INTRODUCTION

In Germany, about 95% of neoplasms of the kidney are renal cell carcinomas (RCC; ICD-10 C66). Overall, RCC account for approximately 3.5% of cancer cases in men and 2.6% in women. In the second quarter of the patients already presents with advanced disease (T3a), lymph node infiltration or metastases at diagnosis. Clear cell carcinomas accounts for more than 80% of all RCCs.

Over the last decade the introduction of multiple novel treatments options led to continuous changes in treatment options for patients with metastatic renal cell carcinoma (mRCC) including several progessive kinase inhibitors (TKIs), mTOR inhibitors (mTORi) 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 care and complement the data generated from the pivotal clinical trials.

METHODS

The Renal Cell Carcinoma Research Platform CARAT is a prospective, observational, open, multicenter, clinical registry, which continues the preceding Tumor Registry Renal Carcinoma (TCC Registry). In Germany, 1,000 patients with advanced renal cell cancer, previously untreated for their advanced disease, will be recruited at the start of first-line treatment. A network of up to 150 study sites of urologists and oncologists from both, hospitals and office-based practices in Germany are participating (Figure 1: CARAT has been reviewed by an independent ethics committee and is registered at Clinicaltrials.gov (NCT03374267).

After informed consent is obtained, data on patients’ demographic and clinical (tumor) characteristics, on molecular testing with advanced clear cell renal cell carcinoma – Analyses from the active registries, on treatment patterns over time since 2008. As of December 2021, about 1277 patients in total have been enrolled with about 790 patients whose therapy started at least one year prior to the database cut. By March 2022, about 2274 patients in total have been enrolled with about 790 patients whose therapy started at least one year prior to the database cut. About 50% of the patients died during first-line treatment. For 16% of the patients neither an end of treatment nor a date of progression(s) and death was documented.

RESULTS

Patients and clinical characteristics

Table 1 shows differences of patients receiving a second-line treatment to patients deceased during first-line or prior to second-line treatment and to patients not yet receiving a second-line treatment. 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 treatment (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 ≥ 2: 62% versus 31%).

Patients with sequential treatments

For the first-line treatment a total of 2172 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 56% of the patients the first-line treatment was ongoing and 3% were lost to follow-up (Figure 2). This means that currently a minimum of 50% and a maximum of 7% of patients will be able to receive second-line treatment.

Change of sequential treatments strategies

To show changes over time, four groups of patients are shown, classified by their start of first-line treatment (2007-2016, 2017-2018, 2019, 2020). After 2019 about 85% of the patients received a TKI first-line, while in 2019 about 63% of the patients were treated with a TKI and about 35% with a CPI or 16% 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 2016 the most frequent second-line strategies were an mTORi (18%) or another TKI (29%) after TKI in the first-line. In the period 2017-2020, a CPI in the second-line (after TKI in the first-line) was already more frequent (29%) than another TKI (21%) in the second-line. In 2019 the most common strategies were TKI in the first-line and CPI in the second-line (20%) and vice-versa (10%, Figure 3).

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.