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Research Article

Treatment, outcome and quality of life of 1239 patients with advanced non-small cell lung cancer – final results from the prospective German TLK cohort study

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ABSTRACT

Objectives: Real-life data on advanced non-small cell lung cancer (NSCLC) are centrally important to complement the results from clinical trials and to improve the standard of care. We present data on the choice of systemic first- and second-line treatment, number of treatment lines, survival and longitudinal data on health-related quality of life (HRQOL) of patients treated by medical oncologists in Germany.

Materials and methods: 1239 patients with advanced NSCLC were recruited at start of first-line therapy into the prospective German clinical cohort study TLK (Tumour Registry Lung Cancer) by 107 sites between February 2010 and December 2013 and followed-up until January 2016. HRQOL was assessed using the EORTC QLQ-C30 and LC13 questionnaires.

Results: Most patients receive carboplatin- or cisplatin-based doublet chemotherapy in first-line treatment. The choice of platinum agent did neither influence the outcome: median overall survival (OS) was 12.2 months for carboplatin combinations (95% confidence interval [CI] 10.0–13.8) and 11.9 months for cisplatin combinations (95% CI 10.2–13.8), nor did it have a marked impact on the HRQOL. Patients receiving cisplatin were younger and fitter at start of therapy than patients receiving carboplatin or mono-chemotherapy. The longitudinal HRQOL analysis revealed the main symptoms that need to be addressed in follow-up care, irrespective of the platinum agent: fatigue, nausea, dyspnoea and pain. The patients receiving targeted therapies with tyrosine kinase inhibitors (TKIs) had a median OS of 22.1 months (95% CI 15.0–35.1) and considerably superior HRQOL.

Conclusion: There was no difference in outcome between the platinum compounds cisplatin and carboplatin in first-line treatment of advanced NSCLC in routine care. This is the first report of longitudinal HRQOL data comparing treatments, showing no difference between carboplatin and cisplatin.

Abbreviations: ALK, Anaplastic Lymphoma Kinase; BMI, body mass index; CCI, Charlson Comorbidity Index; CI, confidence interval; CR, complete response; CRISP, clinical research platform into molecular testing, treatment and outcome of non-small cell lung carcinoma patients; eCRF, electronic case report form; ECOG, Eastern Cooperative Oncology Group; EGFR, Epidermal Growth Factor Receptor; EORTC, European Organisation for Research and Treatment of Cancer; HRQOL, health-related quality of life; LC, lung cancer; mOS, median overall survival; NSCLC, non-small cell lung cancer; OS, overall survival; PD, progressive disease; PFS, progression-free survival; PR, partial response; PRO, patient-reported outcomes; RECIST, Response Evaluation Criteria in Solid Tumors; ROS1, c-ros oncogene 1; TKI, tyrosin kinase inhibitor; SCLC, small cell lung cancer; SD, stable disease; TLK, Tumour Registry Lung Cancer; TTD, time to deterioration

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1. Introduction

Lung cancer is one of the most frequent malignancies in Germany, approximately 59,900 new diagnoses are expected in 2020 [1]. The majority of patients are diagnosed with advanced or metastatic disease. The prognosis for patients with advanced disease is unfavourable, the relative 5-year survival rate is only 4% [2]. The most common histologic subtype is non-small cell lung carcinoma (NSCLC), which accounts for more than 85% of the cases [3]. Recently, the focus of research has shifted to the molecular profiling of lung cancer and genetic alterations in multiple targetable oncogenes have been identified [4,5]. Targeted therapies have been approved for EGFR-mutations (15% of the European NSCLC cases [6]), ALK-translocations (4–5% of the NSCLC cases [7]) and ROS1-rearrangements (1–2% [8]). Tyrosine kinase inhibitors (TKIs) significantly improved the outcome and quality of life of patients with EGFR-mutations . However, about 80% of the patients with NSCLC are not eligible for currently available targeted therapy and receive platinum-based doublet chemotherapy, or mono-chemotherapy in case of very frail patients. The platinum-base (cisplatin or carboplatin) is combined with one of the third-generation drugs paclitaxel, docetaxel, pemetrexed, gemcitabine or vinorelbine, depending on the histological subtype. The choice between the platinum agents cisplatin or carboplatin has been subject of a long debate and was the focus of a review [10] as well as a recent meta-analysis [11]. Summing up the results for patients with advanced NSCLC, there was no difference between cisplatin-based and carboplatin-based therapy regarding overall survival and one-year survival rate [11]. Cisplatin is associated with slightly lower costs than carboplatin [12]. However, cisplatin has a higher toxicity profile including nausea and vomiting, neutropenia, renal insufficiency, neurotoxicity and alopecia [13]. As the balance between health-related quality of life (HRQOL) and survival is paramount in the palliative setting, treatment decision is dependent on the individual patients' performance status and comorbidities. Data on treatment in routine practice are needed to understand treatment decision making and effectiveness of treatments in order to assess and improve quality of care – especially as patients enrolled in clinical trials are often highly selected.

In this article, we present comprehensive real world data from the prospective clinical cohort study TLK (Tumour Registry Lung Cancer), which observed patients with NSCLC treated by office-based medical oncologists and clinics in Germany from 2010 until 2016. We have shown before that, compared to patients enrolled in randomized clinical trials, patients with metastatic NSCLC treated in routine care were on average several years older, a significant proportion had an inferior performance status and more comorbidities at start of first-line treatment [14,15]. In the analysis at hand, we examined the data of 1239

Table 1
Patient and tumour characteristics.

Characteristic	Carboplatin + X[d] (n = 566)		Cisplatin + X[d] (n = 433)		Mono-CTx[d] (n = 184)		TKI (n = 56)		All patients (n = 1239)	
	Median	Min–Max	Median	Min–Max	Median	Min–Max	Median	Min–Max	Median	Min–Max
Age at start of therapy, years	69.0	42–88	62.2	33–82	72.5	28–87	70.8	28–86	67.1	28–88
	Mean	StD	Mean	StD	Mean	StD	Mean	StD	Mean	StD
BMI at enrolment, kg/m^2	25.5	4.9	25.2	4.4	25.5	4.3	25.4	4.2	25.4	4.6
Sex	n	%	n	%	n	%	n	%	n	%
Female	155	27.4%	141	32.6%	52	28.3%	31	55.4%	379	30.6%
Male	411	72.6%	292	67.4%	132	71.7%	25	44.6%	860	69.4%
Patients with comorbidity [a]										
Any comorbidity [b]	457	80.7%	318	73.4%	152	82.6%	46	82.1%	973	78.5%
CCI = 0 [c]	303	53.5%	287	66.3%	81	44.0%	35	62.5%	706	57.0%
CCI ≥1[c]	263	46.5%	146	33.7%	103	56.0%	21	37.5%	533	43.0%
Chronic lung disease	143	25.3%	102	23.6%	62	33.7%	11	19.6%	318	25.7%
Diabetes mellitus	95	16.8%	50	11.5%	43	23.4%	11	19.6%	199	16.1%
Hypertension	239	42.2%	147	33.9%	94	51.1%	25	44.6%	505	40.8%
Performance status [a]										
ECOG = 0	97	17.1%	141	32.6%	39	21.2%	21	37.5%	298	24.1%
ECOG = 1	309	54.6%	197	45.5%	78	42.4%	21	37.5%	605	48.8%
ECOG ≥2	94	16.6%	43	9.9%	44	23.9%	10	17.9%	191	15.4%
Missing	66	11.7%	52	12.0%	23	12.5%	4	7.1%	145	11.7%
Metastasis at start of 1st-line										
Yes	310	54.8%	244	56.4%	90	48.9%	34	60.7%	678	54.7%
No	48	8.5%	30	6.9%	17	9.2%	6	10.7%	101	8.2%
Missing	208	36.7%	159	36.7%	77	41.8%	16	28.6%	460	37.1%
Smoking status [a]										
Current Smoker	114	20.1%	100	23.1%	29	15.8%	5	8.9%	248	20.0%
History of smoking (former or ever)	302	53.4%	258	59.6%	108	58.7%	27	48.2%	695	56.1%
Never Smoker	66	11.7%	36	8.3%	18	9.8%	19	33.9%	139	11.2%
Unknown	84	14.8%	39	9.0%	29	15.8%	5	8.9%	157	12.7%
Histology [a]										
Squamous carcinoma	190	33.6%	105	24.2%	78	42.4%	4	7.1%	377	30.4%
Adenocarcinoma	323	57.1%	300	69.3%	90	48.9%	48	85.7%	761	61.4%
Large-cell carcinoma	22	3.9%	12	2.8%	3	1.6%	2	3.6%	39	3.1%
Other	23	4.1%	11	2.5%	11	6.0%	2	3.6%	47	3.8%
Missing	8	1.4%	5	1.2%	2	1.1%	0	0.0%	15	1.2%

Abbreviations: BMI, body mass index; Car, Carboplatin; Cis, Cisplatin; Max, maximum; Min, minimum; StD, standard deviation; TKI, tyrosine kinase inhibitor; X, any substance other than carboplatin or cisplatin.

[a] At enrolment.

[b] At least one comorbidity according to Charlson or additional concomitant diseases.

[c] Charlson Comorbidity Index (CCI) according to Quan et al. [17,18].

[d] Additional bevacizumab was given to 109 (19%) of the patients receiving Car + X, 66 (16%) of the patients receiving Cis + X and 11 (6%) of the patients receiving mono-chemotherapy.