Comprehensive genomic profiling provides patients access to novel matched therapies in a diverse real-world cohort of advanced lung cancer patients

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INTRODUCTION

- Patients with advanced NSCLC experience improved outcomes when administered therapies targeting specific variants compared to chemotherapy.
- ESMO and NCCN treatment guidelines have recommended comprehensive genomic profiling (CGP) to identify patients eligible for matched targeted treatment.
- Here, we assess adherence with guideline-recommended targeted therapy recommendations and assess the time from genomic sequencing to the initiation of targeted medication in a diverse, real-world dataset of advanced NSCLC patients.

METHODS

- We retrospectively analyzed de-identified metastatic NSCLC records from the Tempus multimodal database, which encompasses molecular and clinical data from diverse clinics across the United States sequenced with the Tempus xT assay from 2018 - 2022.
- The following guideline recommended actionable genomic variants were assessed: *EGFR* mutations, *ALK* fusions, ALK, RET, *ROS1*, and *NTRK 1/2/3* fusions, *KRAS* G12C mutations, *BRAF* V600E, and *MET* exon 14 skipping mutations. Genomic sequencing may have occurred prior to matched therapy recommendation.
- Patients were defined as adherent if they harbored a targetable variant and received a targeted therapy once the matched therapy was included in guidelines.
- Patients were defined as non-adherent if they harbored a targetable variant and did not receive a targeted therapy once it was included in guidelines.

Figure 1. CONSORT diagram

SUMMARY

- In a real-world, retrospective analysis of a cohort of advanced NSCLC patients, most oncologists utilized CGP to identify and treat patients with guideline-recommended variant-matched targeted therapy, with adherence rates varying by variant.
- Importantly, even patients that received CGP results prior to NCCN inclusion of novel therapies, received matched therapy once they were included in guidelines.

RESULTS

Table 1. Cohort Demographics

Characteristic	Overall, N = 1407	Adherent Patients N = 201	Non-adherent patients N = 32	p-value
Age at Sequencing				
Median (IQR)	67.0 (60.0, 74.5)	68.0 (58.0, 76.0)	71.0 (63.0, 78.3)	0.13
Gender, N(%)				
Female	668 (47.0%)	124 (62.0%)	16 (50.0%)	1.0
Male	739 (53.0%)	77 (38.0%)	16 (50.0%)	
Race				
Asian	30 (2.0%)	15 (7.0%)	NA	1.0
Black	145 (10.0%)	20 (10.0%)	1 (2.2%)	
Other	56 (4.0%)	7 (3.0%)	2 (6.0%)	
White	940 (67.0%)	120 (60.0%)	22 (69.0%)	
Unknown	236 (17.0%)	39 (19.0%)	7 (22.0%)	
Smoking Status				
Non-smoker	182 (13.0%)	76 (38.0%)	6 (19.0%)	0.96
Smoker	1161 (83.0%)	118 (59.0%)	24 (75.0%)	
Unknown	64 (5.0%)	7 (3.0%)	2 (6.0%)	
Histology				
Adenocarcinoma	824 (59.0%)	162 (81.0%)	26 (81.0%)	1.0
Carcinoma	32 (2.0%)	1 (0.005%)	2 (6.0%)	
Non-small cell carcinoma	49 (3.0%)	4 (2.0%)	1 (3.0%)	
Squamous cell carcinoma	183 (13.0%)	8 (4.0%)	1 (3.0%)	
Unknown	174 (12.0%)	16 (8.0%)	1 (3.0%)	
Other	145 (10.0%)	10 (5.0%)	1 (3.0%)	
Diagnosis to Sequencing				0.86
Median days (IQR)	27.0 (18.0, 47.0)	26.0 (17.0, 42.0)	24.5 (18.8, 42.3)	
Sequencing to Medication Start				0.71
Median days (IQR)	24.0 (12.0, 85.0)	23.0 (12.0, 104.0)	33.0 (11.5, 116.8)	
Sequencing Date to Last Known Date				0.36
Median days (IQR)	323.0 (203.0, 501.0)	375.0 (247.0, 537.0)	295.0 (168.75, 593.3)	

Table 2. Adherence Rate by Mutational Status

Variant n,(%)		Therapy n,(%)		
		Targeted	Non-targeted	Total
	Targetable Variant	86.3% (n = 201)	13.7% (n = 32)	233
	No Targetable Variant	4.9% (n = 57)	95.1% (n =1117)	1174
	Total	258	1149	

Figure 2. Adherence to Targeted Therapy by Variant
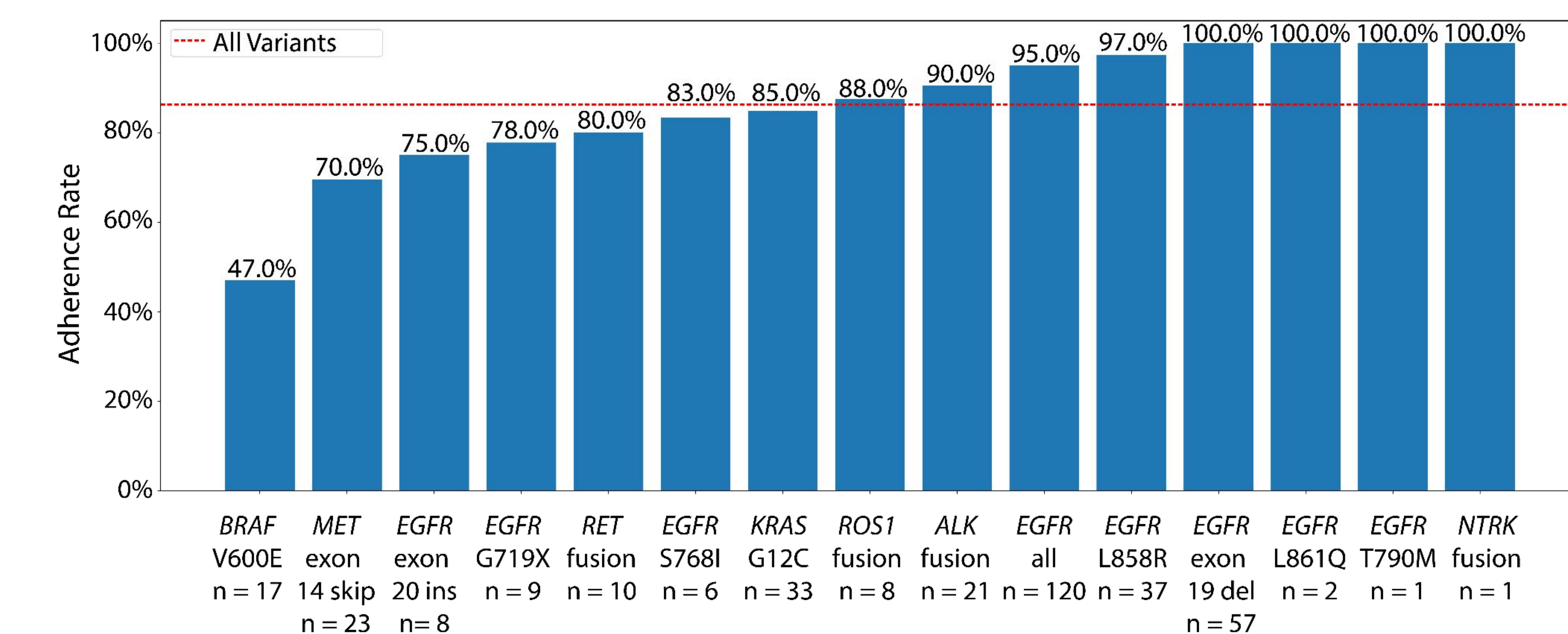
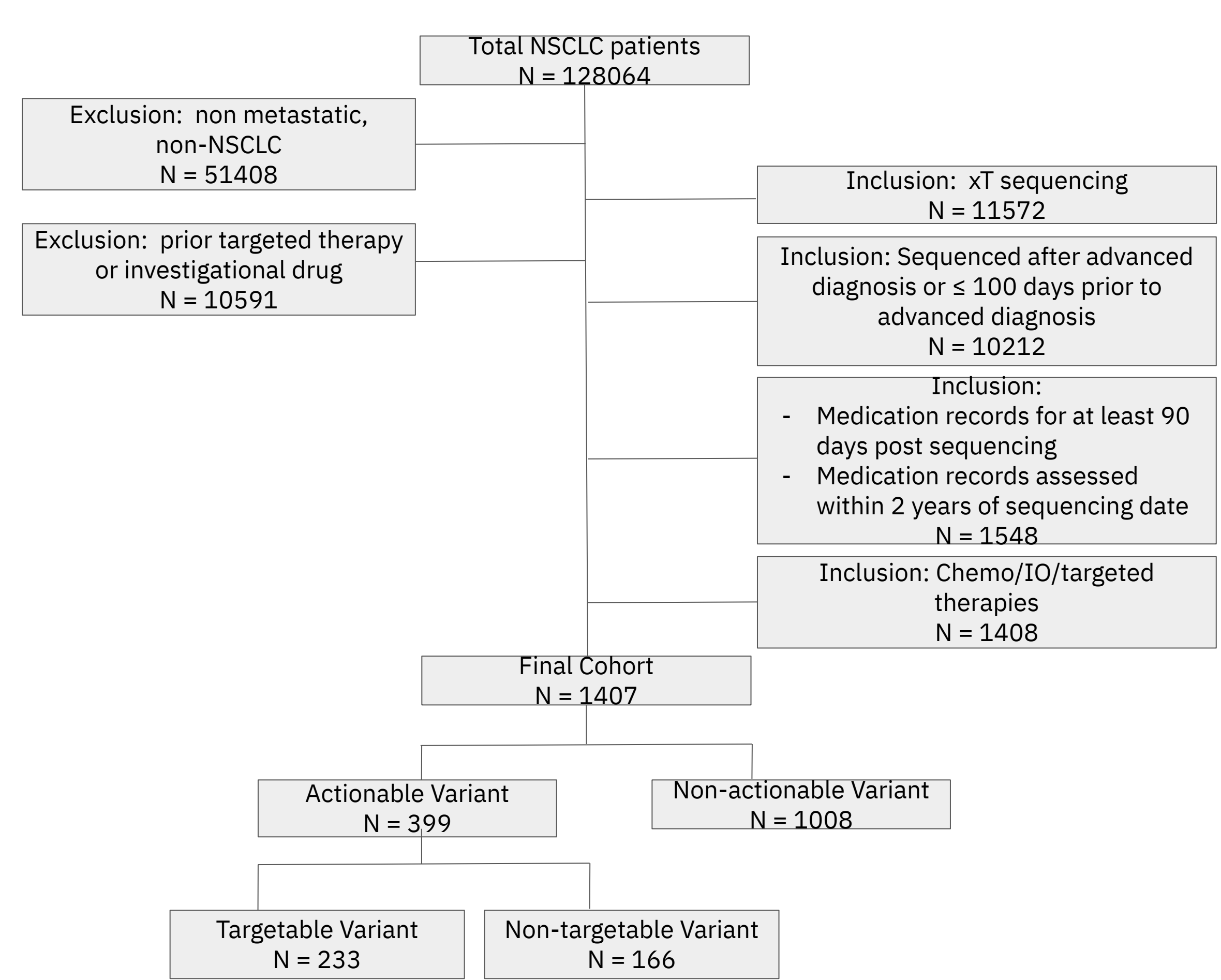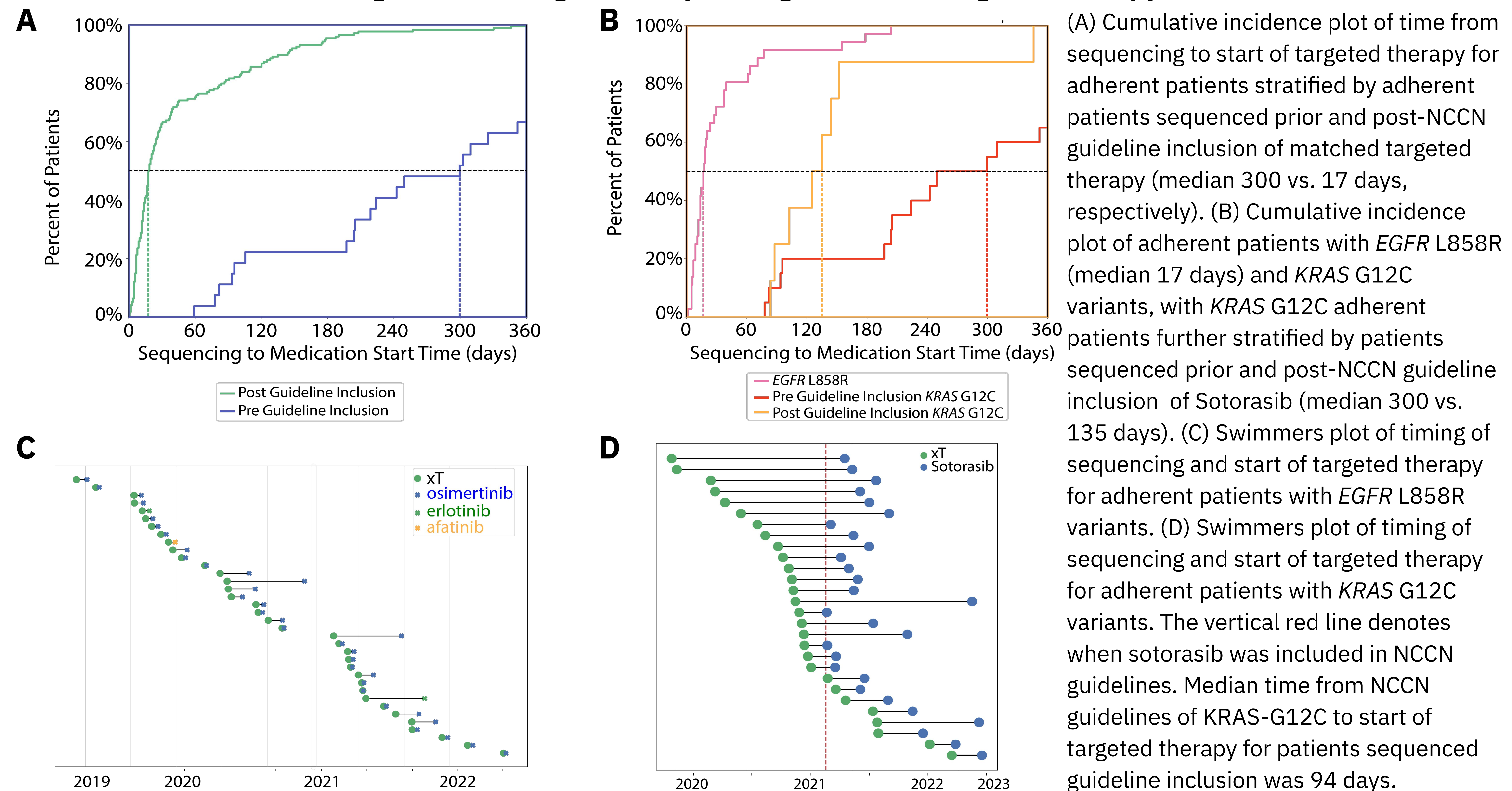### Figure 3. Timing from Sequencing to Start of Targeted Therapy

(A) Cumulative incidence plot of time from sequencing to start of targeted therapy for adherent patients stratified by adherent patients sequenced prior and post-NCCN guideline inclusion of matched targeted therapy (median 300 vs. 17 days, respectively). (B) Cumulative incidence plot of adherent patients with *EGFR* L858R (median 17 days) and *KRAS* G12C variants, with *KRAS* G12C adherent patients further stratified by patients sequenced prior and post-NCCN guideline inclusion of Sotorasib (median 300 vs. 135 days). (C) Swimmers plot of timing of sequencing and start of targeted therapy for adherent patients with *EGFR* L858R variants. (D) Swimmers plot of timing of sequencing and start of targeted therapy for adherent patients with *KRAS* G12C variants. The vertical red line denotes when sotorasib was included in NCCN guidelines. Median time from NCCN guidelines of KRAS-G12C to start of targeted therapy for patients sequenced guideline inclusion was 94 days.