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Treatment adherence and clinical outcomes of osimertinib in minority patients with advanced EGFR mutated NSCLC

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Osimertinib has been one of the most commonly prescribed first-line treatments for EGFR-mutated advanced NSCLC for the last several years for patients with EGFR-mutated non-small cell lung cancer (NSCLC), yet clinical outcomes among racial and ethnic minority patients remain poorly characterized due to underrepresentation in pivotal trials. We conducted a retrospective study of 174 patients with advanced EGFR-mutated NSCLC treated at the Montefiore Einstein Comprehensive Cancer Center (MECCC) from 2015 to 2024 to evaluate real-world survival and treatment adherence. The cohort included 32.2% Hispanic, 28.7% non-Hispanic Black (NHB), 26.4% non-Hispanic White (NHW), and 12.6% Asian patients. In multivariable analyses, NHB patients experienced significantly worse overall survival compared with NHW patients, both in the overall cohort (Hazard ratio (HR) 1.83, 95% confidence interval (CI) 1.02–3.27) and in first-line osimertinib users (HR 3.42, 95% CI 1.48–7.88), despite similar adherence rates. Hispanic and Asian patients also showed trends toward inferior outcomes. These findings highlight survival disparities and underscore the need for inclusive trials and targeted strategies.

Lung cancer remains the leading cause of cancer-related deaths in the United States[1]. Approximately 15–20% of patients with NSCLC in the U.S. have tumors harboring actionable EGFR alterations[2]. Osimertinib, a third-generation EGFR tyrosine kinase inhibitor (TKI), is the most commonly used standard frontline therapy for EGFR-mutated advanced NSCLC and an adjuvant therapy after resection, based on improved survival demonstrated in pivotal trials such as FLAURA[3,4] and ADAURA[5]. However, those trials had limited participation of racial/ethnic minorities (only ~1–5% Black or Hispanic), raising concerns about the generalizability of their findings to underrepresented populations in real-world practice[3–5]. Moreover, recent randomized trials have expanded first-line options, with FLAURA2 demonstrating improved outcomes for osimertinib plus platinum–pemetrexed versus monotherapy, and MARIPOSA showing superiority of amivantamab–lazertinib versus osimertinib; we therefore focused this analysis specifically on osimertinib monotherapy to isolate outcomes for this widely used regimen.

Previous studies have suggested racial disparities in lung cancer outcomes, with Black patients often experiencing worse survival than White patients[6–8]. Additionally, the prevalence of EGFR mutations might differ by ancestry: most analyses report similar or lower EGFR mutation rates in

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African American patients compared to Whites, and similar or higher rates in Hispanic patients[9–25]. Notably, a prior study at our institution found that Black patients with EGFR-mutant NSCLC had inferior survival on first- or second-generation EGFR TKIs compared to White patients[13]. However, data on osimertinib access, adherence, and outcomes in racial/ethnic minority populations remain limited. Given that the Montefiore Einstein Comprehensive Cancer Center (MECCC) serves a predominantly underrepresented minority patient population (>30% Black and >35% Hispanic overall), we sought to evaluate treatment adherence and clinical outcomes of osimertinib in this diverse cohort, to determine whether racial/ethnic disparities observed in earlier generation therapies persist with osimertinib.

Results

Patient demographics and socioeconomic factors

A total of 174 *EGFR*-mutated advanced/metastatic patients with NSCLC treated with osimertinib met the inclusion criteria. Median age was 69 years, and 69.5% were female. The cohort was racially and ethnically diverse: 26.4% were non-Hispanic White (NHW), 28.7% non-Hispanic Black (NHB), 32.2% Hispanic, and 12.6% Asian. Overall, 55.7% were documented to be never smokers with a significantly higher proportion of never-smokers among Asian patients (81.8%) compared to other groups ($p < 0.001$). Baseline body weight and BMI differed by race: NHB and Hispanic patients had higher median weight/BMI than their NHW and Asian counterparts (e.g., median BMI 25.2 and 24.9 for NHB and Hispanic vs. 22.2 and 22.4 for NHW and Asian, $p = 0.011$ for BMI difference). There were no significant differences in age or sex distribution across the groups.

Several socioeconomic factors revealed significant differences across racial and ethnic groups. The majority of Hispanic (75.0%) and NHB (54.0%) patients lived in neighborhoods with a median annual household income of less than $50,000 USD, compared to 8.7% of NHW patients ($p < 0.001$ for income distribution). Insurance coverage also varied: 32% of NHB, 25% of Hispanic, and 31.8% of Asian patients were on Medicaid, versus only 8.7% of NHW patients ($p = 0.025$). Among 63 patients who obtained osimertinib through our institution's specialty pharmacy (enabling detailed cost data), the median total cost for osimertinib per patient per month was $16,734 USD. However, due to insurance and patient assistance programs, the mean out-of-pocket cost to patients was approximately $59.30 USD, with a median out-of-pocket cost of $0 USD for these patients. There were no significant differences in the cost of osimertinib or out-of-pocket expenses across racial and ethnic groups.

Clinical and tumor characteristics

Nearly all patients (96.6%) had adenocarcinoma histology. Regarding EGFR genotypes, 110 patients' tumors (63.2%) had an exon 19 deletion and 45 (25.9%) had an exon 21 L858R point mutation. The remaining 10.9% (19 patients) harbored uncommon EGFR mutations. Baseline disease burden and performance status (PS) were similar among groups: at osimertinib initiation, 74.1% of all patients had Eastern Cooperative Oncology Group (ECOG) PS 0–1, and 25.9% had ECOG PS ≥ 2, with no significant difference in PS distribution by race/ethnicity ($p = 0.573$). Brain metastases were present in 39.7% of patients overall at the start of osimertinib (not significantly different between groups, $p = 0.157$).

Treatment adherence to osimertinib was generally high across the cohort. Among the 76 patients with available pharmacy refill data, 81.6% achieved proportion of days covered (PDC) > 80% and were considered adherent. Adherence rates were 83.3% among NHW patients, 74.1% among NHB patients, 82.8% among Hispanic patients, and 100% among Asian patients. Although these differences were not statistically significant ($p = 0.412$), the approximately 10% lower adherence observed among NHB patients may warrant further investigation. Overall, no definitive racial disparities in medication adherence were identified.

Osimertinib was used as first-line therapy in 111 patients (63.8%), while 63 patients (36.2%) received it as second-line or later. Prior therapies in those who received osimertinib beyond first line included platinum-based chemotherapy in 17.5% and a first- or second-generation EGFR TKI (erlotinib, gefitinib, or afatinib) in 28.2% of patients. The distribution of prior treatments did not differ notably by race/ethnicity (Table 1).

Clinical outcomes

At a median follow-up time of 34.3 months, the median real-world overall survival (rwOS) for the entire cohort was 32.7 months. When stratified by race/ethnicity, median rwOS was shortest in NHB patients at 21.9 months, compared to 40.2 months in NHW, 35.3 months in Hispanic, and 32.7 months in Asian patients (Table 2). Although the log-rank test for overall survival by race/ethnicity did not reach significance ($p = 0.27$), Cox proportional hazards analysis revealed a significant association between NHB race and mortality. In univariable analysis (Fig. 1A), compared to NHW, NHB patients had significantly worse rwOS (Hazard ratio (HR): 1.76, 95% CI: 1.00–3.08; $p = 0.049$), while Hispanic and Asian patients did not show a significant difference in rwOS. In the multivariable model adjusting for sex, BMI, ECOG PS, EGFR mutation type, and line of therapy (Fig. 1B), NHB race remained independently associated with worse rwOS (HR 1.83, 95% confidence interval (CI) 1.02–3.27; $p = 0.042$), while Hispanic and Asian patients remained non-significant. Notably, median household income (as a binary ≥$50,000 vs. < $50,000) was not significantly associated with rwOS ($p = 0.378$), nor was insurance type ($p = 0.391$ for Medicaid vs. others), suggesting that while insurance and income were not independently associated with survival in our models, they may act as mediators rather than confounders and could still contribute to the observed disparities. The Kaplan–Meier plots of rwOS for the entire cohort and by racial and ethnic groups are shown in Figs. 2 and 3. Among other covariates, in multivariable analysis, ECOG PS was strongly predictive of rwOS (ECOG ≥ 2 vs. ECOG 0-1: HR: 3.97, 95% CI: 2.4–6.54; $p < 0.001$). Underweight with low BMI (<18.5) was also associated with significantly worse rwOS (HR 2.30, 95% CI 1.26–4.19; $p = 0.007$).

The median real-world progression-free survival (rwPFS) for the overall cohort was 16.3 months. There were no statistically significant differences in rwPFS or time to treatment discontinuation (TTD) across racial/ethnic groups. However, NHB patients had numerically shorter, but not statistically significant, rwPFS (NHW: 17.3 months; NHB: 15.6 months; Hispanic: 16.1 months; Asian: 17.1 months) and TTD (NHW: 20.5 months; NHB: 19.7 months; Hispanic: 19.6 months; Asian: 23.5 months). In univariable and multivariable analysis, none of the racial/ethnic variables were significantly associated with PFS (Table 2 and Supplementary Tables 1 and 2). These findings suggest that while minority patients had numerically shorter PFS, the study may have been underpowered to detect modest differences. The Kaplan–Meier curves for rwPFS by group are available in Supplementary Figs. 1 and 2. ECOG PS ≥ 2 (multivariable HR of 2.43, 95% CI 1.64–3.60; $p < 0.001$) was the only clinical factor significantly associated with poorer rwPFS.

In subgroup analysis of the 111 patients who received osimertinib as first-line therapy, racial disparities in rwOS outcomes persisted: NHB patients ($n = 31$) had significantly worse rwOS compared to NHW ($n = 28$) in both univariable (HR: 2.16, 95% CI: 1.00–4.65; $p = 0.049$; Fig. 1C) and multivariable analyses (HR: 3.42, 95% CI: 1.48–7.88; $p = 0.004$; Fig. 1D). In multivariable analyses, Hispanic patients also showed a trend toward worse rwOS (HR: 2.19, 95% CI: 0.90–5.35; $p = 0.085$), while outcomes for Asian patients were more comparable to NHW (HR: 1.60, 95% CI: 0.54–4.77; $p = 0.396$). Analyses of rwPFS among first-line osimertinib users did not differ significantly in either univariable (Supplementary Table 3) or multivariable analyses (Supplementary Table 4).

Of 128 patients with disease progression on osimertinib, 51 received a subsequent line of therapy (Supplementary Table 5A). Among these 51 patients, the median rwPFS2 was 4.7 months (Supplementary Table 5B). Median rwPFS2 did not differ significantly among racial and ethnic groups ($p = 0.483$). There was also no significant difference in the proportion of patients receiving next-line therapy ($p = 0.416$), with 38.9% of NHW, 32.4% of NHB, 50% of Hispanic, and 33.3% of Asian patients receiving next-line treatment.

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Table 1 | Demographics and clinical characteristics within each racial/ethnic group of advanced patients with NSCLC treated with osimertinib

		All patients (*n* = 174)	Non-Hispanic Whites (*n* = 46, 26.4%)	Non-Hispanic Blacks (*n* = 50, 28.7%)	Hispanics (*n* = 56, 32.2%)	Asian (*n* = 22, 12.6%)	*P* value
Age at start of osimertinib (years, median, range)		69 (30–92)	72.50 (46–89)	67.5 (30–88)	69 (32–90)	67 (42–92)	0.483
Gender, *n* (%)	Male	53 (30.5)	11 (23.9)	13 (26.0)	20 (35.7)	9 (40.9)	0.353
	Female	121 (69.5)	35 (76.1)	37 (74.0)	36 (64.3)	13 (59.1)	
Smoking, *n* (%)	Smoker (former or active)	77 (44.3)	31 (67.4)	22 (44.0)	20 (35.7)	4 (18.2)	0.001
	Never smoker	97 (55.7)	15 (32.6)	28 (56.0)	36 (64.3)	18 (81.8)	
Weight (kg, median, range)		63.8 (34–128)	58.3 (34–115)	69.5 (39.6–128)	63.6 (37.9–97.0)	58.4 (37.9–85.7)	0.002
BMI (kg/m^2, median, range)		23.9 (12.4–45.6)	22.2 (12.4–37.4)	25.2 (14.2–45.6)	24.9 (15.8–38.0)	22.4 (16.1–33.5)	0.011
	< 18.5	21 (12.1)	8 (17.4)	6 (12.0)	3 (5.4)	4 (18.2)	0.105
	18.5–25	81 (46.6)	26 (56.5)	18 (36.0)	27 (48.2)	10 (45.5)	
	>25	72 (41.4)	12 (26.1)	26 (52.0)	26 (46.4)	8 (36.4)	
Insurance (%)	Commercial	38 (21.8)	13 (28.3)	14 (28.0)	6 (10.7)	5 (22.7)	0.025
	Medicare	95 (54.6)	29 (63.0)	20 (40.0)	36 (64.3)	10 (45.5)	
	Medicaid	35 (20.1)	4 (8.7)	12 (24.0)	12 (21.4)	7 (31.8)	
	Medicare and Medicaid	6 (3.4)	0 (0.0)	4 (8.0)	2 (3.6)	0 (0.0)	
Household income (USD) by Zip Code (median, range)		56,279 (23,337–243,514)	88,795 (37,886–243,514)	47,831 (23,337–97,919)	37,886 (23,337–215,797)	56,410 (35,813–114,698)	<0.001
	<$50,000	82 (47.1)	4 (8.7)	27 (54.0)	42 (75.0)	9 (40.9)	<0.001
	≥$50,000	92 (52.9)	42 (91.3)	23 (46.0)	14 (25.0)	13 (59.1)	
Actual out-of-pocket cost[a] (USD, mean)		59.3	78.3	2.6	116.1	6.0	0.756
	Not available (%)	111 (63.8)	38 (82.6)	26 (52.0)	30 (53.6)	17 (77.3)	
Total cost[a] (USD, median)		16,734	16,734	16,734	16,734	16,734	0.804
	Not available (%)	111 (63.8)	38 (82.6)	26 (52.0)	30 (53.6)	17 (77.3)	
Adherent to osimertinib (PDC ≥ 80%)	Yes	62 (35.6)	10 (21.7)	20 (40.0)	24 (42.9)	8 (36.4)	0.412
	No	14 (8.0)	2 (4.3)	7 (14.0)	5 (8.9)	0 (0.0)	
	Not available	98 (56.3)	34 (73.9)	23 (46.0)	27 (48.2)	14 (63.6)	
ECOG at start of osimertinib, *n* (%)	<2	129 (74.1)	36 (78.3)	36 (72.0)	43 (76.8)	14 (63.6)	0.573
	≥2	45 (25.9)	10 (21.7)	14 (28.0)	13 (23.2)	8 (36.4)	
Brain metastasis, *n* (%)	Yes	69 (39.7)	14 (30.4)	19 (38.0)	23 (41.1)	13 (59.1)	0.157
	No	105 (60.3)	32 (69.6)	31 (62.0)	33 (58.9)	9 (40.9)	
Histology, *n* (%)	Adenocarcinoma	168 (96.6)	46 (100.0)	48 (96.0)	54 (96.4)	20 (90.9)	0.284
	Squamous	6 (3.4)	0 (0.0)	2 (4.0)	2 (3.6)	2 (9.1)	
TRAEs present, *n* (%)	Yes	100 (57.5)	26 (56.5)	26 (52.0)	36 (64.3)	12 (54.5)	0.621
	No	74 (42.5)	20 (43.5)	24 (48.0)	20 (35.7)	10 (45.5)	

Table 1 (continued) | Demographics and clinical characteristics within each racial/ethnic group of advanced patients with NSCLC treated with osimertinib

		All patients (n = 174)	Non-Hispanic Whites (n = 46, 26.4%)	Non-Hispanic Blacks (n = 50, 28.7%)	Hispanics (n = 56, 32.2%)	Asian (n = 22, 12.6%)	P value
Initial EGFR mutation at diagnosis	del19	110 (63.2)	26 (56.5)	34 (68.0)	39 (69.6)	11 (50.0)	0.272
	L858R	45 (25.9)	12 (26.1)	10 (20.0)	14 (25.0)	9 (40.9)	
	Uncommon[b]	19 (10.9)	8 (17.4)	6 (12.0)	3 (5.4)	2 (9.1)	
Prior EGFR TKI (other than osimertinib)	Yes	49 (28.2)	16 (34.8)	11 (22.0)	17 (30.4)	5 (22.7)	0.496
	No	125 (71.8)	30 (65.2)	39 (78.0)	39 (69.6)	17 (77.3)	
Prior chemotherapy	Yes	31 (17.8)	9 (19.6)	6 (12.0)	12 (21.4)	4 (18.2)	0.625
	No	143 (82.2)	37 (80.4)	44 (88.0)	44 (78.6)	18 (81.8)	
Lines of therapy with osimertinib	First line	111 (63.8)	25 (54.3)	38 (76.0)	33 (58.9)	15 (68.2)	0.124
	Second line or beyond	63 (36.2)	21 (45.7)	12 (24.0)	23 (41.1)	7 (31.8)	

PDC Proportion of Days Covered, *USD* United States Dollar, *ECOG* Eastern Cooperative Oncology Group, *TRAE* Treatment-Related Adverse Effect, *TKI* Tyrosine-Kinase Inhibitor.
[a]Costs are per 30-day supply.
[b]Uncommon EGFR mutations include G719X, L861Q, S768I, and exon 20 insertions, alone or in compound mutations.

In the sensitivity analysis using a multivariable model that included all variables except osimertinib adherence, we observed similar results. NHB patients continued to show numerically worse OS (HR 1.74, 95 percent CI 0.92–3.32; $p = 0.090$). Hispanic (HR 1.26, 95 percent CI 0.62–2.59; $p = 0.524$) and Asian patients (HR 1.27, 95 percent CI 0.53–3.03; $p = 0.597$) also demonstrated patterns consistent with the original multivariable model, although these associations were not statistically significant (Supplementary Fig. 3).

Osimertinib-related adverse events (AEs) were generally low-grade, with 58% of patients experiencing rash and 42% reporting diarrhea. There were no significant differences in AE incidence or severity by race (e.g., grade≥3: $p = 0.380$), suggesting similar tolerability across racial/ethnic groups.

Discussion

Despite osimertinib being one of the standard first-line therapies for EGFR-mutated NSCLC, racial and ethnic minority patients, particularly NHB and Hispanic individuals, remain underrepresented in key clinical trials[3,4]. In the present study involving a racially and ethnically diverse U.S. cohort, NHB patients had significantly shorter rwOS, including among those receiving first-line osimertinib for advanced disease (21.9 months), compared to NHW (40.2 months) and the benchmark from the FLAURA trial (38.6 months)[13]. Hispanic and Asian patients did not exhibit significantly shorter rwOS. The rwPFS did not significantly differ by race, which may be attributable to limited statistical power due to sample size constraints. Alternatively, the pattern of similar PFS but divergent OS may indicate that differences in long-term outcomes are potentially influenced by post-progression factors, such as comorbidities or other unmeasured variables. Baseline ECOG PS and stage at initiation did not differ by race, suggesting diagnostic delay may not fully explain the disparity.

Previous studies have not consistently identified such disparities with osimertinib, likely due in part to limited minority representation and/or differing study settings. For instance, Sabari et al.[26] found no OS difference between Black and White patients in a large U.S. dataset (adjusted HR ~ 1.08, $p = 0.57$); however, minority patients comprised a relatively small proportion of the cohort, which may limit power to detect subgroup differences. Similarly, Cardona et al.[27] found no significant racial/ethnic differences among Hispanic patients, and Li et al.[28] reported no race-associated genomic predictors of therapeutic response. In contrast, our study is based on a population where approximately two-thirds of patients identify as Black or Hispanic (substantially higher than the <15% minority representation in prior studies), potentially offering greater power to detect disparities driven by healthcare inequities. Notably, the rwOS among our NHW patients (~40 months) aligns with FLAURA trial outcomes, whereas the significantly poorer rwOS observed in NHB patients underscores an urgent need for further investigation and targeted interventions.

Our subgroup analyses indicated that socioeconomic factors known to influence cancer outcomes may also affect osimertinib use[29]. Despite its high cost[30,31], few studies have explored the impact of cost, insurance status, or income in NSCLC, though prior research suggests private insurance may improve survival in other cancers[32,33]. In our cohort, insurance type, household income, and neighborhood socioeconomic status were not significantly associated with rwOS or rwPFS. Broad access to osimertinib, regardless of race, likely minimized financial barriers and supported treatment access and continuation.

We also assessed treatment adherence, a well-known determinant of outcomes in oral cancer therapies[34–37]. Prior studies involving earlier-generation EGFR TKIs have linked lower adherence to high costs and socioeconomic disadvantage, disproportionately affecting Black patients[38–42], In our cohort, overall adherence to osimertinib was high across all groups (~82% with PDC > 80%). While adherence among NHB patients was modestly lower (74%) compared to other groups (~86%), this difference did not reach statistical significance. Still, the 12% gap may warrant further study to assess its role in outcome disparities.

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Table 2 | Overall survival (OS), progression-free survival (PFS) and time to discontinuations (TTD) of advanced patients with NSCLC receiving osimertinib

		N (%)	OS (median, 95% CI)	*P* value	PFS (median, 95% CI)	*P* value	TTD (median, 95% CI)	*P* value
Overall cohort		174 (100)	32.7 (28.5–41.6)		16.3 (15.0–19.7)		20.2 (16.2–24.3)	
Age	<65	65 (37.4)	31.4 (24.1–44.5)	0.724	16.0 (13.8–21.7)	0.618	19.7 (15.7– 29.6)	0.812
	≥65	109 (62.6)	35.9 (26.6–49.7)		17.3 (14.1–24.1)		20.3 (15.8–25.2)	
Gender	Male	53 (30.5)	31.4 (26.4–NA)	0.802	17.3 (14.1–27.4)	0.782	20.3 (15.7–29.6)	0.790
	Female	121 (69.5)	35.3 (25.0–44.5)		16.0 (13.8–20.2)		19.7 (15.7–24.3)	
Race/ethnicity	Non-Hispanic White	46 (26.4)	40.2 (32.6–NA)	0.268	17.3 (15.7–26.4)	0.863	20.5 (16.2–58.0)	0.268
	Non-Hispanic Black	50 (28.7)	21.9 (14.6–NA)		15.6 (13.2–21.4)		19.7 (14.6–26.6)	
	Hispanic	56 (32.2)	35.3 (26.3–NA)		16.1 (10.9–24.2)		19.6 (11.5–25.2)	
	Asian	22 (12.6)	32.7 (21.2–NA)		17.1 (10.2–32.7)		23.5 (13.9–NA)	
Smoking	Smoker (Former or active)	77 (44.3)	35.9 (28.6–NA)	0.318	17.3 (15.0–27.4)	0.378	24.2 (16.2–37.5)	0.245
	Non-smoker	97 (55.7)	29.6 (25.0–44.9)		16.3 (12.1–19.7)		17.3 (14.5–23.5)	
BMI (kg/m^2)	Underweight (BMI < 18.5)	21(12.1)	17.4 (13.2–NA)	0.015	15.0 (7.8–18.2)	0.006	15.2 (10.6–NA)	0.057
	Normal weight(BMI 18.5 – 25)	81(46.6)	41.6 (32.6–60.1)		21.1 (15.8–28.7)		25.2 (17.3–37.5)	
	Overweight/obese (BMI > 25)	72 (41.4)	31.4 (24.2–NA)		15.7 (11.9–20.2)		17.1 (15.4–21.9)	
Insurance	Commercial	38 (21.8)	32.6 (21.9–NA)	0.644	15.0 (9.3–28.7)	0.767	16.0 (14.5–34.8)	0.145
	Medicare	95 (54.6)	40.2 (28.5–55.7)		17.3 (15.0–21.4)		20.8 (17.2–26.4)	
	Medicaid	35 (20.1)	29.6 (17.7–NA)		16.0 (8.4–27.8)		16.5 (13.5–NA)	
	Medicare and Medicaid	6 (3.4)	NA		NA		6.7 (3.5–NA)	
Household Income by zip code	<50,000	82 (47.1)	29.3 (24.2–47.0)	0.375	17.1 (12.9–21.4)	0.564	17.1 (13.5–24.2)	0.049
	≥50,000	92 (52.9)	37.5 (28.6–55.7)		16.3 (15.0–21.7)		21.4 (16.5–37.5)	
ECOG PS	<2	129 (74.1)	40.2 (32.7–59.7)	< 0.001	19.1 (16.3–26.4)	<0.001	21.9 (19.7–27.7)	<0.001
	≥2	45 (25.9)	14.6 (10.0–NA)		8.3 (6.6–16.1)		11.5 (7.5–17.2)	
Brain metastases	Yes	69 (39.7)	29.3 (24.1–55.7)	0.649	15.6 (12.9–21.1)	0.252	19.6 (14.5–26.1)	0.554
	No	105 (60.3)	35.3 (28.5–49.7)		17.2 (14.6–25.6)		20.8 (16.6–26.6)	
EGFR mutations	Del 19	110(63.2)	37.5 (28.6–55.7)	0.368	17.2 (13.8–26.4)	0.082	24.3(16.0–34.3)	0.025
	L858R	45 (25.9)	31.4(25.0–NA)		16.3 (15.0–20.5)		17.3(15.7–24.2)	
	Uncommon	19 (10.9)	24.1(10.3–NA)		13.8(5.8–NA)		14.1(5.67–NA)	
Adherence	PDC ≥ 80%	14(8.0)	37.5 (29.6–NA)	0.356	21.1(18.5–35.0)	0.569	26.4 (19.7–NA)	0.739
	PDC < 80%	62(35.6)	31.4(17.7–NA)		16.8(12.9–NA)		24.3(14.2–NA)	
Histology	Adenocarcinoma	168(96.6)	32.7 (26.6–41.6)	0.802	16.3 (14.6–19.7)	0.729	19.6(15.8–24.2)	0.733
	Squamous cell carcinoma	6(3.4)	59.7 (21.3–NA)		18.9 (14.6–NA)		24.3(20.8–NA)	
Line of therapy with osimertinib	First line	111 (63.8)	32.7 (26.4–66.0)	0.511	19.7 (17.1–26.6)	0.001	21.9 (17.2–29.6)	0.025
	Second line or beyond	63 (36.2)	35.0 (21.9–47.0)		13.1 (9.4–16.0)		15.2 (13.7–25.2)	

OS Overall survival, *CI* Confidence interval, *PFS* Progression-free survival, *TTD* Time-to-discontinuation, *BMI* Body-mass index, *ECOG* Eastern Cooperative Oncology Group, *PS* Performance status, *NA* Not available due to insufficient sample size or because the value was not reached, *PDC* Proportion of days covered.

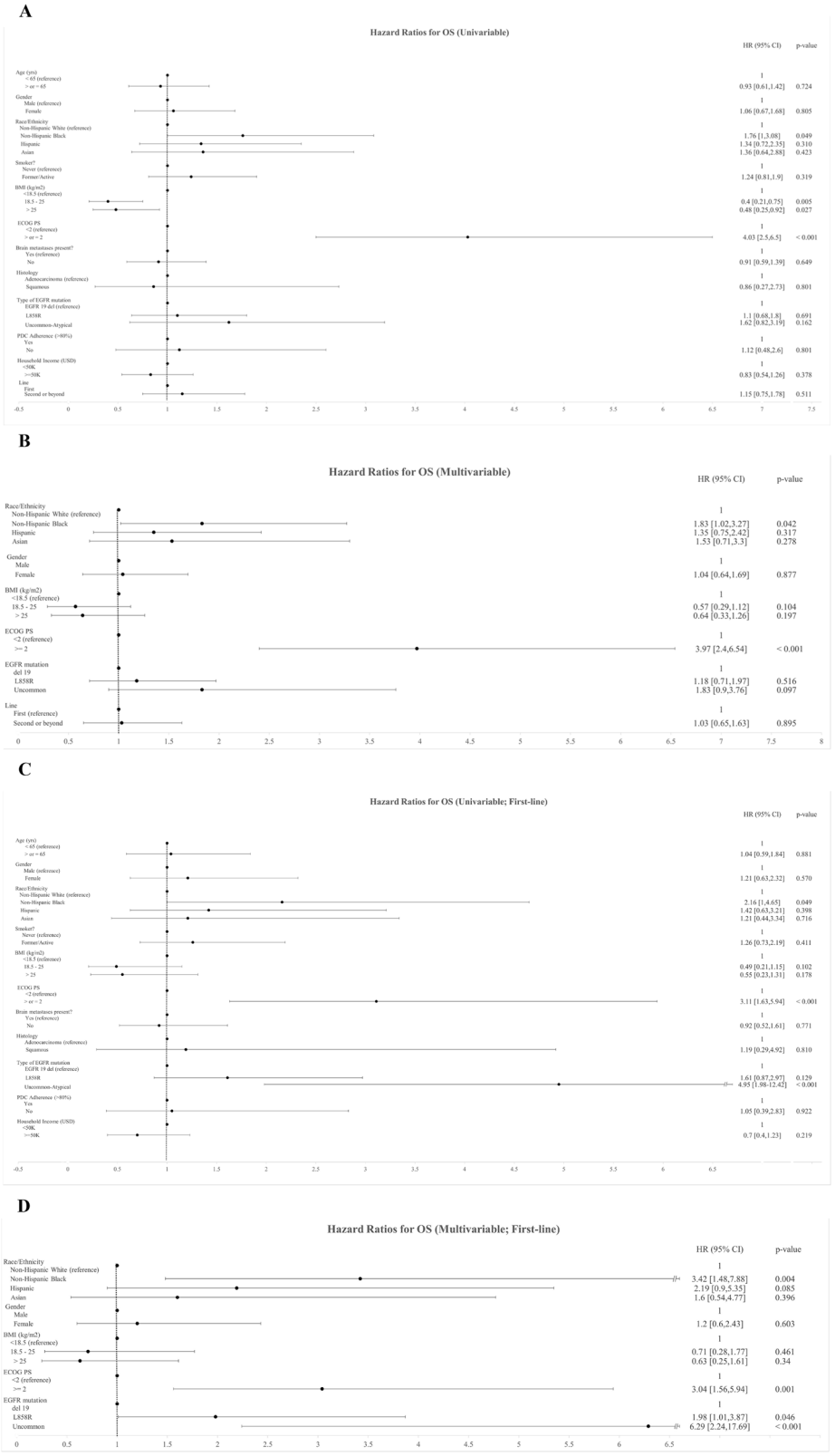

Fig. 1 | Cox Proportional Hazards Analysis of Overall Survival. A Univariable Cox model results for risk of death among patients with metastatic NSCLC on osimertinib (**B**) Multivariable Cox model results (adjusted for multiple covariates simultaneously) (**C**) Univariable Cox model results for risk of death among patients with metastatic NSCLC on first-line osimertinib (**D**) Multivariable Cox model results (adjusted for multiple covariates simultaneously) in patients receiving first-line osimertinib therapy.

Several additional factors may contribute to the observed survival disparities beyond access, cost, and adherence. Biological differences, particularly in pharmacogenomics, may play a role. Osimertinib is metabolized by CYP3A4/5, and Black patients are more likely to carry CYP3A5 and other polymorphisms associated with increased drug clearance, potentially leading to subtherapeutic exposure[43–49]. Similar findings have been reported with other TKIs, including EGFR TKIs, such as erlotinib, raising concerns about suboptimal dosing in Black patients[50–52]. Moreover, NHB and Hispanic patients in our cohort had higher average body weight/BMI, raising concerns about underdosing with osimertinib's fixed-dose regimen.

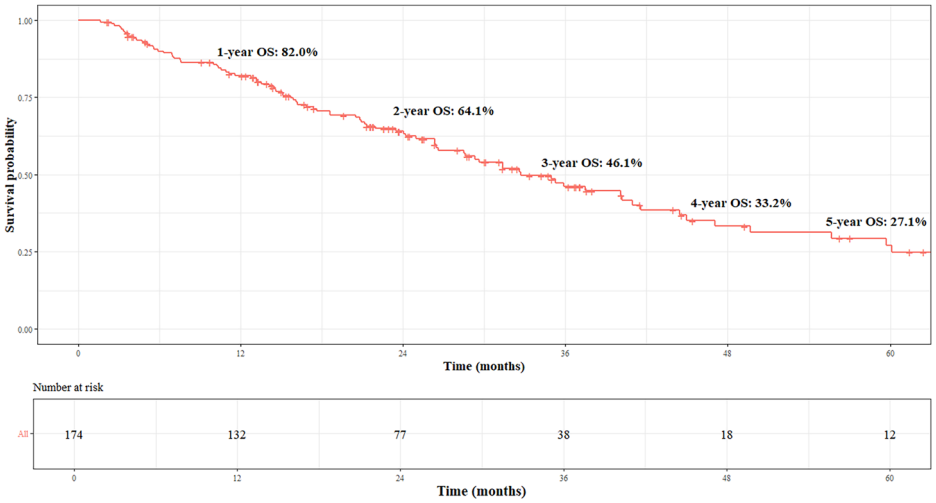

Fig. 2 | Kaplan-Meier estimates of real-world overall survival for the entire cohort.

Pharmacokinetic modeling suggests both weight and ethnicity may affect drug levels, and CYP3A variants have been linked to blood concentrations and outcomes[44].

Tumor genomic differences, such as a higher prevalence of co-mutations like TP53, though not fully captured in our dataset, could further explain differential outcomes. Additional factors, including unmeasured comorbidities, poorer PS, subtle differences in care delivery, or lower rates of second-line therapy, may also contribute. Taken together, these findings suggest that the survival gap likely reflects a multifactorial interplay of pharmacological, biological, and healthcare system influences.

Our study has several limitations. As a retrospective analysis, findings may not be generalizable, and selection bias is possible, particularly given our institution's high proportion of minority and lower socioeconomic status patients. The modest sample size, especially in subgroups, may limit statistical power and increase variability. Socioeconomic status was estimated using neighborhood income and insurance type, which may not fully capture individual or community-level factors, allowing for residual confounding. Adherence and pharmacy cost data were limited to patients using our specialty pharmacy, leading to high missingness that correlated with race/ethnicity. This limitation introduces potential bias and requires cautious interpretation of adherence-related analyses. Some clinical data, such as ctDNA and co-mutation profiles (including TP53), were incomplete, limiting our ability to assess genomic contributors to disparities. Lastly, although follow-up was mature (median 34 months), long-term outcomes for patients on newer therapies may be underrepresented.

Despite these limitations, our study offers novel insights into real-world outcomes with osimertinib in a racially diverse cohort. To our knowledge, it is the first to quantify a significant survival disadvantage for Black patients with EGFR-mutated NSCLC on this therapy. The findings highlight the urgent need for more inclusive clinical trials and targeted efforts to close outcome gaps. Minority patients must be proactively included in research to ensure equitable benefit from emerging cancer therapies.

In conclusion, our real-world analysis shows that racial disparities seen with older EGFR TKIs persist in the osimertinib era, with Non-Hispanic Black patients experiencing significantly worse survival despite similar access, cost, and adherence. This suggests underlying biological or systemic factors. Addressing these disparities requires inclusive research, personalized dosing strategies, and deeper investigation into pharmacogenomics and other risk modifiers. Future studies should explore combination therapies, such as osimertinib with chemotherapy or novel agents, for high-risk subgroups. We have initiated a prospective real-world study on osimertinib and are participating in the ECOG-ACRIN prE1702 trial to better understand outcomes in diverse populations. These efforts reflect growing recognition that equitable precision oncology depends on diverse trial representation and integration of genomic and pharmacologic insights.

Methods

Patient selection and data collection

We conducted a retrospective review of the MECCC cancer registry, identifying 6,019 patients diagnosed with lung cancer (ICD-10 C34.0–C34.9) between January 1, 2015, and December 31, 2024. From these, we included patients who met the following inclusion criteria: (1) histologically or cytologically confirmed advanced or metastatic unresectable NSCLC; (2) age 18 years or older; (3) presence of an EGFR actionable mutation (confirmed by PCR or next-generation sequencing on tumor tissue or plasma); (4) at least two clinical visits at MECCC; and (5) receipt of osimertinib therapy. Patients receiving osimertinib in combination with chemotherapy were excluded from this analysis. EGFR mutations were categorized as common (Exon 19 deletions, L858R) or other (e.g., Exon 20 insertions, S768I, L861Q, G719X).

Baseline patient data were extracted from electronic medical records (EMR), including age, gender, smoking status, weight, body mass index (BMI) at osimertinib initiation, insurance status, median annual income (based on the ZIP code from the patient's EMR address and U.S. Census Bureau data[53]), and tumor histology as reported in the pathology report. Additional clinical factors at osimertinib initiation included Eastern Cooperative Oncology Group (ECOG) PS, presence of brain metastases, line of therapy (first vs. later line) for osimertinib, EGFR mutation subtype, and any prior systemic treatment before osimertinib initiation. A flowchart summarizing the study cohort is presented in Fig. 4.

This study was reviewed and approved by the MECCC institutional review board (IRB Protocol 2022-13806: Assessing clinical outcomes and defining treatment barriers in EGFR-mutated NSCLC patients receiving osimertinib). The current manuscript reports only the retrospective cohort component of this approved protocol. For this retrospective chart review, the requirement for obtaining individual informed consent was formally waived because the study used existing data collected as part of routine clinical care and posed no more than minimal risk to participants.

Pharmacy and adherence data

We collected pharmacy records for osimertinib prescriptions, including fill dates, quantity dispensed, total drug cost, and out-of-pocket cost to patients. Medication adherence was assessed using the PDC method, endorsed by the Pharmacy Quality Alliance as a standard for medication adherence measurement. PDC was calculated as the number of days the patient had osimertinib on hand, divided by the number of days in the observation period (from the first fill to the last fill). We included only

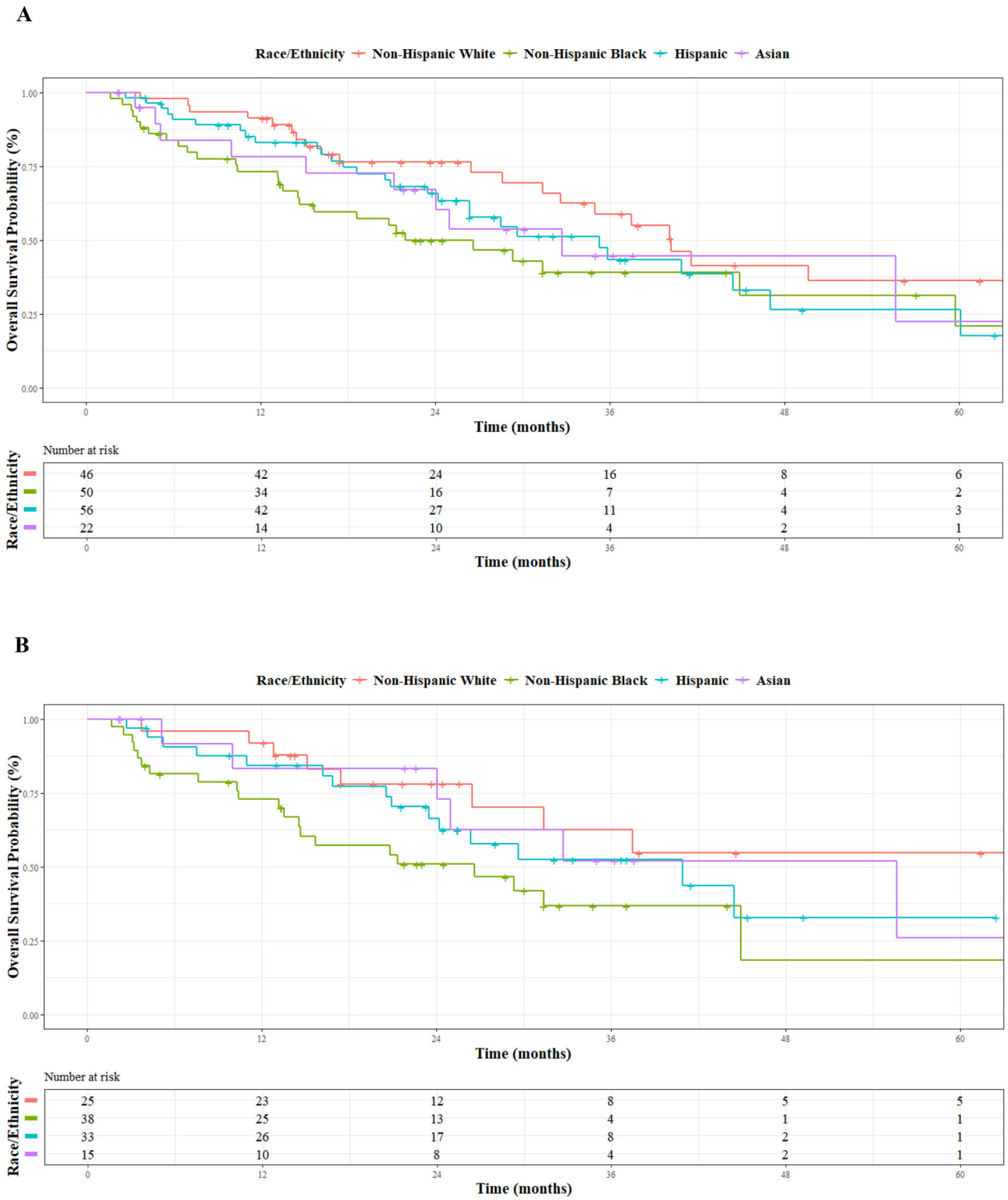

Fig. 3 | Kaplan-Meier estimates of real-world overall survival by race & ethnicity. **A** Total cohort. **B** First-line osimertinib cohort.

patients with at least two fills to accurately calculate PDC. If patients refilled early, resulting in an overlap of medication supply, the excess days were carried over (ensuring PDC did not exceed 100%). Consistent with prior research and the Utilization Review Accreditation Commission guidelines, we defined patients as adherent if PDC > 80%[38,54–56]. We also recorded each patient's total osimertinib drug cost and their out-of-pocket cost after insurance, per our institution's specialty pharmacy records.

Clinical outcomes

rwOS was defined as the time from the date of osimertinib initiation, with death events ascertained via our institutional EMR linked to regional hospital data and obituary/nursing facility records to the date of death from any cause or last contact. rwPFS was defined as the time from osimertinib initiation to disease progression (as determined by clinical assessment and radiographic reports in EMR), or death, whichever occurred first. This was calculated in accordance with the methods used

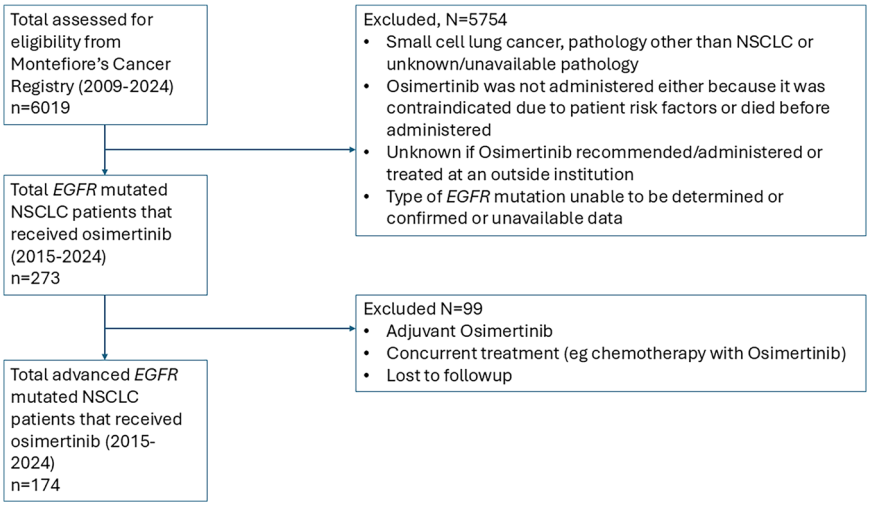

Fig. 4 | Patient selection flowchart: Schematic of cohort selection for patients with advanced NSCLC treated with osimertinib at MECCC.

in prior retrospective studies[31,32]. Treatment duration was measured as time to discontinuation (TTD), defined as the number of days between the first and last dates of osimertinib administration. Additionally, data on osimertinib-related AEs were collected from EMR and categorized by system and grade when available (using CTCAE v5.0 terminology when documented).

Statistical analysis

Demographic and clinical characteristics were compared between racial and ethnic groups using the Wilcoxon rank-sum test or Kruskal–Wallis test for continuous variables, and the chi-squared test or Fisher's exact test for categorical variables. Survival analyses were conducted using Kaplan–Meier curves with log-rank tests for rwOS and rwPFS. Cox proportional hazards models were used to assess differences in rwOS, rwPFS, and TTD. HRs and 95% CIs were calculated. rwOS and rwPFS were evaluated using both univariable and multivariable models, with adjustments for clinically relevant covariates, including gender, race/ethnicity, BMI, ECOG PS, EGFR mutation type, and line of therapy. We also conducted a sensitivity analysis using the full multivariable model to assess the robustness of our findings. Additionally, the real-world progression-free survival for the next line of therapy after osimertinib (rwPFS2), as well as the subsequent treatment type, were determined and analyzed. All statistical analyses were performed using R version 4.4.0, with a significance level set at $p < 0.05$ using two-sided tests.

Data availability

Due to patient privacy and institutional ethical regulations, the datasets from this study are not publicly available but can be requested from the corresponding author upon a reasonable request. The underlying code for this study is not publicly available but may be made available to qualified researchers on reasonable request from the corresponding author.

Code availability

The underlying code for this study is not publicly available but may be made available to qualified researchers on reasonable request from the corresponding author.

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Author contributions

Conceptualization: M.L., B.H., and H.C. Methodology: M.L., J.S., B.H., and H.C. Software: J.S., S.T., and H.C. Validation: M.L., B.H., and H.C. Formal analysis: J.S. and S.T. Investigation: M.L., J.S., E.M., D.S.A., and H.C. Data curation: M.L., J.S., E.M., and D.S.A. Writing—Original draft: M.L., J.S., and H.C. Writing—Review and editing: M.L., J.S., E.M., D.S.A., C.Z., X.X., J.Y., A.D., R.G., B.S., N.O., B.H., and H.C. Visualization: M.L. and J.S. Supervision: B.H. and H.C. Project administration: H.C. Funding acquisition: J.Y., B.S., and H.C.

Competing interests

H. Cheng and J. Yang received research support from AstraZeneca. The other authors declare no financial or non-financial competing interests.

Additional information

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