Analytical Approaches to Estimate Medication Persistence From Electronic Health Record Data: A Study of Tyrosine Kinase Inhibitors in Patients With Epidermal Growth Factor Receptor–Positive Advanced Non–Small Cell Lung Cancer

MSR157

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Background

- Medication persistence is the duration a patient remains on treatment without discontinuation or a permissible interruption, and it is a key metric for assessing real-world effectiveness and tolerability of treatments. Despite the growing use of electronic health record (EHR) data in real-world evidence generation, standardized methods for estimating medication persistence using EHR data alone remain limited
- The objective of this study was to compare two commonly used approaches for estimating medication persistence in the biotech industry: time-to-event (TTE) and non-time-to-event (non-TTE) analyses. The performance of these approaches was compared by estimating medication persistence among patients with advanced non-small cell lung cancer (advNSCLC) who had epidermal growth factor receptor (*EGFR*) mutations and were treated with EGFR-tyrosine kinase inhibitors (TKIs)

Methods

- **Data source:** The Flatiron Health Research Database[1]
- **Setting:** The study included 4851 patients diagnosed with advNSCLC between January 2011 and October 2024, who had a positive *EGFR* result within 60 days prior to or 30 days after initiating the earliest line of therapy (LOT) containing EGFR-TKIs (including erlotinib, gefitinib, dacomitinib, afatinib, osimertinib, and lazertinib)

Table 1. Frameworks for Estimating Persistence: TTE and Non-TTE Approaches

	TTE	Non-TTE
Outcome Measures at 6, 12, and 18 Months	Time to first qualifying discontinuation event including the initiation of subsequent therapy, death, or structured activity record followed by a treatment-free period of more than 60 days	Proportion of patients who remain on TKI at different months, among those who remained under follow-up
Time 0	Initiation of first EGFR-TKI	Initiation of first EGFR-TKI
Censoring	Patients were censored at their last confirmed activity or the data cutoff date	No censoring was applied in the analysis Last confirmed activity date was used to determine if the patient was still under follow-up

Patients were diagnosed with stage IIIB, IIIC, IVA, or IVB NSCLC on or after January 1, 2011, or were diagnosed with early-stage NSCLC and subsequently developed recurrent or progressive disease on or after January 1, 2011

Reference

1. Flatiron Health. Database Characterization Guide. Flatiron.com. Published March 18, 2025. Accessed April 14, 2025. https://flatiron.com/database-characterization

Disclosures: This study was sponsored by Flatiron Health, Inc.—an independent member of the Roche Group. During the study period, XL, BJ, BK, NW, PW, and AP reported employment with Flatiron Health, Inc. and stock ownership in Roche. Data first presented at ISPOR 2025 in Montreal, QC, Canada on May 16, 2025.
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Results

Table 2. Patient Characteristics

Characteristics	N = 4851
Age at the first TKI initiation	
Median (IQR), years	69 (61-77)
Gender, n (%)	
Female	3257 (67.0)
Male	1593 (33.0)
Unknown/missing	1 (<0.1)
Race, n (%)	
White	2778 (57.0)
Black or African American	349 (7.2)
Asian	655 (14.0)
A race not listed above	415 (8.6)
Unknown/missing	654 (13.0)
Ethnicity, n (%)	
Hispanic or Latinx	269 (5.5)
Not Hispanic or Latinx	3559 (73.0)
Unknown/missing	1023 (21.0)
Practice type, n (%)	
Academic	1220 (25.0)
Community	3505 (72.0)
Both	126 (2.6)
Follow-up time	
Median (IQR), months	17 (6-31)

Abbreviations: IQR, interquartile range.

Figure 1. Persistence at Different Timepoints

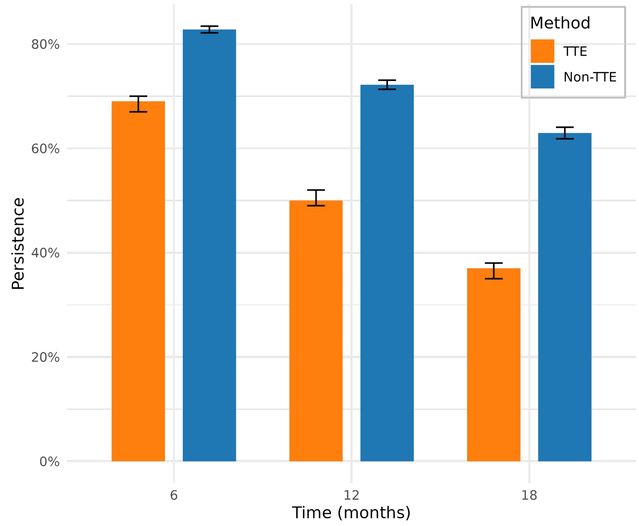

Table 3. Proportion of Patients Who "Persisted" on Treatment at 6, 12, and 18 Months After Initiation Using TTE vs non-TTE Approaches

	Persistence estimates, % (95% CI)		
	6 months	12 months	18 months
TTE	69 (67-70)	50 (49-52)	37 (35-38)
Non-TTE	83 (82-83)	72 (71-73)	63 (62-64)

Conclusions and Main Findings

Persistence estimates differed between the TTE and non-TTE approaches. The TTE approach consistently yielded lower persistence estimates across all time points evaluated. These differences reflect the underlying definitions and handling of censoring in each method: the TTE approach estimates the cumulative persistence and accounts for censoring, whereas the non-TTE approach provides point-in-time snapshots. The TTE approach more accurately reflects the patient journey over time, and is particularly well-suited for longitudinal analyses. The non-TTE approach, on the other hand, offers a quicker and simpler alternative, which may be suitable for exploratory analyses or settings where a high-level snapshot is sufficient.

Future Directions

- Evaluate competing risk framework (e.g., treating death as a competing event) to improve accuracy of persistence estimation
- Develop best practices for persistence estimation using EHR data alone, particularly when claims data are not available

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Brendan Kerr		BK 4/30/25
Patrick Ward	PJW 4/8/25	PJW 4/29/25
Brooke Jarrett	BAJ 4-7-25	BAJ 4/30/25

ISPOR 2025 Research Abstract

Title: Analytical Approaches to Estimate Medication Persistence From Electronic Health Record Data: A Study of Tyrosine Kinase Inhibitors in Patients With Epidermal Growth Factor Receptor–Positive Advanced Non–Small Cell Lung Cancer

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Objectives
Despite the increased use of electronic health record (EHR) data in oncology research, studies estimating medication persistence using EHR data alone remain limited. In the biotech industry, persistence is often assessed using time-to-event (TTE) and non-TTE approaches. This study compared approaches for estimating the persistence of epidermal growth factor receptor (EGFR) tyrosine kinase inhibitors (TKI), including erlotinib, gefitinib, dacomitinib, afatinib, osimertinib, and lazertinib, among patients with *EGFR*-positive advanced non–small cell lung cancer (advNSCLC).

Methods
This retrospective study used the nationwide Flatiron Health EHR-derived deidentified database with a data cutoff of November 30, 2024. Patients with advNSCLC and a positive *EGFR* result 60 days before or 30 days after initiating any EGFR TKI were included. In the TTE approach, persistence was estimated with the time from EGFR TKI initiation until death or the earliest subsequent episode of EGFR TKI followed by more than 60 days of EGFR TKI-free patient activity, whichever occurred first. Patients were censored at their last confirmed activity or data cutoff. In the non-TTE approach, persistence was defined as the proportion of patients remaining on EGFR TKIs at different time points, among those still under follow-up at their last confirmed activity date.

Results
Among 4851 patients, persistence (95% CI) of EGFR TKIs with the TTE approach vs non-TTE approach was 69% (67%-70%) vs 82% (82%-83%) at 6 months, 50% (49%-52%) vs 70% (69%-71%) at 12 months, and 37% (35%-38%) vs 61% (60%-62%) 18 months.

Conclusion
The non-TTE approach estimated higher EGFR TKI persistence than the TTE approach at all timepoints. The TTE approach accounts for censoring and estimates cumulative persistence, whereas the non-TTE approach provides a point-in-time snapshot. The TTE approach may also provide insights into other real-world outcomes, such as real-world treatment duration. Future work could enhance this approach by incorporating competing risks.

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