PROSPECTIVE GERMAN REGISTRY CRISP, AIO-TRK-0315

REAL-WORLD TREATMENT AND OUTCOME OF PATIENTS WITH STAGE II-III NSCLC IN GERMANY FROM 2018-24

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BACKGROUND

In the management of locally advanced non-small cell lung cancer (NSCLC), recent therapeutic advances have significantly expanded treatment options. The approval of TKIs and CPIs has enabled the possibility of individual maintenance therapies following adjuvant therapy or radiochemotherapy. Chemoimmunotherapy in the neoadjuvant setting allows for a reassessment of operability. Treatment options and patient eligibilities are determined by clinical stage, resectability of tumor, biomarker test results and patient characteristics. Limited data exist on the distribution of treatment strategies in real world treatments, and the proportion of patients eligible for emerging therapies. Here we present data on biomarker testing, treatment sequences, and outcomes after the most frequent treatment strategies in real-world patients with stage II and III NSCLC in Germany.

METHODS

CRISP is a prospective, multi-center clinical research platform that observes treatment reality of patients with lung carcinoma in Germany. Between August 2018 and December 2023, 144 sites from all sectors of cancer care in Germany recruited 2376 patients with stage I-III NSCLC at the start of antitumoral treatment (surgery, neoadjuvant systemic therapy, radiotherapy or radiochemotherapy). Information on patients' demographic and clinical (tumor) characteristics, diagnostic measures and biomarker testing are documented at inclusion. During follow-up, data on all antitumoral treatments, further biomarker testing, course of disease including potential palliative treatments and outcome are recorded. Patients are treated according to physician's choice based on the patients' individual needs and schedules. All data are collected from patients' records. Follow-up time for patients within this analysis was between 1.5 and 6 years, at data base cut on March 31, 2025.

RESULTS

Out of 2153 evaluable patients, 1849 patients were diagnosed with NSCLC Stage II (n = 512) or III (n = 1337). Patient and tumor characteristics are displayed in **Table 1.**

For patients with Stage II tumors, testing for PD-L1 expression increased over time rising from 26 % in 2018 to 82 % in 2023. For patients with Stage III tumors, testing for PD-L1 expression was already established, but further increased from 47 % to 83 % between 2018 and 2023. Test rate and details on test results are shown in **Figure 1 A and B.**

Testing for EGFR alterations started with approval of targeted treatments and increased from 13 % in 2018 to 61 % in 2023 in patients with stage II and from 25 % in 2018 to 52 % in 2023 in patients with stage III tumors. Overall, in 13 % of tested patients an EGFR-alteration was detected. **(Figure 1 C and D)**

Patients with stage II tumors went through a variety of treatment paths but mainly had an initial surgery (77 %, n = 392) and afterwards most of these patients received adjuvant systemic therapy (62 %, n = 315) including immunotherapy or EGFR inhibitors. **(Figure 2A)**

Diversity of treatment paths for Stage III patients was even greater than for Stage II patients. 37% of patients (n = 495) underwent initial surgery and for 38 % (n = 502) received definitive radiochemotherapy with and without following consolidation with immunotherapy was documented. **(Figure 2B)**

Median RFS was 66.7 [95 % CI 49.9, NA] months for stage II and 22.6 [95 % CI 17.1, 28.3] for stage III patients with adjuvant systemic therapy after RO resection and independent of the drugs administered. Five-year survival rate for these groups were 81.0 % [95 % CI 73.9, 86.3] and 52.9 % [95 % CI 43.3, 61.6], respectively. **(Figure 3 A and B)**

Median PFS from end of radiochemotherapy was 6.0 [95 % CI 5.1, 7.2] months for stage III patients who did/could not receive immunotherapy and 14.8 [95 % CI 11.8, 19.2] months for patients with immunotherapy. Median overall survival for these groups was 18.5 [95 % CI 16.1, 23.2] and 41.1 [95 % CI 27.7, NA] months, respectively. **(Figure 3 C and D)**

DISCUSSION

Treatment options in stage II-III NSCLC increased, resulting in increasingly complex and diversified treatment sequences. Clinical guidelines regarding molecular biomarker testing and novel therapeutic agents are being rapidly incorporated into standard clinical practice. Real-world effectiveness data demonstrate promising outcomes for patients who are eligible for new therapeutic approaches. Nevertheless, significant challenges persist in optimizing sequential treatment strategies, particularly regarding operability and the implementation of (neo)adjuvant or perioperative therapeutic paradigms across the heterogeneous patient population.

References:

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Conflicts of Interest:
Wilfried E.E. Eberhardt has received honoraria for advisory board function from Astra Zeneca, BMS, MSD, Pfizer, Sanofi, Daiichi-Sankyo, Regeneron, Novartis, Pierre Fabre, Roche, Amgen, Lilly Deutschland, Boehringer Ingelheim.

Further he has received honoraria for educational lectures from Astra Zeneca, BMS, MSD, Pfizer, Sanofi, Daiichi-Sankyo, Regeneron, Novartis, Pierre Fabre, Roche, Amgen, Lilly Deutschland, Boehringer Ingelheim and onkowissen.de.

The institution has received a research grant for an investigator initiated trial from Astra Zeneca.

ClinicalTrials.gov Identifier:
NCT02622581

Additional information:
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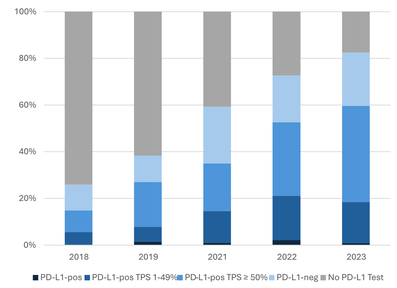
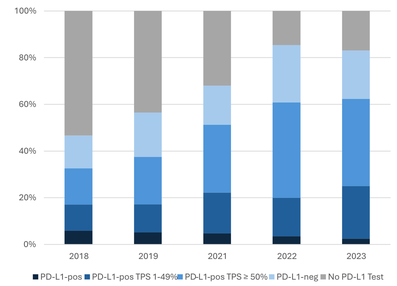
Figure 1: Test rates and results PD-L1 and EGFR

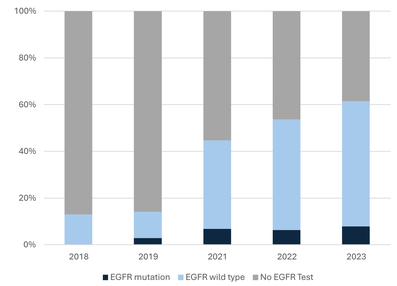
A: PD-L1 stage II



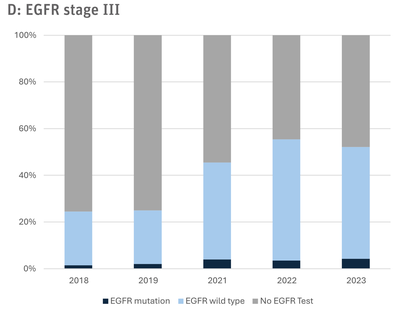
B: PD-L1 stage III



C: EGFR stage II



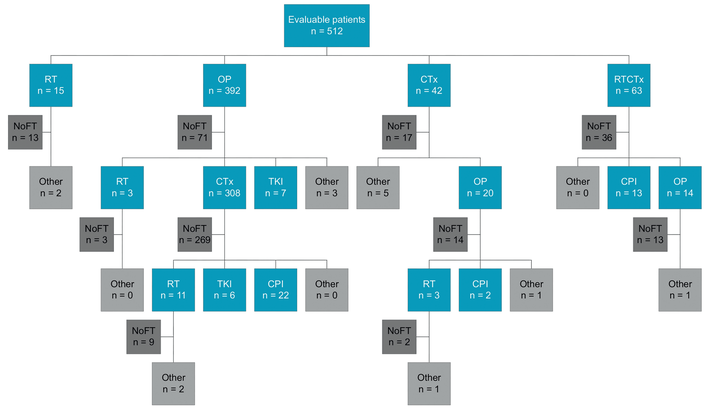
D: EGFR stage III



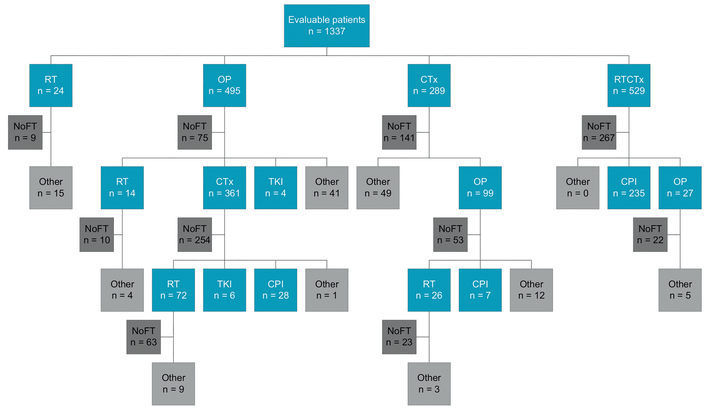
Recruitment was paused from February to December 2020 and since January 2024. Therefore, the years 2020 and 2024 are not shown due to small case numbers. | "PD-L1 pos" includes patients for whom TPS is unknown but documented as "positive". | "EGFR mutation" includes all patients with a detected mutation, regardless of whether the mutation is druggable. | "No Test" includes patients for whom it is unknown whether a test was performed.

Figure 2: Sequential treatment

A: Stage II



B: Stage III



CPI - checkpoint inhibitor | CTx – systemic therapy | NoFT – no further treatment for the primary tumour documented until database cut | OP – surgery | Other – one or more further OP, CPI, CTx, RT, RTCTx or TKI | RT – radiotherapy | RTCTx – radiochemotherapy | TKI – tyrosine kinase inhibitor | Further treatments following TKI or CPI are not shown due to lack of space. | Strategies are presented according to the actual documented sequential treatment. The proportion of documented surgeries only and systemic therapies only is likely over- and the proportion of (neo)adjuvant systemic therapies and radiochemotherapies underrepresented because of delayed documentation of surgery (OP), adjuvant systemic therapy and radiotherapy as part of a radiochemotherapy.

Table 1: Characteristics at diagnosis

	Stage II	Stage III
Patients (N)	512	1337
Sex (n)	512	1337
Female	187 (36.5 %)	547 (40.9 %)
Age at diagnosis in years (n)	512	1337
Median [25 %/75 % quantiles]	68.0 [61.8/72.7]	66.5 [60.8/72.3]
ECOG at diagnosis		
0	244 (47.7 %)	626 (46.8 %)
1	211 (41.2 %)	542 (40.5 %)
≥ 2	28 (5.5 %)	68 (5.1 %)
Unknown to site	29 (5.7 %)	101 (7.6 %)
Charlson Comorbidity Index (CCI [0 – 24] at diagnosis		
0	212 (41.4 %)	627 (46.9 %)
1	187 (36.5 %)	430 (32.2 %)
≥ 2	113 (22.1 %)	280 (20.9 %)

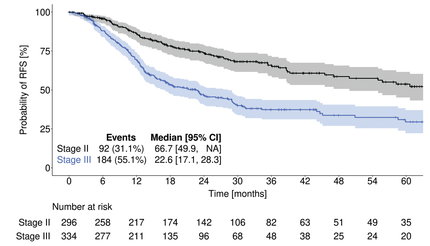
Table 1: Characteristics at diagnosis

	Stage II	Stage III
Smoking status at diagnosis		
Current Smoker	140 (27.3%)	332 (24.8 %)
Ex-Smoker (heavy)	242 (47.3 %)	638 (47.7 %)
Ex-Smoker (intensity unknown)	31 (6.1 %)	102 (7.6 %)
Ex-Smoker (light)	42 (8.2 %)	99 (7.4 %)
Never Smoker	39 (7.6 %)	106 (7.9 %)
Unknown to site	18 (3.5 %)	60 (4.5 %)
Missing	0 (0.0%)	0 (0.0%)
Histology		
Squamous	203 (39.6 %)	529 (39.6 %)
Non-squamous	309 (60.4 %)	808 (60.4 %)
Missing	0 (0.0 %)	0 (0.0 %)

ECOG: Eastern Cooperative Oncology Group performance status
CCI: according to Charlson et al. 1987; current weighting according to Quan et al. 2011. Range 0-24.
Age: For some patients date of diagnosis was not documented yet and age at diagnosis could not be calculated.

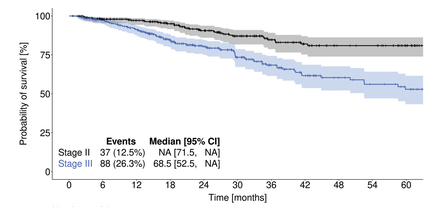
Figure 3: Time to event analyses (calculated by Kaplan-Meier method)

A: Recurrence free survival of Stage II and Stage III patients with adjuvant systemic therapy after RO resection



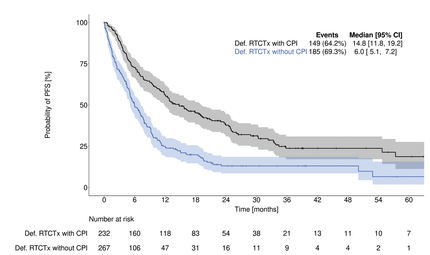
Relapse-free survival (RFS) is defined as the time between RO resection and recurrence of the tumor (local or distant) or death. Patients without event are censored with their individual date of last contact.

B: Overall survival of Stage II and Stage III patients with adjuvant systemic therapy after RO resection



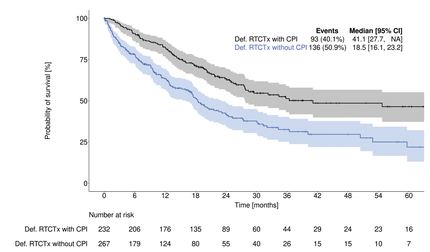
Overall survival (OS) is defined as the time between RO resection and death. Patients without event are censored with their individual date of last contact.

C: Progression free survival of Stage III patients with definitive radiochemotherapy with and without immunotherapy



Progression-Free Survival (PFS) describes the time from the end of definitive radiochemotherapy until first tumor progression or death. Patients without event are censored at last contact.

D: Overall survival of Stage III patients with definitive radiochemotherapy with and without immunotherapy



Overall survival (OS) is defined as the time between end of definitive radiochemotherapy and death. Patients without event are censored with their individual date of last contact.