Poster #RWD86

Healthcare Resource Utilization of United States ROS1+ Non-Small Cell Lung Cancer Patients Treated with Tyrosine Kinase Inhibitors: Analysis of Electronic Medical Transcription Records

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Background

- Lung cancer is a common and deadly cancer in the United States (US),accounting for ~25% of all cancer deaths.[1] Projections suggest that in 2022, there will be 236,000 incident cases and over 130,000 lung cancer-related deaths in the US.[2]
- Non-small cell lung cancer (NSCLC) accounts for an estimated 84% of all diagnosed lung cancers, with a 5-year survival rate of 25% overall and 7% among patients with metastatic disease.[3]
  - Up to 2% of NSCLC patients have rearrangements of the *ROS1* gene (c-ros oncogene) making *ROS1*+ NSCLC a rare cancer.[4]
- Targeted therapies are guideline-recommended early line treatments for *ROS1*+ NSCLC.[5]
  - Crizotinib and entrectinib are the two tyrosine kinase inhibitors (TKI) approved by the US Food and Drug Administration (2016 and 2019, respectively) for front-line treatment of *ROS1*+ NSCLC.[6]
  - Ceritinib, an ALK-TKI, received FDA approval in 2017 for ALK-positive metastatic NSCLC and is used off-label in *ROS1*+ NSCLC while clinical trials are underway.[7]
  - Lorlatinib, approved in 2018 for second/third line treatment of ALK+ metastatic NSCLC, is used off-label as a 2nd line therapy for *ROS1*+ NSCLC patients who have not responded to or have resistance to first-line TKI.[8]
- These agents and related routine medical care may contribute substantially to the high economic burden of *ROS1*+NSCLC.[9]

Study Objective

- This exploratory analysis examined the unexpected healthcare resource utilization (HCRU) of *ROS1*+ NSCLC patients using data from physician narratives of real-world patient encounters in the US routine care setting.

Methods

- Two-phase retrospective, descriptive analysis included:
  - manual record review/abstraction by 2 independent abstractors, followed by
  - meta-data summarization and Natural Language Processing (NLP) text mining

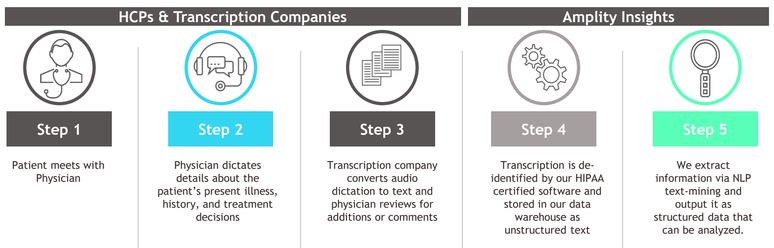
Data Source

- Amplity Insights Database (at time of study; Figure 1):
  - >50 million electronic medical transcription records from >150,000 multi-specialty providers at approximately 40,000 inpatient/outpatient care sites across 50 states and 2 US territories
- Study evaluated data from January 2015 through November 2021.
- All payers: Medicare, Commercial, Medicaid, Uninsured, and Self-Pay.

Study Population

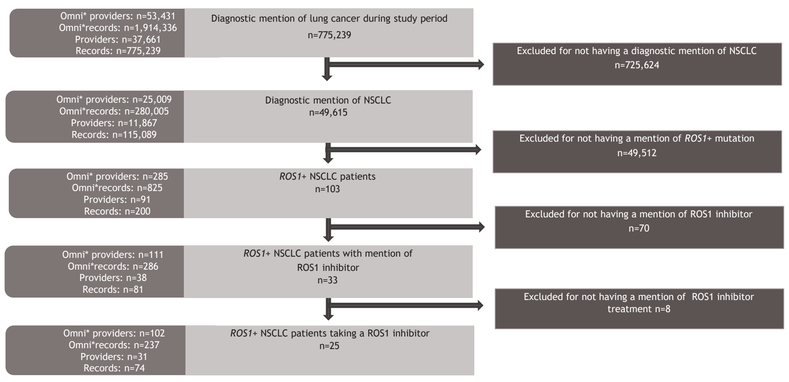
- Adults (age >18 years) *ROS1*+ NSCLC patients treated with crizotinib, entrectinib, ceritinib, and/or lorlatinib.

Figure 1. Overview of Data Capture from Medical Transcription Records



- Total of 389,973 patients with lung cancer and corresponding 775,239 records were identified (Figure 2).
- 49,615 patients had NSCLC.
- 33 patients were confirmed to be NSCLC and *ROS1*+ adults with a mention of ROS1 inhibitor.
- Final patient population for this analysis was narrowed down to 25 representing <0.006% of the total lung cancer population in the Amplity Health transcription records.

Figure 2. Study Population and Amplity Insights Real-World Database

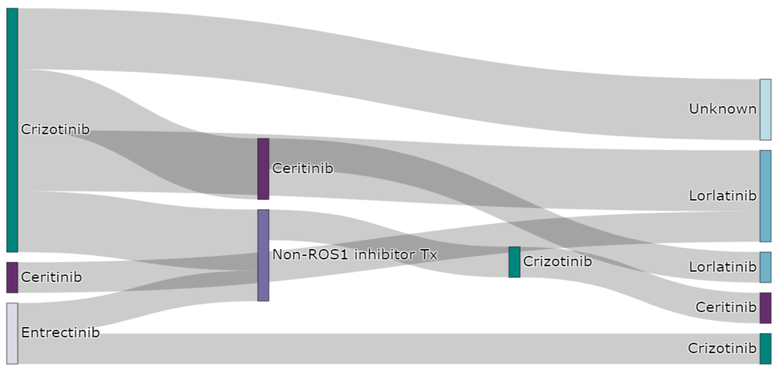


*Omni represents longitudinal records for a patient that may not mention the disease or medication directly
1 at least one record per patient has a mention of any ROS1 inhibitor. The patient has not necessarily ever taken a ROS1 inhibitor
2 at least one record per patient stipulates that the patient has at any time taken at least one ROS1 inhibitor

Results

- 103 *ROS1*+ NSCLC patients were identified; 25 used TKI in any line. The low number of patients identified is consistent with rare nature of ROS1 driver mutation in NSCLC.
  - 23 patients used crizotinib, 4 used lorlatinib, 4 used ceritinib, and 2 used entrectinib (Figure 3).
- The mean age of this treatment cohort was 62 years; 52% of patients were female, 20% had a mentioned history of cancer, and 8% were confirmed current smokers.
- Total time on first-line TKI ranged from 1 to <18 months.
  - In patients who completed their 1L TKI, majority were on crizotinib and 44% treated for 6 to <18 months (n=8); 39% for <6 months (n=7).
- The majority of patients, including 65% (15/23) of crizotinib patients, experienced a TKI treatment disruption (holds, dose reductions, discontinuations or switches).
  - Time to disruption was assessed for 18 patients in whom 9 experienced their first disruption within 3 months after TKI initiation.
  - Progression (53%) and tolerability/adverse effects (AE) (47%) were the most commonly mentioned reasons for disruption, although treatment resistance was not specifically mentioned.

Figure 3. TKI Treatment Patterns in Study Population



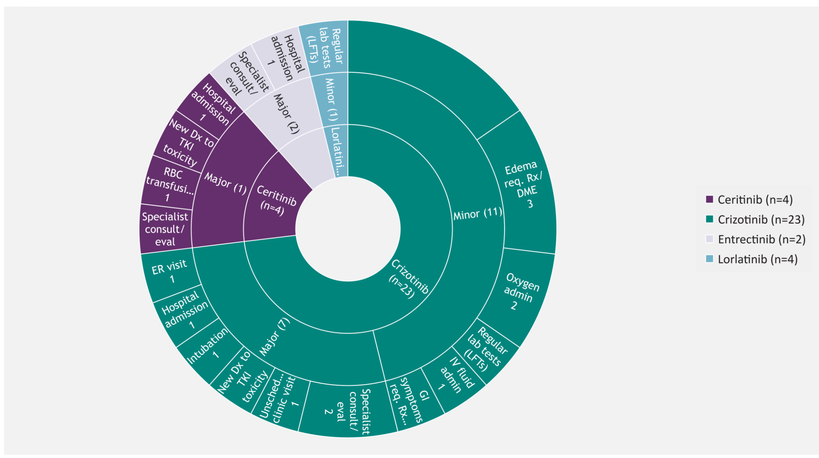
Line	Crizotinib*	Entrectinib	Ceritinib	Lorlatinib	Non-ROS1 inhibitor	None	Unknown
Line 1	22	2	1	0	0	0	0
Line 2	1	0	2	3	3	1	2
Line 3	1	0	0	1	0	0	0
Line 4	0	0	1	0	0	0	0

*1 patient treated with crizotinib in both line 1 and line 3.

Results (continued)

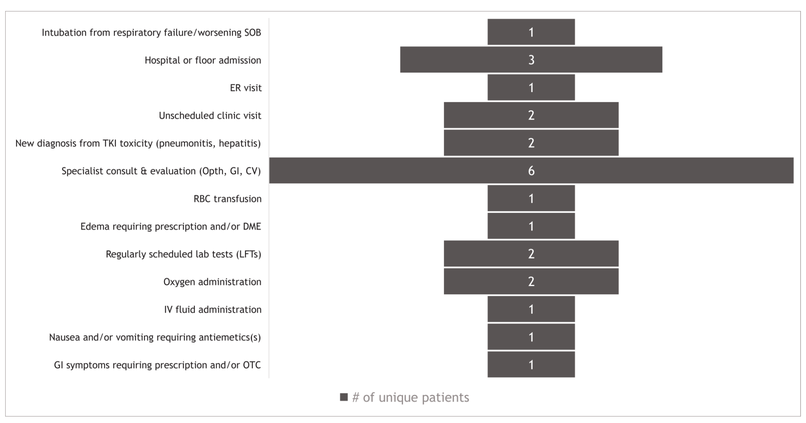
- Majority of TKI-treated *ROS1*+ NSCLC patients (68%) experienced a major or minor health care resource utilization (HCRU) event (Figure 4).
- 35% experienced a MAJOR† HCRU event associated with or while on TKI treatment such as unscheduled visit to Emergency Room (ER) or an unscheduled visit to the clinic.
- 38% experienced a MINOR‡ HCRU event such as symptomatic management of an adverse event with a prescription medication or a new/recurring laboratory test.
- Of the 29 patients with mention of crizotinib, 23 patients were recorded as taking the drug. 61% of these crizotinib-treated patients (14 of 23) had mentions of a major or minor HCRU events. 7 of 23 (30%) experienced major HCRU event.
- Most common major HCRU events mentioned in the transcription record as directly related to patient's TKI by the treating physician were:
  - Referrals to a specialist due to adverse effect/tolerability
  - Unscheduled visits to emergency room or clinic
  - Admittance to a floor unit/hospital
- Additional details of HCRU events are provided in Figure 5 and Figure 6.

Figure 4. Number of HCRU Events Mentioned*



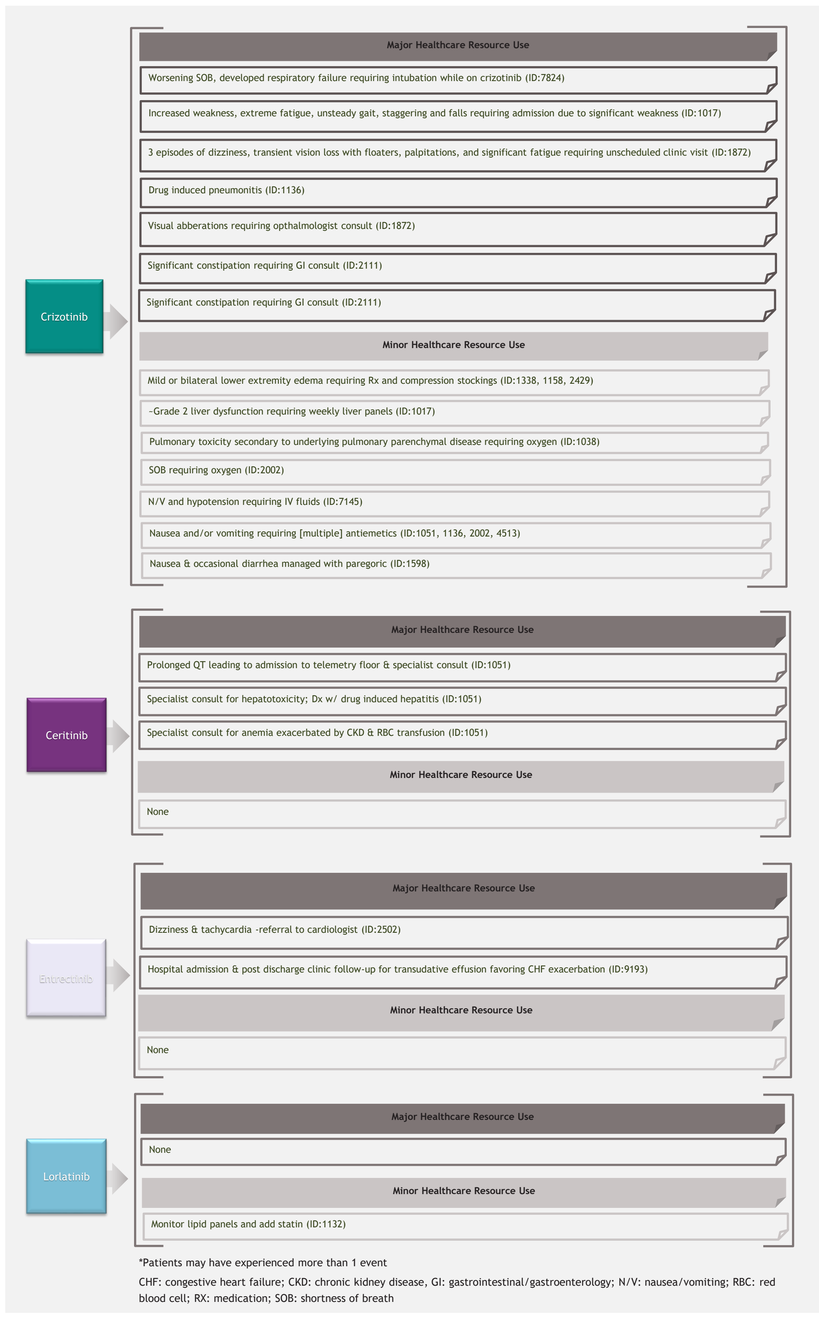
*Some patients used multiple TKI agents during the study
**HCRU mentions by clinician as captured in medical transcription records; probably or likely associated with or during TKI treatment, excluding treatment disruptions or missing records.
†Major HCRU event is defined as admission to hospital/ED, unscheduled clinic visit, specialist referral/consult, new Dx requiring treatment, or medical procedure (e.g., intubation).
‡Minor HCRU event is defined as prescription or use of OTC or prescription drug/DME to manage symptom(s), non-invasive intervention (oxygen, IV fluids), or regularly scheduled labs
DME: durable medical equipment; DX: diagnosis; ER: emergency room; IV: intravenous; OTC: over-the-counter medication; RBC: red blood cell; Rx: prescription medication

Figure 5. Number of Unique Patients* for Each Type of Healthcare Resource Use by Treatment



CT: computerized tomography; DX: diagnosis; HCRU: healthcare resource utilization; PET: positron emission tomography

Figure 6. Healthcare Resource Use Detail

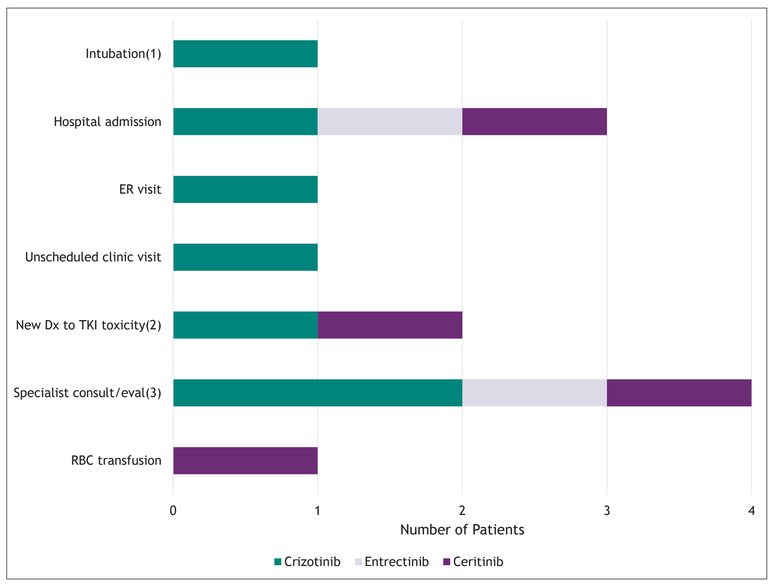


*Patients may have experienced more than 1 event
CHF: congestive heart failure; CKD: chronic kidney disease, GI: gastrointestinal/gastroenterology; N/V: nausea/vomiting; RBC: red blood cell; RX: medication; SOB: shortness of breath

Results (continued)

- Among patients who had a major HCRU event mentioned (Figure 7):
  - 6 patients required specialist consults/evaluations due to adverse effect or toxicity (Ophthalmology, Cardiovascular, or Gastroenterology)
  - 5 patients had unplanned hospital/floor admission, ER, or clinic visit
  - 2 patients received a new diagnosis potentially-related to TKI toxicity
  - 1 patient had to be intubated due to worsening shortness of breath, and another patient received an RBC transfusion

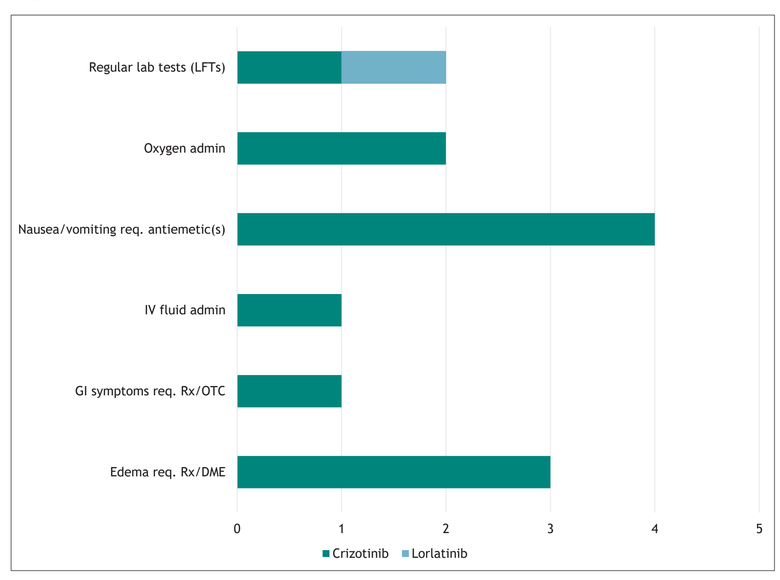
Figure 7. Types of Major HCRU Events Mentioned*



* Healthcare resource use as noted on transcription record.
(1) From respiratory failure/worsening SOB; (2) Pneumonitis, Hepatitis; (3) Ophthalmologist, cardiologist, gastroenterologist.
ER: emergency room; RBC: red blood cell; SOB: shortness of breath.

- Among patients who had a minor HCRU event mentioned (Figure 8):
  - 3 patients required either oxygen or IV fluid administration
  - 2 patients underwent regularly scheduled lab tests
  - 4 patients required the use of antiemetics for nausea/vomiting
  - 3 patients experienced lower extremity edema requiring use of compression stockings and/or prescription medications

Figure 8. Types of Minor HCRU Events Mentioned*



*Healthcare resource use as noted on transcription record.
DME: durable medical equipment; IV: intravenous; LFT: liver function test; OTC: over-the-counter medication; RBC: red blood cell; req: requiring; Rx: prescription medication

Limitations and Conclusions

Limitations

- This was an exploratory, descriptive study.
- Generalizability of results may also be limited by small sample sizes.
- Treatment landscape shifted during the observation period (January 2015 – November 2021) with the approval of entrectinib in late 2019.
- Patients may be lost to follow-up for a variety of reasons, and follow-up may be incomplete for study patients.
- Medical transcriptions are providers' narrative descriptions of patient-provider encounters.
  - As such, only events/terms specifically mentioned by providers (i.e., positive mentions) would be identified in these records.
  - Positive mentions have credibility, but absence of keywords should not be interpreted to mean the event/symptom was necessarily absent.
- Lack of linked adjudicated administrative claims data to confirm whether clinician-mentioned HCRU events actually occurred or to quantify costs and actual economic impact.

Conclusions

- The majority (68%) of all patients experienced a HCRU event.
- 35% experienced major events and 38% experienced minor events.
- The most common major events were consults/referrals to specialist, unscheduled visit to ER/clinic, and admittance to hospital.
- 61% of crizotinib (14 of 23), 67% of entrectinib (2 of 3), 20% of lorlatinib (1 of 5), and 25% of ceritinib (1 of 4) patients had major or minor HCRU events mentioned in their transcription medical records.
- Unexpected HCRU events among *ROS1*+ NSCLC patients treated with crizotinib or other available TKIs may contribute to the total cost of care and should be considered as a relevant and significant additional burden of managing this diagnosis with the current treatment options.

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