

### DATA FROM THE GERMAN RESEARCH PLATFORM CARAT



# **SEQUENTIAL TREATMENT PATTERNS OVER** TIME FOR ADVANCED RENAL CELL CARCINOMA

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# **INTRODUCTION**

In Germany, about 95% of neoplasms of the kidney are renal cell carcinomas (RCC; ICD-10 C64). Overall, RCC account for approximately 3.5% of cancer cases in men and 2.4% in women. Almost one quarter of the patients already presents with advanced disease (T3-4), lymph node infiltration or metastases at diagnosis. Clear cell carcinoma accounts for more than 80% of all RCCs.

Over the last decade the introduction of multiple novel treatments options led to conti-

# **CONCLUSION**

Sequential treatments of patients with mRCC are changing showing that novel treatment options are quickly implemented into routine care in Germany. Currently, sequential use of TKI and CPI are the preferred choice. At least a quarter of patients dies prior to receiving second-line treatment highlighting an unmet medical need for this high-risk population. With longer follow-up, clinical and patient-reported outcomes of sequential treatments we will provide valuable additional evidence to guide treatment strategies in the future.

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nuous changes in treatment options for patients with advanced or metastatic renal cell carcinoma (mRCC) including several tyrosine kinase inhibitors (TKIs), mTOR inhibitors (mTOR), and checkpoint-inhibitors (CPIs).

This raises questions as to how fast newly approved treatments are applied in routine practice and how outcome results translate to patients outside of clinical trials. Systematic, prospective, longitudinal cohort studies providing data on routine care are highly important to assess the state of care and complement the data generated from the pivotal clinical trials.

# BACKGROUND

The Tumor Registry Renal Cell Carcinoma (RCC Registry) analysed treatment and outcome of patients treated in Germany from 2007-2017 (Goebell et al. 2018). The CARAT registry platform, which continues the valuable work from the RCC Registry, continues to assess real world treatment and outcome, complemented by the collection of patient-reported outcomes (PROs) and a decentralized biobanking.

CARAT is the first project of this scale combining medical data, patient characteristics, PROs on quality of life and the potential for

## **METHODS**

translational research. Physicians from all health care sectors – office- and hospitalbased oncologists and urologists – are participating, addressing the unique decentralized structure of the German health care system.

Since treatment reality has been changing rapidly over the last years CARAT will be essential to evaluate current treatments and standard of care, identify unmet needs and develop recommendations to improve quality of care.

Here, we analysed changes in sequential treatment patterns over time since 2008.

Table 1			
	Patients with 2 <sup>nd</sup> -line treatment	Patients deceased during 1 <sup>st</sup> - or prior to 2 <sup>nd</sup> -line treat- ment	Patients not yet in 2 <sup>nd</sup> - line treatment
Number of patients at time of analysis (n)	857	449	267
Gender			
Male	69.9%	66.4%	65.5%
Female	30.1%	33.6%	34.5%
Age at start of respective line of therapy			
Median	68.3 years	72.1 years	68.6 years
IMDC at start of respective line of therapy			
Favourable risk	11.1%	5.3%	18.0%
Intermediate risk	29.2%	23.8%	31.5%
Poor risk	8.3%	19.6%	11.6%
Missing (since 2013)	51.5%	51.2%	39.0%
Comorbidities at inclusion			
CCI O	68.6%	58.4%	66.3%

The Renal Cell Carcinoma Research Plattreatments as well as outcome parameters form CARAT is a prospective, observational, including date of progression(s) and death open, multicenter clinical registry, which are regularly documented. Patients are continues the preceding Tumor Registry followed until death or for a maximum of Renal Cell Carcinoma (RCC Registry) in three years. Germany. 1,000 patients with advanced Data are collected in an electronic data renal cell cancer, previously untreated for capture system with implemented realtheir advanced disease, will be recruited at time plausibility and completeness checks. the start of first-line treatment. A network Manual data management and onsite moniof up to 150 study sites of urologists and toring ensure complement data quality oncologists from both, hospitals and officeassurance measures. based practices in Germany are participating By March 2022, about 2274 patients in total (**Figure 1**). CARAT has been reviewed by an have been enrolled with about 790 patients independent ethics committee and is regissince the start of CARAT in December 2017. tered at Clinicaltrials.gov (NCTO3374267). Patients are recruited at start of first-line After informed consent is obtained, data on treatment, independent of their treatment. patients' demographic and clinical (tumor) For the analyses reported herein, all patients characteristics, on molecular testing with at least one year of follow-up (N=1717, and prior treatments are documented. start of treatment prior to 31/12/2020, data-During the course of therapy, all systemic base cut 31/12/2021) were considered.

### RESULTS

#### Patients and clinical characteristics

**Table 1** shows differences of patients recei ving a second-line treatment to patients deceased during first- or prior to second-line treatment and to patients not yet receiving a second-line. At the time of the respective treatment line, patients who died prior to second-line treatment were older (median 72 years) compared to patients who received a second-line therapy (median 68 years). More than 65% of the patients were male. Patients who died prior to second-line treatment were more often poor risk patients according to the IMDC (20% versus 8%) and/or had more comorbidities (Charlson-Comorbidity-Index ≥1 41% versus 31%).

#### **Change of sequential treatments** strategies

To show changes over time, four groups of patients are shown, classified by their start of first-line treatment (2007-2014, 2015-2018, 2019 or 2020). Because only patients whose therapy started at least one year prior to database cut were considered, no data in 2021 are available yet (**Figure 3**).

Missing	0.0%	0.0%	0.0%		
Treatment duration (months)					
Median	5.7 months	2.9 months	12.8 months		
25-75% Quantile	2.7 - 12.0	1.1 - 6.5	5.6 - 31.3		
No end of treatment documented yet	0.4%	3.6%	56.2%		

41.2%

33.0%

Patients whose therapy started at least one year prior to the database cut

CCI≥1

Treatment duration for first-line treatments calculated only for patients with completed treatments.

31.4%

Table 1 Patient characteristics - patients with and without second-line treatment



Figure 3			
2007 - 2014	2015 - 2018	2019	2020

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#### References

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#### **Conflicts of Interest:**

None of the authors has declared a conflict of interest regarding the subject of this work.

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#### **Patients with sequential treatments**

For the first-line treatment a total of 1717 treatments have been documented until database cut. About 50% of the patients started a second-line treatment, while 26% died during first-line treatment. For 16% of the patients first-line treatment was ongoing and 8% were lost to follow-up (Figure 2). This means that currently a minimum of 50% and a maximum of 74 % of patients will be able to receive second-line treatment.

Overall, the applied first-line strategies have changed over time from mostly TKI to both, TKI-only or CPI-based treatments in recent years. Up to 2018 about 85% of the patients received a TKI first-line, while in 2019 about 43% of the patients were treated with a TKI and about 35% with a CPI or 14% with the combination of TKI and CPI first-line. In 2020, 19% of the patients were treated with a TKI and about 33% with a CPI and about 42%% with TKI and CPI first-line (Figure 3). Up to 2014 the most frequent second-line strategies were an mTORi (19%) or another TKI (19%) after TKI in the first-line. In the period 2015-2018, a CPI in the second line (after TKI in the first-line) was already more frequent (29%) than another TKI (12%) in the second-line. In 2019 the most common strategies were TKI in the fist-line and CPI in the second-line (20%) and vice-versa (10%, Figure 3)



#### Figure 3: Most frequent sequential treatments over time - first to second-line treatments

Patients whose therapy started at least one year prior to database cut.

"Potential" represents patients whose documentation had not been completed yet and who could still receive subsequent treatments. "Docu finished" represents patients whose documentation had been completed.