CLINICAL RESEARCH PLATFORM INTO MOLECULAR TESTING, TREATMENT AND OUTCOME OF NON-SMALL CELL LUNG CARCINOMA PATIENTS (CRISP) – AIO-TRK-0315

REAL-WORLD EVIDENCE OF NSCLC PATIENTS TREATED WITH RADIOCHEMOTHERAPY IN GERMANY

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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.

Locally advanced NSCLC is a heterogenous disease with several treatment approaches possible. Here we present data of patients treated with radiochemotherapy (RTCTx) in routine care in Germany.

METHODS

Since August 2018 over 100 sites in Germany (cancer centres, hospitals and office-based oncologists) have recruited more than 1600 patients diagnosed with NSCLC stage I, II or III. Detailed patient and tumour characteristics, treatment strategies, outcome and PRO (patient-reported outcome) data are collected and analysed. This analysis includes data on 270 patients treated with RTCTx for locally advanced NSCLC followed until 30 June 2021.

Type of radiochemotherapy

Sequential RTCTx is defined as no overlap in timing between chemotherapy and radiotherapy (the chemotherapy starts and ends before the radiotherapy). Induction chemotherapy with simultaneous RTCTx is defined when the chemotherapy starts before the radiotherapy and continues during the radiotherapy. Simultaneous RTCTx (without induction chemotherapy) is considered as a radiotherapy treatment with chemotherapy starting on the same day or later.

RESULTS

Out of 810 evaluable patients enrolled in CRISP until 30 June 2021, 270 were treated with RTCTx, either as definitive RTCTx or in a neoadjuvant/adjuvant setting.

Type of radiochemotherapy

The frequency of each type of RTCTx and the number of patients who had already started receiving an immune checkpoint inhibitor as consolidation treatment is shown in **Figure 1**.

Overall, most of the patients treated with RTCTx received simultaneous RTCTx, either with (n=119, 44%) or without (n=118, 44%) induction chemotherapy. 12% (n=32) of the patients were treated with sequential RTCTx.

Basic demographic characteristics and testing of PD-L1 expression for patients receiving each type of RTCTx are shown in **Table 1**.

Systemic therapy within the radiochemotherapy regimen

The most common chemotherapy regimen within the RTCTx treatment was the doublet cisplatin+vinorelbine (n=100, 37%) (**Figure 2A**). The number of patients treated with cisplatin or carboplatin is shown in **Figure 2B**.

Outcome

Progression-free survival (PFS) and overall survival (OS) were estimated with the Kaplan-Meier method for patients who received radiochemotherapy (RTCTx) and had been under observation for at least one year.

Out of 236 patients diagnosed with stage IIIA and under observation for at least one year, 71 patients (30%) received RTCTx (64 patients received definitive RTCTx). The median PFS [95% CI] of all patients with stage IIIA treated with RTCTx was 10.4 months [7.2-12.2] (**Figure 3A**) and the median OS [95% CI], 21.5 months [15.1-29.6] (**Figure 4A**).

249 patients were diagnosed with stage IIIB/C and had been under observation for at least one year. Out of those, 138 (55%) were treated with RTCTx (131 patients of them with definitive RTCTx). Their median PFS [95% CI] was 9.2 months [6.8-11.2] (**Figure 3B**), and their median OS [95% CI], 22.9 months [19.7-NA] (**Figure 4B**).

Consolidation therapy

80% (n=131) of patients with a non-resectable stage III tumour who received 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 2**).

Of 68 patients eligible for immunotherapy as consolidation treatment (best response CR/PR/SD), 44 received consolidation therapy with durvalumab (**Figure 5**).

CONCLUSION

CRISP presents comprehensive current real-life data of patients with NSCLC in stage I, II or III covering all treatment settings in Germany.

There are multiple different treatment options for patients with NSCLC in stage III. Definitive radiochemotherapy was the treatment of choice for a higher proportion of patients with tumours in stage IIIB/C than in stage IIIA. In line with guidelines recommendations, most of the patients received a platin-doublet and simultaneous radiochemotherapy. In routine care almost half of the patients are treated with a carboplatin-containing therapy. Median OS [95% CI] was 21.5 months [15.1-29.6] and 22.9 months [19.7-NA] for real-world patients with stage IIIA and IIIB/C, respectively, who had been treated with radiochemotherapy.

With a longer recruitment and follow-up time, CRISP will allow to study the efficacy of consolidation therapy after radiochemotherapy in a real-world setting in Germany.

Figure 1

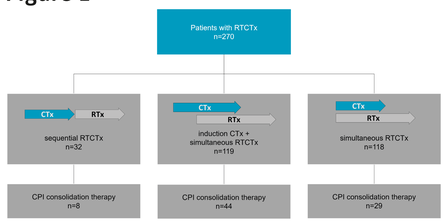

Figure 1: Flowchart - type of radiochemoteragy

CPI - Checkpoint inhibitor | CTx - chemotherapy | RTCTx - radiochemotherapy | RTx – radiotherapy
The number of patients with documented consolidation therapy at the time of database cut does not consider whether these patients fulfilled the requirements to receive consolidation treatment (e.g. response to radiochemotherapy and positive PD-L1 expression). Since follow-up and thus some radiochemotherapies were ongoing at the time of database cut, numbers of patients with consolidation therapy can still increase during the further course of the project.
For one patient the time sequence between chemotherapy and radiotherapy could not be determined due to partially missing dates.

Figure 2

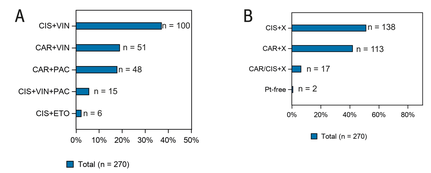

Figure 2: Most frequent chemotherapy regimen within the radiochemotherapy setting

(A) Top5 chemotherapy regimen
CAR - carboplatin | CIS - cisplatin | ETO - etoposide | PAC - paclitaxel | VIN - vinorelbine
(B) Treatments with cisplatin vs. treatments with carboplatin
CIS+X aggregates all the treatments with cisplatin and any other substance(s).
CAR+X aggregates all the treatments with carboplatin and any other substance(s).
CAR/CIS+X indicates a change from CIS+X to CAR+X or vice versa within one course of treatment.
Pt-free aggregates all treatments without CIS and without CAR.

Table 1

	Sequential RTCTx	Induction CTx + simulta-neous RTCTx	Simulta-neous RTC-Tx
Patients (N)	**32**	**119**	**118**
Age at primary diagnosis (years)			
n	32	119	118
Median	66.9	63.5	67.2
25-75% Quantile	61.3 - 74.6	57.5 - 71.2	60.6 - 71.6
Charlson Comorbidity Index at inclusion			
0 n (%)	16 (50.0%)	55 (46.2%)	56 (47.5%)
1 n (%)	9 (28.1%)	42 (35.3%)	39 (33.1%)
≥ 2 n (%)	7 (21.9%)	22 (18.5%)	23 (19.5%)
ECOG at primary diagnosis			
0 n (%)	13 (40.6%)	47 (39.5%)	52 (44.1%)
1 n (%)	11 (34.4%)	48 (40.3%)	46 (39.0%)
≥ 2 n (%)	2 (6.3%)	4 (3.4%)	9 (7.6%)
Unknown to site n (%)	6 (18.8%)	20 (16.8%)	11 (9.3%)
PD-L1 tested (n)	**31**	**116**	**112**
Yes n (%)	25 (78.1%)	96 (80.7%)	90 (76.3%)
No n (%)	6 (18.8%)	19 (16.0%)	20 (16.9%)
Unknown to site n (%)	0 (0.0%)	1 (0.8%)	2 (1.7%)
PD-L1 test results (of all patients)			
Positive n (%)	16 (50.0%)	71 (59.7%)	49 (41.5%)
Negative n (%)	8 (25.0%)	22 (18.5%)	38 (32.2%)

Table 1 Patient characteristics by type of radiochemotherapy

CTx - chemotherapy | RTCTx - radiochemotherapy
ECOG: Eastern Cooperative Oncology Group performance status
For one patient the time sequence between chemotherapy and radiotherapy could not be determined due to partially missing dates.

Figure 3

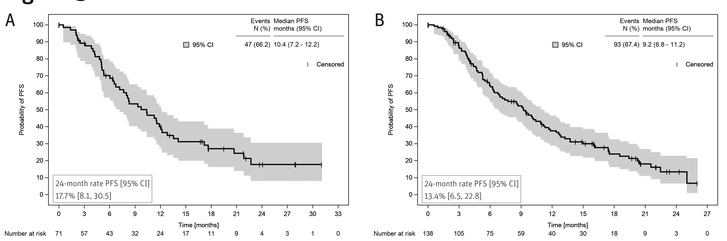

Figure 3: Progression-free survival (PFS) - Patients treated with radiochemotherapy

(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 4

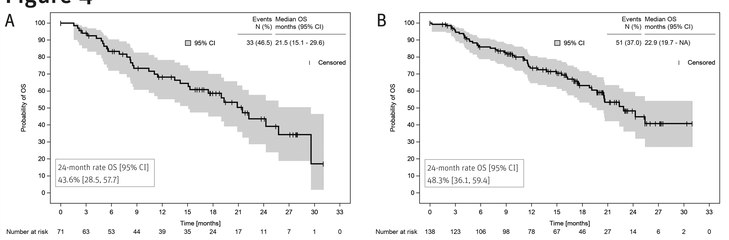

Figure 4: Overall survival (OS) - Patients treated with radiochemotherapy

(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.

Figure 5

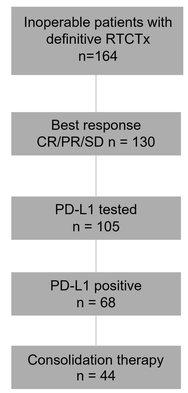

Figure 5: Patients eligible for immunotherapy as consolidation therapy

Please note that documentation was still ongoing for many patients and thus numbers might increase with a longer follow-up.

Table 2

	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 2: 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).
Please note that documentation was still ongoing for many patients and thus numbers might increase with a longer follow-up.