FIRST REAL-WORLD EVIDENCE OF NSCLC STAGE I, II AND III IN GERMANY - AIO-TRK-0315

CLINICAL RESEARCH PLATFORM INTO MOLECULAR TESTING, TREATMENT AND OUTCOME OF NON-SMALL CELL LUNG CARCINOMA PATIENTS

Stuschke M[1],
Eberhardt W[2,3],
Passlick B[4],
Gröschel A[5],
Christopoulos P[6],
Reck M[7],
Grah C[8],
Hoffknecht P[9],
Ludwig P[10],
Hipper A[10],
Chiabudini M[11],
Spring L[12],
Jänicke M[12],
Andres-Pons A[12],
Christoph D C[13],
Bernhardt C[14],
Reiser M[15],
Nusch A[16],
Sebastian M[17],
Griesinger F[18],
Thomas M[6].

[1] Department of Radio Oncology, Westgerman Cancer Centre, Essen/DE,
[2] Department of Medical Oncology, Westgerman Cancer Centre, Essen/DE,
[3] Department of Thoracic Oncology, Ruhrlandklinik, Essen/DE,
[4] Department of Thoracic Surgery, Universitätsklinikum Freiburg, Freiburg/DE,
[5] Department of Internal Medicine, Pneumology, Clemenshospital Münster, Muenster/DE,
[6] Thoracal Clinic and National Center for Tumor Diseases, Translational Lung Research Center Heidelberg (TLRC-H), member of the German Center for Lung Research (DZL), Heidelberg University Hospital, Heidelberg/DE,
[7] Department of Oncology, LungenClinic Grosshansdorf, German Center for Lung Research, Grosshansdorf/DE,
[8] Department of Pneumology and Lung Cancer Centre, Gemeinschaftskrankenhaus Havelhöhe gGmbH, Berlin/DE,
[9] Department of Thoracic Oncology, Niels-Stensen-Kliniken, Franziskus-Hospital Harderberg, Georgsmarienhütte/DE,
[10] Project Management, AIO-Studien-gGmbH, Berlin/DE,
[11] Statistics, IOMEDICO, Freiburg/DE,
[12] Clinical Epidemiology and Health Economics, IOMEDICO, Freiburg/DE,
[13] Medical care centre Hematology and Onocology Essen gGmbH, Essen/DE,
[14] Medical Center for Hematology and Oncology, Dortmund/DE,
[15] PIQM-Office for Internal Oncology and Hematology, Cologne/DE,
[16] Department for Hematology and Internal Oncology, Cancer Centre Ratingen, Ratingen/DE,
[17] Medical Clinic II - Hematology, Oncology, University Hospital Frankfurt, Frankfurt/DE,
[18] Department for Hematology and Oncology, Pius Hospital Clinic Oldenburg, Oldenburg/DE.

Corresponding author:
Dr. med. Martin Stuschke, martin.stuschke@uk-essen.de

Conflicts of Interest:
M. Stuschke: Advisory board function at AstraZeneca, Bristol-Myers Squibb, Sanofi-Aventis and Janssen-Cilag; research grants from AstraZeneca

Funding:
CRISP Satellite NSCLC stage I-III II is supported by grants from AstraZeneca GmbH, Bristol-Myers Squibb GmbH & Co.KGaA, MSD Sharp & Dome GmbH and Roche Pharma AG. None of the funders had any role in study design, data collection and analysis, interpretation of results, decision to publish,or preparation of this analysis.

Acknowledgements:
The CRISP Registry group thanks all participating patients, physicians and study teams.

ClinicalTrials.gov Identifier:
NCT02622581

IASLC 2022 World Conference
6. - 9. August, Vienna, Austria
Programm number: Abstract #2240

BACKGROUND

Lung cancer is the most common cancer diagnosed and the leading cause of cancer death worldwide. In Germany it is the second most common cancer diagnosis in men and the third most common in women. Non-small cell lung cancer (NSCLC) accounts for 85% of the cases.

CRISP (Clinical Research platform Into molecular testing, treatment and outcome of (non-)Small cell lung carcinoma Patients) is a non-interventional, prospective, multi-center clinical research platform whose aim is to understand current treatment reality of patients with lung cancer in Germany. Here we present data of patients diagnosed with early-stage NSCLC I-III (IIIB/C only if treated with curative intent), including first outcome data in routine-care.

METHODS

Since August 2018 over 100 sites in Germany (cancer centres, hospitals and office-based oncologists) have recruited more than 1500 patients diagnosed with NSCLC stage I, II or III (recruitment of stage I possible from December 2020). Detailed patient and tumor characteristics, treatment strategies, outcome and PRO (patient-reported outcome) data are collected and analysed. At the time of database cut (30 June 2021) 1010 patients had been recruited in CRISP with NSCLC in stage I, II or III from 106 study sites (**Figure 1**). Here we present data on the first 810 patients, for whom at least the year of birth, sex and data on the initial treatment had been documented and who had been followed until 30 June 2021. The treatment of non-metastatic NSCLC is mostly driven by detailed therapeutic staging. Accordingly, data are analysed and results are shown in subgroups by clinical stage.

RESULTS

Patient and tumour characteristics

95% of the 810 patients' cases were discussed in a tumour board.

26% of patients were diagnosed with pretherapeutic stage II (5% with stage IIA, 21% with stage IIB), and 66% with stage III disease (32% with stage IIIA, 34% with stage IIIB/C). Only 1 % of the patients had a tumor in stage I; this is due to the difficulty of an early diagnosis as well as due to the later start of recruitment of patients with tumors in stage I in CRISP. The exact early stage could not be determined at diagnosis for 6% of the tumors. The most frequent tumour histologies were adenocarcinoma (52%) and squamous cell carcinoma (39%).

Median age at diagnosis was 66 years, 38% were women, 62% men, 83% of the patients had an ECOG 0/1. 80% of the patients presented with comorbidities; 47% had a Charlson comorbidity index of 0. Almost 70% of the patients were current smokers or heavy ex-smokers, while only 9% were never-smokers. (**Tables 1-2**).

Treatment reality - Sequential treatment

Treatment strategies were analyzed for patients with at least one year follow-up (**Figure 2**).

The most common treatment strategy for patients with clinical stage II tumors (n=188) was surgery (84%, n=157) followed by adjuvant chemotherapy (CTx) (75%, n=140).

For patients with clinical stage IIIA tumors (n=236) the most frequent treatment strategy was surgery (53%, n=124) followed by adjuvant CTx (37%, n=88). 27% of the patients (n=64) were treated with definitive radiochemotherapy (RTCTx).

For patients with stage IIIB/C tumors (n=249) the most frequent treatment was definitive RTCTx (n=131, 53%); 26% (n=64) started with CTx, and 18% (n=44) had initial surgery (followed mostly by CTx, n=36, 15%).

Biomarker Testing

Overall, 484 out of 810 tumors (60%) were tested for PD-L1.

80% (n=131) of the non-resectable stage III tumors who were treated with RTCTx (n=164) were tested for PD-L1 expression. 80 patients had positive PD-L1 expression, which corresponds to 49% of all patients and 61% of tested patients (**Table 3**). Taken together, 44 out of 68 durvalumab-eligible patients (best response CR/PR/SD) received consolidation therapy with durvalumab after RTCTx.

Outcome

Relapse-free survival (RFS), progression-free survival and overall survival (OS) were estimated with the Kaplan-Meier method.

Data for patients who received adjuvant chemotherapy after surgery are presented in **Figure 3** and **Figure 4**. The 2-year RFS rate [95% CI] was 76.9% [66.8, 84.3] and 51.5% [37.2, 64.1] for patients with tumors in stage II and IIIA, respectively. The 2-year OS rate [95% CI] was 90.0% [79.9, 95.1] for patients with tumors in stage II and 79.3% [66.3, 87.7] for patients with stage IIIA tumors.

Data for patients who were treated with radiochemotherapy are shown in **Figure 5** and **Figure 6**. The median PFS [95% CI] was 10.4 [7.2, 12.2] months (stage IIIA) and 9.2 [6.8, 11.2] months (stage IIIB/C). The median OS [95% CI] was 21.5 [15.1, 29.6] and 22.9 [19.7, NA] months for patients with stage IIIA and IIIB/C, respectively.

CONCLUSION

CRISP presents comprehensive current real-life data of patients with NSCLC in stage I, II or III covering all treatment settings in Germany. Patient characteristics reflect a typical population of patients with lung cancer. Most of the patients receive a sequential treatment according to the guidelines. With a longer recruitment and follow-up time, data on patients with stage I will be analysed, and further outcome data, including 5-year survival rates, will be presented.

Figure 1

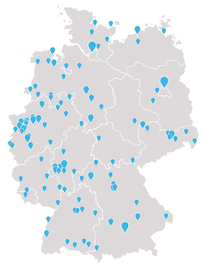

Figure 1: Active sites of the CRISP project in Germany (June 30, 2021)

Figure 2

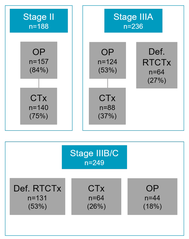

Figure 2: Most frequent sequential treatments by clinical stage

Patients with at least one year follow-up
CTx - systemic chemotherapy | OP - surgery | Def. RTCTx - definitive Radiochemotherapy

Table 3

	Total
Patients (N)	**164**
PD-L1 tested	
Yes n (%)	131 (79.9%)
No n (%)	25 (15.2%)
Unknown to site n (%)	1 (0.6%)
Missing n (%)	7 (4.3%)
Test results PDL1 (of all patients / of tested patients)[a]	
Positive n (%)	80 (48.8% / 61.1%)
Negative n (%)	44 (26.8% / 33.6%)
Unknown to site n (%)	1 (0.6% / 0.8%)
Missing n (%)	6 (3.7% / 4.6%)

Table 3 Testing for PD-L1 in patients with unresectable stage III NSCLC treated with radiochemotherapy.

All tests from diagnose to end of documentation are considered.
[a]Percentages are shown referring to all patients (N) and referring to patients tested for PD-L1 (n).

Table 1

	Stage I	Stage IIA	Stage IIB	Stage IIIA	Stage IIIB/C	Total
Patients (N)	10	38	173	259	279	810
Sex						
Male n (%)	5 (50.0%)	22 (57.9%)	110 (63.6%)	152 (58.7%)	181 (64.9%)	504 (62.2%)
Female n (%)	5 (50.0%)	16 (42.1%)	63 (36.4%)	107 (41.3%)	98 (35.1%)	306 (37.8%)
Age at primary diagnosis (years)						
n	10	38	173	259	279	809
Median	65.1	68.8	64.7	66.4	64.8	65.7
25-75% Quantile	62.9 - 68.8	64.7 - 74.1	59.6 - 71.0	60.0 - 71.4	59.0 - 71.8	59.6 - 71.5
ECOG at primary diagnosis						
0 n (%)	5 (50.0%)	20 (52.6%)	88 (50.9%)	124 (47.9%)	118 (42.3%)	376 (46.4%)
1 n (%)	3 (30.0%)	13 (34.2%)	60 (34.7%)	91 (35.1%)	108 (38.7%)	299 (36.9%)
≥ 2 n (%)	0 (0.0%)	1 (2.6%)	5 (2.9%)	11 (4.2%)	8 (2.9%)	26 (3.2%)
Unknown to site n (%)	2 (20.0%)	4 (10.5%)	20 (11.6%)	33 (12.7%)	45 (16.1%)	108 (13.3%)
Missing n (%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.1%)

Table 1 Patient characteristics by pre-therapeutic tumour stage - basic demographics

The difference between the total number of patients and the sum of patients with stage I, IIA, IIB, IIIA and IIIB/C corresponds to the patients for whom the clinical stage could not be determined.

Table 2

	Stage I	Stage IIA	Stage IIB	Stage IIIA	Stage IIIB/C	Total
Patients (N)	10	38	173	259	279	810
Any comorbidity[a]						
Yes n (%)	8 (80.0%)	33 (86.8%)	140 (80.9%)	211 (81.5%)	217 (77.8%)	648 (80.0%)
No n (%)	2 (20.0%)	5 (13.2%)	33 (19.1%)	48 (18.5%)	62 (22.2%)	161 (19.9%)
Missing n (%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.1%)
Charlson comorbidity index (CCI) [0-24][b]						
0 n (%)	4 (40.0%)	15 (39.5%)	76 (43.9%)	132 (51.0%)	134 (48.0%)	382 (47.2%)
1 n (%)	6 (60.0%)	13 (34.2%)	58 (33.5%)	74 (28.6%)	93 (33.3%)	260 (32.1%)
2 n (%)	0 (0.0%)	4 (10.5%)	23 (13.3%)	32 (12.4%)	30 (10.8%)	98 (12.1%)
3 n (%)	0 (0.0%)	4 (10.5%)	13 (7.5%)	12 (4.6%)	15 (5.4%)	46 (5.7%)
4 n (%)	0 (0.0%)	1 (2.6%)	1 (0.6%)	3 (1.2%)	2 (0.7%)	8 (1.0%)
≥ 5 n (%)	0 (0.0%)	1 (2.6%)	2 (1.2%)	6 (2.3%)	5 (1.8%)	15 (1.9%)
Missing n (%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.1%)
Smoking status[c]						
Current Smoker n (%)	2 (20.0%)	10 (26.3%)	46 (26.6%)	61 (23.6%)	67 (24.0%)	203 (25.1%)
Ex-Smoker (heavy) n (%)	7 (70.0%)	12 (31.6%)	84 (48.6%)	111 (42.9%)	123 (44.1%)	352 (43.5%)
Ex-Smoker (intensity unknown)	1 (10.0%)	3 (7.9%)	12 (6.9%)	27 (10.4%)	32 (11.5%)	81 (10.0%)
Ex-Smoker (light) n (%)	0 (0.0%)	4 (10.5%)	10 (5.8%)	13 (5.0%)	19 (6.8%)	51 (6.3%)
Never Smoker n (%)	0 (0.0%)	7 (18.4%)	12 (6.9%)	29 (11.2%)	19 (6.8%)	72 (8.9%)
Unknown to site n (%)	0 (0.0%)	2 (5.3%)	9 (5.2%)	18 (6.9%)	19 (6.8%)	50 (6.2%)
Missing n (%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.1%)

Table 2 Patient characteristics by pre-therapeutic tumour stage - comorbidities and smoking status at diagnosis

[a] Comorbidities according to CCI (Charlson Comorbity Index) and other comorbidities combined.
[b] Comorbidities by CCI according to Charlson et al. 1987; current weighting according to Quan et al. 2011. Range 0-24.
[c] Ex-smoker (light) - patients who quit smoking more than 15 years before diagnosis or who quit smoking and had smoked less than 10 pack years | Ex-smoker (heavy) - patients who quit smoking less than 15 years ago or who quit smoking but had smoked more than 10 pack years.
The difference between the total number of patients and the sum of patients with stage I, IIA, IIB, IIIA and IIIB/C corresponds to the patients for whom the clinical stage could not be determined.

Figure 3

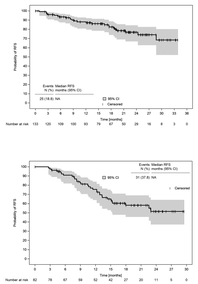

Figure 3: Relapse-free survival - Patients treated with adjuvant chemotherapy

(A) Stage II (B) Stage IIIA
Patients with at least one year follow-up.
Groups according to clinical stage.
RFS estimated with the Kaplan-Meier method.

Figure 4

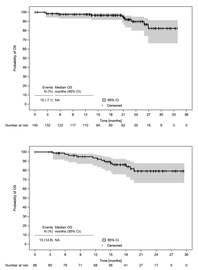

Figure 4: Overall survival - Patients treated with adjuvant chemotherapy

(A) Stage II (B) Stage IIIA
Patients with at least one year follow-up.
Groups according to clinical stage.
OS estimated with the Kaplan-Meier method.

Figure 5

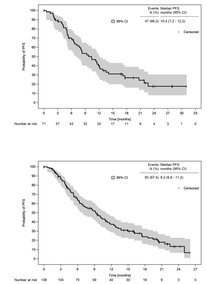

Figure 5: Progression-free survival - Patients treated with radiochemotherapy

(A) Stage IIIA (B) Stage IIIB/C
All patients with at least one year follow-up who were treated with radiochemotherapy.
Groups according to clinical stage.
PFS estimated with the Kaplan-Meier method.

Figure 6

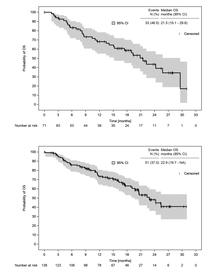

Figure 6: Overall survival - Patients treated with radiochemotherapy

(A) Stage IIIA (B) Stage IIIB/C
All patients with at least one year follow-up who were treated with radiochemotherapy.
Groups according to clinical stage.
OS estimated with the Kaplan-Meier method.