Potential of German claims data to characterize utilization of new cancer drugs - The example of crizotinib
Sarina Schwarz, Katja Anita Oppelt, Miriam Heinig, Ulrike Haug

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Corresponding author
Ulrike Haug

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Abstract

Aims: Premarketing clinical trials are typically conducted under controlled conditions and in selected study populations. Real-world information on the utilization of new cancer drugs is limited. We aimed to explore the potential of German claims data in this regard, exemplified by the ALK-inhibitor crizotinib used in non-small cell lung cancer therapy.

Materials and methods: We identified patients treated with crizotinib in the German Pharmacoepidemiological Research Database (data 2004–2017; 20% of the German population) and assessed patient characteristics, treatment, and survival.

Results: We identified 348 crizotinib patients (56% female, 25% first line users). After two years, overall survival was 48%, with higher survival in men than in women (58% vs. 40%). Overall, 76% of patients discontinued crizotinib treatment. Of those, 41% received another ALK-inhibitor afterwards.

Conclusions: The results underline the potential of German claims data for real-world monitoring of oncologic drug utilization.

Keywords: Crizotinib, non-small cell lung cancer, anaplastic lymphoma kinase, claims data, survival, treatment patterns, real-world analysis
**Introduction**

Cancer is one of the main indications for which new drugs are developed. In solid tumors, the majority of cancer drugs approved over the past years were for the treatment of lung cancer [1]. Several of these drugs were developed for the treatment of advanced non-small cell lung cancer (NSCLC) with anaplastic lymphoma kinase (ALK) rearrangements, occurring in about 3–5% of all NSCLC cases [2, 3]. The first of these so-called ALK inhibitors was crizotinib approved by the European Medicines Agency (EMA) in October 2012 for second or later line treatment of these cancers; in November 2015, the approval was extended to first line treatment and in August 2016, it was also approved for the treatment of patients with C-ros oncogene 1 (ROS1) rearrangements [4, 5].

Premarketing clinical trials investigating the risk-benefit ratio of these drugs are typically conducted under controlled conditions and in selected study populations, which may differ from utilization after market approval. However, information on utilization of these drugs in the real-world setting is limited. To overcome this research gap, there is no optimal data source but various approaches may complement each other. Specific patient registries or medical record reviews provide valuable information but are often costly and partly selective. Large claims databases, which have been used for many purposes in drug monitoring after marketing approval, may also provide information on utilization of new cancer drugs. However, this potential has hardly been evaluated for such databases. This also applies to the German Pharmacoepidemiological Research Database (GePaRD), a large German claims database covering 20% of the German population.

Exemplified by crizotinib, we aimed to explore the potential of German claims data to provide real-world data on utilization of new cancer drugs, treatment patterns, and survival.
**Materials & methods**

**Data source**

We used the German Pharmacoepidemiological Research Database (GePaRD) which contains health claims data from four statutory health insurance (SHI) providers in Germany. GePaRD currently includes information on about 25 million persons who have been insured with one of the participating providers since 2004 or later. Per data year, there is information on approximately 20% of the general population in Germany and all geographical regions of Germany are represented. In addition to demographic data, GePaRD contains information on drug dispensations, outpatient and inpatient services and diagnoses. For this analysis, we used data from 2004 to 2017.

In GePaRD, oral cancer drugs (such as crizotinib) dispensed in the outpatient setting can be identified by the respective Anatomical Therapeutic Chemical (ATC) code including the date of dispensation. Information on parenteral preparations of chemotherapies and monoclonal antibodies in the outpatient setting is typically (for the majority of patients in GePaRD) restricted to the dispensation of such a preparation including the date but without details on the substances included in the preparation. In the inpatient setting, there are general codes for parenteral preparations of chemotherapies and monoclonal antibodies including the date. Furthermore, for certain new and costly drugs (such as crizotinib), specific codes are available to monitor their dispensation in the inpatient setting. Diagnosis codes are registered according to the International Classification of Diseases 10th revision, German modification (ICD-10-GM) in the in- and outpatient setting. For this analysis, we considered hospital discharge diagnoses and outpatient diagnoses with the label “confirmed”.
Study population and study design

We included all patients with an in- or outpatient dispensation of crizotinib between 2012 and 2016 based on the respective codes. Each individual was observed as long as possible, the longest period was from 2004 until 2017. We only included patients with crizotinib initiation until the end of 2016 to allow for a minimum observation period of one year after the first crizotinib dispensation. The observation time was divided into the period before the first crizotinib dispensation (period 1) and after the first crizotinib dispensation (period 2). In period 1, we determined the date of the first diagnosis code of lung cancer (C34) and also assessed whether affected lymph nodes or metastases (C77–C79) were coded. Affected lymph nodes and metastases were defined as being present at diagnosis when they were coded within six months after the first lung cancer diagnosis code in GePaRD. Furthermore, we assessed use of chemotherapy and other targeted therapy in period 1. In period 2, we assessed the number and timing of crizotinib dispensations, the use of chemotherapy, and other targeted therapy as well as survival.

Data analysis

In a first step, we described included patients regarding age at first dispensation of crizotinib, sex, codes for lung cancer and affected lymph nodes or metastases, year of first crizotinib dispensation, number of crizotinib dispensations, and months between first and last crizotinib dispensation. We distinguished between patients using crizotinib as first vs. later line therapy. If a patient did not have chemotherapy or another targeted therapy before crizotinib, crizotinib was classified as first line therapy. Consequently, crizotinib was classified as later line therapy if a patient had chemotherapy and/or another targeted therapy before crizotinib.

For patients with crizotinib as later line therapy, we described the type of therapy before crizotinib. For all patients (i.e., first and later line therapy), we described the course after the first dispensation of crizotinib (i.e., in period 2), distinguishing between the following three groups: A) discontinuation of treatment with crizotinib, B) death while treated with crizotinib, and C) ongoing treatment with
crizotinib at the end of follow-up. Given the package size of crizotinib, we assumed that patients were under treatment with crizotinib for 35 days after each dispensation.

We also assessed absolute survival after crizotinib initiation using Kaplan-Meier estimation with 95% confidence intervals (CI) overall and stratified by sex. We conducted all analyses using SAS software (version 9.4; SAS Institute Inc., Cary, NC).
Results

Overall, we identified 348 patients treated with crizotinib in GePaRD. Table 1 describes the cohort regarding age, sex, available follow-up, relevant diagnosis codes, and crizotinib dispensations. Most patients received crizotinib as later line therapy (75%). Of all patients, the majority (56%) was female and the mean age at first crizotinib dispensation was 58 years (range: 3–87 years); eight patients (2%) were younger than 18 years. The mean observation period before first crizotinib dispensation was about nine years and after the last crizotinib dispensation about seven months. The mean time between the first lung cancer diagnosis code in GePaRD and the first crizotinib dispensation was 16 months. Of patients with lung cancer diagnosis (96% of all patients), 88% had metastases coded at diagnosis and almost all (98%) had at least one metastasis code any time during follow-up. The mean number of crizotinib dispensations per patient was ten and the mean time between the first and last crizotinib dispensation observable in the database was ten months. The proportion of patients receiving crizotinib as first line therapy increased from 5% in 2012 to 40% in 2016. Overall, the characteristics of first and second line users were rather similar, apart from the time between the first lung cancer diagnosis code in GePaRD and the first crizotinib dispensation (8 months vs. 19 months). Supplementary Table 1 shows that patient characteristics such as age and utilization patterns were largely similar between men and women. The proportion of patients with brain metastasis at diagnosis was 5% higher among women than men and the proportion with brain metastasis at any time during the observation period was 10% higher among women than men.

Figure 1 shows the course of patients receiving crizotinib as first line therapy (n=88). Nine patients died during crizotinib therapy (10%), 15 patients still received crizotinib at the end of follow-up (17%), and 64 patients discontinued crizotinib therapy (73%). Of the 64 patients discontinuing crizotinib therapy, i) 17 patients (27%) had a follow-up of less than three months and ten of them died in this time period, ii) 11 (17%) had no further antineoplastic treatment, and iii) 36 (56%) received further antineoplastic
treatment. The latter included ceritinib in 17 patients and alectinib in 13 patients. Three patients received crizotinib, ceritinib, and alectinib.

Figure 2 shows the course of treatment of patients receiving crizotinib as later line therapy (n=260). Before the first crizotinib dispensation, 182 of the patients received chemotherapy, 74 patients received chemotherapy and targeted therapy, and 4 patients only received targeted therapy. Among the 78 patients receiving targeted therapy before the first crizotinib dispensation, no patient received ceritinib or alectinib. Thirty-eight patients died during crizotinib therapy (15%), 22 patients still received crizotinib at the end of follow-up (8%), and 200 patients discontinued crizotinib therapy (77%). Of the 200 patients discontinuing crizotinib therapy, i) 51 patients (26%) had a follow-up of less than three months and 35 of them died in this time period, ii) 36 (18%) had no further antineoplastic treatment, and iii) 113 (57%) received further antineoplastic treatment. The latter included ceritinib in 66 patients and alectinib in 23 patients. Nine patients received crizotinib, ceritinib, and alectinib.

A total of 192 (55%) patients died within the study period. In those who died, the mean time until death following crizotinib initiation was 12 months and 62 patients (32%) died within four months. Figure 3A shows the probability of surviving after the first crizotinib dispensation which was 65% after 12 months and 48% after 24 months. Survival was higher in males than in females; the confidence intervals of the respective survival curves were mostly non-overlapping (Figure 3B). After 24 months, the probability of surviving was 58% in men and 40% in women.

Of the eight patients younger than 18 years, one had diagnosis codes for lung cancer, six had diagnosis codes indicating other cancers (including neuroblastomas (n=2), non-solid tumors (n=2), tumor of connective and soft tissues (n=1), both tumors of the salivary glands and of the thyroid glands (n=1)) and one patient had diagnosis codes for neoplasm of uncertain behavior and neoplasm of liver, gallbladder and/or bile ducts. Five of the eight patients younger than 18 years died within the study period. In those who died, the mean time until death following crizotinib initiation was four months.
Discussion

Our study including an unselected sample of 348 patients receiving crizotinib provides, for the first time, insights into the real-life use of this new cancer drug in Germany based on claims data. On average, the patients were treated with crizotinib for ten months. Overall, 76% of patients discontinued crizotinib therapy. Of those, 41% received another ALK-inhibitor afterwards. A total of 192 (55%) patients died within the study period. Of those who died, 62 (32%) died within four months after crizotinib initiation. The overall 24-month survival probability after the first crizotinib dispensation was 48% and was markedly higher in men (58%) compared to women (40%).

In Europe, crizotinib was approved in 2012, followed by other ALK inhibitors such as ceritinib and alectinib, which were approved in 2015 and 2017, respectively. So far, German-specific data on the real-world use of crizotinib have not been available. There was one study based on a retrospective medical record review (published as an abstract) which included 303 patients from different European countries. One fourth of these patients were from Germany but the results were only reported for the total group of patients. In that study, the mean age was 60 years, a majority was male (60%) and had metastases at the initial diagnosis (89%). The median duration of crizotinib treatment was seven months, 53% of patients were deceased upon record abstraction and the median overall survival was 20 months both in first and second line users of crizotinib [6]. Apart from the higher proportion of men and the shorter treatment duration, patient characteristics and survival estimates were thus similar to our study.

Treatment patterns after crizotinib discontinuation such as the use of second generation ALK-inhibitors were not reported. Other studies, using data from the United States [7, 8], Canada [7, 9], Korea [10, 11], Mexico [10], and Europe [10] reported a mean treatment duration of 9–12 months [7, 8] and also similar treatment patterns after crizotinib discontinuation, i.e., in our study, 44% of the patients received no further therapy, compared to 37%–48% in other studies [9-11], and of those who did receive further therapy, second generation ALK-inhibitors such as ceritinib and alectinib were commonly used (41% in
our study compared to 16%–44% in other studies) [8-11]. When interpreting the proportion of patients receiving second generation ALK inhibitors and comparing it between studies, the approval dates of the second generation ALK-inhibitors must be kept in mind. For example, we included patients who received the first dispensation of crizotinib between 2012 and 2016. Patients included, for example, in 2012 (i.e. receiving the first dispensation of crizotinib in 2012) were thus less likely to receive a second generation ALK-inhibitors as compared to patients included in 2016.

With respect to overall survival after crizotinib initiation, there is one study showing a 24-month survival of 49% (CI 39%–59%), i.e., the estimate is similar to our study (48%) [7]. A study by Reynolds et al. reported a survival of 61% (CI 52%–69%) after 24 months, but the analysis was restricted to patients treated for at least three months [8]. Generally, the comparison of survival estimates is hampered given that the proportions of first and second line users vary between studies. First line users are expected to show a higher survival than second line users if follow-up starts at the time of the first crizotinib use. Apart from the exclusion of persons with a treatment duration of less than three months, this may also explain the higher survival observed in the study by Reynolds et al. where 62% of the patients were first line users of crizotinib.

In this study, we observed higher survival after crizotinib initiation in males than in females. Several aspects need to be taken into account to avoid misinterpretation of this finding. First, only little is known on the natural history of ALK-positive NSCLC. While for NSCLC overall, prognosis has been shown to be higher for females than for males [12, 13], it is not clear whether this also holds true for the small subgroup of ALK-positive NSCLC. So we cannot exclude that the observed differences in survival simply reflect sex differences in the natural history of ALK-positive NSCLC, irrespective of treatment. Second, the reported survival estimates refer to the first crizotinib dispensation as starting point and should thus not be interpreted as prognosis of patients with ALK-positive NSCLC. ALK-positive NSCLC patients not receiving crizotinib, e.g. because they died shortly after diagnosis, were not included in our analysis.
Third, although we did not find relevant differences in patient characteristics and utilization patterns between men and women important information on prognostic factors was lacking in our data (e.g. performance status, number of metastases at diagnosis). It is thus not appropriate to draw any conclusions regarding effectiveness of crizotinib in men vs. women from our study given that the comparison may be biased due to an imbalance in prognostic factors at baseline. In addition to studies on sex differences in the natural history of ALK-positive NSCLC, further real-world studies investigating sex differences in survival of crizotinib patients are needed in order to shed further light on this topic. In a chart review study from Canada the survival analyses focused on patients discontinuing crizotinib treatment and are therefore not comparable to our study [9].

Our study included eight crizotinib users below 18 years. This is plausible given that treatment of pediatric cancers showing ALK gene translocations with crizotinib has been discussed [14-16] and investigated in clinical trials [17]. This includes several cancers, e.g., neuroblastomas and anaplastic large-cell lymphomas. We found codes indicating diagnoses discussed in the literature, in all of the eight patients. This illustrates the potential of large healthcare databases to provide real-life data also on very rare conditions, e.g., in pediatric oncology. Comparison to other studies based on real-life data was not possible as they excluded patients under 18 years [6-11, 18, 19].

We conducted this study not only to describe utilization and survival of crizotinib patients, but also as a use case to assess the potential of German claims data for real-life monitoring of new cancer drugs. The plausibility of our findings is reassuring and our study also suggests that details such as the line of treatment can reasonably be captured in the data. For example, the increase in first line users from 2016 onwards reflects the approval of crizotinib as first line therapy in November 2015. Information on the ingredients of standard chemotherapy, which can partly be highly effective in ALK-positive lung cancers, is limited in GePaRD. Nonetheless, a detailed follow-up is possible regarding the use of new cancer drugs, which are often the main interest of current research. With respect to information on the dose, it
is typically not available for parenteral cancer drugs, but for oral cancer drug such as crizotinib it can be estimated based on the number and timing of dispensations. Unlike chart review studies which may face problems of generalizability, claims data facilitate the identification of unselected patient groups in a rapid and cost-effective way. A specific advantage of GePaRD, which contains data since 2004, is the long and continuous observation period that can be used both to characterize the patients’ medical history including comorbidity as well as to follow up treatment and survival. As opposed to cancer registries, the completeness of claims data does not depend on active reporting by a variety of physicians or institutions, i.e., underreporting of information on cancer treatment is not a concern. Unlike in cancer registries and medical records, cancer histology, results of genetic testing and details on the stage are missing in claims data but the relevance of this limitation depends on the research question. It is less relevant in the context of precision medicine (e.g., crizotinib) where the use of certain drugs is restricted to very specific patients. With respect to information on life-style factors (e.g., smoking) or reasons for the discontinuation of treatment, there are some codes or options to estimate this in claims data, but the quality and completeness of the information is certainly not comparable to primary data where this information can be collected by direct patient or physician contact.

**Conclusion**

Using GePaRD we found treatment patterns regarding crizotinib consistent with other studies and could provide detailed information on its utilization. The overall 24-month survival probability after the first crizotinib dispensation was 48% and was markedly higher in men (58%) compared to women (40%)—a difference that requires further investigation in future studies. The results underline the potential of German claims data for monitoring real-world oncologic drug utilization, which is important in many regards, e.g. to explore their dissemination in clinical practice and to assess whether the use of these drugs in the real world setting differs from premarketing trials, which could also affect the risk-benefit ratio of these drugs.
Summary points

- The potential of claims data for real-world analyses of new cancer drugs has hardly been evaluated.

- We explored this potential for a German claims database covering 20% of the population using crizotinib as an example.

- We identified 348 patients receiving crizotinib between 2012 and 2016.

- The majority (75%) received crizotinib as second or later line therapy.

- 76% of patients discontinued crizotinib therapy. Of these, 41% received a second generation ALK-inhibitor afterwards.

- In total, 192 (55%) patients died within the study period.

- The overall 24-month survival probability after the first crizotinib dispensation was 48% and was markedly higher among men (58%) than women (40%).

- We identified eight crizotinib users under 18 years, of whom seven had diagnosis codes of cancers and neoplasms other than lung cancer.

- The results underline the potential of German claims data for monitoring real-world oncologic drug utilization.
References


**Real-world analysis investigating treatment patterns of 303 patients treated with crizotinib, of those, 75 patients were from Germany.


** Real-world analysis from the US and Canada of 212 crizotinib patients showing overall 24-month survival of 49%.


** Real-world analysis from the US of 199 crizotinib patients showing overall 24-month survival of 61% in crizotinib patients treated for at least 3 months.


*Real-world analysis from Canada including 88 crizotinib patients.

*Real-world analysis including 158 crizotinib patients from the EU (n=99), Korea (n=30), US (n=17), and Mexico (n=12).


*Real-world analysis from Korea including 30 crizotinib patients.


Figure 1. Treatment patterns of patients who received crizotinib as first line therapy.

Crizotinib (n=88)
Year of first dispensation
2012 (n=1)
2013 (n=9)
2014 (n=13)
2015 (n=22)
2016 (n=43)

Discontinued (n=64)\(^a\)
Still on crizotinib at the end of follow-up (n=15)\(^b\)
Died while on crizotinib (n=9)\(^c\)

After the last crizotinib dispensation
Follow-up ≤3 months\(^d\) (n=17) (Of these: 10 deaths)
No further antineoplastic therapy (n=11)
Further antineoplastic treatment (n=36)
Chemotherapy only (n=9)
Other targeted therapy only (n=21)
Chemotherapy and other targeted therapy (n=6)

Of these:
Ceritinib (n=14)
Alectinib (n=10)
Ceritinib and alectinib (n=3)

\(^a\)One patient received another targeted therapy (ceritinib) between the first and the last crizotinib dispensation.
\(^b\)One patient received chemotherapy between the first and the last crizotinib dispensation.
\(^c\)No patient received another antineoplastic therapy between the first and the last crizotinib dispensation.
\(^d\)Without further antineoplastic treatment until death/end of follow-up.
Figure 2. Treatment patterns of patients who received crizotinib as later line therapy.

Before crizotinib therapy

Other antineoplastic therapy:
- Chemotherapy only (n=182)
- Other targeted therapy only (n=4)
- Chemotherapy and other targeted therapy (n=74)

Other antineoplastic therapy:
- Ceritinib (n=0)
- Alectinib (n=0)

Crizotinib (n=260)
Year of first dispensation
- 2012 (n=19)
- 2013 (n=37)
- 2014 (n=63)
- 2015 (n=77)
- 2016 (n=64)

Of these:
- Ceritinib (n=0)
- Alectinib (n=0)

Discontinued (n=200)*

Still on crizotinib at the end of follow-up (n=22)**

Died while on crizotinib (n=38)**

After the last crizotinib dispensation

Follow-up ≤3 months*** (n=51)
(Of these: 35 deaths)

No further antineoplastic therapy (n=36)

Further antineoplastic treatment (n=113)
- Chemotherapy only (n=22)
- Other targeted therapy only (n=73)
- Chemotherapy and other targeted therapy (n=18)

Of these:
- Ceritinib (n=57)
- Alectinib (n=14)
- Ceritinib and alectinib (n=9)

*Eleven patients received chemotherapy between the first and the last crizotinib dispensation, six patients received another targeted therapy and two patients received chemotherapy and another targeted therapy. Five patients received ceritinib.

**One patient received another targeted therapy between the first and the last crizotinib dispensation.

***Two patients received chemotherapy between the first and the last crizotinib dispensation, two patients received another targeted therapy. One patient received ceritinib.

****Without further antineoplastic treatment until death/ end of follow-up.
Figure 3. Overall survival (OS) after the first dispensation of crizotinib. Figure 3A. All crizotinib patients. Figure 3B. Stratified by sex.
<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Overall (n=348; 100%)</th>
<th>Timing of crizotinib therapy</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>First line (n=88; 25.3%)</td>
<td>Later line (n=260; 74.7%)</td>
</tr>
<tr>
<td>Female sex, n (%)</td>
<td>193 (55.5%)</td>
<td>51 (58.0%)</td>
<td>142 (54.6%)</td>
</tr>
<tr>
<td>Age at first crizotinib dispensation (years), mean ± SD</td>
<td>57.9 ± 15.5</td>
<td>60.2 ± 16.5</td>
<td>57.1 ± 15.1</td>
</tr>
<tr>
<td>Follow-up (months) in the database, mean ± SD</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Before first crizotinib dispensation</td>
<td>104.0 ± 42.9</td>
<td>105.3 ± 46.9</td>
<td>103.6 ± 41.5</td>
</tr>
<tr>
<td>After last crizotinib dispensation</td>
<td>7.0 ± 8.8</td>
<td>6.1 ± 5.7</td>
<td>7.3 ± 8.9</td>
</tr>
<tr>
<td>Overall</td>
<td>121.3 ± 44.3</td>
<td>121.7 ± 45.7</td>
<td>121.2 ± 43.8</td>
</tr>
<tr>
<td>Number of patients with at least one lung cancer diagnosis code in the database</td>
<td>333 (95.7%)</td>
<td>83 (94.3%)</td>
<td>250 (96.2%)</td>
</tr>
<tr>
<td>Year of first lung cancer diagnosis code in the database, n (%)</td>
<td></td>
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<tr>
<td>before 2012</td>
<td>55 (16.5%)</td>
<td>4 (4.8%)</td>
<td>51 (20.4%)</td>
</tr>
<tr>
<td>2012</td>
<td>36 (11.1%)</td>
<td>4 (4.8%)</td>
<td>32 (13.2%)</td>
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<tr>
<td>2013</td>
<td>49 (14.7%)</td>
<td>9 (10.8%)</td>
<td>40 (16.0%)</td>
</tr>
<tr>
<td>2014</td>
<td>74 (21.9%)</td>
<td>15 (18.1%)</td>
<td>59 (23.2%)</td>
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<tr>
<td>2015</td>
<td>68 (20.4%)</td>
<td>18 (21.7%)</td>
<td>50 (20.0%)</td>
</tr>
<tr>
<td>2016</td>
<td>51 (15.3%)</td>
<td>33 (39.8%)</td>
<td>18 (7.2%)</td>
</tr>
<tr>
<td>Months between first lung cancer diagnosis code and first crizotinib dispensation, mean ± SD</td>
<td>16.2 ± 23.8</td>
<td>7.9 ± 24.0</td>
<td>19.0 ± 23.1</td>
</tr>
<tr>
<td>Presence of codes for metastases, n (%)</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>at diagnosis</td>
<td>294 (87.7%)</td>
<td>71 (83.5%)</td>
<td>223 (89.2%)</td>
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<tr>
<td>at any time</td>
<td>328 (97.9%)</td>
<td>80 (94.1%)</td>
<td>248 (99.2%)</td>
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<tr>
<td>Presence of codes for brain metastases, n (%)</td>
<td></td>
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<td></td>
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<tr>
<td>at diagnosis</td>
<td>69 (20.6%)</td>
<td>17 (20.0%)</td>
<td>52 (20.8%)</td>
</tr>
<tr>
<td>at any time</td>
<td>166 (49.6%)</td>
<td>34 (40.0%)</td>
<td>132 (52.8%)</td>
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<tr>
<td>Year of first crizotinib dispensation, n (%)</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>2012</td>
<td>20 (5.8%)</td>
<td>1 (1.1%)</td>
<td>19 (7.3%)</td>
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<tr>
<td>2013</td>
<td>46 (13.2%)</td>
<td>9 (10.2%)</td>
<td>37 (14.2%)</td>
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<tr>
<td>2014</td>
<td>76 (21.8%)</td>
<td>13 (14.8%)</td>
<td>63 (24.2%)</td>
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<tr>
<td>2015</td>
<td>99 (28.5%)</td>
<td>22 (25.0%)</td>
<td>77 (29.6%)</td>
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<tr>
<td>2016</td>
<td>107 (30.8%)</td>
<td>43 (48.9%)</td>
<td>64 (24.6%)</td>
</tr>
<tr>
<td>Number of crizotinib dispensations, mean ± SD</td>
<td>10.1 ± 9.2</td>
<td>10.4 ± 9.5</td>
<td>10.0 ± 9.1</td>
</tr>
<tr>
<td>Months between first and last crizotinib dispensation, mean ± SD</td>
<td>10.3 ± 10.4</td>
<td>10.2 ± 9.8</td>
<td>10.3 ± 10.7</td>
</tr>
</tbody>
</table>

1 Of the 15 patients without lung cancer diagnosis, 8 patients were <18 years and had diagnosis codes for neuroblastomas, non-solid tumors, tumors of connective and soft tissues, salivary glands and thyroid glands, as well as neoplasm of uncertain behavior and neoplasm of liver, gallbladder and/or bile ducts. Seven patients were ≥18 years and had diagnosis codes for non-solid tumors, head and neck cancer, tumors of the retroperitoneum and connective and soft tissue or several tumors with the primary site being unspecified.

2 Of those with at least one lung cancer diagnosis code in the database.