Real-world overall survival of patients with advanced non-small cell lung cancer: Results of a claims data study of patients in Germany

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Overview

Research question	Method
➢ What is the real-world overall survival (OS) in incident aNSCLC patients? ➢ Which factors are associated with OS in these patients?	➢ Observational, retrospective claims-data study investigating OS of incident aNSCLC patients, using claims data provided by a large German health insurance fund with about 3.2 million insured patients.
Key results	**Conclusions**
➢ The median overall survival in aNSCLC patients is 351 days ➢ Higher age, male gender, stage IV cancer diagnosis (as opposed to stage IIIb diagnosis) contributed to lower OS. ➢ Positive mutation status (EGFR, ALK, ROS-1) increased OS.	➢ OS of incident aNSCLC patients is still limited and did not improve in recent years, even if new treatments were introduced. ➢ Positive mutation status is strongly associated with better OS.

Background

Non-small cell lung cancer (NSCLC) accounts for about 85% to 90% of all lung cancer diagnoses and is the leading cause of cancer death [1-3]. Despite advances in research and treatment in recent years, it is being discussed whether recent therapy developments that have shown their potential in clinical trials are also associated with better real-world outcomes in advanced NSCLC (aNSCLC) treatment. The objective of this study was to describe the real-world overall survival (OS) of patients with a diagnosis of advanced non-small cell lung cancer (aNSCLC). Moreover, factors associated with OS were explored.

Methods

In this retrospective claims-based data analysis (dataset: AOK PLUS), aNSCLC patients observable for at least 12 months from their incident diagnosis were identified. All patients with an incident diagnosis of aNSCLC between 2012-2015 were included. Patients were selected in a stepwise procedure based on their diagnoses and treatment received:

1. Lung cancer patients were identified based on the record of their diagnosis (documented via relevant ICD-10 code). The inclusion criteria required: (i) at least one inpatient or one outpatient confirmed diagnosis of lung cancer, (ii) documentation of SCLC or NSCLC treatments between 01/01/2012-31/12/2015 and (iii) continuous insurance with the respective sickness fund (death being the only exception) between 01/01/2011-31/12/2016.
2. Non-small cell lung cancer patients were selected from all lung cancer patients, on the account of whether the treatment they received following their lung cancer diagnosis (identified through relevant ATC and OPS codes) was NSCLC-specific, as ICD-10 does not differentiate between SCLC and NSCLC. Treatment was defined as NSCLC-specific by consulting the latest treatment guideline in Germany and the official SMPCs of the respective drugs published by the European Commission's Public Health division. Patients with any treatment for SCLC or only treatment for approved for both SCLC and NSCLC were excluded.
3. Patients with advanced disease were identified based on whether they received a diagnosis of tumor stage IIIb or higher diagnosis (documented via relevant ICD-10 codes), at the time of their diagnosis. Tumor staging was done with respect to the German treatment guidelines and UICC 8. Patients with a first inpatient or outpatient confirmed tumor stage IIIb or higher diagnosis between 01/01/2012-31/12/2015 were included. Only patients with incident disease were selected, ensured by checking whether a patient received an advanced tumor stage diagnosis in the 12 months before, and excluding them if they did.

Index date was alternatively defined as date of first diagnosis of stage IIIB/IV or date of first-line systemic treatment initiation. To address changes in OS in last years, survival of patients first diagnosed in respective calendar years was reported. OS was described using Kaplan Meier curve logic which took into account both death and end of observational period/data availability. A multivariable Cox regression was performed in order to identify the effect of various independent variables on the mortality of patients.

Results

This claims data analysis included 1,741 incident advanced NSCLC patients, with the mean age of 66.97 years and a higher proportion of male patients (70.13%) than female patients (29.87%). Patients received on average 4.7 chronic drug prescriptions and more than half of them (75.99%) had at least 1 all-cause hospitalization in the baseline period.

Table 1 Baseline characteristics

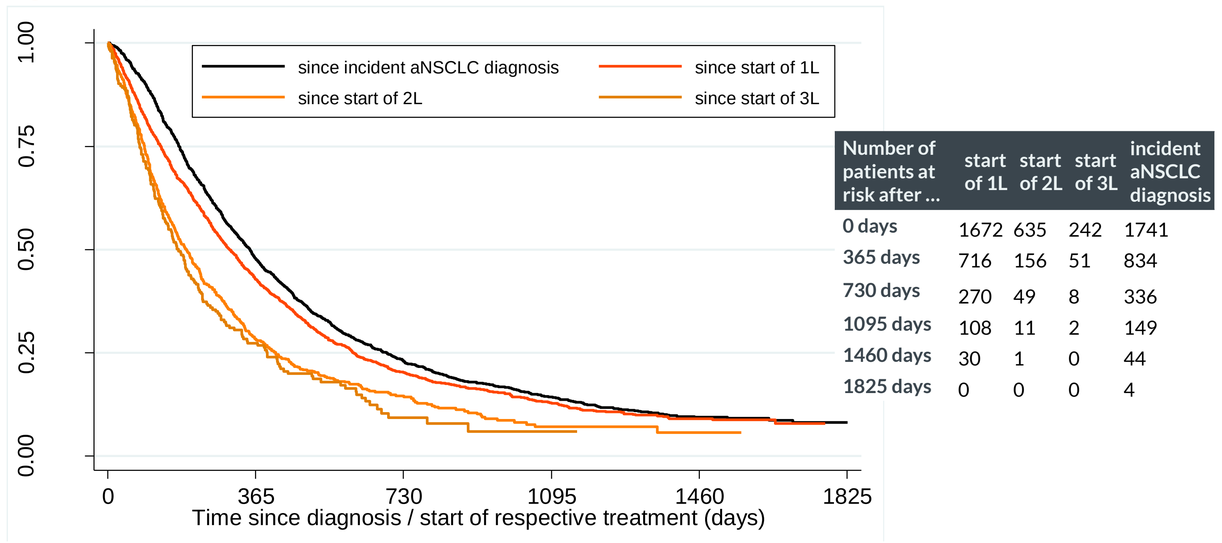
Variable		aNSCLC Patients
N		**1,741**
Age at index date	Mean (Median | SD)	66.81 (68 | 10.16)
Gender	Female, N (%)	520 (29.87)
Charlson Comorbidity Index (CCI)	Mean (Median | SD)	7.02 (7 | 3.55)
TNM status at index date	IIIB (%), % of patient	32.17
	IV (%), % of patient	43.71
	IIIB and IV (%), % of patient	24.12
First aNSCLC diagnosis in		
	2012, % of patient	29.70
	2013, % of patient	25.33
	2014, % of patient	24.70
	2015, % of patient	20.28
Within 12 month baseline period…		
…at least one hospitalization	% of patients	75.99
…number of chronic drugs (defined as at least 2 different prescriptions per ATC class)	Mean (Median | SD)	4.70 (4 | 3.90)

From incident aNSCLC diagnosis, mean survival was 533 days (95% CI: 508-558), and median survival was 351 days (95% CI: 329-366). Percentage of patients still alive after 3/6/9/12 months was 90.47%/73.81%/59.45% and 47.90% respectively. Median OS for mutation-positive patients was 571 days (95% CI: 471–709); mean survival 703 days (95% CI: 621-785).

1,672 patients started a first-line systemic treatment. From date of treatment start, mean survival was 481 days (95% CI: 456-506), and median survival was 301 days (95% CI: 280-321) (see Figure 1); for mutation-positive patients, mean survival was 665 days (95% CI: 582-748) and median survival 513 days (95% CI: 442-647). Percentage of patients still alive 3/6/9/12 months following the start of the 1L treatment was 82.24%/66.45%/53.23%/42.88% respectively.

43.91% of 517 patients diagnosed in 2012 were alive after 12 months, using date of incident aNSCLC diagnosis as index date. For patients first diagnosed in the years 2013/2014/2015, respective numbers were 52.83% (2013); 49.30% (2014) and 45.61% (2015).

Figure 1 Kaplan Meier survival estimates from treatment lines



Number of patients at risk after …	start of 1L	start of 2L	start of 3L	incident aNSCLC diagnosis
0 days	1672	635	242	1741
365 days	716	156	51	834
730 days	270	49	8	336
1095 days	108	11	2	149
1460 days	30	1	0	44
1825 days	0	0	0	4

In a multivariable Cox regression analysis (see Figure 2) exploring predictors of early death, the following were identified as poor prognostic factors: age (HR:1.01), tumor stage IV at diagnosis (HR:1.65), and number of prescribed chronic drugs in the 12 months before diagnosis (HR:1.03). Conversely, female gender (HR: 0.74) and positive mutation status (HR: 0.65 –in comparison to a negative status or no testing) were associated with a decreased risk of mortality.

Figure 2 Multivariate Cox analysis - Contributing factors to overall survival

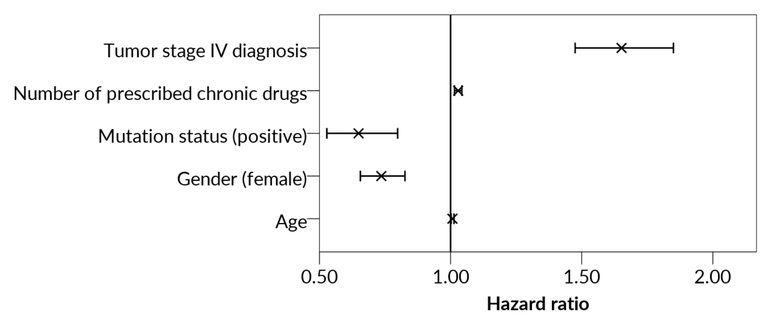


Table 2 Overall Survival

Overall survival of patients since...	N	Median survival in days (CI)	Mean survival in days (CI)
start of 1L	**1,672**	301 (280-321)	481.01 (455.54-506.47)
start of 2L	**635**	194 (170-216)	346.82 (311.70-381.94)
start of 3L	**242**	174 (144-205)	290.11 (247.00-333.23)
incident aNSCLC diagnosis	**1741**	351 (331 - 371)	532.91 (507.59 - 558.23)

Strengths and limitations

In contrast to most real-world evidence collected in e.g. retrospective chart reviews or registry datasets, that consist of highly selected study sites and patient populations, this study could avoid the inherent selection bias. However, as mutation status and staging was not readily available in German health claims data, proxies needed to be defined. Thus there remains a degree of uncertainty with regard to the accuracy of the study findings.

Conclusion

Median OS reported in recent clinical trials for 1L agents new on the market (e.g. Nivolumab and Pembrolizumab) was reported to be between 14.4-22.1 months since start of 1L treatment [4-6]. In our observational cohort it was lower (11.5 months; mutation-positive: 18.8 months), and did not change since 2012. Hence, despite the introduction of new targeted and immunotherapy treatments in aNSCLC, the real-world survival prognosis for patients in advanced stages of NSCLC did not improve. Therefore, there is an urgent need to optimize the real-world treatment of these patients.

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Keywords

Observational research, claims data analysis, non-small cell lung cancer (NSCLC), advanced non-small cell lung cancer (aNSCLC), overall survival (OS), real-world treatment

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