TREATMENT AND OUTCOME DATA FROM THE PROSPECTIVE GERMAN REGISTRY PLATFORM CRISP (AIO-TRK-0315)

CHECKPOINT INHIBITOR MONOTHERAPY IN POTENTIALLY STUDY-ELIGIBLE OR NON-STUDY-ELIGIBLE NSCLC PATIENTS IN THE GERMAN CRISP REGISTRY REAL-WORLD COHORT

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BACKGROUND

Treatment for metastatic non-small cell lung cancer (NSCLC) stratified according to biomarker testing results was shown in clinical trials to have beneficial outcomes. Whether these improvements carry over into real-world routine therapy is of great interest for patients and physicians. Here we used the prospective, national clinical research platform CRISP to compare patient characteristics and outcome of patients with PD-L1 TPS≥50% tumours treated with checkpoint inhibitor monotherapy (CPI) who are deemed either potentially study-eligible or non-study-eligible.

METHODS

CRISP is a prospective, observational, open, multicentre, interdisciplinary clinical research platform that collects data on all (sequential) treatments, patient and tumour characteristics, biomarker testing, clinical and patient-reported outcome in approximately 180 hospitals and practices in Germany. Currently 6300+ patients were recruited, who will be followed until death or end of project. Data from 473 patients with PD-L1 TPS≥50% and no EGFR- or ALK-Mutation recruited between 12/2015 and 06/2019 and receiving CPI monotherapy as 1st-line treatment was analysed. Patients were deemed study-eligible if they had the following characteristics: ECOG=0-1, Stage IV, no brain metastases, no HIV or second tumour and no prior (neo-)adjuvant therapies.

RESULTS

Of 473 analysed patients 191 (40.4 %) were potentially study-eligible in reflection of inclusion criteria for clinical trials KEYNOTE 42 and 24. 282 patients (59.6 %) were thus non-study-eligible representing the real-world patient population. The study-eligible and real-world group are similar in most patient characteristics. However, study-non-eligible-patients have more often an ECOG ≥ 2 (by definition) and non-squamous tumour histology (**Table 1**). In treatment response rates, CR/PR rates were comparable in both groups, but there was a markable greater proportion of patients with stable disease, which is also reflected in a longer median treatment duration for study-eligible-patients (**Table 2**). Rates of discontinued treatments due to toxicity or tumour progression were similar between both patient groups (**Table 2**). Potentially study-eligible patients however, had a longer PFS_{REG} (**Figure 1**) and OS (**Figure 2**), both from start of first-line treatment, than potentially non-study-eligible patients.

DISCUSSION

In our strictly observational study use of CPI monotherapy in PD-L1 TPS≥50% patients is resulting in improved treatment outcome. Potentially study-eligible patients are profiting from this improvement. However, about 60 % of the analysed German patients in routine care are potentially non-study-eligible and for them improvement is substantially less in terms of both PFS_{REG} and OS. As response rates and toxicity are comparable between groups, these differences seem to be mostly due to different rates of stable disease. However, some limitations apply as Best Responses in CRISP are assed by treating physicians at different times and with different methods, as part of real-world routine care. Likewise, the PFS_{REG} can only be seen as the closest possible estimation to PFS in clinical trials, as tests for tumour progression also vary between patients in terms of time intervals and examination methods.

CONCLUSION

In recent years the use of CPI monotherapy in PD-L1 TPS ≥ 50 % patients increased in Germany, resulting in improved treatment outcome. Potentially study-eligible patients account for about 40 % of analysed patients and are profiting more than potentially non-study-eligible patients. The impact of CPI combination therapies or treatment without CPI on both patient groups, will be subject of future analyses.

Figure 1

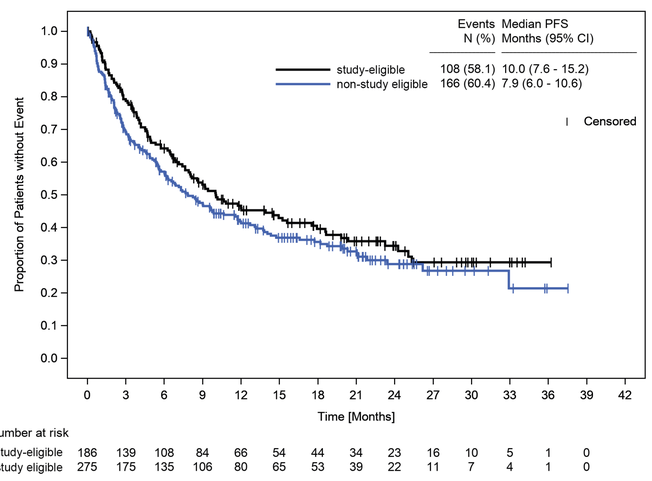

Figure 1: registry specific PFS (PFS_{REG}) by study eligibility

Figure 2

Figure 2: Overall survival by study eligibility

Table 1

	study eligible	non-study-eligible	total
Patients N	191	282	473
Age (n)			
Median (Years)	68.0	68.0	68.0
25th / 75th quantile	62.0 - 75.0	60.0 - 75.0	61.0 - 75.0
Missing n (%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Sex (n)			
Male n (%)	114 (59.7%)	179 (63.5%)	293 (61.9%)
Female n (%)	77 (40.3%)	103 (36.5%)	180 (38.1%)
Missing n (%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
ECOG (n)			
0 n (%)	67 (35.1%)	52 (18.4%)	119 (25.2%)
1 n (%)	124 (64.9%)	89 (31.6%)	213 (45.0%)
≥2 n (%)	0 (0.0%)	65 (23.0%)	65 (13.7%)
Unknown n (%)	0 (0.0%)	73 (25.9%)	73 (15.4%)
Missing n (%)	0 (0.0%)	3 (1.1%)	3 (0.6%)
Histology (n)			
Non-squamous n (%)	139 (72.8%)	229 (81.2%)	368 (77.8%)
Squamous n (%)	52 (27.2%)	53 (18.8%)	105 (22.2%)
Other alteration present			
ROS-1 n (%)	2 (1.0%)	4 (1.4%)	6 (1.3%)
BRAF n (%)	5 (2.6%)	8 (2.8%)	13 (2.7%)
Start year of 1st-line			
2015/16 n (%)	1 (0.5%)	0 (0.0%)	1 (0.2%)
2017 n (%)	63 (33.0%)	75 (26.6%)	138 (29.2%)
2018 n (%)	92 (48.2%)	141 (50.0%)	233 (49.3%)
2019 n (%)	35 (18.3%)	66 (23.4%)	101 (21.4%)
Status of 1st-line treatment (n)	191	282	473
Treatment ongoing n (%)	46 (24.1%)	63 (22.3%)	109 (23.0%)
Treatment discontinued, no 2nd-line n (%)	23 (12.0%)	37 (13.1%)	60 (12.7%)
Documentation completed during/after 1st-line (for other reasons than „death", e.g. LTFU) n (%)	18 (9.4%)	30 (10.6%)	48 (10.1%)
Death n (%)	55 (28.8%)	85 (30.1%)	140 (29.6%)
Treatment in 2nd-line n (%)	49 (25.7%)	67 (23.8%)	116 (24.5%)
PD-L1-targeted n (%)	5 (2.6%)	4 (1.4%)	9 (1.9%)
Pembrolizumab n (%)	5 (2.6%)	4 (1.4%)	9 (1.9%)
Not-PD-L1-targeted n (%)	44 (23.0%)	63 (22.3%)	107 (22.6%)
CT n (%)	38 (19.9%)	55 (19.5%)	93 (19.7%)
Other targeted n (%)	6 (3.1%)	8 (2.8%)	14 (3.0%)

Table 1: Patient characteristics and 1st-line treatment status by study eligibility
Age, ECOG and other alterations at start of 1st-line treatment; CT: chemo therapy

Table 2

	study eligible	non-study-eligible	total
Patients N	191	282	473
PFS_{REG} in months (n)	186	275	461
Median	10.0	7.9	9.0
95% CI	7.6, 15.2	6.0, 10.6	7.3, 10.8
Events n (%)	108 (58.1%)	166 (60.4%)	274 (59.4%)
OS in months (n)	184	274	458
Median	23.3	20.2	21.1
95% CI	16.5, 26.1	15.9, 26.2	16.6, 25.6
Events n (%)	84 (45.7%)	123 (44.9%)	207 (45.2%)
Patients with completed treatments (n)	144	219	363
Treatment duration in days			
Median	128.5	86.0	106.0
25th / 75th quantile	47.0 - 310.5	27.0 - 225.0	43.0 - 253.0
Missing n (%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Reason for end of treatment (n)			
Toxicity n (%)	14 (9.7%)	22 (10.0%)	36 (9.9%)
Progression n (%)	58 (40.3%)	78 (35.6%)	136 (37.5%)
Guidelines n (%)	11 (7.6%)	15 (6.8%)	26 (7.2%)
Other n (%)	58 (40.3%)	100 (45.7%)	158 (43.5%)
Missing n (%)	3 (2.1%)	4 (1.8%)	7 (1.9%)
Best Response (n)			
CR n (%)	2 (1.4%)	4 (1.8%)	6 (1.7%)
PR n (%)	30 (20.8%)	47 (21.5%)	77 (21.2%)
SD n (%)	39 (27.1%)	38 (17.4%)	77 (21.2%)
PD n (%)	32 (22.2%)	45 (20.5%)	77 (21.2%)
Unknown n (%)	40 (27.8%)	80 (36.5%)	120 (33.1%)
Missing n (%)	1 (0.7%)	5 (2.3%)	6 (1.7%)

Table 2: Outcome by study eligibility
CR: Complete remission; PR: partial remission; SD: stable disease; PD: progressive disease
For comparison, median OS was 30.0 months (KEYNOTE-024) and 20.0 months (KEYNOTE-042) in the intervention and 14.2 months (KEYNOTE-024) and12.2 months (KEYNOTE-042) months in the control group. Median PFS was 10.3 months (KEYNOTE-024) and 6.5 months (KEYNOTE-042) in the intervention and 6.0 months (KEYNOTE-024) and 6.4 months (KEYNOTE-042) in the control group. However, in the CRISP registry there are no specifications as to the timing, frequency or criteria of tumor assessment and thus registry-PFS and -response data should be considered as the best clinical approximation and might not be identical to the PFS/response determined in clinical trials.

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