Conflict of Interest Statement

- This study was sponsored by Merck KGaA, Darmstadt, Germany, and is part of an alliance between Merck KGaA and Pfizer, Inc
- MK, FXL, JH, AA, and PV are employees of Merck KGaA or Pfizer
- CK is an employee of HDI which received funding from Merck KGaA and Pfizer

Treatment Patterns, Survival, and Healthcare Resource Use for Locally Advanced or Metastatic Renal Cell Carcinoma in England: Results of a Longitudinal Observational Cohort Study

M. Kearney[1], C. Knott[2,3], F.-X. Lamy[4], J. Harnett[5], A. Amin[6], P. Verpillat[4]

[1]Global Evidence and Value Development, Merck KGaA, Darmstadt, Germany

[2]Health Data Insight CIC, Fulbourn, UK

[3]National Cancer Registration and Analysis Service, Public Health England, London, UK

[4]Global Epidemiology, Merck KGaA, Darmstadt, Germany

[5]Global Medical Epidemiology and Big Data Analysis, Pfizer Inc, New York, NY, USA

[6]Merck Serono Limited, Feltham, UK; an affiliate of Merck KGaA, Darmstadt, Germany

Introduction/Background

- Renal cell carcinoma (RCC) is ranked as the sixth and tenth most common malignancy in men and women in the United States, respectively[1]
  - The estimated number of diagnosed cases in 2018 was 65,340, and the estimated number of deaths was 14,970[2]
- An estimated 115,174 kidney, renal pelvis, and ureter cancers were diagnosed in Europe in 2012, with approximately 49,000 deaths due to kidney cancer in the same year[3]
- Limited studies report real-world evidence representing routine clinical practice in patients with RCC in Europe
- Recent approval of immune checkpoint inhibitor (ICI) and tyrosine kinase inhibitor (TKI) combination therapies has altered the first-line (1L) standard of care for patients with advanced RCC (aRCC)
- This observational study describes clinical management of and outcomes in patients with aRCC in England prior to the introduction of immunotherapy-based combination treatments in the 1L setting

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2. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2018. CA Cancer J Clin. 2018;68(1):7-30.
3. European Network of Cancer Registries. Kidney Cancer (KC) Factsheet. https://www.encr.eu/sites/default/files/factsheets/ENCR_Factsheet_Kidney_2017.pdf. Accessed May 5, 2020.

Study Objectives

- Describe real-world patient demographics and comorbidities, tumour characteristics, and healthcare resource utilization (HRU) among patients with newly diagnosed aRCC in England
- Describe treatment patterns following diagnosis, including lines of systemic therapy, radiation therapy, and surgical resections
- Report key clinical outcomes, including overall survival (OS) from diagnosis and from start of 1L treatment

Methodology

Design

- A descriptive, noninterventional study of a real-world cohort of patients with aRCC as defined using routine patient-level data hosted by the National Cancer Registration and Analysis Service (NCRAS) in England:
  - Incident primary cases of advanced or metastatic RCC (stage III/IV) were captured from January 2013 to June 2017, inclusive
  - Patients were followed up until the earliest of death, loss to follow-up, or end of study period (March 2018)

Statistical Analyses

- Descriptive statistics were used to describe baseline characteristics and treatment patterns
- OS data were analysed from diagnosis and the start of 1L systemic therapy using Kaplan–Meier survival curves

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Eligibility Criteria

Inclusion Criteria

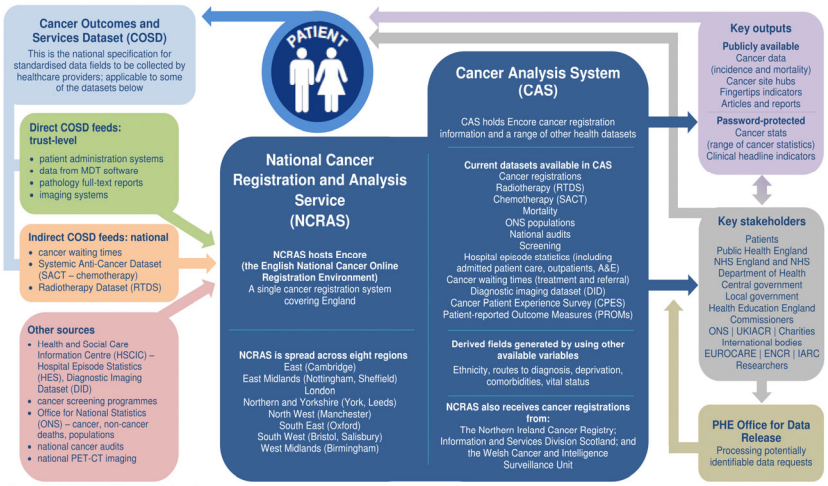
- Resident in England at the date of diagnosis
- Aged ≥18 years at the date of diagnosis
- At least 1 incident primary diagnosis of advanced or metastatic RCC, dated between January 1, 2013 and June 30, 2017

Exclusion Criteria

- No recorded date, stage of diagnosis
- No recorded age at diagnosis
- Cases identified via death certificate only
- Receipt of a nonsponsor systemic therapy funded through the Cancer Drugs Fund
- Participation in a clinical research trial

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Data Linkages: Cancer Data Flow in Public Health England (PHE)



Data Extracted:

- NCRAS: patient identification, demographics
- SACT: systemic cancer treatment identification
- RTDS: cancer-specific radiotherapy
- HES: hospital treatments including surgical procedures, diagnoses, and comorbidities
- ONS: routine death registration data

➔ All nationwide databases

7 **COSD**, Cancer Outcomes and Services Dataset; **HES**, Hospital Episode Statistics; **NCRAS**, National Cancer Registration and Analysis Service; **ONS**, Office for National Statistics; **PHE**, Public Health England; **RTDS**, Radiotherapy Data Set; **SACT**, Systemic Anti-Cancer Therapy

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Results

Baseline Characteristics*

Incident aRCC patients	N=14,629
Age at diagnosis, years	
Mean (SD)	68.3 (12.3)
Median (Q1, Q3)	69.0 (60.0, 77.0)
Sex, n (%)	
Male	9,597 (65.6)
Female	5,032 (34.4)
Morphology, n (%)	
Clear cell renal carcinoma	12,206 (83.4)
Stage at diagnosis, n (%)	
III	6,213 (42.5)
IV	8,416 (57.5)
Duration of follow-up from diagnosis, months†	
Mean (SD)	19.4 (17.2)
Median (Q1, Q3)	14.6 (4.1, 31.0)
Modified Deyo-Charlson Comorbidity Index score	
Mean (SD)	2.8 (1.7)
Median (Q1, Q3)	3.0 (2.0, 4.0)

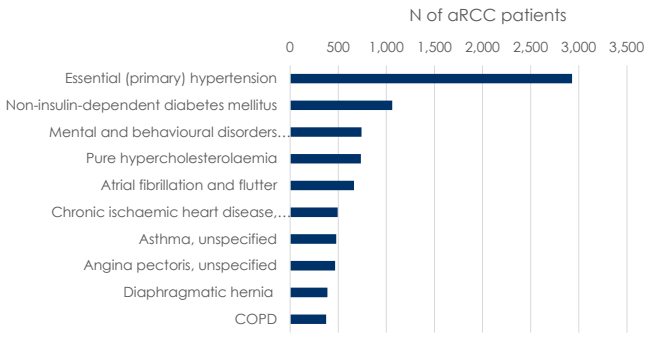
8 * Baseline = between 27 to 3 months prior to index
† Follow-up period was defined from the date of the first aRCC diagnosis to the date of death, loss to follow-up, or the end of the observation period, whichever came first

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Results

Most frequent comorbidities documented during the baseline period*

- Hypertension (n=2,930 [20.0%])
- Type 2 diabetes mellitus without complications (n=1,061 [7.3%])
- Mental and behavioral disorders due to use of tobacco (n=742 [5.1%])
- Hypercholesterolemia (n=735 [5,0%])



9 * Baseline = between 27 to 3 months prior to index
COPD, chronic obstructive pulmonary disease

9

Results

Treatment Patterns in Overall Population (n=14,629)

- During follow-up, 51.5% of patients underwent ≥1 surgical resection, and 13.7% received radiation therapy
- Overall, 3,549 patients (24.3%) received systemic therapy: 11.8% of patients with stage III disease and 33.5% with stage IV
- Among 3,549 patients receiving 1L therapy, 1,379 (38.9%) also received 2L, 491 (13.8%) received 3L, and 173 (4.9%) received ≥4L
- Targeted therapies were the most frequently (>70%) administered agents across all lines; ICIs were the second most common agents, ranging from 1.7% in 1L to 31.8% in ≥4L (overall: 8.6%)

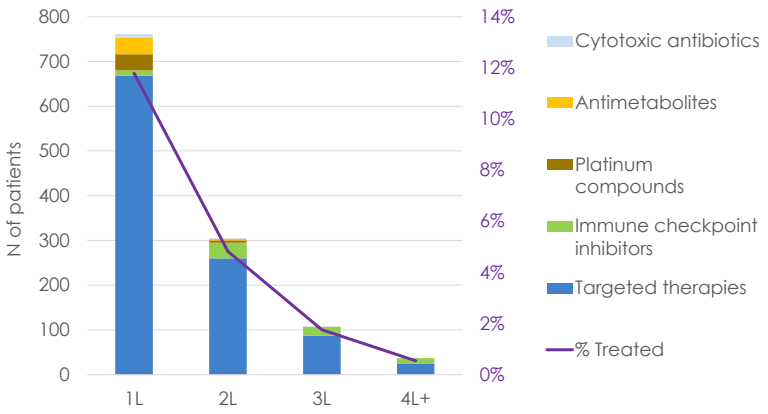
10 **2L**, second line; **3L**, third line; **4L**, fourth line

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Results

Treatment Patterns—Stage III (n=6,213)

Treatment classes by line of treatment



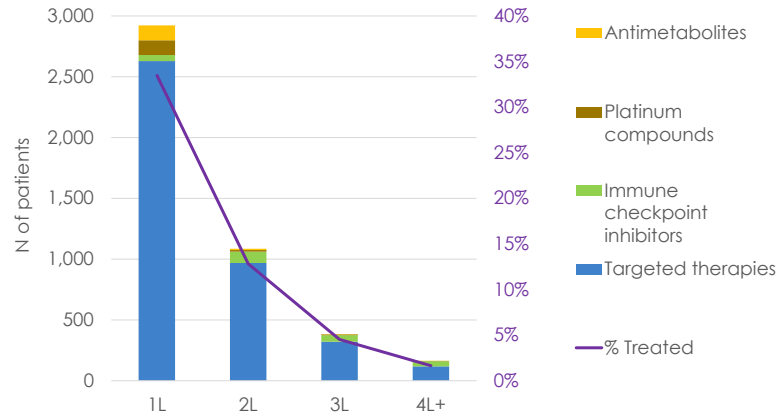
- 87.6% had ≥1 resection during follow-up
- 11.8% had ≥1 line of systemic therapy
- Targeted therapies were the most frequently (>70%) administered agents across all lines
- ICIs were the second most common agents
- High attrition across all lines of treatment

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Results

Treatment Patterns—Stage IV (n=8,416)

Treatment classes used by line of treatment



- 24.9% had ≥1 resection during follow-up
- 33.5% had ≥1 line of systemic therapy
- Targeted therapies were the most frequently (>80%) administered agents across all lines
- ICIs were the second most common agents
- High attrition across all lines of treatment

Results

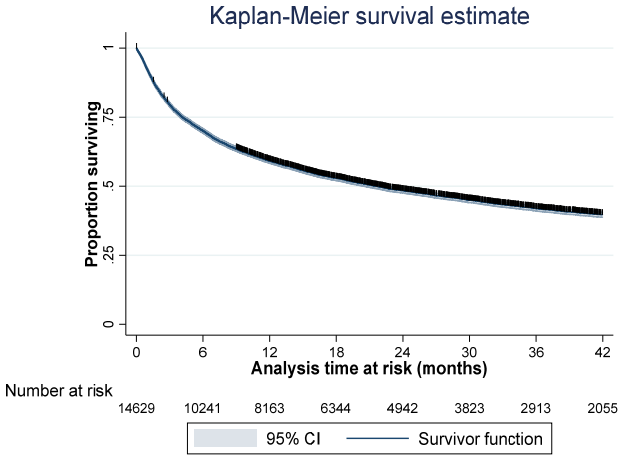
HRU per patient per year (PPPY)

Incident aRCC patients	N=14,629
Hospital admissions	
Mean (SD)	4.8 (10.1)
Median (Q1, Q3)	1.7 (0.2, 6.1)
Outpatient visits, n (%)	
Mean, SD	19.8 (28.1)
Median	13.5 (5.9, 25.7)
Emergency department visits, n (%)	
Mean (SD)	2.0 (4.6)
Median (Q1, Q3)	0.5 (0.0, 2.1)
Specialist consultations*, n (%)	
Urologist	11,088 (75.8)
Oncologist	8,518 (58.2)
Computerised tomography (CT) scans, n (%)	
Mean (SD)	10.3 (42.9)
Median (Q1, Q3)	2.8 (1.1, 7.2)

13 *At least one encounter with a consultant, regardless of the reason.

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Kaplan-Meier Curve of OS From Diagnosis: aRCC



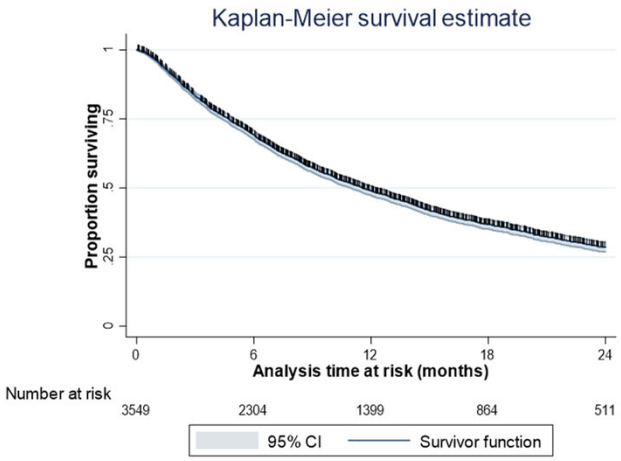
Survival from diagnosis (n=14,649)

There were 8,130 deaths (55.6%) following diagnosis, resulting in a median survival of 21.6 months from diagnosis and a 24-month survival rate of 48.4% (95% CI: 47.5%-49.2%)

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Kaplan-Meier Curve of OS From Start of 1L Systemic Therapy: aRCC



Survival from start of 1L systemic therapy (n=3,549)

There were 2,371 deaths (66.8%) during follow-up, resulting in a median survival of 11.6 months from 1L initiation and a 24-month survival rate of 28.6% (95% CI: 26.9%-30.3%)

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Strengths

- Data from a national cancer registry in England, with linkage to other relevant datasets
  - Real-world data relating to the epidemiology, outcomes, and HRU of patients with incident advanced or metastatic RCC
  - Comprehensive data, with records for every patient with a diagnosis or treatment for aRCC provided or funded by the NHS
- The cancer registry benefits from mandatory data submission and robust validation procedures, maximizing completeness as well as standardizing recording to reduce the risk of misclassification
- Documentation of the full continuum of care in all NHS-funded settings and longitudinal tracking of patient information

16 **NHS**, National Health Service

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Limitations

- The cancer registry and its linked datasets lack information on health outcomes such as cancer recurrence and disease progression
- Under-reporting of tumour staging or histology (17% missing stage)
- SACT dataset only contains systemic therapy data administered in secondary care; it does not include details of treatment delivered in primary care or private care settings
- Drugs funded through the Cancer Drugs Fund (CDF) are not included
- Lines of systemic therapy were derived using an algorithm
- Incompleteness of data items such as ICD-10 diagnosis codes and OPCS-4 procedure codes in HES

17 **OPCS-4**, OPCS Classification of Interventions and Procedures

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Conclusions

- This study provides important insights into historic treatment patterns, outcomes, and HRU among patients with newly diagnosed aRCC in England identified from January 2013 to June 2017 with follow-up until March 2018
  - This data is derived from linking databases that capture clinical data on cancer and its treatment in routine day-to-day practice in England
- Systemic cancer therapy use was limited, ie, only 11.8% of patients with stage III disease and 33.5% with stage IV received 1L treatment, with high attrition observed across lines of treatment
- Median OS was approximately 21.6 months from diagnosis and 11.6 months from the initiation of 1L systemic therapy
- The treatment landscape for aRCC continues to evolve, with new agents and combinations (eg, ICI/TKI) being adopted following this study period
- Thus, it is important to evaluate outcomes, patient characteristics, prognostic factors, and treatment patterns associated with the management of aRCC in contemporary healthcare settings
- This study can serve as a useful benchmark for future real-world studies in aRCC, thereby enabling clinicians to better understand the utilization of and outcomes associated with newer systemic agents

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Acknowledgments

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Contact Details of Presenting Author

Dr. Mairead Kearney

Email: mairead.kearney@merckgroup.com