Assessing Missing Antineoplastic Therapy Prior to Electronic Health Record (EHR)-Derived First Line of Therapy after Advanced Non-Small Cell Lung Cancer (aNSCLC) Diagnosis

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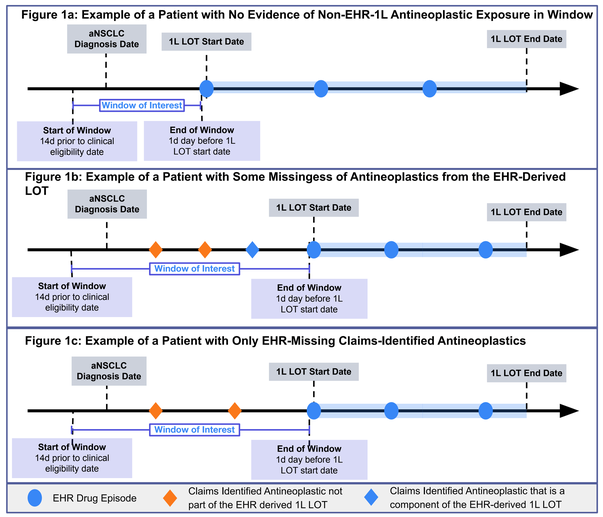
Objectives

- In oncology populations, treatment and line of therapy information is crucial in understanding the patient journey and is necessary to understand exposure and subsequent outcomes. Oncology Electronic Health Record (EHR) is a source of patient treatment exposures, but there is a potential for missingness due to a variety of different mechanisms.
- To better understand potential treatment missingness in EHR data, this study utilized an administrative health claims linked EHR database in an aNSCLC population to identify antineoplastic exposure in claims prior to the first recorded EHR documented exposure.

Methods

- The Flatiron Health Research Database (FHRD) is a nationwide EHR-derived longitudinal database comprised of de-identified patient-level structured and unstructured data, curated via technology-enabled abstraction. During the study period, the de-identified data originated from approximately 280 US cancer clinics (~800 sites of care).[1,2] Komodo Health is a healthcare technology company and its Healthcare Map™ consists of proprietary real-time commercial claims activity data on 330 million US patients and their interactions with the US healthcare system.
- Retrospective longitudinal clinical data were derived from EHR data, comprising patient-level structured and unstructured data, curated via technology-enabled abstraction, and were linked to closed claims coverage within the Komodo Healthcare Map using a third-party linking software to probabilistically match patients.
- Patients selected were diagnosed with aNSCLC between 2013 and 2022 who were treated with a common rule-based National Comprehensive Cancer Network (NCCN Guidelines Version 3.2023) designated first line of therapy (1L)[3]
- Antineoplastics were identified in claims during the window of interest defined as between 14 days prior to advanced diagnosis through the day before EHR-based 1L start to identify potential missingness in EHR-derived 1L treatment data. (Figure 1)
- Patients were classified by the degree of missingness between the EHR-derived 1L treatment components and the claims identified antineoplastics in the window of interest. (Figure 1)

Figure 1: Classifications of Patients' based on Claims Identified Antineoplastics within the Window of Interest Compared to the EHR-derived 1L Components and Start Date



Results

- 5,863 patients were included in this analysis (Figure 2); Of whom, 876 (14.9%) were treated with 1L oral tyrosine kinase inhibitors, and 4,987 (85.1%) were treated with 1L intravenous (IV) regimens (Table 2).
- The duration of the window of interest was a median of 48 days (0-379 days). There were 24 patients who had a window of interest of 0 days, which are included in the present analysis despite not having any time at risk of unobserved antineoplastic exposure.
- Overall, 221 patients (3.8%) had either some missingness or only missing antineoplastics.
  - Of those 221 patients, the majority of the observed antineoplastic components did not have a labeled indication for aNSCLC; common agents observed included imatinib (n=56), hormonal therapies (n=33), and methotrexate (n=27). (Table 3)
- 473 patients (8%) had claims identified antineoplastics during the window of interest, all of which were the same components of the EHR-derived 1L. Seventy-nine percent of them were for patients who had an oral medication in their 1L.
- In a post hoc analysis, we investigated an NCCN recommended second line of therapy, Nivolumab, when identified as the EHR-derived 1L. 268 patients received nivolumab as EHR-derived 1L. 47 (14.7%) had evidence of some missing components and only missing components in claims data during the window of interest.

Figure 2: Cohort Selection

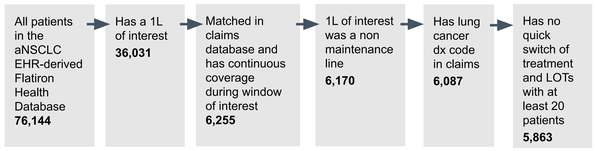


Table 1: Baseline Characteristics

Characteristic	Total n = 5,863	No evidence of non-EHR-1L antineoplastic exposure in window n = 5,658	Evidence of antineoplastic exposure not observed in EHR-derived LOT▲ n = 205
Median Age at advanced diagnosis [IQR]	66 (60, 74)	66 (60, 74)	65 (58, 74)
Gender			
Male	2,854 (49%)	2,764 (49%)	90 (44%)
Female	3,009 (51%)	2,894 (51%)	115 (56%)
Race			
Asian	220 (4.1%)	211 (4.1%)	9 (4.8%)
Black or African American	623 (12%)	603 (12%)	20 (11%)
Other Race	671 (13%)	649 (13%)	22 (12%)
White	3,795 (71%)	3,659 (71%)	136 (73%)
Hispanic or Latinx ethnicity	215 (4.7%)	205 (4.6%)	10 (6.3%)
Extent of disease at initial diagnosis			
Advanced disease (stages IIIB-IV)	4,758 (81%)	4,613 (82%)	145 (71%)
Early stage disease (stages I-IIIA)	1,105 (19%)	1,045 (18%)	60 (29%)
Practice type			
Academic	687 (12%)	661 (12%)	26 (13%)
Community	5,131 (88%)	4,953 (88%)	178 (87%)
Both	45 (0.8%)	44 (0.8%)	1 (0.5%)
Region			
Midwest	963 (16%)	939 (17%)	24 (12%)
Northeast	1,139 (19%)	1,098 (19%)	41 (20%)
South	2,178 (37%)	2,106 (37%)	72 (35%)
West	714 (12%)	682 (12%)	32 (16%)
Unknown	869 (15%)	833 (15%)	36 (18%)

▲ **Evidence of antineoplastic exposure not observed in EHR-derived LOT:** Total number of patients with either some missingness or only missing components. (Figure 1)

Table 2: Counts per EHR-Derived 1L Line Name Stratified by Evidence of Claims-Identified Exposure During the Window of Interest

EHR Derived 1L LOT	Total n(%)	No evidence of non-EHR-1L Antineoplastic▲ n (%)	Some Missingness‖ n (%)	Only Missing Antineoplastics ♦ n(%)
Orals (overall)	**876 (100%)**	**816 (93.2%)**	**24 (2.7%)**	**36 (4.1%)**
Afatinib	95 (100%)	86 (90.5%)	4 (4.2%)	5 (5.3%)
Alectinib	67 (100%)	62 (92.5%)	1 (1.5%)	4 (6.0%)
Crizotinib	76 (100%)	70 (92.1%)	4 (5.3%)	2 (2.6%)
Erlotinib	303 (100%)	283 (93.4%)	10 (3.3%)	10 (3.3%)
Osimertinib	335 (100%)	315 (94.0%)	5 (1.5%)	15 (4.5%)
IVs (overall)	**4987 (100%)**	**4842 (97.1%)**	**123 (2.5%)**	**22 (0.4%)**
Bevacizumab, Carboplatin, Paclitaxel	174 (100%)	172 (98.9%)	2 (1.1%)	0 (0%)
Bevacizumab, Carboplatin, Pemetrexed	398 (100%)	389 (97.7%)	7 (1.8%)	2 (0.5%)
Carboplatin, Paclitaxel	1400 (100%)	1369 (97.8%)	29 (2.1%)	2 (0.1%)
Carboplatin, Paclitaxel, Pembrolizumab	224 (100%)	223 (99.6%)	1 (0.4%)	0 (0%)
Carboplatin, Pembrolizumab, Pemetrexed	1130 (100%)	1093 (96.7%)	30 (2.7%)	7 (0.6%)
Carboplatin, Pemetrexed	851 (100%)	827 (97.2%)	21 (2.5%)	3 (0.4%)
Pembrolizumab	810 (100%)	769 (94.9%)	33 (4.1%)	8 (1.0%)

Table 2 Legend:

▲ **No evidence of non-EHR-1L antineoplastic exposure in window:** There was no observed claims identified antineoplastics in the window of interest, or the observed claims identified antineoplastics were the same components of the EHR 1L treatment components. (Figure 1a)

‖ **Some Missingness:** The observed claims identified antineoplastics in the window of interest had some components of the EHR 1L treatment and a claims identified antineoplastic that was not observed in the EHR-derived 1L treatment. (Figure 1b)

♦ **Only Missing Components:** All observed claims identified antineoplastics in the window of interest were different then the EHR-derived 1L treatment components. There was Only EHR-missing claims identified antineoplastics. (Figure 1c)

Table 3: Ten Most Frequent Antineoplastics Observed in Claims That Were Not Seen in the EHR-Derived LOT

Antineoplastic	Total n(%)
Imatinib*	56 (21%)
Carboplatin	32 (12%)
Pemetrexed	32 (12%)
Methotrexate*	22 (8.4%)
Bevacizumab	14 (5.2%)
Paclitaxel	12(4.5%)
Pembrolizumab	10 (3.7%)
Anastrozole*	9 (3.4%)
Cisplatin	8 (3%)
Durvalumab	8 (3%)

*Indicates antineoplastic components that do not have a labeled indication for aNSCLC

Discussion

- Initial investigation was limited to standard of care first line regimens as indicated in NCCN guidelines,[3] and the present work is limited in generalizability to such regimens.
  - Post-hoc analysis of nivolumab (a common second line regimen) as identified in EHR 1L revealed a greater proportion of missing antineoplastics. However, a majority (85%) of patients had no missingness identified when using nivolumab as 1L.
- This study included patients who may have additional malignancies, these patients may commonly have line misclassification if they are being treated for multiple malignancies at the same time and some of these oral medications are not abstracted in the EHR as part of oral treatment in aNSCLC.
- We did not classify patients as having missing treatment components when the claims identified antineoplastics were the same components as the EHR-derived 1L since this likely represents a correctly identified first LOT. These cases may indicate a difference in start date or be a result of differences in data generating mechanisms (pharmacy fill date vs abstracted start date).
- Since we included patients who could have been receiving adjuvant treatment, or treatment for early stage disease, some antineoplastics identified could have been used for treatment of disease prior to advanced diagnosis.

Conclusions

- A low proportion of claims-derived antineoplastic drug exposures were observed prior to the EHR-based 1L start date that were not present in the EHR.
  - Among exposures observed in the window of interest, many were antineoplastics typically used for the treatment of other malignancies. Limiting to putative aNSCLC-directed 1L regimens, alignment is greater than statistics here may suggest.
- These findings can inform exposure misclassification quantitative bias analysis.

References

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