy (15.3 months; 95% CI = 11.5-19.7),[6] and no treatment (5.4 months; 95% CI = 2.8-9.2)[2] within each practice scenario was used to estimate the incremental number of life-years lost among PMTT-eligible patients receiving nontargeted therapy. Estimates of OS were similar across published studies for PMTT (range = 24.6-30.0 months) and nontargeted therapy (15.3-19.5 months), further supporting selection of the inputs.[2,3,6–8] CIs reported within each source study were considered for sensitivity analysis (Table 1).[2,6]

To estimate the population impact of testing in Optimal Practice vs Observed Practice on survival, the median OS was applied to the corresponding number of patients in each testing scenario for each treatment assignment (PMTT, nontargeted therapy, and no treatment) as estimated in our analysis. OS in patients with mNSCLC is relatively short (median ≤30 months among those receiving targeted therapy and shorter for those who do not[2,3,6–8]), and this analysis is not modeling survival longitudinally, thus survival was not discounted.

MODEL ASSUMPTIONS

This analysis focused on the survival impact of expanding guideline-concordant comprehensive genomic profiling (CGP) testing in patients with mNSCLC and does not model specific therapeutic choices for first-line or subsequent therapy. Rather, the downstream impact of testing uses aggregate estimates of survival determined by genomic sequencing results and the category of resulting treatment assignment (ie, PMTT, nontargeted therapy, or no treatment). PD-L1 testing was excluded from the analysis, because the NCCN guidelines endorse MGPT independent of PD-L1 status. In Optimal Practice, all patients received guideline testing (100%). A proportion of patients (5.4%) were not treated regardless of mutation status, assuming other factors affecting the decision (eg, mortality, hospice/palliative care, or decision to forego therapy).[19]

UNCERTAINTY ANALYSES

Beyond the baseline estimates, the prevalence of patients with at least 1 actionable biomarker was considered over a range of values reported in the literature (23%-54%).[2,3,6] To account for uncertainty in the proportion of patients with known targets receiving matched therapy following guideline-concordant testing in observed practice, the estimate was varied from 46% to 86%.[19] Third, rates of guideline-concordant testing in observed practice were evaluated over a range of potential estimates (45%-75%) encompassing those reported in the literature.[5,6,16,17,25] Fourth, a sensitivity analysis was conducted setting the uptake of guideline testing in Optimal Practice to 90%, assuming some patients may refuse testing. Lastly, estimates of median OS for treatment assignments of PMTT and nontargeted therapy were varied independently over 95% CIs reported within the source study.[6] No sensitivity analysis was performed on the median OS for no treatment as the proportion of untreated patients was the same under the observed practice and optimal practice scenarios. Thus, applying different OS values would not change the life-years lost outcome from baseline.

Results

Among the estimated 92,401 patients with new metastatic adenocarcinoma or large cell carcinoma histology, 49,427 patients were projected to have at least 1 of the 10 NCCN-recommended genomic variants with a known targeted first-line therapy[12] (Figure 2). Among those harboring actionable alterations, we applied a published rate of 5.4% for patients who did not pursue active treatment,[19] leaving 46,757 assumed to be identified and treated with PMTT in the Optimal Scenario vs 28,177 in Observed Practice. The 46,757 patients receiving PMTT in Optimal Practice realized a total of 113,417 life-years, a gain of 20,901 more than the patients treated in Observed Practice (Table 2). In Observed Practice, based on a baseline rate of comprehensive biomarker testing rates of 60%, 28,177 patients with actionable mutations were treated with PMTT and 18,580 were treated with nontargeted therapy.

UNCERTAINTY ANALYSIS

Incremental LYG under Optimal Practice ranged from a low of 9,018 to a high of 20,901 when a range of actionable biomarker prevalence (23%-53%) was examined (Table 2 and Figure 3).

In analyses varying the rate (46%-86%) of patients with known actionable targets who receive PMTT, incremental life-years gained (LYG) under Optimal Practice vs Observed Practice was 15,897 and 29,242 at the low and high ends of the range of input values, respectively (Table 2 and Figure 3).

Over the range of pessimistic and optimistic targeted testing rates (45%-75%) in Observed Practice, the incremental increase in LYG with Optimal Practice was 19,174 and 22,628, respectively (Table 2 and Figure 3). When a lower rate

TABLE 2 Summary of Modeled Outcomes Among Biomarker-Prevalent Patients

Input/analysis	Observed Practice	Optimal Practice	Incremental harms (net Observed vs Optimal)
Base case			
Appropriately treated	28,177	46,757	No harms
Missed PMTT	21,250	2,670	18,580 missed
Total LY	92,516	113,417	20,902 LYL
Prevalence of actionable biomarker uncertainty			
Appropriately treated	12,158-28,177	20,175-46,757	No harms
Missed PMTT	9,169-21,250	1,152-2,670	8,017-18,580 missed
Total LY	39,920-92,516	48,938-113,417	9,018-20,901 LYL
PMTT following guideline-consistent testing uncertainty			
Appropriately treated	20,763-32,626	46,757	No harms
Missed PMTT	16,801-28,663	2,670	14,131-25,993 missed
Total LY	84,175-97,520	113,417	15,897-29,242 LYL
Targeted testing in current practice			
Appropriately treated	26,643-29,712	46,757	No harms
Missed PMTT	19,715-22,785	2,670	17,045-20,115 missed
Total LY	90,790-94,243	113,417	19,174-22,628 LYL
Overall survival (PMTT), median			
Appropriately treated	No impact	No impact	No impact
Missed PMTT	No impact	No impact	No impact
Total LY	79,601-106,135	91,987-136,016	12,386-29,882 LYL
Overall survival (nontargeted treatment), median			
Appropriately treated	No impact	No impact	No impact
Missed PMTT	No impact	No impact	No impact
Total LY	86,632-99,328	113,417	14,089-26,785 LYL

Values are presented as a range or n.
LY = life-years; LYL = life-years lost; PMTT = precision-matched targeted therapy.

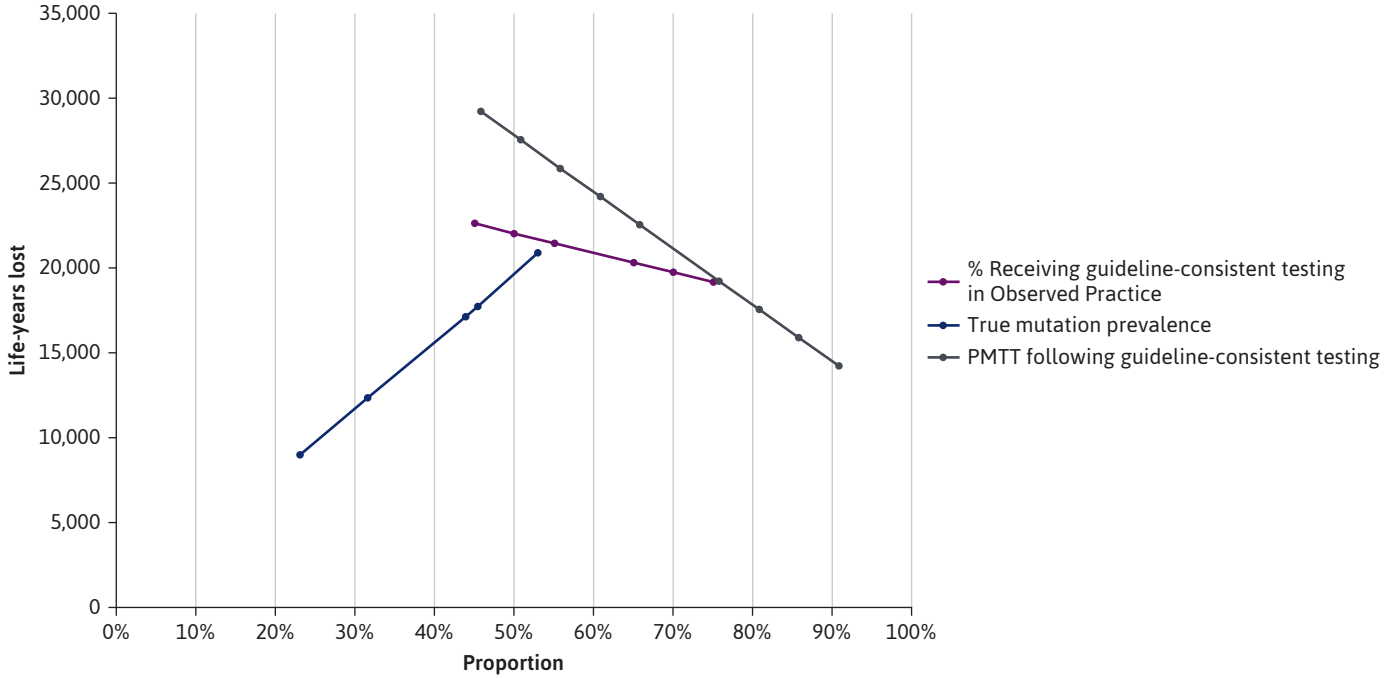
of targeted biomarker testing (90%) was considered in Optimal Practice, 15,642 additional LYG were estimated vs Observed Practice.

Variation in median OS associated with PMTT (23.3-34.6 months) resulted in incremental LYG with Optimal Practice ranging from 12,386 to 29,882. Median OS for nontargeted therapy (11.5-19.7 months) led to incremental LYG of 26,785 and 14,089, respectively, with Optimal Practice.

Discussion

We estimated the life-years lost from suboptimal delivery of precision oncology (suboptimal biomarker testing and/or use of PMTT) in observed practice for patients with advanced or metastatic lung cancer. Among the 49,427 patients with an actionable mutation, 21,250 did not receive PMTT in Observed Practice, resulting in a loss of 20,902 life-years that

FIGURE 3 Incremental Life-Years Lost Because of Lack of Testing and Associated Undertreatment Over Range of Uncertainty in Key Parameters[a]



[a]*The uncertainty parameters are those described in Tables 1 and 2.*
PMTT = precision-matched targeted therapy.

could be realized through Optimal Practice implementation of precision oncology.

Beyond the risk of premature mortality, administering nontargeted therapy to patients who are eligible for targeted treatment exposes them to significant avoidable morbidities and diminished quality of life. Estimates from real-world data suggest hospitalization rates for patients receiving immunotherapy are an absolute 10% higher than in patients receiving targeted therapy (12% vs 2%).[26] Patients optimally treated based on CGP results have fewer emergency department and outpatient visits.[27] Although beyond the scope of this article, the average cost of immunotherapy per patient with mNSCLC is approximately $30,000 over 3 cycles of therapy and upwards of $1.7 billion for a cohort of approximately 50,000 patients.[28] Thus, inappropriate immunotherapy from failure to employ a precision oncology approach results in survival deficits as well as financial waste. Although adequate testing alone does not ensure test-concordant therapy, comprehensive testing has been associated with lower costs than single-gene testing.[29–32]

Moreover, recent studies demonstrate a reduction in resource utilization and overall patient costs associated with implementation of Optimal Practice, including comprehensive genomic testing and appropriate PMTT.[27,33–35] Our findings take a broader view by quantifying the impact at a US population level in terms of the total number of patients undertreated and the resulting life-years lost because of suboptimal implementation of guideline-informed precision oncology in actual practice.

The failure to fully implement a precision medicine approach reflects a range of clinical practice gaps, including barriers in biomarker testing, data interpretation (eg, sample quality), treatment selection, and access to care (eg, practice setting, cost of testing, and reimbursement).[5,36,37] A recent study estimated that as many as half of patients with newly diagnosed mNSCLC do not get access to precision medicines because of factors associated with testing.[5] A separate retrospective study from a US community health system noted that of patients with advanced NSCLC who received biomarker testing, only 20% had comprehensive testing vs small-panel

testing, potentially owing to being in a community setting, yet more actionable mutations were identified through comprehensive testing, resulting in better patient outcomes. Moreover, disparities in testing and treatment associated with sex, race and ethnicity, smoking status, practice type, and insurance type further contribute to the gap in optimal treatment.[20,22,38]

Multiple strategies have been proposed to close these gaps, with the goal of ensuring that patients consistently receive the most effective precision therapies.[5,39,40] Strategic investment in programs to improve the use of comprehensive biomarker testing panels and PMTT holds significant potential to offset both program and testing costs by minimizing the use of ineffective therapies and reducing morbidity and mortality.[29,30] Quality measures that assess the magnitude of undertesting and the discordance between genomic testing results and prescribed therapies could demonstrate national progress toward reducing the number of patients receiving a suboptimal therapy. Adoption of a national quality metric focused on appropriate testing in NSCLC would not only quantify practice gaps reflecting suboptimal testing but also quantify progress toward reducing harms associated with no or inadequate testing.[16] The application of testing and treatment concordance metrics across all racial and ethnic groups would permit an assessment of the impact on reducing disparities in access to standard of care testing and treatment.

LIMITATIONS

This analysis is likely a conservative estimate of the true impact of inappropriate therapy that underestimates the harm implied. As previously noted, our estimate does not explicitly account for the immediate or downstream cost impact of discrepancies in diagnostic testing. This explicitly omits cost discrepancies associated with prescribed therapy, morbidity, and mortality. Further, our definition of non–guideline-driven testing likely oversimplifies the complex set of factors that can contribute to suboptimal implementation of precision medicine. These factors may include inappropriate treatment selection, test selection, errors in test handling, inconclusive results, timing and receipt of results, and the occurrence of false negative and positive findings, among others.

Second, a simplifying assumption in our analysis was the use of literature-based evidence that combined these 2 steps (test result and treatment decision) into a single input. Thus, the potential discrepancy between the results of biomarker testing and the receipt of subsequent treatments owing to any number of factors (eg, delayed reports) was not modeled explicitly and may overestimate the use of concordant therapy. Reliance on literature-based estimates from varying studies may also be perceived as a limitation of this approach. We note that the studies selecte to inform the treatment pathways based on testing outcome were separate reports from the same study.[5,19] Inputs for test use, prevalence, and survival were selected from studies that were conducted in populations consistent with our analysis (eg, patients with advanced NSCLC eligible for first-line treatment) and those that provided internally consistent estimates.

Third, the model does not account for potential false positives/negatives of biomarker testing. Well-validated comprehensive biomarker testing panels report precision, accuracy, and specificity greater than 99%.[41,42] Although intertest variability is well-known,[43,44] the impact of false positive/false negative tests on premature mortality is small compared with absent or inadequate testing.

Fourth, we applied a constant proportion of patients who go untreated across and within Observed and Optimal Practice. Although this may underestimate the absolute number of patients who forego treatment, the assumption was applied equally and is not expected to impact the incremental differences between Optimal and Observed Practice.

Finally, our Optimal Practice is presented as a reference for best case and unlikely to be achieved fully in practice. Observed Practice used the most recent and representative data specific to the population of patients with mNSCLC who are eligible for first-line therapy from the literature at the time of analysis and considered outcomes over a range of uptake assumptions. Because practices are changing rapidly these numbers might not reflect current practice, nor should they be generalized to other populations of patients with NSCLC or solid tumors.

This study shows that suboptimal implementation of precision medicine in mNSCLC leads to premature deaths. Consequently, there is potentially wasted health care spending on the use of suboptimal treatments for patients who would otherwise benefit from targeted therapy. To understand the economic value and downstream costs associated with PMTT requires formal cost analysis. A recent analysis found that the incremental cost-effectiveness of CGP vs small-panel testing was inversely related to the number of patients with advanced NSCLC receiving treatment.[45] The budget impact of comprehensive testing to a US payer has also been reported to be relatively small (ie, ≤$0.035 per member per month) in comparison with the clinical benefit of extended life expectancy.[46,47] Although improving testing rates would facilitate initiation of PMTT resulting in improved OS, other system changes are required to optimize PMTT. Policy changes, including adoption of national quality measures, would further help more patients get precision-targeted treatments and support changes in policy to make personalized cancer care the standard.

Conclusions

Among patients with mNSCLC in the United States, suboptimal use of recommended panel testing at diagnosis is associated with significant clinical harm associated with life-years lost. Investments in effective programs that improve adherence to NCCN guideline recommendations and promote test-concordant therapy could increase life expectancy for up to 20,000 patients annually.

DISCLOSURES

Ms Migliaccio-Walle, Dr Veenstra, and Dr Ramsey are employees of Curta Inc., which received research support for this project from Illumina. Dr Spencer was an employee at Illumina at the time of this research and is a shareholder of Illumina. Mr Dumanois is an employee and shareholder of Thermo Fisher Scientific. Thermo Fisher helped fund this research study. Dr White is an employee and shareholder of Eli Lilly and Company. Dr Langer is an employee and shareholder of United Healthcare. Dr Pritchard received research support from Illumina and Thermo Fisher Scientific to help fund this research. Dr Fox is an employee and shareholder of Illumina.

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