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Healthcare resources utilization and exploration of the patient journey through claims database: an application on advanced renal cell carcinoma patients in France

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Background

- In 2018, kidney cancer was the 7th most common cancer in France, with 15,323 incident cases. The median age at diagnosis is 68 years, and 67% are diagnosed in men.[1]
- Most common type of kidney cancer is renal cell carcinoma (RCC), of which 80% are clear cell carcinoma, the most common and aggressive type of RCC.[1, 2]
- A third of RCC patients present distant metastases at diagnosis, and around 20-50% will eventually have advanced or metastatic RCC (aRCC).[2]
- The available therapeutic options to treat RCC are evolving very rapidly. Over the last ten years, tyrosine kinase inhibitors (TKI) monotherapies (*e.g.* sunitinib and pazopanib) were the standard of care for first-line treatment (1L). In some cases, such as poor-prognosis aRCC, a mTOR inhibitor (*e.g.* temsirolimus) was administered.[3, 4]
- With the approval of immunotherapy as second-line (2L) treatment in 2016, the aRCC patients' treatment pathways has changed. With immunotherapy infusion performed in hospital setting substituting oral treatment administered at home, the role and the coordination requirement between office-based practitioners and hospitals may have been modified.[5]
- The analysis of the healthcare resources utilization (HCRU) of 2L aRCC patients and the care journey according to the 2L treatment before 2019 is essential to understand and characterize the impact of a treatment with a new mechanism of action on the patients care journey, and the study objective was to describe this.

Methods

Data source

- This cohort study was build based on the French nationwide healthcare insurance system claims database ("*Système National des Données de Santé*", SNDS). The SNDS includes anonymous individual data for all affiliated persons, covering at least 99% of French residents (around 66 million individuals).[6]
- The following categories of data are available in the SNDS:
  - socio-demographic characteristics,
  - ambulatory care,
  - hospital discharge summaries,
  - registration status for 30 long-term diseases (LTD).[6]
- In the SNDS, drugs are coded according to the Anatomical Therapeutic Chemical (ATC) classification, hospital diagnoses and LTD are coded with the International Classification of Diseases, 10th Revision (ICD-10), and medical and surgical procedures are coded according to the *Classification Commune des Actes Médicaux* (CCAM).[6]
- The study protocol was approved by *the Comité éthique et scientifique pour les recherches, les études et les évaluations dans le domaine de la santé* (CESREES; file number 1622015) and by the *Commission nationale de l'informatique et des libertés* (CNIL; file number 920314).

Selection of the population

- Cohort of patients initiating systemic 1L therapy for aRCC in 2016.
- Inclusion criteria:
  - Initiation of one of the following treatments: aldesleukin, sunitinib, pazopanib, sorafenib, bevacizumab, interferon alfa-2a, axitinib, temsirolimus, everolimus, cabozantinib, nivolumab between 01/01/20216 and 31/12/2016 (first dispensing = index date),
  - Diagnosis of aRCC during the study period (hospitalization diagnosis or LTD C64, or renal biopsy in the six months period preceding the index date).
- Exclusion criteria:
  - Age <18 years at index date,
  - Another cancer diagnosis prior to index date for which the first systemic treatment is reimbursed (*e.g.* sunitinib and gastric cancer, bevacizumab and colorectal cancer),
  - Another aRCC treatment prior to index date,
  - Less than one year history prior to index date,
  - Standard SNDS criteria (*e.g.* same-sex twins, Mayotte, *etc.*).
- Study periods (**Figure 1**):
  - Inclusion period: 1st January to 31st December 2016,
  - Historical period: 1st January 2006 to the index date,
  - Follow-up period: until death from any cause, loss to follow-up (*i.e.*, absence of care consumption for at least six months) or end of the study period on 31st December 2019, whichever occurred first.
- In this analysis, we focused on all patients initiating a 2L aRCC treatment, among those meeting the inclusion criteria.

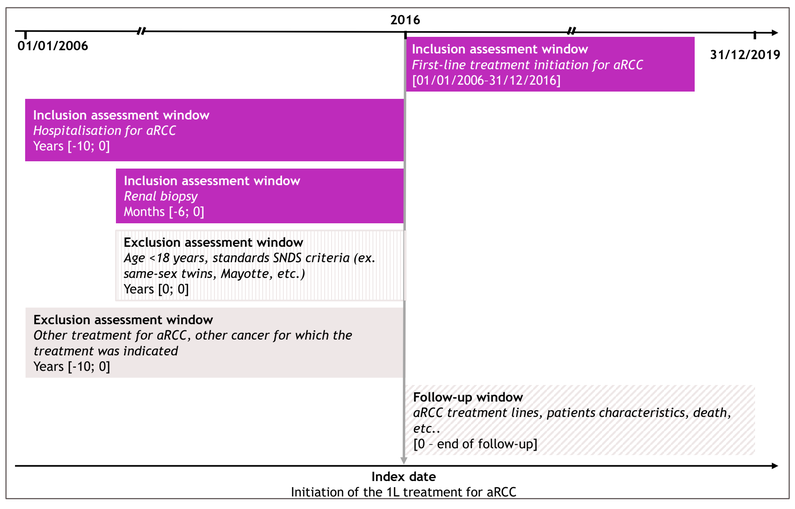


Figure 1. Study design

Statistical analyses

- HCRU analysis were performed during 2L treatment (from 2L initiation to end of 2L treatment), over the treatment period and on a per month of treatment basis.
- Kaplan-Meier approach was applied to estimate the median time to 2L treatment discontinuation (TTD).
- As required by the French General Data Protection Regulation (GDPR), all results for less than 11 patients were not presented.
- Statistical analysis was carried out using SAS version 9.4 software (SAS Institute Inc., Cary, NC).

Results

Selection of the population

- Among 1,629 patients (27.7%) initiated 1L treatment for aRCC in 2016, 872 (53.5%) received a 2L treatment over the follow-up period (**Figure 2**).
- Within 2L, patients mainly received nivolumab (43.7%) and TKIs (42.2%, notably axitinib and cabozantinib).

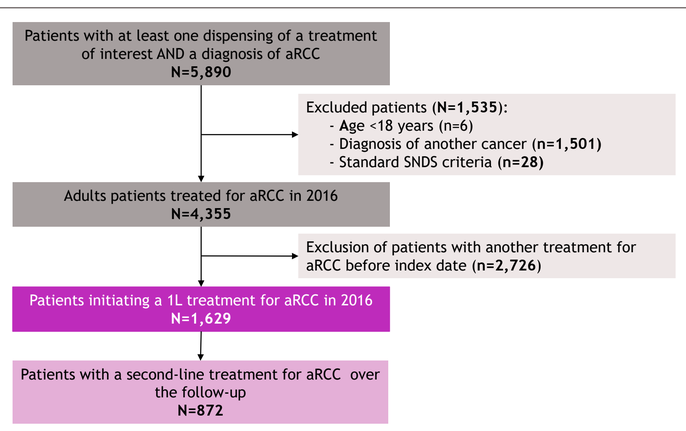


Figure 2. Selection of the population

Characteristics of patients at initiation of 2L treatment (Table 1)

- Three-quarters (76.7%) of patients were male and the median age was 66.5 ears.
- Circa two-thirds (66.3%) of patients had at least one metastatic site and 51.3% had synchronous diagnosis.
- Main localizations for metastases were lung (75.4%) and bones (50.2%).
- 69.2% of patients had undergone total nephrectomy.
- Most of patients had at least one comorbidity other than their aRCC: 17.1% of patients had diabetes and 12.4% had chronic lung disease.
- Patients treated with nivolumab seemed different from those treated with TKI. Patients treated with nivolumab:
  - Had fewer synchronous metastases (56.8% *versus* 60.9%), but more localized lung (56.4% *versus* 44.0%) and liver (18.1% *versus* 13.0%) metastases,
  - Had more diabetes (19.4% *versus* 13.6%).
- Overall, the median TTD was 4.5 months. It was 5.1 months for nivolumab ; for TKIs the median TTD was 4.9 months.

Table 1. Characteristics of patients at initiation of the second line of treatment

Characteristics, *n (%)*	Total N=872	Nivolumab n=381	TKI n=368	Other treatments n=123
Median age, years	66.5	67.4	65.5	66.3
Men	669 (76.7)	300 (78.5)	277 (75.3)	93 (75.6)
Age-adjusted Charlson score ≥7[a]	822 (94.3)	361 (94.8)	348 (94.6)	113 (91.9)
Median delay between diagnosis of aRCC and 1L initiation, months	7.9	8.4	8.7	5.2
Synchronous metastases[b]	349 (60.4)	142 (56.8)	156 (60.9)	51 (70.8)
Lung metastases[c]	436 (75.4)	215 (86.0)	162 (63.3)	59 (81.9)
Bones metastases[c]	290 (50.2)	132 (52.8)	122 (47.7)	36 (50.0)
Anterior local treatment				
Total nephrectomy	603 (69.2)	270 (70.9)	257 (69.8)	76 (61.8)
Partial nephrectomy	71 (8.1)	33 (8.7)	33 (9.0)	<11[d]
Metastasectomy	68 (7.8)	30 (7.9)	26 (7.1)	12 (9.8)
Radiotherapy	213 (24.4)	106 (27.8)	92 (25.0)	15 (12.2)
Median time to discontinuation (TTD), months	4.5	5.1	4.9	3.0

[a] The minimum possible score was six, all patients have un cancer; [b] Metastases diagnosed <6 months after the diagnosis of aRCC, [c] Among patients with at least one metastasis; [d] As required by the French GDPR, all results for less than 11 patients were not presented.
TKI: tyrosine kinase inhibitors

HCRU during the 2L treatment

Overall HCRU over the treatment duration (Figure 3)

- Almost half of the patients had at least one hospital doctor visit, a complete hospitalization and imaging or procedures performed in hospital setting over the treatment period.
- More than 95% of patients saw their pharmacist at least once a month.
- The nurse is a key player in patient follow-up in terms of both frequency and intensity of interaction.
- The general practitioner (GP) is involved in the management of 70% of patients on 2L aRCC treatment with a median number of consultation per month <1.
- Patients treated with nivolumab had similar patient journey in comparison to patients treated with TKI, expect for treatment infusion (session at hospital for aRCC treatment).

All patients n=872			% of patients with HCRU during 2L (all patients)	Median PPPM (patients with a care consumption)
Hospital HCRU	Session at hospital for aRCC treatment		43.0	1.7
	Other hospital Care	Session at hospital for another treatment	20.0	0.7
		Visit to any doctor in inpatient setting (without hospit.)	59.6	0.6
		Complete MSO hospitalization excl. palliative care	48.3	0.4
		Complete MSO hospitalization for palliative care	11.2	0.4
		Day hospitalization	22.4	0.2
		Emergency room	30.8	0.3
Dispensation of aRCC treatment			100.0	1.1
Retail pharmacy		Dispensation of another drug in community pharmacy	95.1	2.2
		Dispensation of another drug in hospital pharmacy	4.6	0.3
Ambulatory care		Visit to GP in outpatient setting only	72.6	0.8
		Nurse care received in outpatient setting only	81.7	2.4
		Imaging exams and procedures recorded in ambulatory	48.9	0.4

Nivolumab n=381			% of patients with HCRU during 2L (all patients)	Median PPPM (patients with a care consumption)
Hospital HCRU	Session at hospital for aRCC treatment		93.2	1.7
	Other hospital Care	Session at hospital for another treatment	28.9	0.7
		Visit to any doctor in inpatient setting (without hospit.)	56.2	0.4
		Complete MSO hospitalization excl. palliative care	55.1	0.4
		Complete MSO hospitalization for palliative care	11.8	0.4
		Day hospitalization	24.9	0.2
		Emergency room	34.4	0.3
Dispensation of aRCC treatment			100.0	1.7
Retail pharmacy		Dispensation of another drug in community pharmacy	94.2	2.2
		Dispensation of another drug in hospital pharmacy	6.8	0.3
Ambulatory care		Visit to GP in outpatient setting only	70.3	0.7
		Nurse care received in outpatient setting only	82.2	2.5
		Imaging exams and procedures recorded in ambulatory	53.3	0.4

TKI n=368			% of patients with HCRU during 2L (all patients)	Median PPPM (patients with a care consumption)
Hospital HCRU	Session at hospital for aRCC treatment		*n<11*	NR
	Other hospital Care	Session at hospital for another treatment	11.7	0.7
		Visit to any doctor in inpatient setting (without hospit.)	65.5	0.8
		Complete MSO hospitalization excl. palliative care	40.5	0.3
		Complete MSO hospitalization for palliative care	9.5	0.3
		Day hospitalization	20.1	0.2
		Emergency room	37.2	0.3
Dispensation of aRCC treatment			100.0	1.0
Retail pharmacy		Dispensation of another drug in community pharmacy	97.0	2.2
		Dispensation of another drug in hospital pharmacy	3.3	0.2
Ambulatory care		Visit to GP in outpatient setting only	72.8	0.7
		Nurse care received in outpatient setting only	84.0	2.1
		Imaging exams and procedures recorded in ambulatory	46.2	0.4

]75%, 100%]]50%, 75%]]25%, 50%]]0%, 25%] n[1-11[

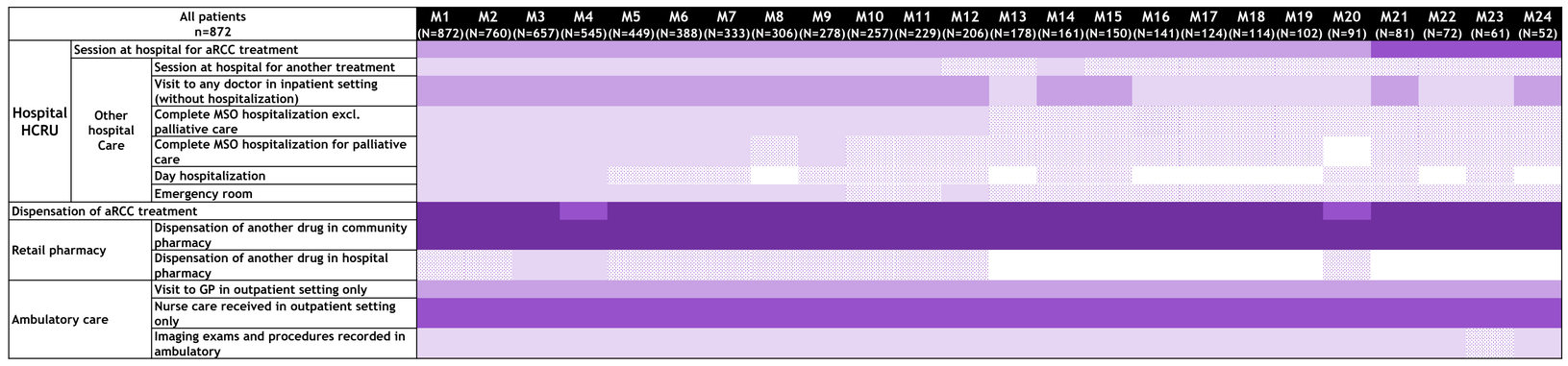
Figure 3. Overall HCRU during the 2L treatment

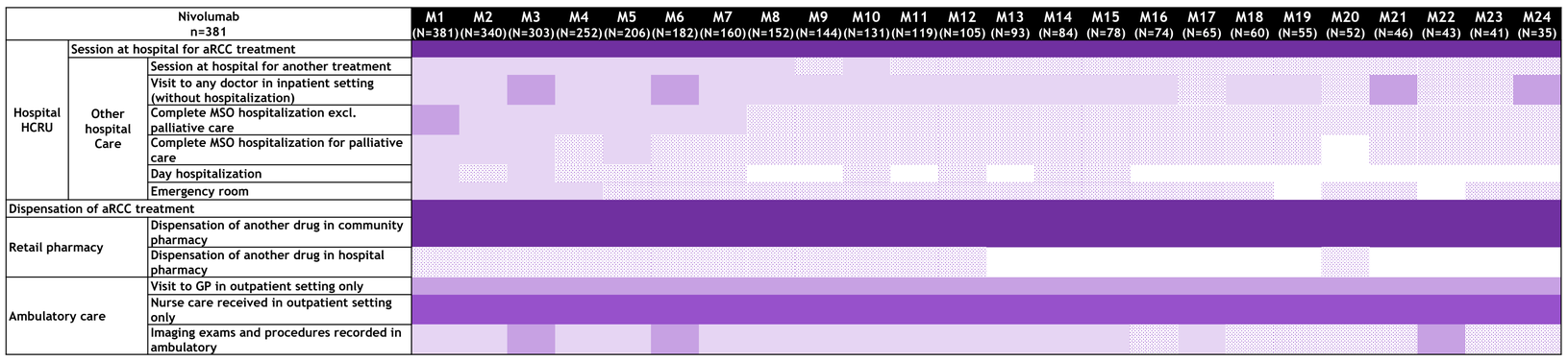
PPPM: per patient per month; NR: not reported
Interpretation example: among the 872 patients with a second line treatment, 43.0% have at least one session at hospital for aRCC treatment during second line treatment, with a median of 1.7 sessions per month of 2L treatment.

HCRU per month of 2L treatment (Figure 4)

Figure 4 represents the HCRU on a per month basis and allows to analyze whether the HCRU are constant or not over the treatment period.

- Hospital and outpatients care remained relatively steady each month over the 2L treatment period.
- Pharmacists and nurses are not only major interlocutors but also constant contacts all along the 2L patient journey : >75% of patients visits a community pharmacy each month; 50% to 75% of patients have nurse care each month, even among patients treated with nivolumab.
- The description of the care pathway specific to each type of treatment over the follow-up period is limited regarding the decreasing number of patients and the SNDS analysis rules but in both cases pharmacists and nurses seem to be a major point of contact with RCC patients.





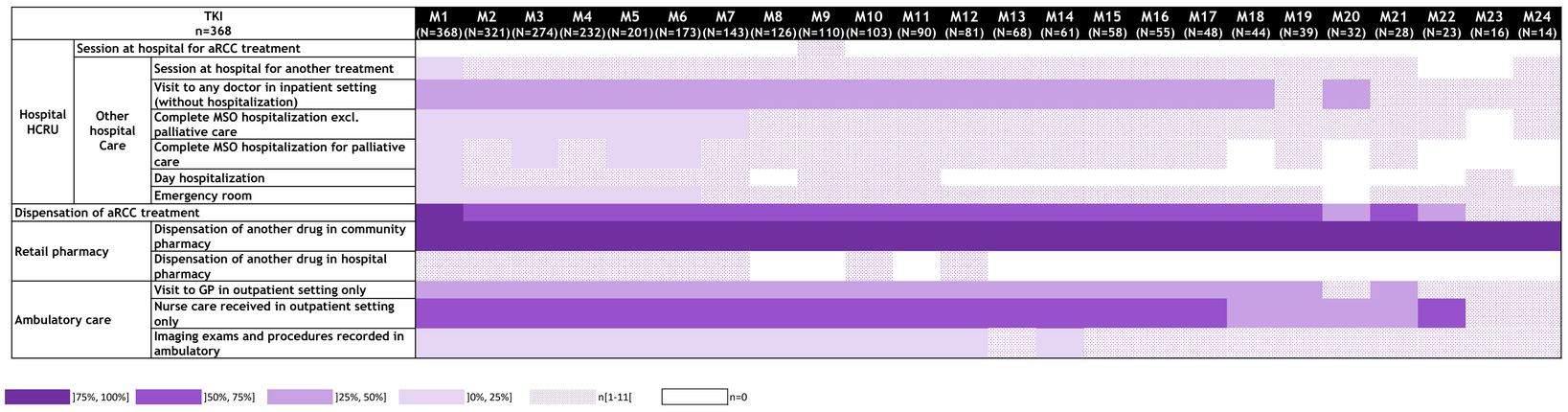


Figure 4. HCRU during 2L treatment, per month of 2L treatment

Interpretation example: among all patients, between 25% to 50% of patient had at least one session at hospital for aRCC treatment from the first month of 2L treatment to the 20th month. From the 21st month, between 50% to 75% of patients had at least one session at hospital for aRCC treatment, yet less than 81 patients are always under 2L treatment.

Conclusion

- To our knowledge, this is the first national cohort of aRCC patient population describing the HCRU and the care journey in France.
- The representativeness of this cohort and the detailed description of the patients' care journey at the start of the immunotherapy era in aRCC provides an important insight into the use of treatments in daily clinical practice.
- Results of this study highlight the importance of hospital HRCU regardless of treatment received, and the significant role of nurses and retail pharmacists in ambulatory setting.
- The identification of all hospital and ambulatory care providers involved in the management of aRCC patients may contribute to better address care management and coordination changes related to the availability of immunotherapy in 2L, and more recently in association in 1L of treatment. Therefore, data regarding first-line immunotherapy must also be rapidly evaluated.

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