# INSPIRE: kidney cancer

## Systemic anti-cancer treatment

**Public, private and Non-Governmental Organisation partnership**

Pfizer MERCK MSD Bristol Myers Squibb™

HELSE SØR-ØST HELSE MIDT-NORGE HELSE VEST HELSE NORD

Kreftregisteret KREFTFORENINGEN invenz LMI

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# Foreword

INSPIRE Kidney cancer is the third project initiated to investigate systemic anti cancer treatment (SACT) in Norway. This is the first time the Cancer Registry of Norway (CRN) publishes results on systemic anti cancer treatment for a cancer type where there is no clinical registry. Thus, the report represents a first assessment on how SACT-data can be used together with the basic core variables in the CRN, to obtain an understanding of the treatments used in clinical practice within kidney cancer.

INSPIRE Kidney cancer is a collaboration between the CRN, INVEN2 (technology transfer office), LMI (Pharmaceutical Industry in Norway), four pharmaceutical companies (Merck, Pfizer, MSD and Bristol Myers Squibb), The Norwegian Cancer society and the four regional Health Authorities.

We would like to emphasize how important this collaboration has been to be able to collect and assess information about SACT for a patient group where there is no clinical registry.

The lack of a clinical registry for kidney cancer limits the amount, and detail, of data that is possible to collect. Hence, this leads to limitations on what analyses it is possible to perform. Even so, this project has shown that it is possible to evaluate some parts of the patient treatment pathways, if the core variables are sufficient for the analyses.

Oslo, 1. February 2023

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Chapter 1

# Summary

"INSPIRE: kidney cancer. Systemic anti-cancer treatment of kidney cancer" is the third report of the INSPIRE project. The report shows results for kidney cancer and systemic anti-cancer treatment and evaluates opportunities and limitations when using only data from the incidence registry (core variables) in the time period 2019–2021.

The specific data available for kidney cancer in the Cancer registry of Norway (CRN) are the core variables, derived from pathology reports and clinical notifications. The core variables are the basic variables available for all cancer cases. In the analysis for metastatic kidney cancer, the SEER staging is used, as there is a lack of information on the TNM staging. The CRN captures data on systemic anti-cancer treatment (SACT) regularly from three of the four regional health authorities (HA) in Norway; South East HA, Western HA and Central Region HA.

The incidence and the relative survival of kidney cancer has increased over the last 20 years (see figure 5.1, table 5.1 and 5.2). The incidence for men is twice as high as that for women.

There has been an increase in the use of immunotherapy among patients receiving 1st line SACT, both mono or in combinations (IO/IO or IO/TKI). In 2019, among patients receiving 1st line SACT about 12% of primary mRCC patients received 1st line immunotherapy alone or in combination. In 2021, that percentage has increased to 87%.

Combination therapy with IO/IO is mainly used in 1st line therapy and some patients receive IO as monotherapy or in combination with TKI, as 2nd line therapy. TKI is the most used therapy for second, and subsequent lines of therapy.

This report shows that there are differences in treatment given to patients across the health regions. The patient groups are small, however, and those differences may be due to random (and natural) variation in the patient population.

The lack of a clinical registry for kidney cancer limits the amount, and detail, of data that is possible to collect. This project has shown that it is possible to evaluate some parts of the patient pathways, if the core variables are sufficient for the analyses.

SACT data will be available for all cancers towards the summer of 2023. Access to such data requires applications via www.helsedata.no and the necessary approvals.

# Chapter 2

# Definitions

**Table 2.1:** Definitions

| Abbreviations and terminology | Explanations |
|---|---|
| ATC [1] | Anatomical Therapeutic Chemical (ATC [1]). A classification system where the active substances are grouped according to the organ or system on which they act and their therapeutic, pharmacological and chemical properties. |
| Core variables [2] | The basic variables the CRN has on all cancer sites on diagnostic work-up and treatment. |
| CRN | The Cancer Registry of Norway. |
| DCO | Death Certificate only. Refers to cancer cases where the only documentation on the cancer diagnosis is a death certificate. The CRN always tries to backtrace clinical information from cancers reported on death certificates, but in about 2% of all cancer cases no additional information is available. |
| H-prescriptions | Refers to prescriptions prescribed and financed by the specialist health care. May also refer to the medications that are prescribed using H-prescriptions. These medications are often capsules, tablets, or simple injections the patient takes at home. |
| Incidence | The number of new cancer cases. Incidence can be expressed as the absolute number, or as the rate, taking into account the size of the population at risk. |
| INSPIRE | Abbreviation for INcreaSe PharmaceutIcal REporting. A project aiming to capture data on systemic anti-cancer therapy to the Cancer Registry of Norway. The project also aims to analyse and present results for systemic anti-cancer therapy for specific cancer sites. |
| IMDC [3] | International mRCC Database Consortium. In this report we use IMDC as a reference to factors for risk stratification of metastatic kidney cancer. |
| IO | Immune oncology, a type of systemic anti-cancer therapy, ATC group L01F. |
| Line of treatment | Refers to treatment of metastatic disease. 1$^{st}$ line is the first SACT given, 2$^{nd}$ line is the second SACT given. Changing the line of treatment is often due to progression or severe side effects. |
| LMI | The Association of the Pharmaceutical Industry in Norway. |
| mTOR-I | mechanistic Target of Rapamycin Inhibitors, a type of systemic anti-cancer therapy, ATC group L01EG. |
| mRCC | Metastatic renal cell carcinoma, refer to "RCC" for a list of included morphologies. |
| National guidelines | National guidelines with recommendations for diagnostic work-up, treatment and follow up of cancer patients. Please note that the present national guidelines for kidney cancer dates back to 2015 and are undergoing updates during the fall of 2022. |
| NOK | Norwegian Kroner, the currency of Norway. |
| NOS | Not otherwise specified. |
| NPR | The Norwegian Patient Registry. NPR has information on all out-patient and in-patient visits in the specialist health care system in Norway. |
| Primary mRCC | Patients with metastatic renal cell carcinoma, at initial diagnosis. |
| RCC | Renal cell carcinoma, including clear cell adenocarcinoma, papillary adenocarcinoma and RCC not otherwise specified (NOS). |
| RHA | Regional Health Authority. |
| RT | Radiation therapy, aka radiotherapy. |
| SACT | Systemic anti-cancer therapy. |
| SACT data [4] | Data on systemic anti-cancer therapy from both hospitals and H-prescriptions. |

| Abbreviations and terminology | Explanations |
|---|---|
| SACT H-prescriptions | Systemic anti-cancer therapy from H-prescriptions only. |
| SACT hospitals | Systemic anti-cancer therapy from hospitals only. |
| Secondary mRCC | Renal cell carcinoma where the patient initially was diagnosed with localised or regional metastasis, and later developed distant metastasis. |
| SEER stage[5] | Summary stage that defines the extent of cancer disease as either localised, regional metastasis, distant metastasis or unknown. It is consistent with stage as given in the U.S. National Cancer Institute's Surveillance, Epidemiology and End Results (SEER) Program. |
| TKI | Tyrosine Kinase Inhibitors, a type of systemic anti-cancer therapy, ATC group L01E (excluding M-TOR I) |
| TNM, cTNM, pTNM | Tumour, Node, Metastasis. A global standard for classifying the extent of spread of cancer. cTNM refers to clinical TNM and pTNM to pathological TNM. |
| Treatment cycle | Repeated treatments of the same regimen, referred to as cycle 1, cycle 2, etc. |
| Treatment regimen | A specific combination of medications given, a predefined template for treatment. |

Chapter 3

# Introduction

## 3.1 INSPIRE kidney cancer

The INSPIRE kidney cancer project started in April 2022 and is the third INSPIRE project (for more information on INSPIRE, see below in chapter 3.2). The first two INSPIRE projects on lung cancer and breast cancer were based on data from the respective clinical registries as well as data on systemic anti-cancer therapy (SACT data). In contrast, no clinical registry exists for kidney cancer, and hence there is a significant difference in terms of quantity and quality of available data in the kidney cancer project, compared to the projects on lung and breast cancer.

The treatment options for kidney cancer have evolved rapidly over the last few years, with numerous SACT combinations being approved and made available for Norwegian patients (for example [6] and [7]). Although the registry based studies demonstrate survival benefits, little is known on whether comparable outcomes can be expected in a real-world setting on a national level. Moreover, potential regional differences in diagnostic work-up, treatment and follow-up have not been systematically analysed so far.

There is no national clinical registry on kidney cancer in Norway, and there are no current plans to establish one. However, the Cancer registry of Norway (CRN) still collects a lot of basic data on kidney cancer via the cancer incidence registry (core variables, refer to figure 4.1), the Norwegian Patient Registry (NPR) and the Cause of Death Registry, as well as information on SACT (refer to figure 4.2).

This INSPIRE kidney cancer project was initiated to investigate if the available real-world data can be used to close the knowledge gaps described above. More precisely, using the existing data, we want to evaluate whether the analyses in this report are relevant and detailed enough for stakeholders, but also to critically assess any limitations due to the lack of a clinical registry for kidney cancer. The latter is also of importance when assessing the feasibility of future analyses for other types of cancer, where no clinical registry exists.

The purpose of this report is therefor twofold;

1. Analyse systemic anti-cancer therapy for kidney cancer, refer to chapter 5
2. Evaluate possibilities and limitations when using SACT data with core variables (for cancers without a clinical registry), refer to chapter 6

## 3.2 The INSPIRE projects

The first INSPIRE project started in January 2019. Its aim was to extract data on SACT from hospitals in Norway on all cancer types, with a focus on lung cancer. That report includes analyses on treatment pathways, both generally for all lung cancer patients but also for SACT used in subgroups of lung cancer patients. The report on INSPIRE lung cancer was published in April 2021. A total of 12 pharmaceutical companies and the Norwegian Cancer Society supported the project financially, making it a success in terms of national collaboration efforts, involving private, voluntary, and public stakeholders from the health care sector.

A second INSPIRE project focused on breast cancer, and a report on SACT and general treatment pathways was published in April 2022. This project included five pharmaceutical companies.

This INSPIRE kidney cancer project is the third and final project. There are currently no plans for additional INSPIRE projects focusing on specific cancer types. The three INSPIRE projects have sufficiently demonstrated that SACT data can be accessed, collected, and processed, and thus there is no need for further funding via additional INSPIRE collaborations. For information on access to data, see 6.4.

For a more extensive background on the INSPIRE projects, please refer to

- INSPIRE: lung cancer report from 2021 (only in Norwegian) [8]
- INSPIRE: breast cancer report from 2022 (only in Norwegian) [9]
- INSPIRE: a new opportunity for cancer pharmacoepidemiology research from 2021 [10]

## 3.3 Participants, organization, and financing

The INSPIRE kidney cancer project is managed by the CRN, and run by an internal project group. The INSPIRE kidney cancer project received financial support from four pharmaceutical companies; Merck, Pfizer, MSD and Bristol Myers Squibb (BMS), in addition to a contribution for operational costs from the CRN. The companies have contributed over 1.5 million NOK.

A steering committee, led by the CRN, has been established to ensure close monitoring of the progress and development of the project, while providing an opportunity for regular discussions between the different stakeholders. Participants of the steering committee were representatives from each of the four Regional Health Authorities in Norway, the Association of the Pharmaceutical Industry in Norway (LMI), the CRN, two of the participating companies (BMS and MSD), Inven2 (technology transfer office, observer) and the Norwegian Cancer Society (observer) (refer to table 7.8).

An analysis group was established, involving additional stakeholders from both the public and private sector (refer to table 7.10). This includes the two other pharmaceutical companies supporting INSPIRE kidney cancer; Pfizer and Merck. The aim of the analysis group was to obtain clinically relevant advice on the planned analyses of SACT in kidney cancer.

In addition, a sub-board involving the representatives from all participating pharmaceutical companies, led by LMI, ensured the alignment of interests between the different sponsors (refer to table 7.9).

Chapter 4

# Data sources and data quality

## 4.1 Kidney cancer and available data in the CRN

The CRN collects cancer-specific data from several different sources, and can combine these data to generate cancer cases for each individual patient, as illustrated in figure 4.1. However, not all data sources are available for all cancer types. This mainly depends on whether there is an established national clinical registry for the specific cancer type. As of 2022, there are eight clinical cancer registries with national status[1] in Norway (colorectal cancer, childhood cancer, breast cancer, gynaecological cancer, lung cancer, lymphoid malignancies, melanoma, and prostate cancer), providing detailed data on diagnosis, treatment and follow-up. Some clinical registries also include patient reported outcome measures. For cancer types without existing national registries, the quality and quantity of available data is limited. Nevertheless, core variables derived from pathology reports and clinical notifications are collected for all cancer types in Norway and can provide basic information without a clinical registry, see table 4.1. In addition, the CRN collects data on radiation therapy and systemic anti-cancer therapy (SACT [4]) on all cancer types.

[1] National status means the registries have to abide by specific requirements for reporting and progress, they are evaluated yearly, and they receive extra funding.

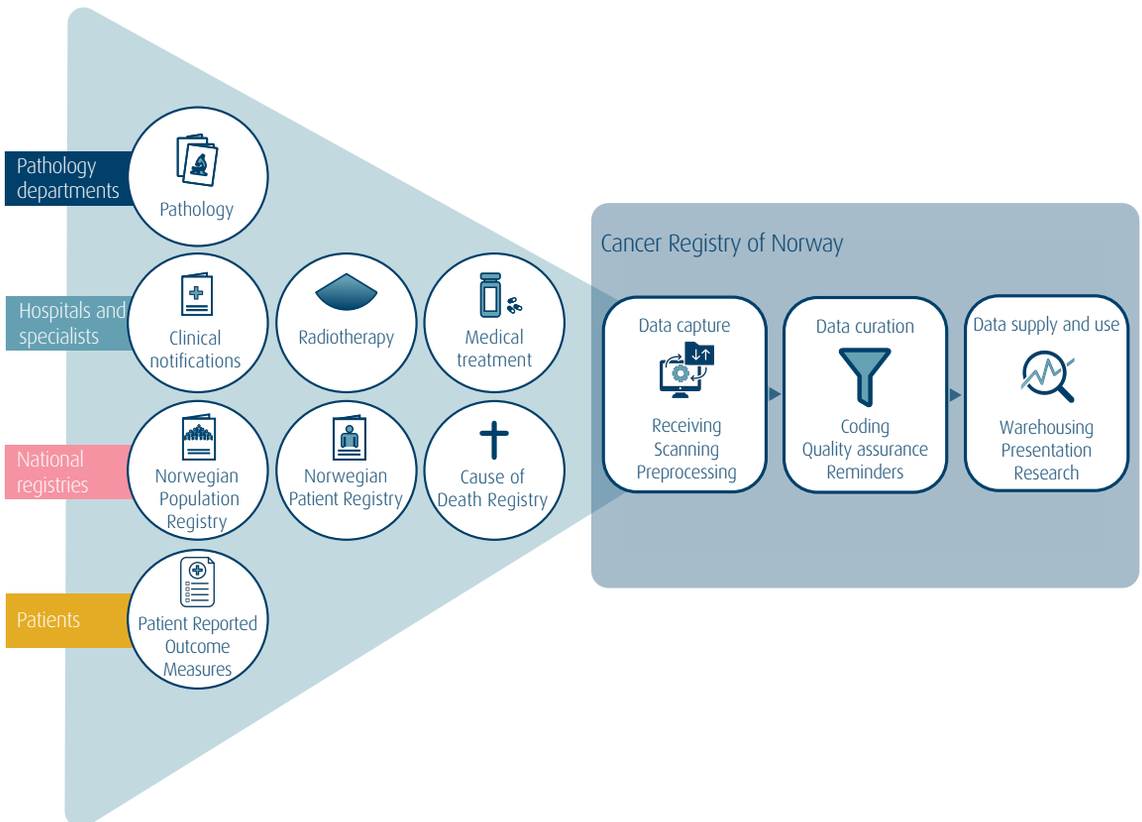



**Figure 4.1:** Data sources for information on cancer cases

With no existing clinical registry for kidney cancer in Norway, the available data in the CRN relevant for the IN-SPIRE kidney cancer project includes the core variables, as well as data on radiation therapy and SACT. This is described in more detail below:

- Incidence, mortality and survival of kidney cancer
  - Incidence, mortality and survival data for all cancer cases in Norway. The CRN publishes statistics annually for all cancer types, including kidney cancer.
- Identifying kidney cancer and subgroups
  - Histology, making it possible to differentiate on kidney cancer subgroups.
  - Staging according to the SEER classification.
  - Progression: Only partly available as this requires confirmation by pathology reports.
  - Risk group stratification: not available.
  - Any other cancer diagnoses in the patient group (available for all cancers).
  - Co-morbidity: not available.
- Patient demographics and region of residence
  - All cases in the CRN can be differentiated by demographic parameters and region of residence at the time of diagnosis.
- Diagnostic work-up (including immunohistochemistry)
  - The CRN has limited information on diagnostic work-up on kidney cancer patients. The information available is mainly derived from pathology reports stating whether the tissue sample stems from a biopsy or from surgery. Other types of information requires that a report on diagnostic work-up has been sent from the physician, but this reporting is not complete for kidney cancer.

  - There is information on whether immunohistochemistry has been performed on the tissue sample. This information is available from pathology reports for all cancer types. However the CRN does not register the result or method for immunohistochemistry for kidney cancer. The result and method is generally only available for cancer types where there is a clinical registry in place, but the information and level of details differ.

- Treatment
  - Surgery: There is information on nephrectomies and partial nephrectomies on kidney cancer patients, but no more details on the surgical method is available.
  - Radiation therapy: The CRN has data on all external radiation therapy in Norway for all cancer types, including kidney cancer. The information includes doses (fractions and total), region (part of the body treated), and the number of fractions administered.
  - SACT: The CRN has detailed data on SACT, for all cancer patients, including kidney cancer. However, SACT data has so far only been curated for cancer cases in the clinical registries, with the exception of kidney cancer for this report.

The specific data available for kidney cancer in the CRN are the core variables[2], derived from pathology reports and clinical notifications. Core variables are the basic variables available for all cancer cases, refer to table 4.1.

**Table 4.1:** Core variables, selected

| Variable name | Variable description |
|---|---|
| Age at diagnosis | Age of the patient at the time of diagnosis. |
| Basis for the diagnosis | The most reliable method used to confirm the diagnosis for the cancer case. |
| Categorisation of underlying cause of death | Describes whether the patient has died from cancer or from another cause. |
| Certainty of diagnosis | How reliable the diagnosis of cancer is. The reliability is assessed based on certainty of tumour malignancy and certainty of the primary site of the tumour. |
| County | County of residence at time of diagnosis. |
| Date of birth | Date of birth. |
| Date of diagnosis | Date of diagnosis. |
| Gender | The gender of the person. |
| Localisation | Origin of primary tumour according to a Cancer Registry of Norway-specific version of ICD-7. There are rules in place to determine the localisation for a cancer case if the individual messages received have various localisations. |
| Metastasis | Extent of the disease found in current examination (refer table 4.2) |
| Morphologically verified | Whether or not the diagnosis is verified through a morphological examination. |
| Morphology | Tumour type of the cancer case, the histopathological classification of the tumour. |
| Person status | Information on whether the patient is alive and living in Norway, dead or lost to follow-up. |
| Radiotherapy | Information about radiotherapy. |
| SEER stage | Summary stage which is consistent with stage as given in the U.S. National Cancer Institute's Surveillance, Epidemiology and End Results (SEER) Program. |
| Status date | Date of emigration or death. Blank/missing if the patient is still alive. |
| Surgery | Most comprehensive surgery performed as primary treatment for the cancer case. |
| Topography | Origin of the primary tumour. |

### 4.1.1 Staging and risk factors of kidney cancer

Kidney cancer in the CRN is staged using SEER stage[5] (refer to definitions in chapter 2). SEER stage is divided into localised, regional metastasis, distant metastasis, and unknown. In clinical practice however, the commonly used staging system is TNM staging. TNM staging is a more detailed classification describing the size and extent of tumour growth (T), the degree of spread to regional lymph nodes (N), and the presence of distant metastasis (M). As there are differences between the SEER staging and the TNM staging, and the CRN uses the SEER staging for

this report, we cannot adjust or differentiate analyses according to the TNM classification, neither clinical TNM nor pathological TNM. In table 4.2 there is a description of SEER staging for kidney cancer in the CRN.

**Table 4.2:** SEER staging for kidney cancer

| Value | Description | SEER staging |
|---|---|---|
| 0 | Invasive tumour, no spread to neighbouring structures or organs, no lymph node or organ metastasis | Localised |
| 1 | Metastasis to lymph nodes in the abdomen (but not the pelvis) | Regional metastasis |
| 2 | Metastasis to lymph nodes outside the abdomen | Distant metastasis |
| 3 | Metastasis to organs in the abdomen (but not the pelvis) | Distant metastasis |
| 4 | Metastasis outside the abdomen | Distant metastasis |
| 5 | Microscopic spread to fatty tissue, vena cava, or the renal vein (T3a/T3b) | Regional metastasis |
| 6 | Macroscopic spread to nearby structures, adrenal gland or through gerotas fascie (T4) | Regional metastasis |
| 7 | Information on the presence of metastasis, but no information on where | Unknown |
| 9 | No information on whether or not the patient has metastasis | Unknown |

IMDC risk factors [3] is used by clinicians for patients with metastatic kidney cancer as a prognostic tool and support for therapy selection. The risk model uses six criteria[2] to differentiate risk into favourable-risk disease, intermediate-risk disease, and poor-risk disease. Out of the six criteria, the only one available to the CRN is time from diagnosis to systemic therapy. The lack of information on risk factors means this report cannot adjust or differentiate analyses based on the IMDC risk model.

[2] Karnofsky Performance Status <80, <1 year from time of diagnosis to systemic therapy, Haemoglobin < lower limit of normal, Neutrophils > upper limit of normal, Platelets > upper limit of normal, and Corrected calcium > upper limit of normal

## 4.2 Information on systemic anti-cancer treatment

### 4.2.1 Data capture – overview

The CRN captures data on systemic anti-cancer treatment (SACT) regularly from hospitals in Norway. A prerequisite is that the hospitals use an IT system designed for administering SACT, and that that data can be exported. Of the four Regional Health Authorities in Norway, the hospitals within one region, the North Regional Health Authority, lack the required IT system, and is hence not a part of the data capture from hospitals[3]. The Northern region has about 10% of the cancer cases in Norway. This means that current data capture of SACT in hospitals cover about 90% of the cancer cases from 2019. Figure 4.2 shows the data capture from the different hospitals, and what year SACT data became available. Information on medication taken at home by cancer patients (referred to as SACT H-prescriptions), is collected from the Norwegian Patient Registry about three times a year. The data is available from 2019 and onwards (figure 4.2).

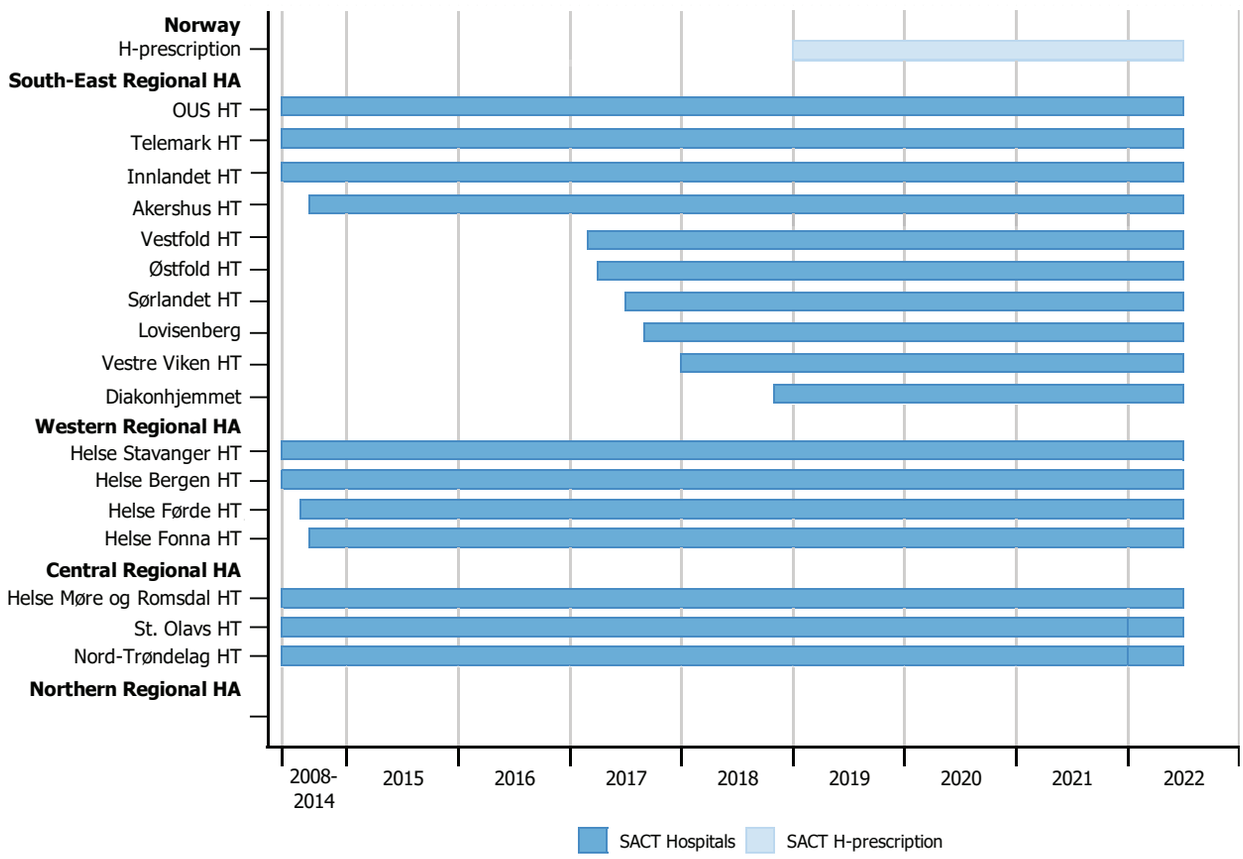



**Figure 4.2:** Data capture SACT, hospitals and H-prescriptions

**Figure 4.2**

**Data source**
- SACT hospitals
- SACT H-prescription

**Inclusion**
- SACT from 1st January 2008
- All cancer sites

**Comments**
- Period 2008–2014 is merged

[3]The Northern region is in the process of acquiring an IT system for SACT administration.

### 4.2.2 SACT data from hospitals

The SACT data from the hospitals are transferred directly from the IT systems used in patient care. The variables collected are the same as those needed for administrating chemotherapy (and other antineoplastic substances). As shown in table 4.3 the level of reporting for mandatory variables is very high.

**Table 4.3:** Variables on systemic anti-cancer treatment from hospitals (mandatory variables only)

| Variable | Description | Example | Level of reporting |
|---|---|---|---|
| **Personal identification number** | Norwegian personal identification number, 11 digits | 12034598765 | 100% |
| **Institution** | Institution/hospital where the patient was treated | Oslo University Hospital | 95.5% |
| **Weight** | Patients weight at time of treatment, kg | 76.5 | 98.6% |
| **Height** | Patients height at time of treatment, cm | 174 | 98.0% |
| **Administration date** | Date the substance was given to the patient | 23.04.2019 | 99.3% |
| **Substance** | Name of active substance | Pembrolizumab | 100% |
| **Dose of substance** | Dose of active substance | 200 | 95.5% |
| **Dosage unit** | Unit of measurement for the substance | mg | 95.5% |
| **Route of administration** | Intravenous, orally, etc. | intravenous | 95.5% |

**Table 4.3**

**Data source**
- SACT hospitals

**Inclusion**
- All cancer patients with SACT in the CRN, from the South East, West and Central regions
- Treated 2008–2021

**Exclusion**
- Cancer patients with SACT from the Northern region

### 4.2.3 SACT data from H-prescriptions

Cancer medications taken by the patient at home are usually tablets, capsules or simple injections. Cancer medications taken at home are prescribed using ”H-prescriptions” (refer to chapter 2). The SACT data on H-prescriptions are considered reliable, as the information is used directly in patient care. As shown in table 4.4 the level of reporting is very high. Note that all regions in Norway are included in the SACT H-prescription data capture.

**Table 4.4:** Selected variables on systemic anti-cancer treatment from H-prescriptions

| Variable | Description | Example | Level of reporting |
|---|---|---|---|
| **Diagnosis code** | Diagnosis according to ICD-10 | C50 | 99,5% |
| **Prescribing institution** | The institution where the H-prescription was prescribed | Oslo University Hospital | 100% |
| **Date of prescription** | Date when the prescription was written by the physician | 23.02.2020 | 100% |
| **Personal identification number** | Norwegian personal identification number, 11 digits | 12034598765 | 100% |
| **Dispensed date** | Date the prescriptions was filled by a pharmacy | 24.02.2020 | 100% |
| **Product name** | Product name for medicine delivered to the patient | Inlyta tab 5 mg | 100% |

**Table 4.4**

**Data source**
- SACT H-prescriptions

**Inclusion**
- All cancer sites
- All of Norway
- Prescriptions were filled 2019–2021

### 4.2.4 Limitations in SACT data capture

The most significant limitation in data capture for SACT is the lack of data from the Northern region, which accounts for around 10% of all cancer patients in Norway. The Northern region will be acquiring an IT system for SACT, hopefully during 2023. For a full list of data capture limitations, refer to table 4.5.

Private clinics in Norway do not report SACT data to the CRN, mainly due to lack of necessary IT systems for SACT administration. Hence, the number of cancer patients receiving cancer medication in private clinics is not known but we assume the number is small for RCC (based on clinical experience).

**Table 4.5:** Limitations in SACT data capture

| Type of information | Included in data capture | Comment |
|---|---|---|
| **Adverse events or drug reactions** | No | Please refer to "Clinical evaluations" commented below. |
| **Clinical evaluations** | No | Clinical evaluations, like how the patient responds to treatment or side effects, are not documented in the IT systems SACT data is captured from. |
| **Early trial drugs** | Yes | Drugs administered as part of an early trial are included in the data capture, but not in the data set for this report. These drugs often lack official names and/or ATC codes. There are usually few patients receiving these drugs. |
| **Hormonal therapy** | No | Hormonal therapy is not part of the drugs available using H-prescription and is not administered through the SACT hospital systems, therefor hormonal therapy is not available. However, hormonal therapy is not common in kidney cancer. |
| **Medication in clinical trials** | Partly | Drugs administered as part of a clinical trial are included in the data capture, if they are administered through the SACT-software that data is captured from. We know that drugs given orally, as part of a clinical trial, usually are not administered via the SACT software, and therefor are not included in the data capture. Another exclusion is drugs administered as a part of blinded studies. |
| **Northern region (hospitals)** | No | The Northern region does not have an IT system for administering SACT, and is not included in the data capture from hospitals. |
| **Response or progression** | No | Please refer to "Clinical evaluations" commented above. |
| **Side effects** | No | Please refer to "Clinical evaluations" commented above. |
| **Treatments at private clinics** | No | Treatments given outside the official health care system, in private clinics, is not included in the data capture. |

## 4.3 Data curation

The SACT data extracted from the hospital's IT systems are raw data, meaning there has been very few, or no, changes, aggregations or validations performed before it reaches the CRN. Data curation consists of many steps and was described in detail in both the INSPIRE lung cancer report and the INSPIRE breast cancer report [8] [9].

Data curation is essential in order to aggregate, compare and analyse data. A large amount of the SACT data are text variables and do not adhere to standards for spelling or abbreviations. That being said, there are few national standards in place for variables in the SACT data. The list below, shows the major steps of data curation performed on the SACT data, with a few examples. Please refer to the other INSPIRE reports on lung and breast cancer for more information.

- Initial validation and clean up:
  Initial validation and clean up, is done to ensure the data has a valid format. This includes checking that numerical values are within a predefined range, and removing duplicates.

- Mapping of variables:
  Mapping is done to make the data sets comparable. Names of substances are spelled in different ways at different hospitals, and may contain pre- and post-fixes. All substances are mapped to the official Norwegian spelling, and pre- and post fixes removed. Mapping is also performed for variables such as route of administration and unit of dose.

- Creating new variables:
  Creating new variables is done partly to make the data sets comparable, but also to make the data sets easier to handle. Names of treatment regimens are often unique for each hospital, making them difficult to compare. We created new names of regimens using the names of substances the patient has received and putting them in alphabetical order separated by "+". We can also create treatment cycles in order to simplify counting the number of treatments.
- Link SACT data to individual cancer cases:
  The SACT data needs to be linked to an individual cancer case. This is straightforward when the patient has only one cancer diagnosis. For patients with more than one cancer diagnosis, we use data from NPR on coinciding dates for hospital visits and dates for SACT to link the treatment to the correct diagnosis. We also check which diagnosis is recorded in NPR for those visits and match them to the cancer diagnosis. Any SACT that occurs before the kidney cancer diagnosis date or contains chemotherapy are removed from the data set.

## 4.4 Prerequisites for the analysis

This report presents descriptive analyses based on averages and proportions. No statistical tests for differences among groups has been performed.

In some analyses we show the number of patients, even though there are 5 or less patients, which we normally do not do. In this report we have chosen to include analyses with a small number of patients because the inclusion criteria for the analyses are made by the CRN based on the available data and requires knowledge of how each case has been staged in the database. Outsiders do not have this knowledge and can therefore not identify individual patients.

This report includes patients diagnosed with kidney cancer from 1$^{st}$ of January 2019 to 31$^{st}$ of December 2021. We include data on SACT (from hospitals and H-prescriptions) from 1$^{st}$ of January 2019 until the 30$^{th}$ of June 2022. The data extraction took place on the 1$^{st}$ of November 2022.

For patients receiving surgery more than once, we have only used the first date of surgery in the analyses.

Treatment duration for SACT in hospitals is time from first administration date, until the last administration date, for the same regimen.

For SACT H-prescriptions, treatment duration is defined as the time from the first filled prescription until the last filled prescription + 30 days, for the same substance. We choose to add 30 days because the TKI-packages contain treatment for 30 days. It will therefore provide a more correct view of the actual treatment duration than using the last dispensed day as end of treatment.

Results in this report are based on a small patient population and interpretations and conclusions must take into account that results may be influenced by random (and natural) variations.

Chapter 5

# Kidney cancer and systemic anti-cancer therapy

## 5.1 Kidney cancer

### 5.1.1 Trends in incidence, survival and mortality (kidney cancer)

In 2019, 2020 and 2021 there were 911, 894 and 930 new cases of kidney cancer diagnosed per year, respectively (excluding cancer in the renal pelvis). The incidence of kidney cancer has increased for both men and women over the last 20 years (figure 5.1). The incidence for men is twice as high as that for women. That is, about 67% of all kidney cancers occur in men (calculated average for 2019–2021). The 5-year relative survival increased from 50–55% in 2000, to about 80% in 2020 (the green and brown lines).

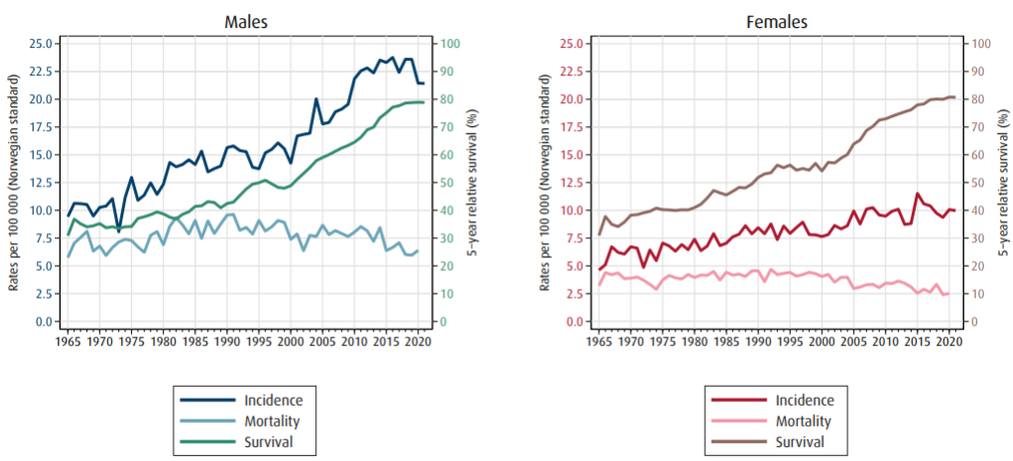



**Figure 5.1:** Trends in incidence, mortality and survival in kidney cancer (all stages combined)

**Figure 5.1**

**Data source**
- Cancer Registry

**Inclusion**
- Kidney cancer, ICD-10 C64

**Comments**
- The graph is copied from Cancer in Norway 2021, page 108 [11]
- Please note that information on mortality for 2021, was not available when the graph was published

Table 5.1 and 5.2 shows five-year relative survival by stage and period of diagnosis, 2002–2021, for both males and females. For kidney cancer patients, the relative survival has increased in the time period 2002–2021 for localised, regional and distant stage cancers.

**Table 5.1:** Five-year relative survival by stage and period of diagnosis, 2002–2021, males

| Stage | Relative survival (%), males | | | |
|---|---|---|---|---|
| | 2002-2006 | 2007-2011 | 2012-2016 | 2017-2021 |
| **Localised** | 85.0 | 87.1 | 91.9 | 92.6 |
| **Regional** | 55.6 | 57.9 | 64.9 | 70.2 |
| **Distant** | 8.4 | 9.3 | 17.3 | 21.9 |
| **Unknown** | 68.2 | 70.5 | 50.4 | 59.7 |
| **Total (all stages)** | 60.1 | 66.3 | 77.2 | 78.9 |

**Table 5.2:** Five-year relative survival by stage and period of diagnosis, 2002–2021, females

| Stage | Relative survival (%), females | | | |
|---|---|---|---|---|
| | 2002-2006 | 2007-2011 | 2012-2016 | 2017-2021 |
| **Localised** | 88.1 | 91.0 | 91.4 | 93.2 |
| **Regional** | 50.7 | 49.0 | 65.1 | 72.3 |
| **Distant** | 12.8 | 18.3 | 15.4 | 18.8 |
| **Unknown** | 65.4 | 81.5 | 40.6 | 52.5 |
| **Total (all stages)** | 65.3 | 73.9 | 78.3 | 80.7 |

**Table 5.1 and 5.2**

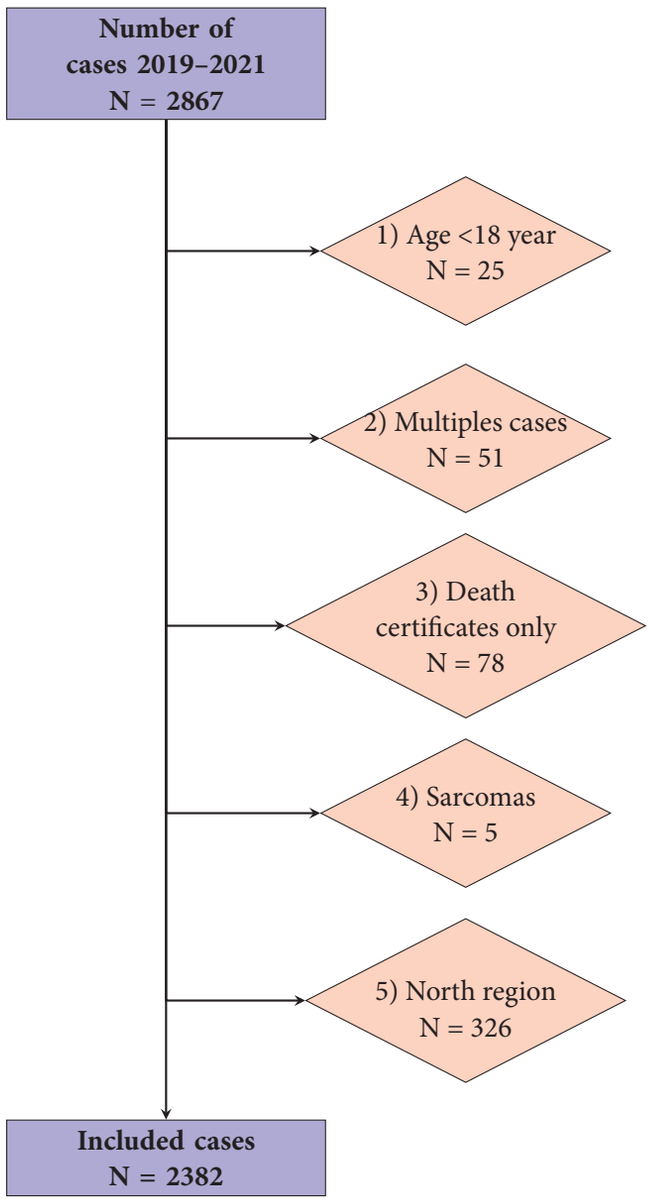
**Data source**
- Cancer Registry
**Inclusion**
- Kidney cancer, ICD-10 C64
**Comments**
- Stage refer to SEER stage, see table 4.2
- The table is copied from Cancer in Norway 2021, page 89 (males) and 91 (females) [11]

### 5.1.2 Patient population and exclusions

The patient population in this report are patients diagnosed with kidney cancer in Norway between 1st of January 2019 and 31st of December 2021. Follow-up data on SACT for those patients is available until 30th of June 2022. For exclusions in the data set, refer to the list below and the flow chart.

The numbering refers to the flowchart, see below.

1. 25 cases were excluded because the patients where under the age of 18.
2. 51 cases were excluded, because the patients presented multiple cases of kidney cancer. In these instances we have kept the first kidney cancer case, and excluded the later cases from the data set.
3. 78 cases were excluded due to the death certificate being the only source for kidney cancer report (DCO = Death Certificate Only).
4. Five cases of sarcomas (not sarcomatoid carcinomas) located in the kidney was also excluded, both due to the difference in therapy and the small number of patients. The excluded sarcomas are sarcoma (NOS), small cell carcinoma, malignant angiomyolipoma, and leiomyosarcoma (NOS).
5. Finally, all kidney cancers in the North region of Norway are excluded, 326 cases. The North region does not have a SACT system in place so there is no SACT data on those patients.


Number of cases 2019–2021 N = 2867
1) Age <18 year N = 25
2) Multiples cases N = 51
3) Death certificates only N = 78
4) Sarcomas N = 5
5) North region N = 326
Included cases N = 2382

### 5.1.3 Patient characteristics (study population and cohorts)

The study population consist of 2382 kidney cancer patients (table 5.3). There is a 1:2 ratio between female and male patients. In the study population, 61% are identified as having localised disease, and clear cell carcinoma is the predominant histology, making up 66% of the cases.

The number of patients with other histologies or unknown histology are relatively few and seldom treated with SACT, so the main focus in the following chapters will be the three groups; clear cell and papillary carcinomas and RCC NOS. These three groups together constitutes renal cell carcinomas (RCC). For an overview of all kidney cancer morphologies and grouping, see chapter 7.1.

The main focus of this chapter is SACT in kidney cancer. The most relevant patient group for SACT are metastatic renal cell carcinoma patients (mRCC). Table 5.3 presents baseline characteristics for both primary and secondary mRCC. The patient population with metastatic RCC at initial diagnosis (primary mRCC) consists of 259 patients. Secondary metastatic renal cell carcinoma are patients that initially were diagnosed with localised disease or regional metastasis, and later developed distant metastasis (secondary mRCC) and consists of 123 patients. How these groups are identified is further described in chapter 5.3.

**Table 5.3:** Baseline characteristics and SACT treatment proportions

| | Kidney cancer | | | Primary mRCC | | | Secondary mRCC | |
|---|---|---|---|---|---|---|---|---|
| | Patients | SACT treated | | Patients | SACT treated | | Patients | SACT treated |
| | N | n | (%) | N | n | (%) | N | n |
| **Total (N)** | 2 382 | 376 | 15,8 | 259 | 203 | 78,4 | 123 | 98 |
| **Age** | | | | | | | | |
| 18-49 | 247 | 29 | 11.7 | 18 | 17 | 94.4 | 9 | 7 |
| 50-59 | 444 | 87 | 19.6 | 54 | 48 | 88.9 | 27 | 24 |
| 60-69 | 664 | 104 | 15.7 | 67 | 52 | 77.6 | 35 | 27 |
| 70-79 | 756 | 127 | 16.8 | 89 | 70 | 78.7 | 45 | 36 |
| 80+ | 271 | 29 | 10.7 | 31 | 16 | 51.6 | 7 | 4 |
| **Gender** | | | | | | | | |
| Male | 1 652 | 274 | 16.6 | 190 | 147 | 77.4 | 84 | 70 |
| Female | 730 | 102 | 14.0 | 69 | 56 | 81.2 | 39 | 28 |
| **Region** | | | | | | | | |
| South East | 1 437 | 230 | 16.0 | 163 | 127 | 77.9 | 78 | 63 |
| West | 546 | 78 | 14.3 | 56 | 44 | 78.6 | 28 | 23 |
| Central | 399 | 68 | 17.0 | 40 | 32 | 80.0 | 17 | 12 |
| **Year of diagnosis** | | | | | | | | |
| 2019 | 804 | 140 | 17.4 | 81 | 65 | 80.2 | 58 | 45 |
| 2020 | 777 | 120 | 15,4 | 87 | 67 | 77.0 | 38 | 29 |
| 2021 | 801 | 116 | 14.5 | 91 | 71 | 78.0 | 27 | 24 |
| **Histology** | | | | | | | | |
| Clear cell carcinoma | 1 575 | 265 | 16.8 | 186 | 146 | 78.5 | 100 | 81 |
| Papillary carcinoma | 380 | 42 | 11.1 | 20 | 14 | 70,0 | 21 | 15 |
| RCC NOS | 112 | 50 | 44.6 | 53 | 43 | 81.1 | 2 | 2 |
| Other histologies (incl chromophobe) | 180 | 15 | 8.3 | 0 | 0 | 0 | 0 | 0 |
| Unknown histology | 135 | 4 | 3.0 | 0 | 0 | 0 | 0 | 0 |
| **Stage at diagnosis** | | | | | | | | |
| Localised | 1 458 | 50 | 3.4 | 0 | 0 | 0 | 54 | 37 |
| Regional | 361 | 68 | 18.8 | 0 | 0 | 0 | 69 | 61 |
| Metastatic | 295 | 213 | 72.2 | 259 | 203 | 78.4 | 0 | 0 |
| Unknown | 268 | 45 | 16.8 | 0 | 0 | 0 | 0 | 0 |
| **Surgery at diagnosis** | | | | | | | | |
| Nephrectomy | 985 | 149 | 15.1 | - | - | - | - | - |
| Resection | 899 | 26 | 2.9 | - | - | - | - | - |
| No surgery | 498 | 201 | 40.4 | - | - | - | - | - |
| **Metastasis pathologically verified** | | | | | | | | |
| Yes | - | - | - | - | - | - | 50 | 34 |
| No | - | - | - | - | - | - | 73 | 73 |

**Table 5.3**

**Data source**
- Cancer Registry

**Inclusion**
- Kidney cancer ICD-10 C64
- Diagnosed 2019–2021
- Treated from 2019 until 30$^{th}$ June 2022

**Comments**
- Nephrectomy means the entire kidney is removed
- Resection means that a part of the kidney is removed
- Metastasis pathologically verified is only shown for secondary mRCC
- "-" , data not shown
- Surgery is only presented for the overall kidney cancer population
- For secondary mRCC, percentages for SACT are not shown as they can be misleading since being treated with SACT is used to identify a subset of the patients
- Chromophobe is the largest histology group in "Other histologies" (see table 7.1)

### 5.1.4 Implementations of kidney cancer treatment in Norway

Norway has a publicly financed health care system, and all citizens are entitled to equal health care. Whenever a new treatment fulfills the three national priority criteria it can be implemented and made available to all patients through public reimbursement. If more than one treatment is available, a national tender will be initiated, thus the market is tender-driven which could guide choice of treatment, in addition to guidelines. Table 5.4 lists drugs that have received a positive reimbursement decision for the treatment of kidney cancer, since 2017 by The National System for Managed Introduction of New Health Technologies within the Specialist Health Care Service in Norway. In figure 5.4 we show trends in treatment choices that also relates to the positive reimbursement decisions listed below.

**Table 5.4:** Treatments with positive reimbursement decision for kidney cancer (selection)

| Date | Active substance (trademark) | Type | Reimbursements decisions (shortened text) | Reference |
|---|---|---|---|---|
| 27.02.2017 | Nivolumab (Opdivo®) | IO | Nivolumab as 2nd line treatment for advanced RCC | [12] |
| 23.10.2017 | Kabozantinib (Cabometyx®) | TKI | Kabozantinib as treatment for advanced RCC after 1st line treatment | [13] |
| 27.01.2020 | Ipilimumab (Yervoy®) / Nivolumab (Opdivo®) | IO/IO | Ipilimumab/Nivolumab combination as treatment for former untreated patients with advanced or metastatic RCC with intermediate-/high-risk profile | [14] |
| 31.08.2020 | Pembrolizumab (Keytruda®) / Aksitinib (Inlyta®) | IO/TKI | Pembrolizumab/Aksitinib as 1st line treatment for former untreated patients with advanced or metastatic RCC Reimbursed for treatment of patients with favourable-risk profile first then for intermediate/high-risk profile | [15] |
| 22.11.2021 | Kabozantinib (Cabometyx®) / Nivolumab (Opdivo®) | IO/TKI | Kabozantinib/Nivolumab combination as 1st line treatment of advanced RCC | [16] |
| 20.06.2022 | Lenvatinib (Kisplyx®) / Pembrolizumab (Keytruda®) | IO/TKI | Lenvatinib/Pembrolizumab combination as 1st line treatment of advanced RCC in adults | [17] |

## 5.2 Primary metastatic renal cell carcinoma

### 5.2.1 Treatment trajectories (kidney cancer)

The treatment trajectories for the kidney cancer study population are shown in figure 5.2. The figure shows SEER staging to the left and subsequent treatments to the right (refer to table 4.2 for information on SEER staging). Please note that the SEER stage refers to stage at initial diagnosis.

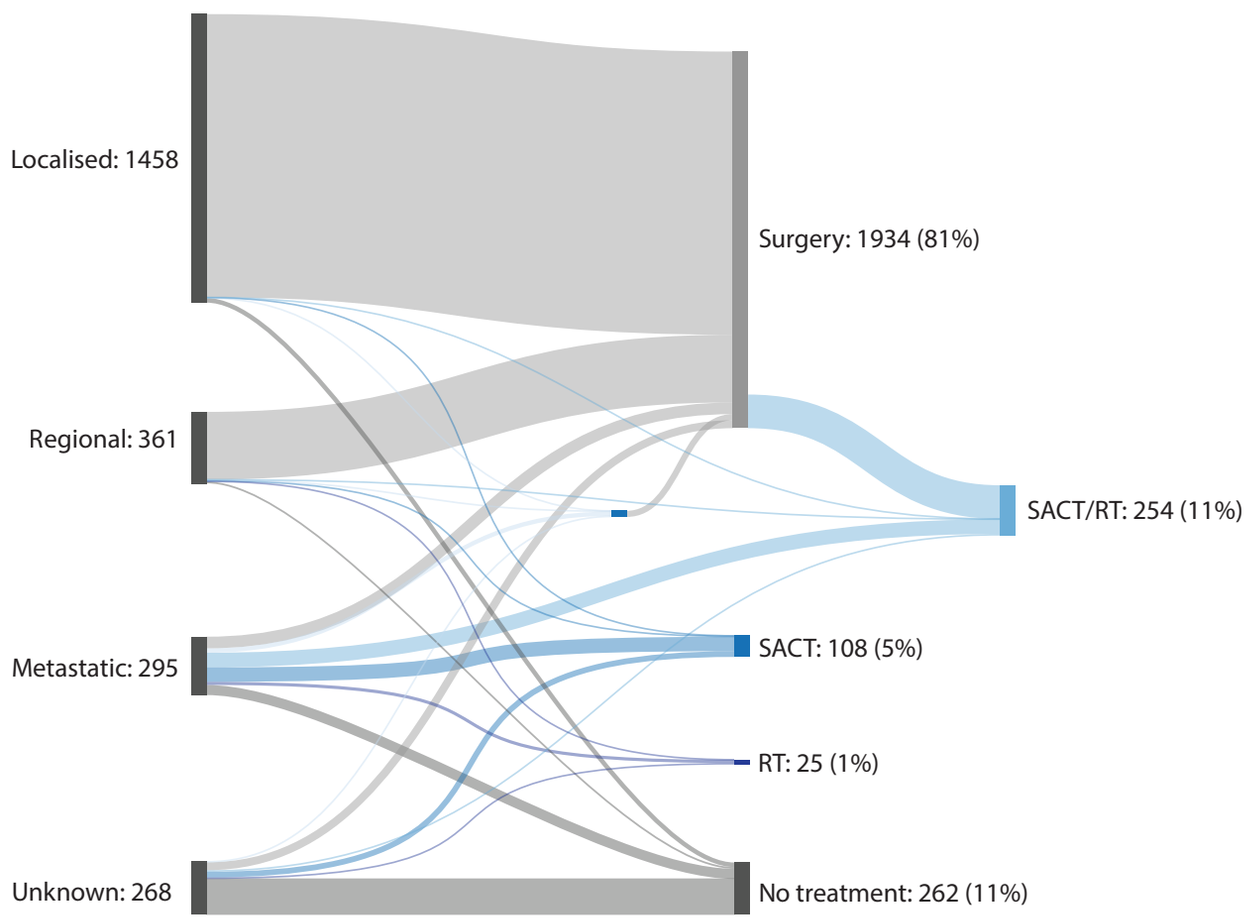



**Figure 5.2:** Overall treatment trajectory of kidney cancer by stage

**Figure 5.2**

**Data source**
- Cancer registry
- SACT data
- Radiation therapy data (RT)

**Inclusion**
- Overall study population (N=2382) with kidney cancer
- Diagnosed 2019–2021
- Treated from 2019 until 30th June 2022

**Comments**
- Stage refers to SEER stage at initial diagnosis
- Surgery includes nephrectomy and resection and is not restricted to surgery at time of diagnosis as in table 5.3
- The group unknown are patients where CRN dose not have information on stage
- Subsequent SACT regimens are collapsed into one event (e.g. two different SACT following each other appear as one event)
- SACT/RT = Patients receiving both RT and SACT irrespective of order
- A small group of patients (31 patients) were treated ahead of surgery with either SACT and/or RT (dark blue box)
- Coloring reflects treatment that includes SACT therapy (blue) and RT only (purple)

Almost all (98%) of kidney cancer patients with localised disease or regional metastasis at initial diagnosis receive surgery. Very few are treated with SACT and/or radiation therapy (RT) before surgery (only 31 patients, with 29 starting with SACT treatment). Less than one-fourth of patients with metastatic disease at initial diagnosis receive surgery.

The overall proportion treated with at least one SACT regimen is 15.8% (376 patients) while 72% (213 patients) of the patients with metastatic disease at diagnosis, receive SACT (table 5.3).

Those treated with SACT and RT after surgery (254 patients), include both patients initially diagnosed with metastatic disease and patients where the cancer has spread after initial diagnosis. Patients receiving only SACT are mainly those with primary metastatic disease, but also includes patients with locoregional disease where the cancer has spread at a later stage. Very few patients receive only RT [1].

The primary mRCC group constitutes 259 (88%) of the 295 metastatic kidney cancer patients. Of the 259 mRCC patients, 203 (78%) were treated with SACT (table 5.3). The secondary metastatic mRCC group constitutes 123 patients.

The group categorized as stage unknown at diagnosis are patients where the CRN do not have information on the extent of the kidney cancer (268 patients). The majority of this group have not received any treatment. This may be because they have not begun treatment before the cut off date for data collection, 30th June 2022, or because they are too ill to benefit from treatment. As figure 5.2 shows, this also applies to about one-fifth of patients with primary metastatic disease.

Figure 5.2 shows that approximately 1700 patients in the study population have not received any additional treatment following surgery during the time period examined in this report. Patients diagnosed with localised or regional kidney cancer have a high 5-year relative survival rate, over 70% for regional metastasis and over 92% for localised disease (please refer to table 5.1 and 5.2).

Clear cell carcinoma is the largest histological group, while it is the renal cell carcinoma not otherwise specified (RCC NOS) that have the highest proportion of SACT treated patients with 45% (table 5.3). The group RCC NOS includes renal cell carcinoma sarcomatoid type and two more histologies in addition to RCC NOS (table 7.1).

Only four patients with unknown histology are treated with SACT.

This report does not show the time from diagnosis to surgery. Some patients have only been reported to the registry by pathology report. This means there is no prior diagnosis date before surgery for these patients, and that the time interval between diagnosis and surgery will be 0.

### 5.2.2 Patient characteristics (primary mRCC)

The patient population with metastatic renal cell carcinoma at initial diagnosis (primary mRCC) is 259 patients, see table 5.3. The majority (60%) of primary mRCC patients are diagnosed between the ages 50–79 years. There is an overweight of men with mRCC, which coincides with a generally higher overall incidence of kidney cancer in males (refer table 5.3).

The majority (78.4%) of primary mRCC patients receive SACT. However, the number of cases are small in many subgroups in the table. The proportion of SACT treated patients is highest in patients aged 18–49 years (94.4%) and 50–59 years (88.9%). The age groups between 60–69 years and 70–79 years receive SACT in respectively 77.6% and 78.7% of the cases.

### 5.2.3 Treatment trajectories (primary mRCC)

In figure 5.3 we present different lines of treatment. To describe treatment trajectories, regimens have been grouped based on the type of treatment according to ATC-classification (ATC/DDD Index 2021) into IO, TKI and mTOR-I, see explanation below. The classification of the active substances can be found in the metadatabase.

[1] Includes all radiation therapy

- IO = Immune Oncology, ATC group L01F
- TKI = Tyrosine Kinase Inhibitors, ATC group L01E (excluding mTOR-I, ATC L01EG)
- mTOR-I = mechanistic Target of Rapamycin Inhibitors, ATC group L01EG

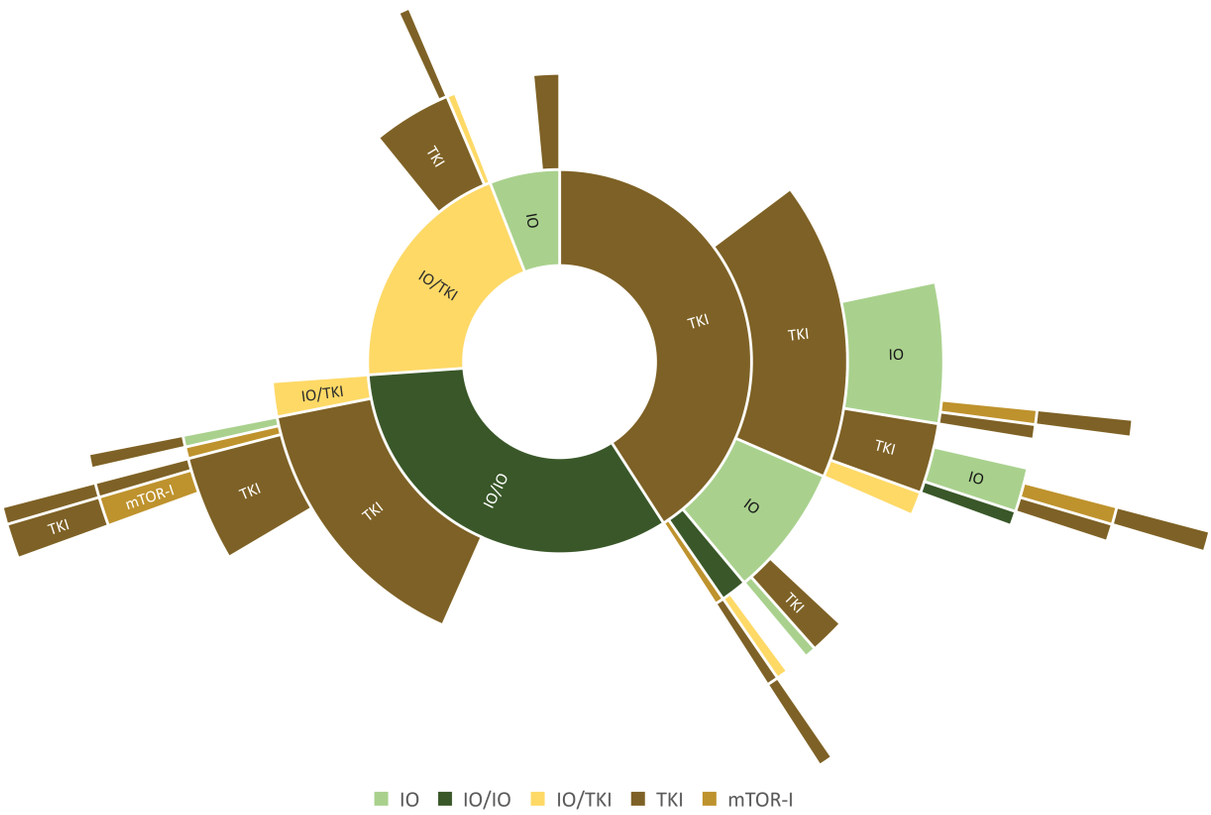



**Figure 5.3:** Treatment trajectories of patients with primary mRCC

**Figure 5.3**

**Data source**
- Cancer Registry
- SACT data

**Inclusion**
- Primary mRCC
- Diagnosed 2019–2021
- SACT from 2019 until 30th June 2022

**Comments**
- N = 203 patients
- The sunburst diagram is read from the center showing first line treatment, and subsequent lines of treatment outwards.

Figure 5.3 shows that immunotherapy, either as monotherapy or in combination with TKI or other IO (IO/TKI, IO/IO and IO), is a common choice of 1st line therapy during this 3.5-year period. TKI is the most common monotherapy in both 1st and 2nd line treatment. A tabulation of the diagram can be found in the appendix, refer to chapter 7.7. In the next section, we describe trends in 1st line therapy (refer to chapter 5.2.4).

### 5.2.4 Treatment trends (primary mRCC)

There has been a change in treatment of mRCC patients over the last few years, as new therapies has been made available (refer to table 5.4 for more information). In figure 5.4 we show the type of first line treatments, grouped by year, and the proportion of patients receiving the various 1st line treatments. The treatments are grouped into TKI and/or IO, monotherapy or in combinations (refer to chapter 5.2.1 or 2 for explanation of the groups).

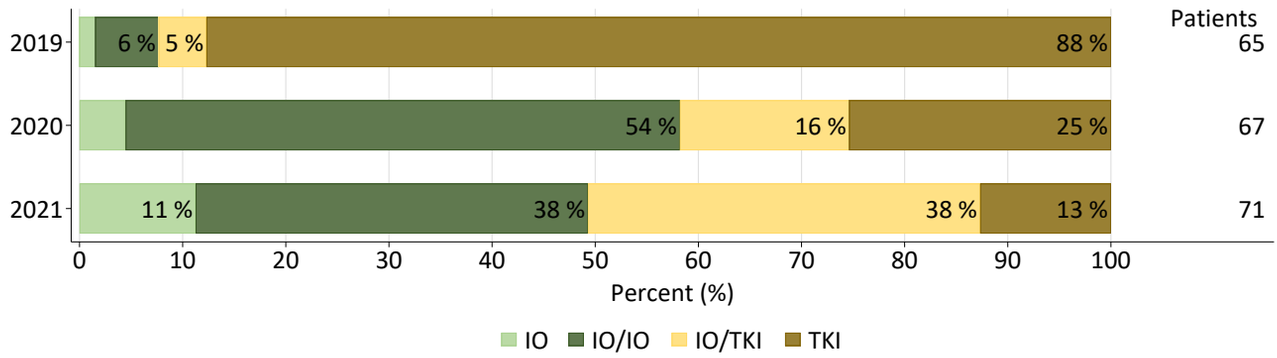



**Figure 5.4:** 1st line SACT for primary mRCC, by year of diagnosis

**Figure 5.4**

**Data source**
- Cancer Registry
- SACT data

**Inclusion**
- Primary mRCC
- SACT from 2019 until 31st December 2021

**Comments**
- Any surgery or RT information is ignored

Figure 5.4 presents the 1st line SACT for primary mRCC by year of diagnosis. In contrast, figure 5.3 presents the 1st line treatment for the same 3.5 year period combined.

Figure 5.4 shows that there was a clear change in 1st line therapy for primary mRCC between 2019 and 2021. This is not visible in figure 5.3, because it shows 1st line treatment for 3.5 years combined. The proportion of patients receiving monotherapy as 1st line therapy (either TKI or IO) decreased from 89% in 2019 to 24 % in 2021. In 2019 the dominant 1st line therapy was TKI monotherapy, which was given to 88% of patients. In 2021 this therapy was given to 13% of patients.

In 2021, 87% of patients with primary mRCC (treated with SACT) received immunotherapy as part of their 1st line treatment, compared to 12% in 2019.

In 2021, the dominant therapies were combinations of either IO/IO (38%) or IO/TKI (38%). This constitutes an increase from 11% in 2019 to 76% in 2021 in the proportion of patients receiving IO combination treatments for primary mRCC.

The changes in treatment reflects positive reimbursements decisions for the use of the IO/IO combination therapy ipilimumab/nivolumab in advanced and metastatic mRCC patients with intermediate or high-risk profile (27.01.2020)([14]) and the IO/TKI combination pembrolizumab/aksitinib (31.08.2020)([15]). Although there are no current approvals for IO monotherapy as 1st line treatment for mRCC patients, 11% received this as 1st line treatment in 2021. However, it should be noted that this only constitutes 8 patients, and that ongoing trials in this group of patients may explain this result.

### 5.2.5 Time to treatment initiation (primary mRCC)

In Norway there are national recommendations in place to ensure that diagnostic work-up is performed and treatment has been commenced in due time following a referral stating a possible kidney cancer. From the patient's first visit until a diagnosis has been confirmed, the lead time is 25 days for kidney cancer (for the overall group, refer to[18]). From a diagnosis has been confirmed until commencement of SACT, the lead time is 11 days. This means that the recommended lead time from the patient's first visit until they start treatment, is 36 days.

Figure 5.5 shows the number of days from diagnosis date in the CRN, to treatment initiation. The diagnosis date in the CRN is defined as the first date where the diagnosis is confirmed after tissue samples and/or other examinations. The date refers to when the biopsy or surgery was conducted. The date of diagnosis may differ from the patient's

first visit to the health care service, but it is the most reliable information in the CRN for the purpose of analysing lead times.

The recommended lead times applies for kidney cancer in general, but the following figure focuses on primary mRCC. Please note that the figure only shows number of days from diagnosis to start of SACT. Any surgery or radiation therapy is ignored in this analysis.

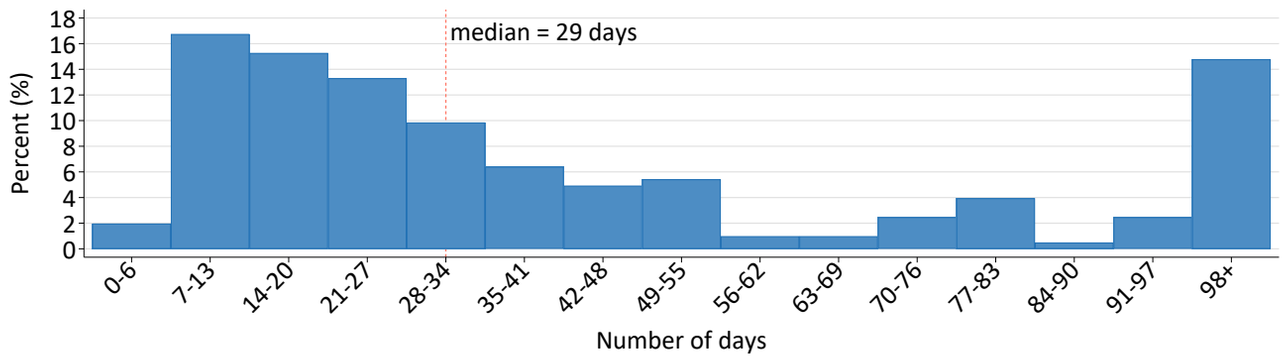



**Figure 5.5:** Time to treatment initiation with SACT from diagnosis for patients with primary mRCC

**Figure 5.5**

**Data source**
- Cancer Registry
- SACT data

**Inclusion**
- Primary mRCC
- Diagnosed 2019–2021
- SACT from 2019 until 31st December 2021

**Comments**
- Total = 203 patients
- Any surgery or RT information is ignored

Median number of days from the diagnosis date to the initiation of SACT for primary mRCC, was 29 days (figure 5.5). This is within the recommended lead time of 36 days. Approximately 72% of patients have begun SACT within 56 days following diagnosis. Figure 5.5 also shows that about 15% start SACT after 98 days or more following the time of diagnosis.

### 5.2.6 Time on treatment (primary mRCC)

Figure 5.6 shows the duration of the time period that patients with primary mRCC has been treated with different kinds of therapies, 1st line therapy only. Some patients in this analysis are still receiving treatment (table 7.5), which may affect treatment duration. For an overview of the number of patients and treatment duration, refer to table 7.6 in the appendix. Discontinuation of one of the two active substance in a combination treatment is not taken into account.

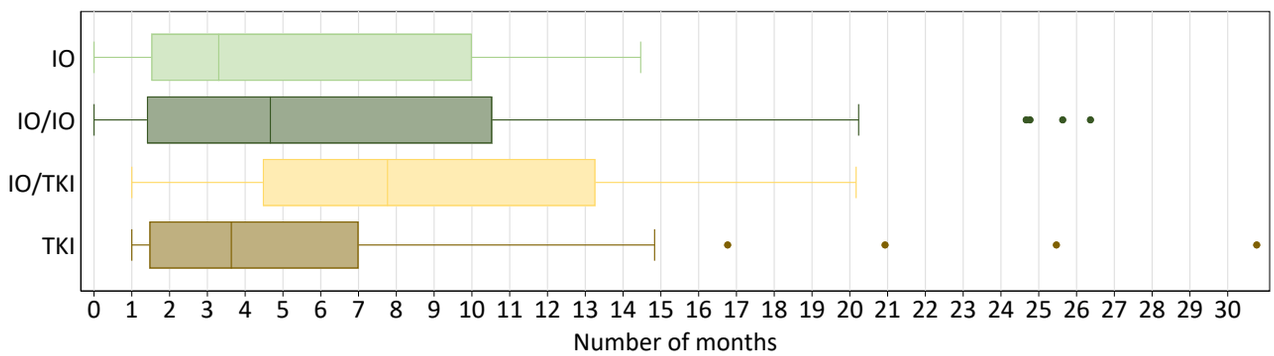



**Figure 5.6:** Time on 1st line treatment for patients with primary mRCC

**Figure 5.6**

**Data source**
- Cancer Registry
- SACT data

**Inclusion**
- Primary mRCC

**Comments**
- Definition of treatment duration (refer to chapter 4.4)
- Patients that have received only one course of IO or IO/IO, and no further treatments, will have treatment length = 0 months
- Total = 203 patients

Figure 5.6 shows that the lower 25% of the patients received IO treatment for up to 1.5 months (light green line to the left). About 50% of patients underwent IO for 1.5 to 10 months approximately (the light green rectangle). The upper 25% received IO treatment for 10 to 14.5 months (light green line to the right). The median time on IO treatment was 3.3 months (vertical green line within the green rectangle). Refer to chapter 7.2 for more information.

Patients receiving the combination IO/IO had 4.7 months median time on treatment. Of the patients receiving IO/IO, the lower 25% received treatment for 0 to 1.4 months, while 50% of patients received treatment for 1.4 to 10.5 months, and the upper 25% received treatment for 10.5 to 20.2 months. There are also four outliers receiving treatment for an even longer period of time.

The combination IO/TKI had 7.8 months median time on treatment, which is the longest median time on treatment in this analysis. Of the patients receiving IO/TKI, the lower 25% had a treatment duration of between 1 and 4.5 months, while 50% of patients received treatment for 4.5 to 13.3 months, and the upper 25% received treatment for 13.3 to 20.2 months.

Patients receiving TKI monotherapy had 3.6 months median time on treatment. The lower 25% of the patients had a treatment duration of between 1 to 1.5 months, while 50% of patients received treatment between 1.5 to 7 months, and the upper 25% had a treatment duration of between 7 and 14.8 months.

## 5.3 Secondary metastatic renal cell carcinoma

### 5.3.1 Patient characteristics (secondary mRCC)

Patients with secondary metastatic renal cell carcinoma were initially diagnosed with localised disease or regional metastasis, and developed distant metastasis at a later stage. However, the CRN does not have a clear picture of all these patients, since not all cases of secondary metastasis are reported. All pathology reports showing cancer are automatically reported to the CRN, but not all patients receive a biopsy of secondary metastasis (for example if the patient is too ill too cope with the procedure or too ill to benefit from treatment). To get an overview of this patient group we have created a group based on the following criteria;

1. Patients with localised disease or regional metastasis at initial diagnosis.
2. Pathology report showing distant metastasis, at least 4 months after initial diagnosis[2].
   OR
3. Patients receiving SACT at least 4 months after initial diagnosis (refer to footnote). SACT is primarily given to RCC patients with advanced disease. Information on SACT is hence used to identify patients who most likely have distant metastasis, even though the CRN does not have a pathology report verifying metastasis.

Table 5.3 shows that the majority of secondary mRCC patients are identified using SACT data (73 out of 123 patients). There are limitations to using this method for identifying this group of patients, but it is the most appropriate method for the objective of this report.

In table 5.3 there seems to be a decline in the number of patients each year diagnosed with secondary mRCC. This is a result of both the expected course of the disease and the method we have used to identify the group. It is more likely that patients diagnosed in 2019 have developed metastasis, than those diagnosed in 2021. Over time the number of patients developing metastasis is expected to increase for 2020 and 2021, coming closer to the number of patients with secondary mRCC in 2019.

### 5.3.2 Treatment trajectories (secondary mRCC)

For secondary mRCC we use the same grouping of therapies as described in section 5.2.3 and the sunburst diagram below begins with 1st line therapy in the center and subsequent lines of therapy outwards. For supplementary information on the number of patients and proportions of 1st line treatment, refer appendix table 7.7.

[2]The initial four months after diagnosis are included in the initial diagnosis period in CRN

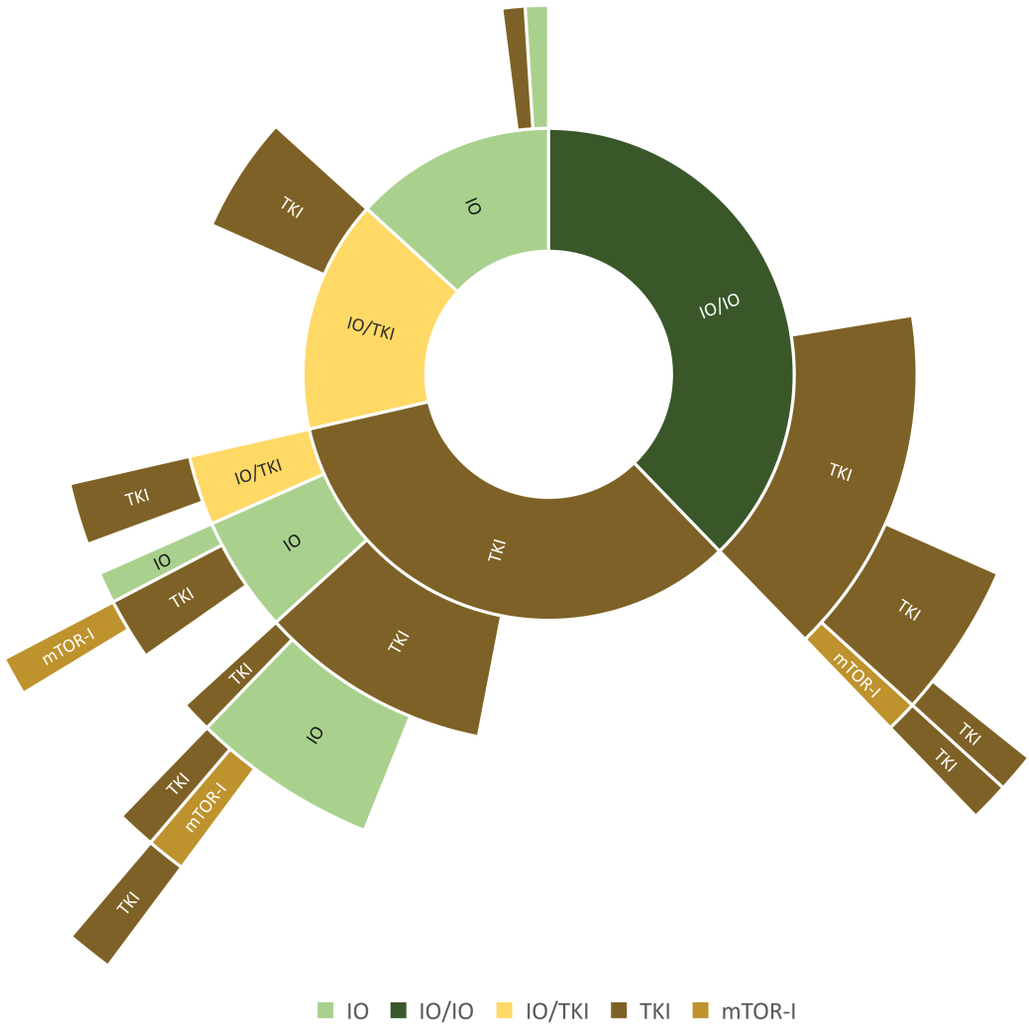



**Figure 5.7:** Treatment trajectories for patients with secondary mRCC

**Figure 5.7**

**Data source**
- Cancer Registry
- SACT data

**Inclusion**
- Secondary mRCC (refer to chapter 5.3.1 for more information)
- Initially diagnosed 2019–2021 with localised disease or regional metastasis
- Treated from 2019 until 30th June 2022

**Comments**
- Some patients may still be on treatment

Figure 5.7 shows that the majority of patients receive 1st line mono or combination therapy that includes immunotherapy (over 60% IO/IO, IO and IO/TKI) for this 3.5 year period. The combination therapy IO/IO is the most used 1st line therapy for secondary mRCC. TKI is used as monotherapy or in combination with IO, in almost 50% of patients (TKI and IO/TKI). The figure also shows that TKI monotherapy is the most dominant therapy in use for 2nd and 3rd line therapy. The treatment trajectories for secondary mRCC are similar to the overall structure of the treatment trajectories of primary mRCC in figure 5.3. For more details refer to table 7.7.

Figure 5.7 shows data for the 3.5 year period in question. Earlier in this report we showed that there has been a change towards more use of immunotherapy from 2019 to 2021 for primary mRCC (refer figure 5.1). We have not done an analysis for treatment choices grouped by year for secondary mRCC.

### 5.3.3 Time on treatment (secondary mRCC)

Figure 5.8 shows time on 1st line treatment for secondary mRCC, by type of therapy. Some patients in this analysis are still receiving treatment, which may affect treatment duration. See table 7.5 for an overview of the number of patients, and table 5.8 for the duration of treatments. Refer to appendix figure 7.2 for grouping of regimens to types of treatment.

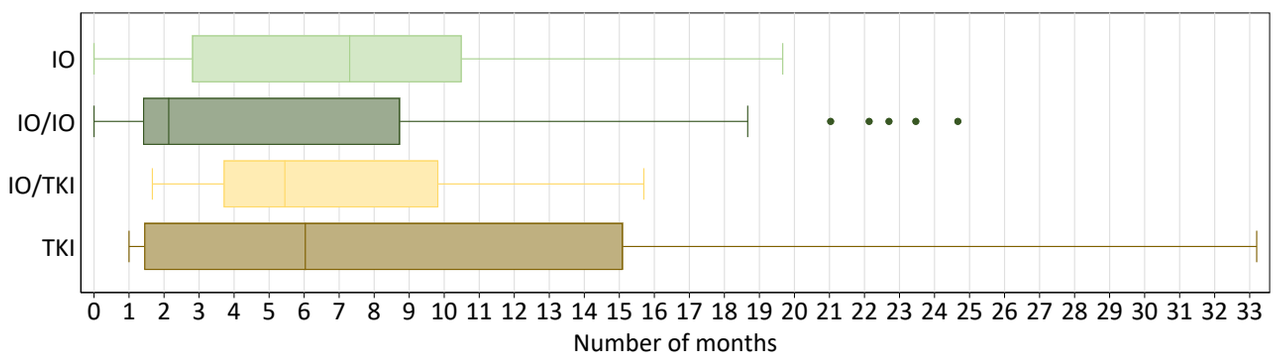



**Figure 5.8:** Time on 1st line treatment for patients with secondary mRCC

**Figure 5.8**

**Data source**
- Cancer Registry
- SACT data

**Inclusion**
- Secondary mRCC, initially diagnosed 2019–2021 with localised disease or regional metastasis
- Treated from 2019 until 30th June 2022

**Comments**
- Definition of treatment duration (refer to chapter 4.4)
- Total = 123 patients

Starting with immune monotherapy (IO), figure 5.8 shows that the median time on treatment is 7.3 months. Of the patients receiving IO, the lower 25% had a treatment duration between 0 to 2.8 months, while the middle 50% of patients received between 2.8 to 10.5 months, and the upper 25% had a treatment length between 10.5 to 19.7. These results show that time on treatment for secondary mRCC, generally are longer than those for primary mRCC, however the number of patients with secondary mRCC is small which may affect results (123 patients).

The combination IO/IO had 2.1 months median time on treatment for secondary mRCC. Of the patients receiving IO/IO , the lower 25% of patients had treatment durations between 0 to 1.4 months, the middle 50% of patients received treatment between 1.4 to 8.7 months, and lastly, the upper 25% had a treatment duration between 8.7 to 18.6 months. The treatment lengths for IO/IO in secondary mRCC are generally shorter than those for primary mRCC. However, a higher proportion of patients with secondary mRCC than primary mRCC is still on treatment at end of follow-up time (table 7.5).

The combination IO/TKI had 5.5 months median time on treatment for secondary mRCC. Of the patients receiving IO/TKI, the lower 25% had a treatment duration between 1.7 to 3.7 months, while the middle 50% of patients received treatment between 3.7 to 9.8 months, and lastly, the upper, 25% receive IO/TKI for 9.8 to 15.7 months. Treatment durations for IO/TKI in secondary mRCC are shorter compared to primary mRCC. However, also here a higher proportion of patients with secondary mRCC than primary mRCC is still on treatment at end of follow-up time (table 7.5).

TKI monotherapy had 6.0 months median time on treatment. Of the patients receiving TKI monotherapy, the lower 25% had a treatment duration between 1 to 1.4 months, the middle 50% of patients received treatment between 1.4 to 15.2 months, and lastly, the upper 25% of had a treatment duration between 15.2 to 33.2 months. Time on treatment for monotherapy TKI in secondary mRCC is longer than those for primary mRCC.

## 5.4 Treatment of mRCC for primary and secondary metastasis combined

### 5.4.1 First line therapy by age and gender (mRCC)

In this section, primary and secondary mRCC are combined into one group consisting of 301 patients. The following analysis focus on SACT for mRCC by age, gender, histology and region of residence.

**Table 5.5:** 1st line therapy of patients with mRCC by age and type of treatment

| | | Age | | | | | |
|---|---|---|---|---|---|---|---|
| | **N** | 18-49 | 50-59 | 60-69 | 70-79 | 80+ | **Median age** |
| **IO** | 25 | 4% | 24% | 24% | 36% | 12% | 69 |
| **IO/IO** | 104 | 12% | 27% | 32% | 28% | 2% | 64 |
| **IO/TKI** | 56 | 5% | 23% | 25% | 43% | 4% | 69 |
| **TKI** | 116 | 7% | 22% | 22% | 37% | 11% | 69 |
| **Total number of patients** | 301 | | | | | | |

**Table 5.6:** 1st line treatment of patients with mRCC by gender and type of treatment

| | | **Total** | IO | IO/IO | IO/TKI | TKI |
|---|---|---|---|---|---|---|
| **Male** | N | 216 | 16 | 65 | 40 | 95 |
| | % | | 7% | 30% | 19% | 44% |
| **Female** | N | 85 | 9 | 39 | 16 | 21 |
| | % | | 11% | 46% | 19% | 25% |

**Table 5.5 and 5.6**

**Data source**
- Cancer Registry
- SACT data

**Inclusion**
- mRCC
- Diagnosed 2019–2021
- SACT from 2019 until 30th June 2022

**Comments**
- 301 patients = 203 Primary mRCC treated with SACT + 98 Secondary mRCC treated with SACT (refer to table 5.3)

The age distribution of 1st line treatment in table 5.5 shows that median age for IO/IO is 64 years, compared to 69 years for the other three therapy groups. Table 5.6 also presents the gender distribution for the treatment groups. The table shows that 44% of the men in this group receive TKI as 1st line therapy, compared to 25% of the women. The combination IO/IO is given to 46% of women with mRCC as 1st line therapy, while 30% of the men receive the same therapy. The results indicate that there are differences in the choice of 1st line therapy for men and women. However, we have not analysed the specific age or histology distribution for men and women separately, and do not know if differences in age or histology could explain some of these results. Again it is noteworthy that the groups are small and that random (and natural) variation may also contribute to these differences.

### 5.4.2 First line therapy by histology (mRCC)

Figure 5.9 shows 1st line therapy for mRCC grouped by histology.

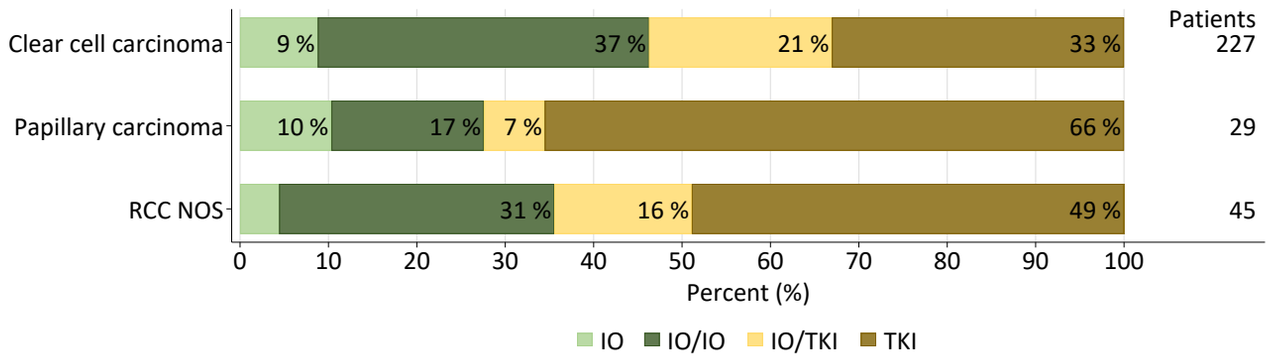



**Figure 5.9:** 1st line treatment of patients with mRCC by type of histology

**Table 5.9**

**Data source**
- Cancer Registry
- SACT data

**Inclusion**
- mRCC
- Diagnosed 2019–2021
- SACT from 2019 until 30th June 2022

**Comments**
- Total = 301 patients

Clear cell carcinoma is the most common histology (75% of patients) among mRCC patients receiving 1st line SACT. About 67% of patients with clear cell carcinoma received immunotherapy as part of their 1st line treatment either as monotherapy or in combination with IO or TKI. The combination IO/IO therapy was the most common 1st line therapy (37%), while 33% and 21% received TKI and IO/TKI, respectively.

Papillary carcinoma is the smallest group, consisting of 29 patients. This means that random (and natural) variation may impact the results to a larger extent than for the group of clear cell carcinoma. Papillary carcinoma seems to be treated mostly with TKI as 1st line therapy (mono or in combination with IO, 73%). About 34% receive immunotherapy (monotherapy or in combinations) as 1st line therapy.

The group with RCC NOS consists of 45 patients. About 65% of patients received 1st line therapy with TKI, alone or in combination, while 51% of patients received immunotherapy as monotherapy or as a combination.

Figure 5.9 shows results for a time period of 3.5 years combined. Figure 5.4 showed that 1st line therapy had changed from 2019 until 2021 for primary mRCC, towards an increase in the use of immunotherapy. A similar analysis has not been conducted for treatment choices grouped by year and histology.

### 5.4.3 First and second line therapy by region (mRCC)

Figure 5.10 presents the proportions of treatment groups among patients receiving 1st line therapy. For percentage of patients receiving 1st line therapy among all patients diagnoses with kidney cancer or primary mRCC, see table 5.3.

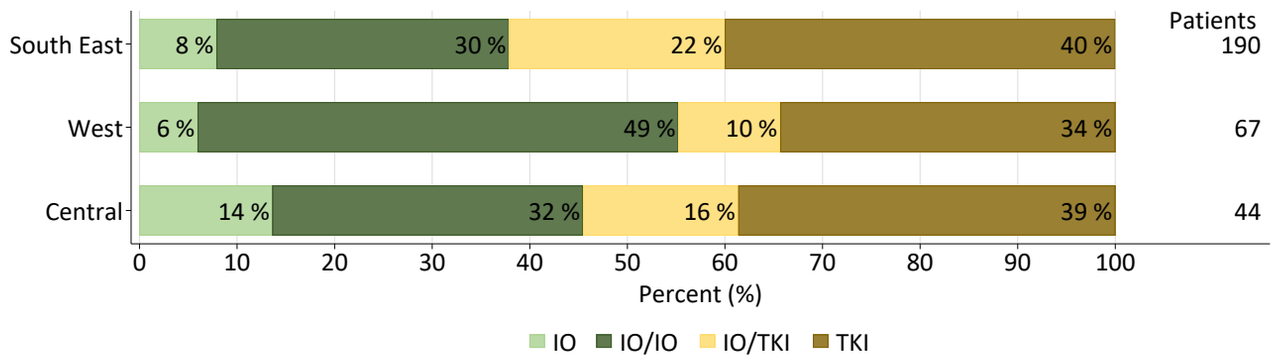



**Figure 5.10:** 1st line treatment of patients with mRCC by health region

Figure 5.10 illustrates that the South East region uses TKI (as monotherapy or in combinations) more than the other regions as 1st line treatment, as 62% of patient receive this therapy. The Western region uses TKI as part of 1st line therapy for mRCC in 44% of patients. The figure also show that the Western region use more immunotherapy as 1st line, especially the combination IO/IO, which is given to 49% of the patients receiving 1st line therapy.

First line therapy proportions seems to differ between the regions among the patients receiving 1st line treatment, but the Western and Central regions have few patients (67 and 44 respectively). These results may be affected by variations in patient characteristics (age, comorbidity, histology et.c.) and may not show actual differences in treatment. If followed over time, the results may give a clearer indication on, whether or not, there are regional variations in care. No statistical testing of differences among the group has been performed.

Among the 301 patients receiving 1st line SACT a subset of patients went on to receive 2nd line therapy. Figure 5.11 presents the proportion that received 2nd line therapy by region among the patients receiving 1st line (figure 5.10). The overall average in Norway is also presented.

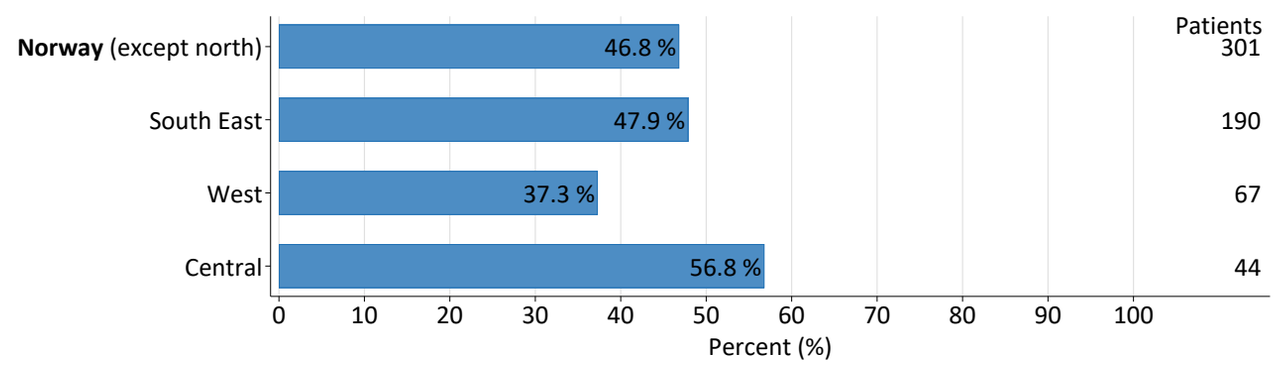



**Figure 5.11:** 2nd line treatment of patients with mRCC by health region

**Figure 5.10 and 5.11**

**Data source**
- Cancer Registry
- SACT data

**Inclusion**
- mRCC
- Diagnosed 2019–2021
- SACT from 2019 until 30th June 2022

**Comments**
- Total = 301 patients
- Region refers to region of residence at time of diagnosis
- Third line therapy is not presented, as the number of mRCC patients are 56 in total
- For an overview of hospitals in each region refer to figure 4.2

Figure 5.11 presents the 2nd line treatment for patients with mRCC by region. In this figure the number of patients is even smaller than in figure 5.10. Even small differences in patient populations may have a large impact on the results (because of few patients), so this figure should be interpreted with care.

There is no figure showing 3rd line therapy by region, because the number of patients is too small (in total 56 patients). For the Western and Central region there are less than ten patients per region in this group.

# Chapter 6

# Conclusion

The purpose of this report is twofold (as explained in the introduction); 1) analyse systemic anti-cancer therapy for kidney cancer and 2) evaluate possibilities and limitations when using SACT data with core variables (for cancers without a clinical registry). In this chapter these two goals are summarized and evaluated.

## 6.1 Analyse systemic anti-cancer therapy for kidney cancer

To conclude on the first point, the specific aims in the project plan are summarized below, with comments and references.

- Identifying and curating relevant data:
  Refer to chapter 4
- Describe kidney cancer patients with respect to demographic parameters:
  Refer to chapter 5.1.3, 5.2.2 and 5.3.1.
- Describe earlier cancer cases in the population:
  Not done in this report, apart from excluding multiple cases of kidney cancer in the same patient, refer to chapter 5.1.2. Other cancer diagnoses in the study population has been relevant to assess, in order to link SACT with the correct diagnosis (if the patient has more than one cancer in the CRN), refer to chapter 4.3.
- What type of treatment does kidney cancer patients receive:
  Refer to chapter 5.
- Has immunohistochemistry been used to confirm the diagnosis:
  Not done. The CRN does not register the actual results of the analyses. Analysing whether immunohistochemistry has been performed, has not been prioritised. Refer to chapter 4.1 for a description of available data.
- Which hospital treated the patient:
  The report shows number of patients divided by region and treatment choices by region, refer to chapter 5.1.3, 5.2.2, 5.3.1 and 5.10. The number of patients is too small to differentiate between hospitals.
- Mortality for kidney cancer and whether the cause of death was related to kidney cancer or not:
  The report present trends for mortality over the last five decades, refer to chapter 5.1, but not cancer related cause of death. The report focuses on kidney cancer diagnosis starting i 2019 until 2021 because the SACT data is not available from all sources until 2019. This means that there is limited follow up time on these patients, which is one of the reasons for not including mortality.
- Assess routine analysis and publication of results for kidney cancer:
  Annual reporting focusing on kidney cancer will probably not be possible, until there is a clinical registry for kidney cancer.

- Document data, quality of data, analysis, possibilities and limitations:
  Refer to chapters 4 and 5. A discussion on possibilities and limitations follows below.

This report have looked at SACT in kidney cancer, and provided a short overview of incidence, survival, mortality and overall treatment for all kidney cancer cases (with the exceptions listed above). This report does not analyse survival, apart from the overall trend figure in the beginning of chapter 5. The patient population is small and the follow-up time is short for some of these patients, therefor a more in-depth analysis on survival has not been done.

## 6.2 Evaluate possibilities and limitations when using SACT data with core variables

The second purpose of this report was to evaluate possibilities and limitations when using SACT data in cancers where only core variables are available. In conclusion, the CRN can provide an overview of treatment for many different cancer types, as long as the core variables in the CRN (together with treatment data) are sufficient for the analyses. An example from this report is the use of SEER staging to differentiate between groups of patients (refer to table 4.2. For metastatic renal cancer, SEER staging proved sufficient to identify the primary metastatic patients. The report has therefor been able to show analyses on patient characteristics and treatment trajectories for primary metastatic RCC.

Even if the overall mRCC population could be identified using SEER stage, the lack of TNM staging and IMDC risk assessment are still major limitations for analysing treatment of kidney cancer. For example the combination ipilimumab/nivolumab has a positive reimbursement decision for former untreated patients with advanced mRCC in intermediate-/high-risk profile patients. The lack of data on IMDC risk assessments and TNM-staging in the CRN limits how the analyses in this report can be stratified and the results can not show if treatment is given according to this reimbursement decision or not.

The mRCC patient group is also small and even if further sub-grouping could be done (for example using TNM), dividing the cases into even smaller groups could possibly lead to problems in interpreting results because of random (and natural) variation.

For secondary metastatic RCC patients, there are limitations in data capture that makes it difficult to identify the patients. Not all cases of secondary metastasis are confirmed with a biopsy and there are no clinical notifications in use to report secondary metastasis in cancers with no clinical registry. To compensate for this, the patient population were partly identified by the fact that they had received SACT after an initial diagnosis with locoregional disease (in the cases where there was no pathological report present to confirm secondary metastasis). There are limitations to using SACT to identify secondary metastasis and a recommendation for future analyses is to also use NPR data to identify this patient group.

For most cancer types the recommendations for diagnostic work-up, treatment and follow-up requires more detailed information on the tumour, how it affects nearby structures, lymph node status, metastasis, immunohistochemistry results etc., than what SEER staging offers. For cancer types with clinical registries, the CRN can register more diagnostic details and the hospitals are also required to report more clinical details on each patient. This increases the amount of data available and makes it possible to analyse more aspects of diagnostic work-up, treatment and follow-up, than what is possible on cancer types without clinical registries.

There are also limits to how the hospitals report data to the CRN. Data needs to be reported automatically, or at least with as little manual labour as possible. This requires structured electronic patient charts where the reporting is built into the system. This work has been initiated in Norway but there is still a long way to go.

The lack of a clinical registry for kidney cancer limits the amount, and details, of data we are able to collect. For kidney cancer specifically, the lack of automatically reported data means that the CRN will not be able to extend the available data on kidney cancer and use it in annual reports, until this situation changes.

## 6.3 Expected benefits and recommendations

One of the aims has been to understand and present the extent of information that can be extracted from the CRN, for a cancer type without a clinical registry and present how it can be combined with SACT data. This project has shown that it is possible to evaluate some parts of the patient pathways, as long as the core variables are sufficient for the analyses. It is recommended to do a feasibility analysis before starting a project, to assess whether or not the core variables (together with treatment data) will be sufficient, and if it is possible to compensate for the limitations. One example of compensating for the limitations is by using other data that indicates that an event has taken place, like change in treatment indicates that a patient has had unacceptable side effects or did not respond to treatment.

There have been discussions in Norway on whether or not data from the CRN (and other registries) can be used to follow the implementations of new drugs and the effect on patients' survival. This report shows that it is possible to follow the implementation of new drugs, as long as the limitations in available data are taken into account. This report uses data from the CRN and documents both possibilities and limitations in using CRN registry data for evaluating kidney cancer care and the use of SACT. Together with the reports from INSPIRE lung cancer and INSPIRE breast cancer, this report hopefully gives a view of the possibilities in using CRN data for evaluating SACT use.

The partners in INSPIRE kidney cancer wanted to look at the use of immunotherapy in kidney cancer and if there were unwanted variations in treatment choices. The report has been able to look at trends in treatment choices, together with analyses on first and subsequent lines of therapy, and treatment in the different regions. This report presents data demonstrating the implementation and establishment of newly approved immunotherapy combinations as the new standard of care for the majority of mRCC patients. There are variations between the regions but the patient group is small and the follow-up time short, and the results should be interpreted with care.

Lastly the project aimed to provide an overview of treatment for metastatic kidney cancer within the rapidly evolving treatment landscape. This report will help to motivate safe and equal access to new therapies in Norway. This report presents the information we have available on kidney cancer treatment in Norway from 2019 until June 2022. It would be beneficial to follow these results over time, to look more closely at treatment choices in the different regions for example, but that is not a part of this project.

## 6.4 Access to data

SACT data will be accessible towards the summer of 2023. This includes all types of cancers, both with and without clinical registries. Access to such data requires applications via www.helsedata.no and the necessary approvals. The SACT data set will need adjustment and curation by the applicant, for example by linking SACT data to individual cancer cases, aggregating treatment regimens and cycles et.c. according to the specific needs of the study in question.

# Chapter 7

# Appendix

## 7.1 Kidney cancer morphologies and grouping

**Table 7.1:** Kidney cancer morphologies and grouping

| Morphology code (ICDO3) | Morphology | Group | Cases |
|---|---|---|---|
| 83103 | Clear cell adenocarcinoma | Clear cell carcinoma | 1844 |
| 82603 | Papillary adenocarcinoma | Papillary carcinoma | 463 |
| 69999 | Microscopic examination not done or not known whether or not a microscopic examination is performed | Other histologies | 190 |
| 83173 | Renal cell carcinoma, chromophobe type | Chromophobe*, Other histologies | 152 |
| 83123 | Renal cell carcinoma, NOS | RCC NOS | 112 |
| 80003 | Neoplasm, malignant | Other histologies | 31 |
| 69009 | Microscopic examination performed, but no morphology is reported | Other histologies | 12 |
| 80103 | Carcinoma, NOS | Other histologies | 12 |
| 83183 | Renal cell carcinoma, sarcomatoid | RCC NOS | 8 |
| 83163 | Cyst-associated renal cell carcinoma | Other histologies | 6 |
| 84803 | Mucinous adenocarcinoma | Other histologies | 0-5 |
| 83113 | Hereditary leiomyomatosis and renal cell carcinoma - syndrome associated renal cell carcinoma | RCC NOS | 0-5 |
| 82903 | Oxyphilic adenocarcinoma | Chromophobe*, Other histologies | 0-5 |
| 80013 | Tumour cells, malignant | Other histologies | 0-5 |
| 80133 | Large cell neuroendocrine carcinoma | Other histologies | 0-5 |
| 80703 | Squamous cell carcinoma, NOS | Other histologies | 0-5 |
| 81403 | Adenocarcinoma, NOS | Other histologies | 0-5 |
| 83203 | Granular cell carcinoma | RCC NOS | 0-5 |

**Table 7.1**

**Data source**
- Cancer registry

**Inclusion**
- Kidney cancer ICD-10: C64
- Diagnosed 2019–2021

**Comments**
- *Chromophobe are grouped with "other histologies" in the analysis
- "Renal cell carcinoma, sarcomatoid" accounts for 8 patients. Sarcomatoid dedifferentiation is not considered to be a unique histological subtype of RCCs; rather, it can be present within any subtype of RCCs[19] (e.g Clear cell carcinoma with sarcomatoid dedifferentiation is classified as Clear cell carcinoma).
- The morphology code for Renal cell Carcinoma, NOS is used on samples that are not further classified (not otherwise specified).
- 0-5: In groups with five or less cases, the actual number of cases will not disclosed

## 7.2 Regimens and type of treatment

**Table 7.2:** Grouping of regimens to type of treatment, only regimens received by 10 patients or more

| Regimen | Type |
|---|---|
| Aksitinib | TKI |
| Aksitinib + Pembrolizumab | IO/TKI |
| Atezolizumab | IO |
| Everolimus | mTOR-I |
| Ipilimumab + Nivolumab | IO/IO |
| Kabozantinib | TKI |
| Kabozantinib + Nivolumab | IO/TKI |
| Lenvatinib | TKI |
| Nivolumab | IO |
| Pazopanib | TKI |
| Pembrolizumab | IO |
| Rituksimab | IO |
| Sunitinib | TKI |

## 7.3 Active substances and number of patients

**Table 7.3:** Number of RCC patients receiving at least one dose of active substance

| Active substance | ATC code | N |
|---|---|---|
| Nivolumab | L01FF01 | 190 |
| Kabozantinib | L01EX07 | 122 |
| Ipilimumab | L01FX04 | 119 |
| Pazopanib | L01EX03 | 113 |
| Aksitinib | L01EK01 | 94 |
| Pembrolizumab | L01FF02 | 84 |
| Sunitinib | L01EX01 | 51 |
| Lenvatinib | L01EX08 | 12 |
| Everolimus | L01EG02 | 12 |

## 7.4 Proportion of patients receiving SACT within 6 months of the following year

**Table 7.4:** Proportion of patients receiving SACT within 6 months of the following year

| Year | Patients (study population) | SACT treated | |
|---|---|---|---|
| | N | n | % |
| 2019 | 804 | 108 | 13.4 |
| 2020 | 777 | 103 | 13.3 |
| 2021 | 801 | 116 | 14.5 |

**Table 7.4**

**Data source**
- Cancer registry
- SACT data

**Inclusion**
- Study population, refer to 5.1

**Comments**
- 2019 with follow-up 30.06.2020
- 2020 with follow-up 30.06.2021
- 2021 with follow-up 30.06.2022

## 7.5 Time on treatment

**Table 7.5:** Number of patients still on treatment at end of follow-up, from figure 5.6 and 5.8

| | Primary metastatic RCC | | | | Secondary metastatic RCC | | | |
|---|---|---|---|---|---|---|---|---|
| | IO | IO/IO | IO/TKI | TKI | IO | IO/IO | IO/TKI | TKI |
| Total patients (N) | 12 | 67 | 45 | 79 | 13 | 37 | 18 | 30 |
| Patients still on treatment at end of follow-up (N) | 5 | 16 | 27 | 4 | 4 | 13 | 8 | 7 |
| Patients discontinued (N) | 7 | 51 | 18 | 75 | 9 | 24 | 10 | 23 |

**Table 7.6:** Tabular representation of time on treatment box plots, from figure 5.6 and 5.8

| | Primary metastatic RCC | | | | Secondary metastatic RCC | | | |
|---|---|---|---|---|---|---|---|---|
| | IO | IO/IO | IO/TKI | TKI | IO | IO/IO | IO/TKI | TKI |
| Total patients (N) | 12 | 67 | 45 | 79 | 13 | 37 | 18 | 30 |
| $25^{th}$ percentile (months) | 1.5 | 1.4 | 4.5 | 1.5 | 2.8 | 1.4 | 3.7 | 1.4 |
| Median (months) | 3.3 | 4.7 | 7.8 | 3.6 | 7.3 | 2.1 | 5.5 | 6.0 |
| $75^{th}$ percentile (months) | 10 | 10.5 | 13.3 | 7 | 10.5 | 8.7 | 9.8 | 15.1 |

**Table 7.6 and 7.5**

**Data source**
- Cancer registry
- SACT data

**Inclusion**
- Study population, refer to section 5.1.2

**Comments**
- Discontinued is defined as either dead or have not received SACT (both active substances if combination) for 60 days prior to end of follow-up time (30.06.2022)
- Time on treatment does not take into account if one of the active substances in a combination treatment is discontinued

## 7.6 Treatment trajectories (mRCC)

Figure 7.1 presents the treatment trajectories for all primary and secondary mRCC SACT treated patients (301 patients). Patients not receiving SACT is not included. A tabular representation of the 1st and 2nd line treatment group proportions can be found in table 7.7.

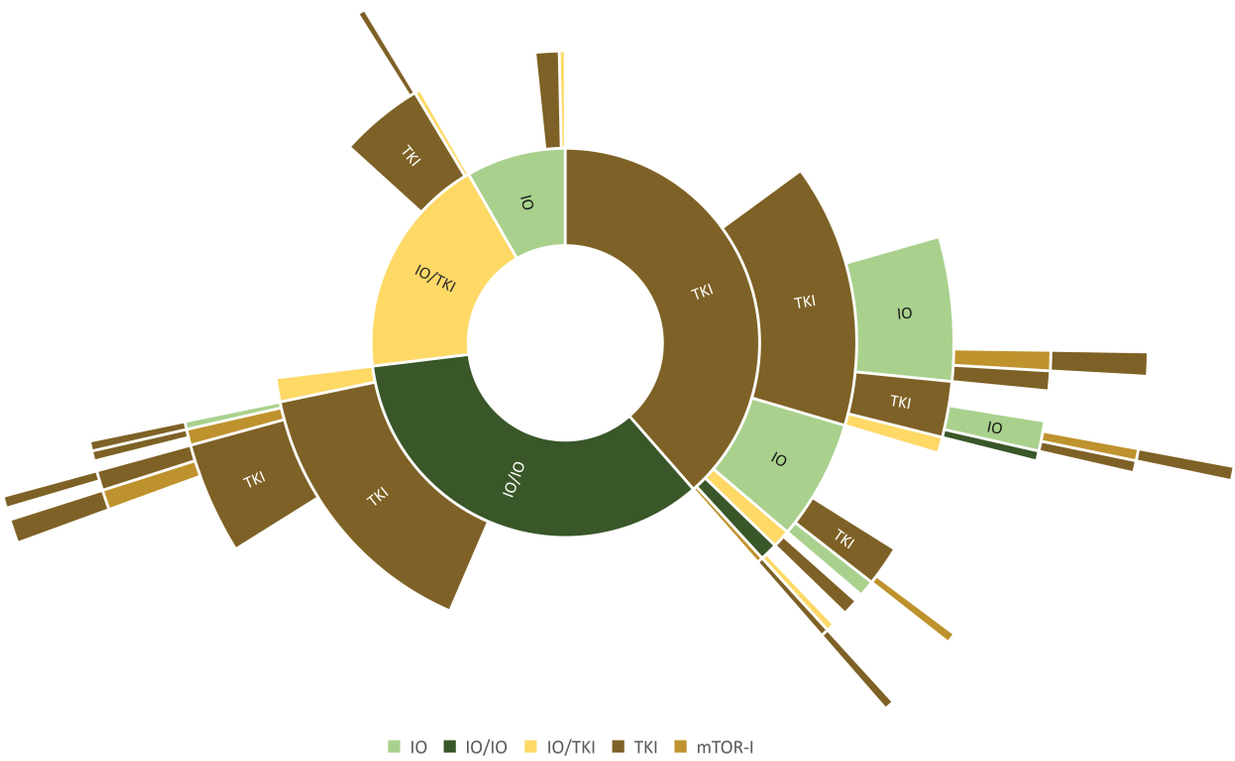



**Figure 7.1:** Treatment trajectories of patients with mRCC

**Figure 7.1**

**Data source**
- Cancer registry
- SACT data

**Inclusion**
- mRCC
- Diagnosed 2019–2021
- SACT from 2019 until 30th June 2022

**Comments**
- Total = 301 patients

## 7.7 Tabulation of patient trajectories

**Table 7.7:** Tabular representation of 1st and 2nd line treatment proportions (among 1st line SACT patients) from figure 5.3, 5.7 and 7.1

| | | Primary mRCC | | Secondary mRCC | | mRCC | |
|---|---|---|---|---|---|---|---|
| | | N | % | N | % | N | % |
| Total patients | | 203 | | 98 | | 301 | |
| 1st line treatment | | | | | | | |
| IO | | 12 | 6 % | 13 | 13 % | 25 | 8 % |
| IO/IO | | 67 | 33 % | 37 | 38 % | 104 | 35 % |
| IO/TKI | | 41 | 20 % | 15 | 15 % | 56 | 19 % |
| TKI | | 83 | 41 % | 33 | 34 % | 116 | 39 % |
| 1st line treatment | 2nd line treatment | | | | | | |
| IO | IO | - | - | - | - | - | - |
| | IO/IO | - | - | - | - | - | - |
| | IO/TKI | - | - | <5 | NA | <5 | NA |
| | TKI | <5 | NA | <5 | NA | <5 | NA |
| IO/IO | IO | - | - | - | - | - | - |
| | IO/IO | - | - | - | - | - | - |
| | IO/TKI | <5 | NA | - | - | <5 | NA |
| | TKI | 31 | 15 % | 15 | 15 % | 46 | 15 % |
| IO/TKI | IO | - | - | - | - | - | - |
| | IO/IO | - | - | - | - | - | - |
| | IO/TKI | <5 | NA | - | - | <5 | NA |
| | TKI | 9 | 4 % | 5 | 5 % | 14 | 5 % |
| TKI | IO | 15 | 7 % | 5 | 5 % | 20 | 7 % |
| | IO/IO | <5 | NA | - | - | <5 | NA |
| | IO/TKI | - | - | <5 | NA | <5 | NA |
| | TKI | 34 | 17 % | 10 | 10 % | 44 | 15 % |
| | mTOR-I | <5 | NA | - | - | <5 | NA |

## 7.8 Figure explanation for treatment duration (box plots)

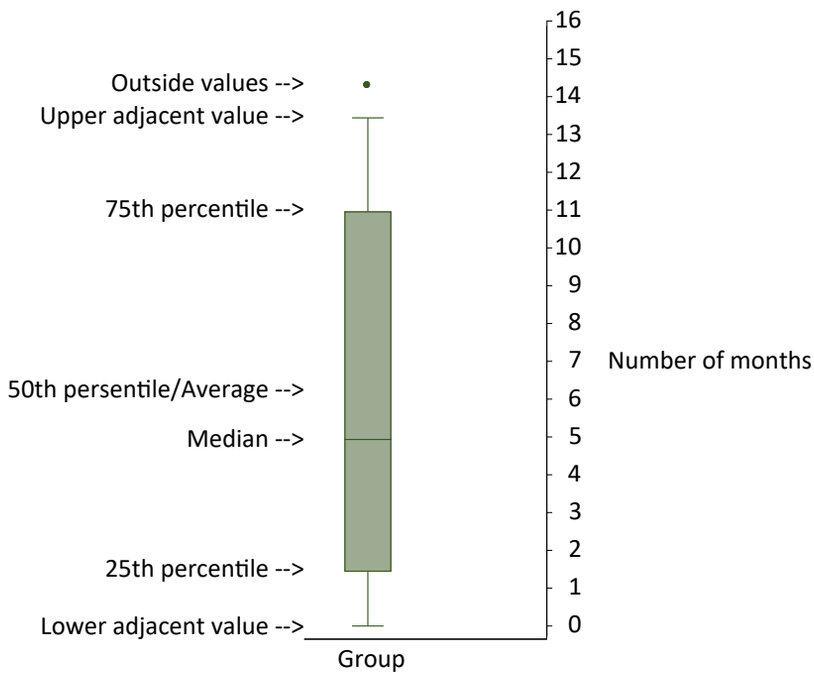



**Figure 7.2:** Illustration on how to interpret time on treatment box plots

## 7.9 Members of the steering committee, sub board and analysis group, INSPIRE kidney cancer

**Table 7.8:** The steering committee

| Name | Organisation |
|---|---|
| Lena Holmström | Cancer Registry of Norway |
| Giske Ursin | Cancer Registry of Norway |
| Bjørn Møller | Cancer Registry of Norway |
| Jan Nygård | Cancer Registry of Norway |
| Sigbjørn Smeland | Oslo University Hospital |
| Katrine Bryne | LMI - Association of the Pharmaceutical Industry in Norway |
| Lisa Gerner | Bristol Myers Squibb (BMS) |
| Sylvi Nguyen | MSD |
| Arn Meland | South East Regional Health Authority |
| Kristine Kloster-Jensen | Western Regional Health Authority |
| Henrik Sandbu | Central Regional Health Authority |
| Synøve Kalstad | Northern Regional Health Authority |
| Siri Kolle | Inven2 |
| Stine Bergliot Høibak-Nissen | Cancer Society of Norway |

**Table 7.9:** The sub board

| Name | Organisation |
|---|---|
| Katrine Bryne | LMI - Association of the Pharmaceutical Industry in Norway |
| Lisa Gerner | Bristol Myers Squibb (BMS) |
| Sylvi Nguyen | MSD |
| Siri Børø | Merck |
| Cathrine Notland | Pfizer |

**Table 7.10:** The analysis group

| Name | Organisation |
|---|---|
| Espen Enerly | Cancer Registry of Norway |
| Anna Skog | Cancer Registry of Norway |
| Kristin Oterholt Knudsen | Cancer Registry of Norway |
| Tom Børge Johannesen | Cancer Registry of Norway |
| Lena Holmstrøm | Cancer Registry of Norway |
| Silje Spinnangr Olsen | Cancer Registry of Norway |
| Inga Hatle | Cancer Registry of Norway |
| Heidi Knobel | St. Olavs Hospital |
| Christoph Müller | Sørlandet Hospital |
| Siri Børø | Merck |
| Cathrine Notland | Pfizer |
| Anja Schiel | Norwegian Medicines Agency |
| Helle Nærsnes Endresen | Norwegian Hospital Procurement trust |
| Mohammad Nouri Sharikabad | Norwegian Institute of Public health |
| Lotte Strandjord | Norwegian Patient Registry |
| Stine Bergliot Høibak-Nissen | Norwegian Cancer Society |
| Katrine Bryne | LMI - Association of the Pharmaceutical Industry in Norway |

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