2025 IKCS: EUROPE

INTERNATIONAL KIDNEY CANCER SYMPOSIUM

Abstract Book

2025 INTERNATIONAL KIDNEY CANCER SYMPOSIUM: EUROPE

1–3 May, 2025 | Amsterdam, the Netherlands

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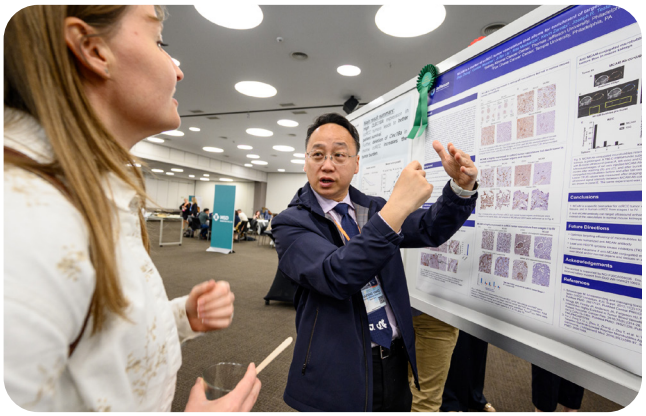

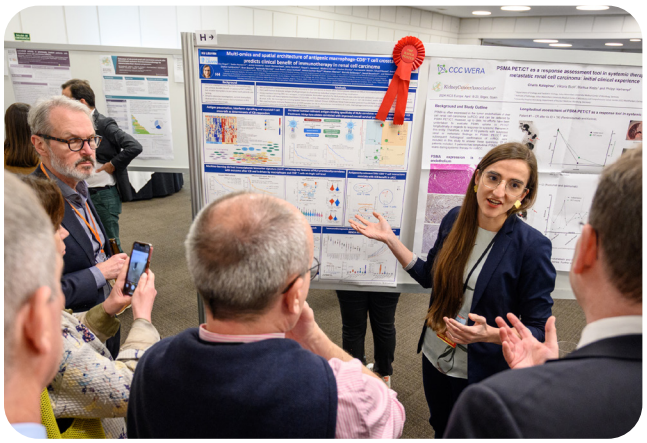

Introduction

We are pleased to present the abstracts accepted for the 2025 IKCS: Europe meeting! The research detailed here will be presented on stage and exhibited during our meeting, representing the best of what our scientific community has to offer. The ideas you will hear are both a review of what we understand so far about kidney cancer and an exciting look towards the future of how we can change the landscape for fellow researchers, practicing clinicians, and the patients and families who are relying on us to give them hope as they face challenging diagnoses. Special thanks to our Scientific Planning Committee for their dedication in reviewing and selecting the research with the highest impact, the most creative ideas, and the most relevancy. I encourage you to engage with the science you hear as well as the people bringing these ideas forward! Together, we have the challenge and the privilege of shaping the future of kidney cancer.

Dr. Salvatore La Rosa
Chief Scientific Officer, KCA

We're excited to welcome IKCS Europe 2025 attendees to Amsterdam! This meeting offers kidney cancer research that will spark academic debate, help us see new ways to treat patients in our care, and improve their quality of life. Congratulations to all the researchers selected to share their discoveries with us here in Amsterdam and congratulations to all the speakers who will bring you their reflections on state of the art care for patients with kidney cancer.

Dr. Axel Bex

Dr. Ignacio Duran

Dr. Lisa Pickering

Co-Chairs, 2025 IKCS: Europe Scientific Planning Committee

Thank You 2025 IKCS: Europe Scientific Planning Committee

We extend our heartfelt gratitude to our dedicated planning committee for their exceptional contributions to this year's symposium. Your commitment and expertise have been invaluable in making this event a success.

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Abstracts

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A1 • POST-TREATMENT SURVEILLANCE

Pattern of disease recurrence and clinical management of localized high-risk renal cell carcinoma (RCC) patients treated with adjuvant (adj) immunotherapy.

BACKGROUND Standard treatment for high-risk localized RCC is radical or partial nephrectomy followed by adj pembrolizumab. However, about 40% of patients progressed despite adj immunotherapy within 5 years. We sought to investigate the pattern of disease recurrence and the clinical management of RCC patients treated with adj immunotherapy.

MATERIALS AND METHODS Patients with high-risk RCC who received adj immunotherapy after radical surgery in our Institution were collected. The primary endpoint was the rate and pattern of disease recurrence. Secondary endpoints: patients' outcomes in terms of disease-free survival (DFS) and overall survival (OS).

RESULTS From March 2018 to January 2025 58 patients were included in the analysis. Patients characteristics are shown in the table. 13 patients (22%) had disease recurrence; in 8 cases (61%) the absolute number of metastases was ≤3, with a number of diverse metastatic sites ranging from 1 (n=6, 46%) to maximum 3 (n=1, 8%). The most frequent sites of metastasis included lung (54%), lymph node (38%), renal bed (15%), and bone (15%). In case of disease recurrence, 7 patients (54%) started systemic first-line therapy, 5 patients (38%) received loco-regional treatment (i.e. radiotherapy or metastasectomy). After a median follow-up of 22.3 months (17.9–26.7 months), the 30-months DFS rate was 73% and 71% for patients treated with adj pembro. The 30-months OS rate was 95% in the overall population and 96% after adj pembro.

Table 1: Baseline characteristics of the patients

Baseline characteristics	Patients (n = 58)
Median age (range)	62.5 (34.7 – 83.7)
Male sex, n (%)	40 (69)
Primary tumour stage, n (%)	
T1	4 (7)
T2	5 (9)
T3	47 (81)
T4	2 (3)
Tumour nuclear grade, n (%)	
Grade 1	1 (2)
Grade 2	14 (24)
Grade 3	22 (38)
Grade 4	18 (31)
Lymph node stage, n (%)	
N0	54 (93)
N1	4 (7)
Metastatic stage, n (%)	
M0	54 (93)
M1 NED	4 (7)
Clear cell histology, n (%)	55 (95%)
Presence of sarcomatoid features, n (%)	14 (24)
Risk category according to KN-564, n (%)	
Intermediate-high	43 (74)
High	2 (3)
M1NED	13 (22)
Type of Adj IO, n (%)	
Pembrolizumab	38 (66)
Nivolumab + ipilimumab	11 (19)
Nivolumab	9 (15)
Compliance to Adj IO, n (%)	
Completed treatment	29 (50)
Discontinued for toxicity	10 (17)
Discontinued for disease progression	6 (10)
Treatment ongoing	13 (22)

CONCLUSIONS

Patients with RCC treated with adj immunotherapy are confirmed to be at high risk of recurrence (27% at 30 months), reinforcing the need of efforts to further improve therapeutic strategies in the adj setting. A loco-regional approach in case of oligometastatic recurrence can be a valid option for the management of these patients.

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A2 • POST-TREATMENT SURVEILLANCE

How is the efficacy of patient selection criteria for adjuvant pembrolizumab after curative surgical treatment of clear cell renal cell carcinoma with intermediate to high risk of recurrence? A real-life data analysis from single institutional experience.

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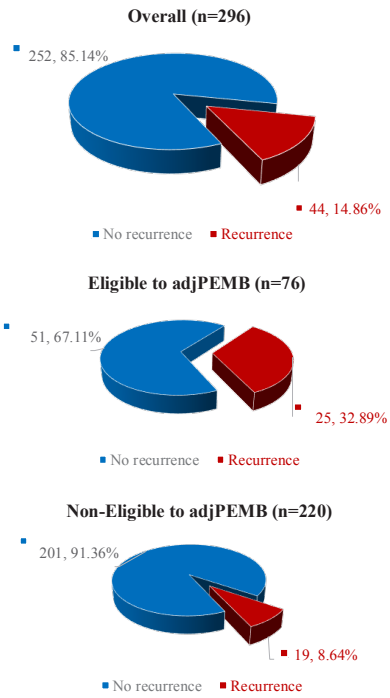
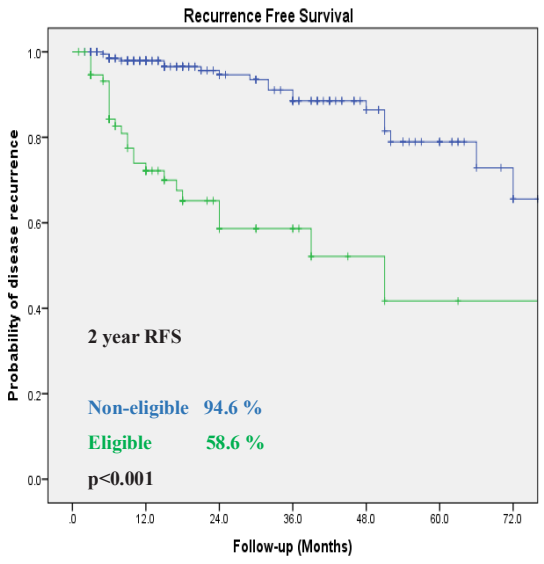
INTRODUCTION & OBJECTIVES Adjuvant pembrolizumab (adjPemb) is recommended for reducing recurrence risk after curative surgical treatment of intermediate to high risk non-metastatic clear cell renal cell carcinoma (ccRCC). This study investigated the natural course of non-metastatic ccRCC after curative surgery in patients classified by the KEYNOTE-564 patient selection criteria.

MATERIALS AND METHODS A total of 531 curative and cytoreductive nephrectomies were performed between January 2015-March 2023 in a tertiary single institution. After exclusion of 235 patients (n=201 non-ccRCC, n=20 incomplete follow-up, n=14 cytoreductive nephrectomy for metastatic renal tumor), a total of 296 non-metastatic ccRCC patients were included into this study. The clinical, histopathological and survival parameters were retrospectively documented from prospectively collected real life database. Chi-square and Mann-Whitney U tests were used for the comparisons of parameters. Kaplan-Meier Analysis was used for survival outcomes.

RESULTS Overall, 76 (25.7%) patients were defined as eligible for adjPemb (n=66, 86.8%; intermediate-high risk, n=10, 13.2%; high risk). The eligible patients had larger median tumor size in clinical (7.5 vs. 3.9 cm, p<0.001) and pathological (7.8 vs. 3.65 cm, p<0.001) assessments, and underwent more often radical nephrectomy (95.9 vs 27.7%, p<0.001). Two-year recurrence free survival (RFS) was lower (58.6 vs. 94.6%, p<0.001) in eligible patients. A total of 44 (14.9%) patients recurred in overall cohort at median follow-up of 18 months, 25 (32.9%) in eligible group and 19 (8.6%) in non-eligible group. Median pathologic tumor size were larger (9 vs 5 cm, p<0.001) and median time to recurrence were earlier (8 vs. 32 months, p<0.001) in eligible group. Fifty-one (67.1%) patients in eligible group did not experience any recurrence at a median follow-up of 15 months.

CONCLUSIONS This real-life data showed that ccRCC recurred after curative surgery in 32.9% of patients defined eligible for adjPemb, and in 8.5% of patients defined non-eligible. The remaining 67.1% of eligible patients did not recur at median follow-up of 15 months. These results suggested that selection criteria defined in KEYNOTE-564 needs to be improved to optimize individualized treatment strategies.





B1 • OTHER

Does cherry angioma have association with kidney cancer? The preliminary report of an observational study

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INTRODUCTION & OBJECTIVES Cherry angioma (CA) is the most common benign vascular proliferation of the skin, particularly in the aging population. On the basis of clinical observation, we hypothesized that the number of CAs may increase in renal tumors. Accordingly, the aim of this study is to investigate the relationship between CAs and renal tumors.

METHODS Between September 2022-October 2024, a total of 167 patients underwent partial or radical nephrectomy for localized suspected renal mass in a tertiary institution. Among them, 98 patients underwent a detailed whole body skin examination, including the scalp and genital areas, by a dermatologist using a digital handheld dermatoscope one day before surgery. The counted number of CAs was prospectively registered for either total body and for each body region. The overall cohort were assessed by descriptive statistics, and clear cell renal cell carcinoma(ccRCC) subgroup were separately investigated by comparative statistics. For the comparison of ccRCC subgroup, the patients were stratified into two groups according to the counts of CAs ≥ 1mm in the ipsilateral operative side; Group 1 (the number of CAs < 2, less ipsilateral CAs) and Group 2 (the number of CAs ≥ 2, more ipsilateral CAs). The descriptive statistics and comparative analyses were performed by using prospectively recorded demograpical, clinical and histopathological parameters.

RESULTS In overall cohort, the median age was 60 (IQRs:28-86) years and 64 (65.3%) patients were male. Median pathological tumor size was 4.6 (IQRs:1.2-11.0) cm. Fifty-eight (59.2%) patients had at least one CA lesion with a median number of 3 (IQRs:1-14) in ipsilateral operative side,and 91 (92.9%) patients with a median number of 24 (IQRs:2-38) in total body. Eighty-five(86.7%) nephrectomy pathologies were malign while 13 (13.3%) were benign. In the comparative analyses of 62 ccRCC patients, the median age was 59 (IQRs:51-68) years and it was not different between two groups. (p:0.159) Body mass index was noted to be higher in Group 1 (28.5 vs 25.7 kg/m2, p:0.009). Both clinical (4.7 cm vs. 8 cm, p:0.01) and pathological tumor size (4.0 cm vs. 5.5 cm, p:0.021) were significantly higher in Group 2, while pT stage did not differ significantly between two groups. The nuclear grade was significantly different between two groups. (Grade 1-2: 83.3% vs. 53.1%; Grade 3-4: 16.7% vs. 46.9%, p:0.011). In addition, the percentage of CAs in ipsilateral operative side to CAs in total body was significantly higher in Group 2. (0% vs. 13.2%, p<0.001) Lack of a control group and metastatic patient group areaccepted as limitations in this study.

CONCLUSIONS The preliminary report of this observational study suggested that cherry angioma might be associated with renal tumors. The association of CA between pathological tumor size and nuclear grade in clear cell RCC might be an area of future researchs.

Parameters	Overall	Group 1	Group 2	p
n	62	30	32	
Age (years)	59 (51-68.3)	57 (47.5-68.8)	60.5 (54-68.8)	0.159
Male Gender (n, %)	44, 71	22, 73.3	22, 68.8	0.691
Diabetes Mellitus (n, %)	13, 21.3	7, 24.1	6, 18.8	0.608
Hypertension (n, %)	29, 47.5	13, 44.8	16, 50	0.686
Body Mass Index (kg/m²)	**27.2 (23.8-30.3)**	**28.5 (25.5-31.8)**	**25.7 (23.1-28.4)**	**0.009**
Left side (n, %)	28, 45.2	15, 50	13, 40.6	0.459
Clinical tumor size (cm)	**6.0 (3.95-10.2)**	**4.7 (3.4-7.0)**	**8 (4.5-10.2)**	**0.01**
Clinical Stage (n, %)				**0.018**
cT1-T2	**58, 93.5**	**30, 100**	**28, 87.5**	
cT3-T4	**4, 6.5**	**-**	**4, 12.5**	
Pathological tumor size (cm)	**4.5 (3.2-6.5)**	**4.0 (2.5-5.6)**	**5.5 (3.9-8.8)**	**0.021**
Pathological tumor size group (n, %)				**0.026**
0-4 cm	**27, 43.5**	**16, 53.3**	**11, 34.4**	
4-7 cm	**22, 35.5**	**12, 40.0**	**10, 31.3**	
>7 cm	**13, 21.0**	**2, 6.7**	**11, 34.4**	
Pathological Stage (n, %)				0.278
pT1-T2	48, 77.4	25, 83.3	23, 71.9	
pT3-T4	14, 22.6	5, 16.7	9, 64.3	
Nuclear Grade (n, %)				**0.011**
Grade 1-2	**42, 67.7**	**25, 83.3**	**17, 53.1**	
Grade 3-4	**20, 32.3**	**5, 16.7**	**15, 46.9**	
Nuclear Grade (n, %)				**0.035**
Grade 1	**7, 11.3**	**3, 10.0**	**4, 12.5**	
Grade 2	**35, 56.5**	**22, 73.3**	**13, 40.6**	
Grade 3	**16, 25.8**	**5, 16.7**	**11, 34.4**	
Grade 4	**4, 6.5**	**0, 0.0**	**4, 12.5**	
Sarcomatoid dedifferantation (n, %)	5, 8.1	1, 3.3	4, 12.5	0.170
Necrosis (n, %)	14, 22.6	4, 13.3	10, 31.3	0.092
Lymphovascular Invasion (n, %)	8, 12.9	2, 6.7	18.8	0.147
Ipsilateral abdominal wall cherry angioma ≥ 1 mm	5 (3-7)	0 (0-1)	4 (2-7)	<0.001
Total body cherry angioma ≥ 1 mm	10 (5-31)	5.5 (2-10)	30 (11-56)	<0.001
Ipsilateral abdominal wall / Total body (%)	10.0 (0-18.9)	0 (0-8.1)	13.2 (10.6-24.31)	<0.001
Contralateral abdominal wall cherry angioma ≥ 1 mm	1 (0-3)	0 (0-0)	1 (0-2)	<0.001

B2 • OTHER

Convergent Mixed Methods Evaluation of a Prototype Health Data Management and Sharing App: A Study with Kidney Cancer Support Charity Members

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BACKGROUND Health data is a critical asset for individuals and the broader healthcare ecosystem. However, common industry practices rely on harvesting from fragmented sources, often without meaningful patient control, participation or reward. This 'data abandonment' model contributes to gaps in care, inefficiencies in research, and ethical concerns around data use. By designing systems that prioritize user agency and transparency, it is possible to improve data quality, facilitate responsible sharing, and ensure that patients—not just industry stakeholders—derive value from their own health information.

METHODS At the end of February 2025, 100 members (patients and family) of a kidney cancer support charity were invited to test the Smartomics personal health data management application over a two-week period. Activity logs were collected to analyze feature utilization and engagement. Participants completed in-app surveys to explore attitudes toward active data sharing, including perceptions of incentive mechanisms. A roundtable discussion was conducted with purposely sampled participants to explore user experiences, ethical concerns, and feedback issues raised.

RESULTS Although engagement with the study was limited (n=7), a diverse group of testers found the proof of concept application had good-excellent user-friendliness, with high Net Promoter Score (75%, and 80% for the envisioned finished product). More than half the users explored donating a proportion of their compensation to a Patient Association and using the app to manage their health data. Survey results revealed reasons for sharing health data ranged from: coordinating care with family and clinicians; helping clinical trials; and receiving compensation. Confidence for sharing was related to security safeguards and knowing who was using data and why. The roundtable also uncovered concerns regarding privacy and sustainability, and unmet needs in condition self-management and carer wellbeing.

CONCLUSIONS There is evidence of a potential gap in services for a patient- and carer-centric data sharing and reward application.

B3 • OTHER

ROB'N'SAFE – Robot-assisted radical Nephrectomy as SAFE same-day surgery now and in the future

BACKGROUND Robot-assisted radical nephrectomy (RARN) is a well-established treatment for localized kidney cancer. However, identifying frail patients at increased risk of postoperative complications remains a key challenge to future same-day RARN. The project aims to identify key predictors to refine preoperative frailty assessment by identifying key predictors of postoperative complications to refine patient selection and develop targeted pre- and postoperative care strategies.

METHODS The following three studies will be conducted.

- **Study I:** A prospective observational cohort study assessing preoperative predictors of frailty and their impact on same-day discharge feasibility. Variables include Clinical Frailty Scale, handgrip strength, chair stand test, CT-derived body composition, and wearable-derived biometric data. Primary outcome: 24-hour readmission rate. Secondary outcomes: 30-day complications and readmission, health literacy, and patient reported quality of life.
- **Study II:** An observational cohort study evaluating postoperative recovery in relation to frailty, using validated questionnaires and pain management assessments. Primary outcome: Patient-reported quality of recovery. Secondary outcomes: opioid consumption, functional recovery metrics, and frailty progression.
- **Study III:** A qualitative study exploring the role of relatives in supporting patients postoperatively, focusing on preparedness, satisfaction, and health literacy in home-based care.

RESULTS & CONCLUSIONS Our expected outcomes include improved patient selection criteria for same-day RARN through the integration of wearable technology, CT-based body composition analysis, and AI-driven predictive models, ultimately optimizing surgical safety. Furthermore, insights into the role of relatives in postoperative support may strengthen home-based care while increasing confidence and reassurance among healthcare professionals and patients.

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B4 • OTHER

A Phase 1, Multiple-dose Study to Evaluate the Safety and Tolerability of First-in-class XmAb819 (ENPP3 x CD3) in Subjects with Relapsed or Refractory Clear Cell Renal Cell Carcinoma (ccRCC)

BACKGROUND Despite advances in the treatment of metastatic ccRCC few patients are cured. Therapies exploiting novel targets are needed. Antigen screening identified ENPP3 (ectonucleotide pyrophosphatase/phosphodiesterase family member 3) as having consistent high expression in ccRCC and low expression in normal tissue. ENPP3 is a transmembrane ectoenzyme involved in hydrolysis of extracellular nucleotides. XmAb819 is a 2+1 (high-avidity bivalent ENPP3 binding with low-affinity monovalent CD3 binding) bispecific antibody. XmAb819 is engineered for preferential engagement of high ENPP3-expressing cancer cells to induce T-cell-mediated cytolysis of cancer cells.

METHODS This is a multicenter, open-label, dose-escalation/expansion study enrolling up to 190 participants with advanced ccRCC. The primary objective is safety and tolerability; the secondary objective is preliminary anti-tumor activity. Part A, dose escalation, establishes a priming dose, step-up dose(s), a cohort-limit dose, and the dosing schedule for both intravenous (IV) and subcutaneous (SC) administration. Part B, dose expansion, evaluates the safety and efficacy of the recommended dose established in Part A. All subjects will have disease progression on standard-of-care therapies. XmAb819 will be administered weekly; cohort-limit doses will be administered in 21-day cycles until disease progression or unacceptable toxicity. Adverse events are graded using CTCAE v5.0; CRS using ASTCT Consensus Grading (Lee, 2019). Efficacy is assessed per investigator using RECIST v1.1.

Enrollment has been initiated, and dose escalation continues in both the IV and SC cohorts. Clinical trial information: NCT05433142.

RESULTS & CONCLUSIONS Our expected outcomes include improved patient selection criteria for same-day RARN through the integration of wearable technology, CT-based body composition analysis, and AI-driven predictive models, ultimately optimizing surgical safety. Furthermore, insights into the role of relatives in postoperative support may strengthen home-based care while increasing confidence and reassurance among healthcare professionals and patients.

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C1 • TUMOR BIOMARKERS AND PATHOLOGY

Predictors of Cabozantinib Response in Patients with Advanced Renal Cell Carcinoma

INTRODUCTION Paired samples from the CABOPRE trial were used to determine the differential expression of miRNAs and key genes associated with response to neoadjuvant cabozantinib treatment in patients with metastatic renal cell carcinoma. This analysis aimed to identify potential biomarkers that could predict treatment efficacy and provide insights into the molecular mechanisms underlying cabozantinib's therapeutic effects.

RESULTS Paired and sequential samples from 15 patients were used to evaluate treatment responses. Fourteen differentially expressed miRNAs were identified pretreatment between responders and non-responders, including miR-549a, with the majority associated with the upregulation of VEGFA and CCND1 in responders. Additionally, nine miRNAs were differentially expressed (six down-regulated and three up-regulated) following cabozantinib treatment compared to baseline, which could serve as predictive biomarkers for cabozantinib response.

Furthermore, the comparison of miRNA levels in plasma and exosomes revealed that only miR-873-3p exhibited concordant expression changes in both compartments, suggesting a potential role for this specific miRNA in mediating the effects of cabozantinib. The analysis of long-term responders (PFS >12 months) exhibited a distinct miRNA signature characterized by the downregulation of two miRNAs and upregulation of four miRNAs compared to the baseline.

Digital spatial profiling was performed on tissue samples from eight nephrectomized patients categorized as responders (n=3) and non-responders (n=5). The analysis revealed a pre-treatment increased expression of 10 genes in the tumor, including VEGFA and CCND1 in responders to cabozantinib. Conversely, CCND1 expression displayed an increase in non-responders post-treatment, suggesting a potential resistance pathway.

Finally, cabozantinib treatment in responders was associated with the upregulation of adhesion molecules ITGAV and ICAM1, which may explain neutrophil infiltration into the tumor microenvironment. Additional MPO staining on the tissue samples showed increased neutrophil expression after treatment in 66% of responders, compared to 40% of non-responders.

CONCLUSION The biomarker analysis reveals that increased VEGFA and CCND1 expression, along with differential miRNA expression and neutrophil infiltration, can predict cabozantinib response in RCC patients.

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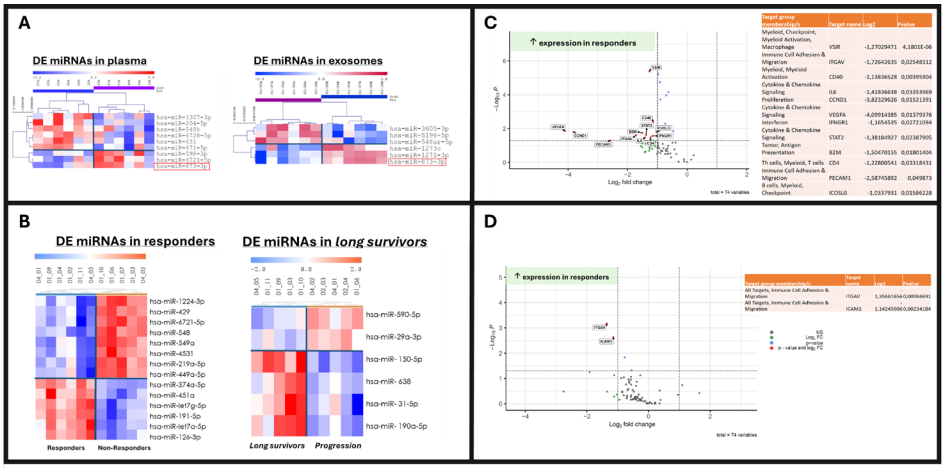

Figure 1. A) Analysis of the differential expression of miRNA levels in plasma and exosomes, highlighting miR-873-3p concordant expression in both settings. B) Analysis of the differential expression of miRNA depending on the response to treatment and the duration of response. C) Digital spatial profiling analysis shows increased expression pre-treatment of 10 genes across responders to cabozantinib. D) Digital spatial profiling analysis reveals an increased expression post-treatment of ITGAV and ICAM1 in responders, which suggest an enhanced neutrophil infiltration in responders to cabozantinib.

ORAL PRESENTATION

C2 • TUMOR BIOMARKERS AND PATHOLOGY

A biomarker analysis of Tide-A, a phase 2 study of first-line avelumab plus intermittent axitinib: circulating kidney injury molecule-1 (KIM-1) in mRCC.

KIM-1 is a plasma biomarker of microscopical residual disease, disease recurrence after nephrectomy and potential benefit from adjuvant immunotherapy (IO). No data is available about it's role in mRCC. We explored KIM-1 in the prospective cohort of Tide-A study: intermittent strategy of axitinib plus avelumab in treatment-naïve mRCC. We performed a proteomics analysis with the aptamer-based technology SomaScan 7K (Somalogic, USA). KIM-1 levels were analyzed in baseline samples and normalized by Adaptive Normalization by Maximum Likelihood to combine samples and correct for batch-effects. KIM-1 cut-off (10.456 relative fluorescence units) was determined by Maximally Selected Rank Statistics using maxstat R package, with Van der Waerden test and log-rank score. KIM-1 levels were evaluated at baseline in the overall population, adjusted for IMDC and for DOR with avelumab maintenance.Data for KIM-1 analysis at baseline were available for 69 pts; 13% were KIM-1-high and 87% KIM-1-low. KIM-1-high was related with shorter mOS (24.2 months [95%CI 21.1–NR] in KIM-1-high vs. not reached (NR) in KIM-1-low; p=0.0019). 2-yOS rate was 90% in KIM-1-low vs. 56% in KIM-1-high (p=0.002). KIM-1 levels was correlated with OS when adjusted for IMDC. No correlation was observed between KIM-1 levels and mPFS (22.9 vs. 29.9 months in KIM-1-high and low, respectively; p= 0.4). KIM-1 data were available for 28/29 pts that discontinued axitinib; the mDOR of ave-maintenance was 15.9 wks in 25 pts with KIM-1-low and NR in 3 pts with KIM-1-high, (p=0.19).High baseline plasma KIM-1 level is an independent negative prognostic factor, regardless IMDC in mRCC treated with VEGFR-TKI+IO. KIM-1 seems not to have a pivotal role for selecting TKI-intermittent strategy.

	2-year OS (%)		
	KIM-1 High	KIM-1 Low	P value
IMDC favourable	80	95	0.045
IMDC Int/Poor	25	86	0.006

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POSTER AD

C3 • TUMOR BIOMARKERS AND PATHOLOGY

How different are the expression levels of immune checkpoint molecules and their roles on the prognosis in surgically treated non-metastatic clear cell, papillary and chromophobe subtypes of renal cell carcinoma?

BACKGROUND & OBJECTIVES The immune checkpoint inhibitiors (ICIs), either as adjuvant treatment in intermediate-high risk non-metastatic disease or as first line treatment in metastatic disease, are approved as standart of care in clear cell renal cell carcinoma (ccRCC). However, there is limited evidence suggesting ICIs in the management of non-clear cell subtypes. This study aims to compare the expression levels of immune checkpoint molecules in tumor cells and tumor microenvironment and their role on prognosis, among surgically treated non-metastatic three RCC subtypes including ccRCC, papillary (papRCC) and chromophobe (chRCC).

METHODS This study included 103 non-metastatic RCC patients undergoing partial or radical nephrectomy between 2015 and 2022 at a tertiary institution. Immunohistochemical methods were used to assess the expression of PD-L1 (Tumor Proportion Score-TPS, Combined Positivity Score-CPS, Immune Cell-IC), PD-1 and CTLA-4 in the paraffin-embedded tissue samples of patients. The threshold was defined as % 1 for immunohistochemical positivity. The present study seeks answers for two questions as co-primary outcome 1) whether the expression levels of ICI molecules differ between subtypes, and 2) whether the positivity of ICI molecules predict RFS after curative surgery in each subtype. The secondary outcomes were defined as whether the positivity of ICI molecules predict CSS and OS.

RESULTS PD-L1 (IC) (p=0.047) and PD-1 (p=0.006) positivity were significantly higher in ccRCC with compared to papRCC and chRCC. PD-L1 (TPS), PD-L1 (CPS) and CTLA-4 positivity were similar between three subtypes. The median follow-up was 49 months, and 10 (9.7%) patients recurred during this follow-up. Kaplan-Meier survival analyses found that PD-1 positivity significantly predicted worse RFS (p=0.008), CSS (p=0.009), and OS (p=0.008) in papRCC, and worse RFS (p=0.014) and OS (p=0.029) in overall cohort. CTLA-4 positivity predicted worse OS (p=0.002) in papRCC while PD-L1 (CPS) positivity predicted better CSS (p=0.036) in ccRCC. PD-L1 (TPS) positivity did not predict any survival outcome either in overall cohort or in each subtype.

CONCLUSIONS These findings suggest that the expression levels of immune checkpoint molecules in tumor and its microenvironment differs among RCC subtypes, and PD-1 is a promising target for further researchs on ICIs in papillary RCC, as it significantly predicts worse prognosis.

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C4 • TUMOR BIOMARKERS AND PATHOLOGY

BAP loss in renal cancer predisposes in spinal cord metastatic early presentation? Two cases reported and review of Relevant literature

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BACKGROUND Mutations drive renal cell carcinoma biology and tumor growth. The BRCA1-associated protein-1 (BAP1) gene is frequently mutated in clear cell renal cell carcinoma (ccRCC) and has been focused as potential worse prognostic and predictive biomarker. We review two cases and discuss the role of BAP1 as a signature event of a subtype of RCC underlying aggressiveness in presentation and possibly a minor response to immunotherapy hinting resistance of unknown mechanism.

PURPOSE To present two cases of Patients with extensive metastatic disease in thoracic vertebra associated with confirmed clear renal cell cancer which documented BAP1 immunostaing loss and demonstrated worse prognosis and outcome.

PATIENTS AND METHODS Two patients were assigned with established clear cell renal cancer diagnosis and simultaneously metastatic disease histological confirmed in thoracic vertebra.

RESULTS Both of them showed negative-expression of BAP1.They presented with disease in Spinal area at the onset of their first symptoms complain .They did not easily responded to local treatment of palliative radiotherapy and to subsequent immunotherapy plus axitinib treatment offered

They both experienced adverse events of colitis and thyroid dysfunction ;easily manipulated but they did not have even 3 months response to 1rst line treatment. Subsequent molecular and chromosomal analysis was demonstrated which will be disposed.

CONCLUSIONS The molecular detection of BAP loss may be associated with both poor survival and an increased rate of worse outcome in patients with clear cell renal cancer; this approach may make aware physician's to early detect metastatic cascade in renal cancer patients and offer them novel approaches with promising anticancer benefit.

D1 • REAL-WORLD EVIDENCE

Adjuvant Pebrolizumab in Renal cancer patients. Real data of a Single Greek Centre

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INTRODUCTION & OBJECTIVES Pebrolizumab is the only adjuvant approved treatment promising improvement in disease free and overall survival in clear renal cell cancer patients post-surgical procedures.

Herein, we report our real world data experience, since its approval in 2022, to reconfirm Keynote trial's conclusions

MATERIALS & METHODS All Medical electronic data of renal cancer patients candidates for adjuvant therapy were reviewed between October 2022 to date.

Data demographics , pathology features, multidisciplinary discussion referrals and all stated reasons of co-decisions for treatment or not ,and noticed toxicity will be presented.

RESULTS Data from 48 patients, eligible for adjuvant pebrolizumab treatment based on pathology criteria as they are identified in Keynote 564 trial , have been recorded from multi-disciplinary team discussion.

All referred patients had intermediate or high risk resected disease.

Only 5 had Sarcomatoid features and nobody had microscopically resected tumoral deposit

15 discussed patients in multidisciplinary team were excluded due to comorbidities hinting high risk of revealing immune related

EVENTS So, 32 had been offered pebrolizumab adjuvant treatment.

25 patients completed 1 year of adjuvant treatment successfully .The rest 7 are still on ongoing adjuvant treatment .One patient post adjuvant completion therapy, presented metastatic brain disease hinting underneath coexistence with no clinical signs .

All rest 24 patients are still being monitored and still free of any metastatic disease.

Immune related adverse events of any grade recorded were: fatigue, pneumonitis, and thyroid dysfunction, presented in 5

PATIENTS No grade III / IV related events were noticed.

Two patients with pneumonitis were offered steroid treatment; their recovery was easy with no hospitalization requirement.

All rest adverse events were easily resolved.

CONCLUSIONS Our real data demonstrate that the majority of patients identified as eligible for adjuvant pebrolizumab when discussed

in multi-disciplinary team are prone to afford immune related adverse events and experience the clinical benefit of the existed

Therapeutic adjuvant renal cancer algorithm

Real-world evidences on adjuvant Pembrolizumab for Renal Cell Carcinoma (ARON-1)

BACKGROUND Pembrolizumab as an adjuvant treatment strategy after radical surgery has demonstrated to improve the disease-free survival (DFS) and overall survival (OS) when compared with placebo in patients with clear cell RCC at a higher risk of relapse. In this study from the ARON-1 dataset we analyzed real-world data on the use of adjuvant pembrolizumab on ccRCC patients.

METHODS We retrospectively collected data from ccRCC patients who received adjuvant pembrolizumab at 56 hospitals from 12 countries. Patients were assessed for DFS, OS and severe adverse events (SAEs). The statistical analysis encompassed the Kaplan-Meier methodology, the log-rank test, as well as univariable and multivariable Cox proportional hazards regression models.

RESULTS 311 patients were included from the ARON-1 dataset. The median age was 61y (range 25–85y); 257 (83%) presented T3 stage at diagnosis, with 17% of cases reporting sarcomatoid differentiation. The median follow-up was 15.4 months (95%CI 11.2–18.8). The median OS and DFS were not reached (NR), with 95% of 2y-OS rate and 69% of 2y-DFS rate. Sixty-one patients (20%) recurred. Lungs (11%) and bones (5%) were the most common distant sites of recurrence. The time to local recurrence was 5.4 months (95%CI 3.0–31.0), while the time to distant recurrence was 6.7 months (95%CI 5.2–31.0). The median DFS was impaired in patients aged <65y (NR vs NR, HR 2.14, 95%CI 1.26–3.63, p=0.005), in the N1 subgroup (HR 5.42, 95%CI 1.72–17.1, p=0.004) and in subjects with sarcomatoid de-differentiation (21.5 months, 95%CI 17.1–25.8 vs NR, HR 2,54 1.29–4,98, p=0.007). Discontinuation rate due to SAEs was 19%; the most common SAEs were colitis (4%), hepatopathy (4%) and nephritis (3%).

CONCLUSIONS In this large real-world study pembrolizumab demonstrated to be an effective and tolerable treatment fort he adjuvant setting of ccRCC at a higher risk of relapse.

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POSTER AD

D3 • REAL-WORLD EVIDENCE

CABONEXT: Advanced renal cell carcinoma treatment following Cabozantinib: a retrospective analysis of sequencing therapies

Cabozantinib combined with nivolumab is considered as a standard of care in first-line treatment for metastatic renal cell carcinoma (mRCC). Cabozantinib is a TKI targeting VEGFR, MET and AXL and showed efficacy as a monotherapy or combined with checkpoint inhibitors (CPI). Little is known about subsequent systemic therapy following cabozantinib. This study aimed to report clinical outcomes from subsequent lines following a 1st or 2nd line treatment in mRCC pts treated by cabozantinib.

METHODS We performed a multicentric retrospective study in 12 French centers. All included pts that received at least one treatment after first or second line based on cabozantinib for mRCC, from August 2018 to December 2024. The primary endpoint was time to treatment failure (TTF). Secondary endpoints included objective response rate (ORR), disease control rate (DCR) and safety.

RESULTS Sixty-five pts were included, 80% males with a median age of 61 years. Thirteen pts (20%) received cabozantinib with nivolumab as first-line therapy (group A), and 80% in second line pretreated with dual CPI in 35% and CPI with TKI in 45% (group B). In group A, 63% received axitinib, 27% received a first generation TKI and one pt received lenvatinib. Median TTF was 4.98 months with an ORR of 44.4% and a DCR of 88.9%. Six pts (55%) had a subsequent line, three pts were still on treatment and two died before starting a new line. In group B, 29% received axitinib, 25% everolimus, 18% lenvatinib, 12% CPI including two in combination with tivozanib and one with belzutifan. Median TTF was 3.21 months with an ORR of 9.3% and a DCR of 46.5%. Nine pts (18%) were still on treatment, 24 pt (47%) had a subsequent line, 21 (41%) died before. Additional data will be added until May 2025.

CONCLUSIONS In our cohort, TKI demonstrated meaningful activity after cabozantinib and nivolumab. TKI after 2nd line cabozantinib had modest activity and treatment targeted acquired resistance or new antitumoral pathway are needed.

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D4 • REAL-WORLD EVIDENCE

Impact of Cabozantinib Monotherapy Starting Dose on Survival in Metastatic Renal Cell Carcinoma: A Real-World Cohort Study

Cabozantinib is a tyrosine kinase inhibitor used for treatment of metastatic renal cell carcinoma. This study describes patient characteristics in 1L and 2L+ and evaluates the effect of starting dose, 60mg vs. 40mg daily, on survival.

Adult patients diagnosed 1996–2021 and treated with cabozantinib monotherapy 2018–2021 at the Hospital District of Southwest Finland were included. Patient characteristics, treatment patterns, and survival were analyzed stratified by the treatment line and starting dose.

In total, 34 (48%) patients received cabozantinib in 1L (60mg n=14, 40mg n=20) and 37 (52%) in 2L+ (60mg n=10, 40mg n=27). Patients in 1L were older (median age 69 vs 65 years) and had poorer prognosis (IMDC favorable 7% vs. 32%, intermediate 54% vs. 59%, and poor risk 39% vs. 9%) compared to 2L+. Patients had undergone prior nephrectomy 14 (41%) in 1L and 24 (65%) in 2L+.

The median duration of treatment in 1L was 9 months (IQR 4.8–11.8) for 60mg starting dose and 13 months (IQR 4.3–19.5) for 40mg starting dose, and in 2L+ 6 (IQR 3.0–8.8) and 4 (3.0–11.0), respectively. Dose reductions were more common with 60mg vs. 40mg starting dose (64% vs. 5% in 1L and 40% vs. 11% in 2L+). The median OS was 22 months (95%CI 20–NA) vs. 28 (95%CI 15–NA) with 60mg vs. 40mg starting dose in 1L, and 12 months (95%CI 5.3–NA) vs. 9.6 months (95%CI 5.9–NA), respectively, in 2L+.

Patients with 1L treatment had poorer prognostic characteristics vs. patients with 2L+ treatment. Patients with 60mg starting dose had also poorer characteristics compared to patients starting with 40mg. There were no significant differences in overall survival between patients with 60mg vs. 40mg starting dose in 1L or 2L. Dose reductions were required to manage side effects.

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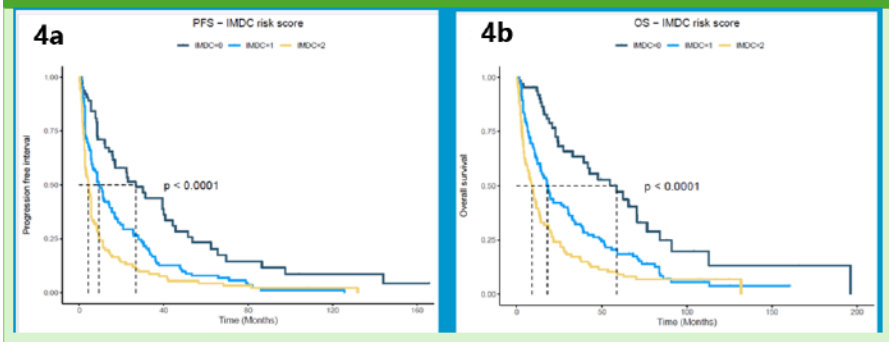
D5 • REAL-WORLD EVIDENCE

Sunitinib for Metastatic Renal Cell Carcinoma. A Real-World Evidence Study in Denmark.

BACKGROUND Sunitinib, a multitarget TKI, has been a cornerstone in mRCC treatment since 2007. Until 2019, it was the preferred first-line treatment, but dual-immunotherapy has since shifted treatment guidelines, limiting sunitinib use primarily to patients in the IMDC favorable prognosis group. While multiple RWE studies have assessed the effectiveness of sunitinib, this study represents the first Danish RWE study, providing data on treatment outcomes.Objectives:The aim of this thesis is to characterize mRCC patients treated with sunitinib at Aarhus university hospital(AUH) and evaluate their PFS and OS. PFS and OS will be compared with other RWEs and RCTs, and the impact of characteristics such as ECOG-PS and IMDC score on PFS and OS will be analyzed.Methods:Lists of patients treated with sunitinib for mRCC from 01-01-2010-to 01-09-2024 were extracted from a Sunitinib registry at Department of Oncology, AUH. Patient data were collected through medical record review in Electronic patient-journals and the pathology database. The data were then organized and entered RedCap. Analyses were conducted and presented as forest plots and KM-curves.Results:Median PFS was 8.43 months (95%CI:6.47–11.2) and mOS was 18.6 months (95%CI:14.73–22.8). In the favorable risk group (IMDC=0), mPFS reached 26.26 months (95%CI:16.52–43.67) and mOS 57.73 months (95%CI:38.62–75.31). For ECOG-PS 0, mPFS was 11.05 months (95%CI:8.05–16.46) and mOS 23.77 months (95% CI:19.05–36.92).ConclusionsWhen compared to other RWEs, our mPFS and mOS fell within the spectrum of previously published results. ECOG-PS and IMDC were identified as the most significant factors in both PFS and OS. Adjusted for IMDC-0, the PFS and OS in our study were among the highest reported in existing RWE's.

Figure 4a and 4b.



Progression-free survival and Overall survival among IMDC groups 0-2. (IMDC-0=Favorable risk group), (IMDC-1=Intermediate risk group), (IMDC-2=Poor risk group).

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Retrospective observational real-life study on metastatic renal cell carcinoma treated in first line with axitinib + pembrolizumab: a project of the Campania Oncology Network

BACKGROUND Several combination therapies are used as first-line treatments for metastatic renal cell carcinoma (mRCC). However, clinical trial populations often differ from the general population, resulting in varied outcomes and toxicities in real-world settings. Oncology Networks are key in generating Real-World Data (RWD) and supporting clinical decision-making through Real-World Evidence (RWE). We retrospectively analyzed mRCC patients treated with first-line pembrolizumab plus axitinib in the Campania Oncology Network (ROC).

METHODS This multicentre retrospective study included untreated mRCC patients receiving pembrolizumab plus axitinib at eight ROC centers. Primary endpoints were progression-free survival (PFS) and overall survival (OS), while secondary endpoints were objective response rate (ORR) and safety.

RESULTS From January 2021 to November 2023, 117 mRCC patients were treated with pembrolizumab plus axitinib at eight ROC centers. International Metastatic RCC Database Consortium (IMDC) risk was favourable in 19.6%, intermediate/poor in 65%, and unknown in 15.4%. Median age at diagnosis was 59 years, with 53.8% having ECOG Performance Status (PS-ECOG) ≥ 1. Clear cell histology was most common (87.2%), and main metastatic sites included brain (36%), lungs (35%), bones (30%), and lymph nodes (29%). After a median follow-up of 12.8 months, median PFS was 15.1 months, ORR was 27.3%, and median OS was not reached. PD caused 49% of treatment discontinuations, and adverse events (AEs) were responsible for 6%. Most adverse events (AEs) were G1-2, including diarrhea (23.9%), asthenia (18%), hypothyroidism (12.8%), and hypertension (9.4%). An indirect comparison with Keynote 426 at first Interim Analysis (2019) showed minimal differences (Table 1).

CONCLUSIONS Our study supports the applicability of pembrolizumab plus axitinib in a real-world setting. As no frontline regimen has proven superior, RWD comparisons may help personalize treatment strategies in clinical practice.

	ROC-RWD	KEYNOTE 426 (First Interim Analysis-2019)
Sample size (n)	117	432
Follow up Median months (IQR)	12.8 (4.7-19.1)	12.8 (0.1-22.0)
Overall Survival Median (95% CI)	Not reached	Not reached
Disease Progression N (IQR)	57 (49%)	264 (61%)
Progression Free Survival Median (95% CI)	15.1 (9.63-NA)	15.1 (12.6-17.7)
Objective Response Rate % (95% CI)	27.3% (19.7-36.5)	59.3% (54.5-63.9)
Duration of treatment Median months (IQR)	10.8 (3.81-18.86)	10.4 (0.03-21.2)
Still receiving treatment N (%)	52 (44%)	253 (59%)
Subsequent therapy N (%)	27 (41%)	88 (50%)

Table 1 An indirect comparison between results from the first interim analysis (at a similar follow up) of the pivotal trial KeyNote 426 and our RWD.

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D7 • REAL-WORLD EVIDENCE

A two-center real-world observational study of ipilimumab + nivolumab in advanced renal cell carcinoma (aRCC)

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INTRODUCTION We aim to report outcomes from patients with aRCC who received first line ipilimumab and nivolumab (I + N) at 2 tertiary cancer centres across England and Wales between June 2019 and July 2023.

METHODS Retrospective study. We included aRCC patients with a minimum follow up of 18 Months, intermediate/poor IMDC status, clear cell aRCC and age ≥18 years.

RESULTS 117 patients were included, with 44.9% patients >65 years-old and 68.4%, males. Most patients had an intermediate IMDC risk status (71.8%) and completed 4 cycles of I+N (73.4%). 41% patients undergone prior nephrectomy. Median follow up was 40 months. Overall, median overall survival (mOS) and median progression free survival (mPFS) were 27.9 and 15.3 months, respectively. 18-months OS was 62.4%. Complete response (CR), partial response (PR), stable disease (SD) and progressive disease (PD) were 11.1%, 48.7%, 58.8%, 22.2% and 14.5, respectively. m OS and mPFS in those with objective response (CR+PR) were 45 and 25.5 months, respectively. mOS in CR, PR, SD, and PD were not reached, 40.8, 21.7 and 7.3 months, respectively. Significantly greater mOS was associated with prior nephrectomy (38.3 months vs 18.7 months, HR: 0.54 [95% CI 0.32-0.89], p=0.015), intermediate IMDC status (35.8 months vs 11.8 months, HR: 0.51 [95% CI 0.31-0.84], p=0.007) and completing 4 cycles of I+N (39.3 months vs 10.6 months, HR: 0.28 [95% CI 0.16-0.51], p<0.001).

DISCUSSION In the real-world setting, vast majority of patients achieved durable response. Those who received 4 cycles of I+N, had a prior nephrectomy and those who were intermediate IMDC risk status had significantly greater survival.

D8 • REAL-WORLD EVIDENCE

Metastatic renal cell carcinoma (mRCC) primary refractory patients to first-line IO-TKI and IO-IO combinations (Meet-URO 33 analysis)

INTRODUCTION Immune-combinations are the standard first-line of mRCC patients, but direct comparisons are lacking and few real-world studies are available. Little evidence is known on primary refractory patients (disease progression as best response), who have poor prognosis and lower treatment possibilities.

METHODS The Meet-URO 33 is an Italian ambispective study of the first-line setting of mRCC patients (CESC IOV 2023-78, PMID: 38914928) to answer unmet clinical questions. This analysis focused on assessing baseline characteristics and survival/response outcomes of primary refractory mRCC patients to first-line immune-combinations.

RESULTS Among 892 patients from 40 centres, 166 (13%) were primary refractory: 37 (31.9%) received IO-IO, 68 (58.6%) IO-TKI and 11 (9.5%) TKI. Compared to other patients, primary refractory patients had: worse IMDC score (favorable-risk: 7.1% vs 23.8%, poor-risk: 36.3% vs 18.6%, p<0.001), Meet-URO score (group 1: 7.5% vs 19.5%, group 5: 12.9% vs 6.4%, p<0.001) and performance status (ECOG PS 2-4: 19.8% vs 7.9, p<0.001); higher pre-therapy steroid use (11.2% vs 6.2%, p=0.046); lower percentage of nephrectomy (50% vs 65.3%, p=0.001), clear-cell histology (75% vs 83%, p=0.037) and sarcomatoid features (51.7% vs 58.3%, p=0.066); higher percentage of lung (69% vs 56.1%, p=0.09), lymph-node (55.2% vs 43.4%, p=0.018) and bone metastases (38.8% vs 27.8%, p=0.016); lower percentage of pancreatic metastases (4.3% vs 9.3%, p=0.076). Primary refractory patients received a higher percentage of IO-IO (31.9% vs 19.3%) and a lower percentage of TKI (9.% vs 20.6%) (p<0.001). After a mFUP of 6.9 months, mPFS was 2.8 months and mOS 8.2 months, with no differences between IO-TKI vs IO-IO (HR for PFS: 0.75, p=0.17; HR for OS: 1.06, p=0.81).

CONCLUSION These preliminary analyses showed distinct baseline characteristics of primary refractory mRCC patients to first-line immune-combinations. No survival differences were recorded according to the type of immune-combination (IO-TKI vs IO-IO). Futher analyses are planned with longer follow-up.

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D9 • REAL-WORLD EVIDENCE

Real-life, first-line treatment with cabozantinib and nivolumab in advanced/metastatic renal cell carcinoma (aRCC): interim analysis of the non-interventional CaboCare study

In this prospective, non-interventional study, aRCC patients from Germany and Austria treated first-line with cabozantinib and nivolumab (CaboNivo) or cabozantinib monotherapy were observed in routine clinical practice. The study aims to assess the number of dose reductions, therapy interruptions and discontinuations due to adverse events (AEs), serious or not. Efficacy outcomes, e.g. objective response rate (ORR) and disease control rate (DCR), were investigated. Physical activity was monitored (Actigraph® GT9X device) at therapy start and every three-months to explore possible correlations between physical activity levels and outcome parameters. Here we present the first interim analysis results of patients treated with CaboNivo.At time of interim analysis, the first 61 patients treated with CaboNivo were included, which had either completed the study by attending their last scheduled study visit (~12 months) or discontinued prematurely for any reason. Mean ± standard deviation age of patients was 67.2 ± 11.7 years, with 57.4% being ≥65 years. Male patients comprised 67.2% of the cohort and 53.6% of patients had an ECOG performance status of 0. Most patients (59.0%) were grouped into the intermediate-risk group. Higher baseline physical activity levels were more frequently reported by patients in the favorable-risk group (83.3%) compared to those in the intermediate-risk (50.0%) and poor-risk (28.6%) groups. Overall, 51.2% of patients reported physical activity levels above this threshold. The median daily cabozantinib dose was 29.9 mg, with dose reductions due to AEs occurring in 37.7% of patients. The DCR was 83.7%, and the ORR was 59.2%. Treatment-emergent AEs were reported by 96.7% of patients.

These interim data on real-world first-line CaboNivo treatment are broadly consistent with phase 3 trial findings, further supporting its efficacy and safety in the management of aRCC.

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D10 • REAL-WORLD EVIDENCE

Integration of First-line Nivolumab-Cabozantinib Combination with Radiotherapy: Achieving Complete Response in Metastatic Fumarate Hydratase-Deficient Renal-Cell Carcinoma, a Case Series

INTRODUCTION Fumarate hydratase-deficient renal-cell carcinoma (FH-d RCC) is an aggressive disease, characterized by poor prognosis and often presenting as metastatic with an earlier age of onset than clear-cell RCC (ccRCC). To date, there is no clear evidence of the best therapeutic algorithm, borrowed from ccRCC.

CASE PRESENTATIONS In June 2023, a 33-year-old woman affected by Hereditary Leiomyomatosis and Renal-Cell Cancer (HLRCC) started first-line therapy with nivolumab and cabozantinib for mediastinal and abdominal lymph node recurrence (short axis of 29, 21 and 21 mm) of a previously radically resected FH-d RCC. After one year of treatment, almost all the lymphadenopathies achieved a radiologic partial response, which was then consolidated with radiotherapy. Four months later, the most recent CT scan showed complete response, and the treatment is still ongoing.

A second case of FHd-RCC in a young male patient came to the attention of our department in July 2023. Following radical nephrectomy, post-operative CT scan showed the presence of two pathological abdominal lymph nodes (short axis of 11 mm). Hence, the patient started first-line nivolumab-cabozantinib. Radiotherapy was performed as consolidative treatment six months after the start of systemic therapy, with a CT scan showing a radiological complete response. Fourteen months from the start of treatment, the patient is still with no evidence of disease and continuing nivolumab-cabozantinib therapy.

CONCLUSION These cases provide the occasion to appreciate the outstanding efficacy of an integrated multimodal therapeutic approach that combines systemic therapy with Vascular Endothelial Growth Factor Receptor Tyrosine Kinase Inhibitor and Immune Checkpoint Inhibitors combination associated to radiotherapy for the management of metastatic FH-d RCC. Enrollment of patients with rare RCC histologies in clinical trials is widely advocated to improve evidence in daily clinical practice.

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ORAL PRESENTATION

D11 • REAL-WORLD EVIDENCE

Genomic Profiling of Non-Clear Cell Renal Cell Carcinoma: Insights for Prognosis and Treatment

BACKGROUND Non-clear cell renal cell carcinoma (nccRCC) is an uncommon and heterogeneous entity characterised by distinctive histological, genetic, and molecular features. This results in nccRCCs exclusion from randomised clinical trials and the adoption of the same therapeutic strategies used for ccRCC in clinical practice, with unfavourable clinical outcomes.

METHODS We analysed real-world data from the nationwide deidentified Flatiron Health-Foundation Medicine nccRCC clinico-genomic database, which integrates clinical and genomic data from approximately 280 US cancer clinics. The genomic profiles of 300 patients with metastatic nccRCC were evaluated, and the prognostic value (overall survival, OS) of the most frequent genomic alterations (GA) was assessed using the Kaplan-Meier method and Cox proportional hazards model.

RESULTS The most prevalent nccRCC subtypes were papillary RCC (pRCC, 74.3%) and chromophobe RCC (chRCC, 16.0%), followed by translocation RCC (tRCC, 4.0%), collecting duct RCC (cdRCC, 4.0%), and renal medullary RCC (RMC, 1.7%). In pRCC, the most common GAs were CDKN2A (30%), CDKN2B (25.1%), TERT (20.2%), and NF2 (15.7%). Among the chromatin-modifying genes, SETD2, BAP1, and PBRM1 mutations were observed in 14.3%, 9.0%, and 5.8%, respectively. In chRCC, the most prevalent GAs were TP53 (68.8%), PTEN (33.3%), and RB1 (18.8%), and other GAs, including CDKN2C, MYC, TERT, VHL, ATRX, CHEK2, and TSC1, were identified in less than 10% of chRCC patients. Survival analyses revealed three genes with prognostic value in pRCC cases: CDKN2A/B GAs (HR 2.59 and 2.45, respectively; p < 0.001) and TERT GAs (HR 1.66, p=0.022) were significantly associated with poor prognosis. MET and PBRM1 GAs showed a trend towards better OS, while TP53 appeared to portend a poor prognosis.

CONCLUSIONS This real-world analysis provides insights into the genomic landscape of nccRCC. The distinctive mutational assets identified in this study warrant further investigation to support the tailoring of treatment strategies and improve outcomes for nccRCC patients.

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Relevance of IMDC risk model in real world setting: single institution experience

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BACKGROUND Systemic therapy landscape for metastatic renal cell carcinoma (mRCC) has evolved rapidly over the recent years and use of combination treatment regimens has shown improved outcome compared to VEGF TKIs. IMDC has been validated and widely used as a prognostic tool for patients with mRCC treated with VEGF TKI and immunotherapy (IO). Aim of this study was to assess outcomes of patients treated with IO based combination treatments and VEGF TKI in relation to IMDC prognostic groups and the impact of previous nephrectomy (Cyto-reductive or radical) in a real-world setting.

METHODS This single centre retrospective study included 112 patients with mRCC receiving first line systemic therapy as of January 2018 to March 2022. PFS and OS were analysed using descriptive statistics and Kaplan-Meier curves.

RESULTS Median age was 66 years (35-85). More than half of the patients were IMDC intermediate risk group (54.5%). Combination treatments were used in about 30% and 42% received only 1 line of therapy.

There was statistically significant difference in median PFS and OS based on IMDC risk groups [median PFS 31.5, 21, 8.7 months and median OS 87, 36, 9 months respectively in favourable, intermediate, and poor groups; (P <0.0001)].

Previous nephrectomy was performed in 48.2% of patients. Median PFS and OS were significantly longer in nephrectomy group. [PFS was 29Vs 10.9 months and OS was 55 vs 21 months;(P < 0.0001)]

DISCUSSION Our study included more patients treated with VEGF TKI monotherapy as it included patients treated in pre-combination therapy era. Similar to other reports, our study also indicates higher proportion of dropouts between lines of therapy.

The results of our retrospective study highlight that IMDC risk groups can be readily used in clinics and remain relevant to predict the prognosis in real world setting. Our study also suggests that patients who had a previous nephrectomy had possible overall survival and progression free survival advantage.

Real world usage of Cabozantinib at University Hospitals Plymouth NHS Trust between 2020 and 2024: does dose reduction affect progression free survival (PFS)?

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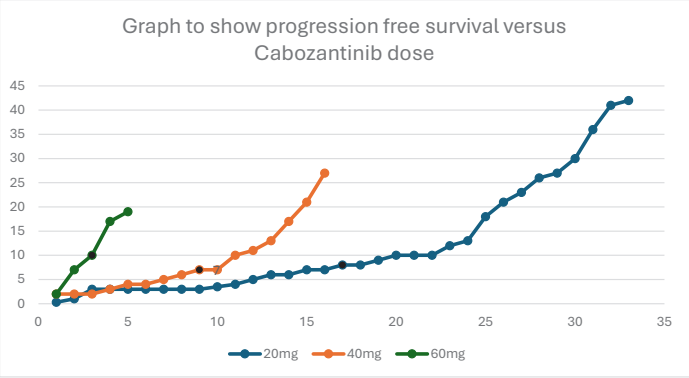
54 patients (15 women, 39 men), ranging in age from 42 to 83 (median age = 64) were treated with single agent Cabozantinib between 2020 and 2024 at University Hospitals Plymouth NHS Trust. The majority of these were treated in the second line setting. 11 (20%) were favourable risk, 18 (33%) were intermediate risk, and 25 (46%) were poor risk (which was a much more unfavourable patient group than in the 2015 METEOR trial, where 43% were favourable risk, 43% intermediate risk and 14% poor risk).Only 5 out of 54 (9%) of patients completed their Cabozantinib course at 60mg. The majority were eventually dose reduced to 20mg (33/54 patients) due to side effects, and 16/54 ended up taking 40mg daily. Dose reductions usually occurred early, most frequently for cycle 2 or 3.In the majority of cases (32/55), Cabozantinib was being utilised in the second line setting, most commonly after progresion on first line immunotherapy.Median PFS of our patients was 7 months. The median PFS is reflective of the 7.4 month median PFS seen on the METEOR trial. The METEOR trial showed an ORR of 21%, which is lower than the ORR seen in our real world patients, of 43%.From our data, the dose of Cabozantinib made no difference to median overall survival, as shown on the below graph, in fact, most of our long term responders are taking 20mg only. This data shows that we are achieving similar PFS results and improved ORR compared to the trial, despite having a much older patient population with poorer risk disease. These impressive results are almost certainly achieved with lower levels of treatment toxicity given timely and aggressive dose reductions.



D14 • REAL-WORLD EVIDENCE

Trends in Kidney cancer: Exploring the impact of sex and age on stage of disease, and prognosis during the past three decades in Denmark – a DaRenCa study

BACKGROUND & OBJECTIVE Renal cell carcinoma (RCC) management has advanced due to increased imaging-based diagnoses and improved therapies for metastatic disease. This nationwide registry-based cohort study investigates how the number of RCC cases, stage at diagnosis, and prognosis have changed during the past 30 years in Denmark, and how these are associated with sex and age.

METHODS All Danish patients aged 18 and older diagnosed with RCC from 1992 to 2021 and without prior cancer history, except for non-melanoma skin cancer, were included, and followed from diagnosis until death or end of follow-up (31-12-2023).

RESULTS 17,423 RCC patients were identified. RCC cases increased from 2,244 in 1992-1996 to 3,947 in 2017-2021. The proportion of male patients increased from 59% in 1992-1996 to 72% in 2017-2021 (P<0.001), and male patients were younger at diagnosis than female patients (median age 65 vs 69 years, P<0.001). Localized cancer cases increased from 51% (N=983) in 1992-1996 to 79% (N=2,766) in 2017-2021, while metastatic cases declined from 34% (N=640) to 19% (N=652). Median survival for metastatic RCC improved from 4.1 months in 1992-1996 to 13.3 months in 2017-2021.

CONCLUSION During the past 30 years, the number of RCC cases in Denmark has increased, particularly in male patients, primarily driven by localized tumors, providing additional pressure for urological departments. The number of metastatic cases has remained stable, while survival has increased, highlighting the impact of early detection and treatment advancements over time.

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POSTER AD

D15 • REAL-WORLD EVIDENCE

Comparison of IO-TKI vs IO-IO combinations in IMDC poor-risk metastatic renal cell carcinoma (mRCC) patients (Meet-URO 33 analysis)

BACKGROUND Immune-combinations are the first-line treatment cornerstone of mRCC patients, but head-to-head comparisons are lacking and few real-world data are available. In this context, little evidence is available for IMDC poor-risk patients, who have the worst prognosis and lowest response to standard treatments.

METHODS The Meet-URO 33 study is an Italian ambispective registry of the first-line mRCC setting (CESC-IOV-2023-78, PMID: 38914928) to answer as many clinical questions as possible. This analysis focused on the different baseline characteristics, response and survival performance of patients receiving IO-TKI and IO-IO combinations.

RESULTS 892 patients were enrolled from 40 centres; 772 (87%) were evaluable for survival analyses and 160 (21%) had IMDC poor-risk: 42 (26%) received IO-IO, 105 (66%) IO-TKI and 13 (8%) TKI. Poor-risk patients receiving IO-IO were older (mean age: 68 vs 64, p=0.03), had more cardiovascular comorbidities (74% vs 56%, p=0.048) and lower frequency of bone metastases (29% vs 57%, p=0.002) compared to IO-TKI-treated patients. After a mFU of 6.9 months, the overall mOS was 11.3 months, higher with IO-IO than with IO-TKI [20.6 vs 11 months, HR 1.65 (0.97-2.82); p=0.067]. The overall mPFS was 6.4 months, higher with IO-IO than IO-TKI [11 vs 5.8 months, HR 1.70 (1.05-2.75); p=0.031]. After multivariable analysis the difference between IO-IO and IO-TKI was not statistically significant for both OS [HR 1.37 (0.78-2.40); p=0.27] and PFS [HR 1.58 (0.95-2.63); p=0.078]. The general ORR was 46%, higher with IO-TKI than with IO-IO [71% vs 29%, OR 0.70 (0.21-1.56); p=0.38].

CONCLUSIONS These first analyses show no clear survival advantage in choosing an IO-TKI combinations instead of an IO-IO combination in IMDC poor-risk patients. These results are in line with the well-known small benefit of TKI in poor-risk patients (more immunogenic / less angiogenic; COSMIC-313 trial results). Future analyses with longer follow-up are planned.

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E1 • IMAGING

Identifying Cancerous and Non-Cancerous Areas in Isolated Kidney Samples via Infrared Visualization

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The objective of this study was to create a novel technique for distinguishing between malignant and healthy areas in isolated kidney samples taken during surgery and determining the margins between the two types of tissue. In our earlier research, differences in infrared images between tumors and non-cancerous tissue were studied.

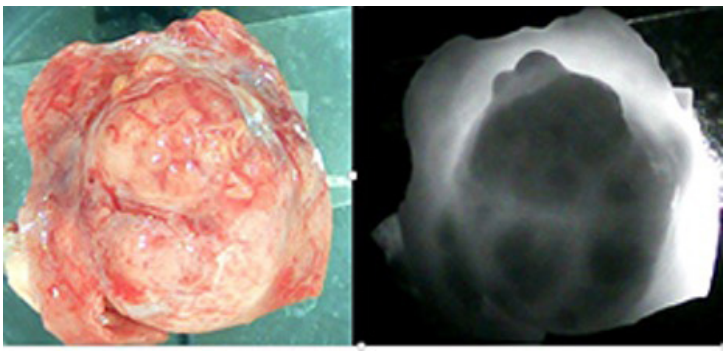
We analyzed kidneys acquired post-open radical nephrectomy. We removed the malignant tissue from these kidneys along with some nearby healthy tissue. The specimens were positioned between the infrared light (IR) source and the CCD camera. IR contains information about the inhomogeneity of the tissue after exiting it. Our developed software highlighted areas associated with both malignant and healthy tissues, assessed their average brightness, computed the ratio of the average brightness (RAB) of the malignant area to that of the healthy area, and stored it in memory. After 32 operations, the software calculated the interval for RABs with a 95% probability.

The IR imaging technology successfully distinguishes between areas of health and malignancy in the image, clearly defining their boundaries (figure 1). This is achieved using our developed software. The findings of IR investigations were in all cases validated by histomorphological studies. The software calculated the range for RABs at 0.38 to 0.42.

Figure 1. A cancerous kidney specimen (left) alongside its IR image. The dark area in the IR image represents malignant tissue, while the light area indicates healthy tissue in the image.

The proposed technique can be applied during partial nephrectomy and may assess margins at the nephrectomy site. It will drastically shorten the time of ischemia, enhance patient outcomes, and limit tissue damage.

This work was supported by the Shota Rustaveli National Science Foundation of Georgia, grant FR-22-195. Title: “Development of the new infrared imaging method for avoiding cancer recurrence after radical prostatectomy and partial nephrectomy.”



E2 • IMAGING

A Phase Ib trial to assess the effects of belzutifan on 89Zr-DFO-girentuximab uptake as a surrogate to determine CAIX tumor expression in patients with clear cell Renal Cell Carcinoma

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INTRODUCTION Despite the clear advancement in the treatment of advanced clear cell renal cell carcinoma (ccRCC) there is still a significant number of patients who progress and eventually succumb to the disease. Belzutifan, a hypoxia inducible factor-2 alpha (HIF-2α) inhibitor is currently FDA approved for patients with relapsed ccRCC who have progressed on a checkpoint inhibitor (CPI) and a vascular endothelial factor tyrosine kinase inhibitor (TKI). Nevertheless, treatment resistance to belzutifan is common and new approaches are needed to improve the durability of response to belzutifan. Here, we aim to evaluate the effect of belzutifan on carbonic-anhydrase IX (CAIX) expression using 89Zr-deferoxamine (DFO) - girentuximab PET in a prospective clinical trial to lay the foundation of a novel combination treatment strategy with future CAIX targeted agents.

Through its inhibition of HIF2α, belzutifan leads to fundamental changes in cell signaling downstream of VHL. VHL mutation is the main driver of ccRCC tumorigenesis through constitutive stabilization of HIFs which then promote the transcription of several key genes involved in tumorigenesis. HIF1 and HIF2 are the key HIF isoforms and have distinct roles. HIF-1α is implicated in the expression of CAIX, a metalloprotease involved in pH regulation. This is clinically relevant as CAIX is an emerging diagnostic and therapeutic target for RCC. Previously, downregulation of HIF-2α in vitro has been shown to lead to overexpression of HIF-1α in tumor cells and thus increased CAIX expression in preclinical models. We hypothesize that belzutifan treatment will lead to increased HIF1 transcriptional activity thereby increasing CAIX expression.

METHODS This is a phase Ib single arm, single center study to evaluate the effects of belzutifan on 89Zr-DFO-girentuximab PET uptake measured in SUVs, in ccRCC lesions. Patients who have > 1 evaluable lesion by RECIST 1.1 and avid disease on 89Zr-DFO-girentuximab PET defined as any uptake above background, will be included. Patients must be candidates for treatment with belzutifan. We expect to enroll 12 patients over 12 months. Primary endpoints will include: 1) SUV max and SUV peak uptake at baseline and after 28 days of treatment with belzutifan, 2) safety. This is an investigator-initiated trial. Telix Pharmaceuticals provided funding and 89Zr—DFO-girentuximab.

Empowering Choices: Insights from Healthcare Professionals on Shared Decision-Making in Kidney Cancer

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INTRODUCTION Shared decision-making (SDM) is essential in cancer care, as treatment options can have a significant impact on both prognosis and patients' quality of life. Patients with small renal masses (SRM) wish to be actively involved in their treatment decisions; however, research shows that the definition and practice of effective SDM in the context of SRM are not yet well established. Additionally, Health Care Professionals' (HCPs) perspectives on the facilitators and barriers to SDM in SRM management remain unclear. This study aims to investigate HCPs' views on factors driving SDM in SRM treatment, beginning with a systematic review to identify factors influencing SDM across cancer care, followed by qualitative interviews across three countries.

METHODS A comprehensive search was conducted to identify qualitative interview studies focused on HCPs being interviewed on drivers for SDM in cancer care. The identified drivers helped to establish a discussion guide which structured the complementing interviews conducted in Germany, the Netherlands and the UK.

RESULTS After removing duplicates, 1,274 records were identified. Following title and abstract screening, 1,117 studies were excluded, leaving 147 studies for full-text review. Ultimately, 13 studies met the inclusion criteria. Through analysis, nine key drivers of SDM were identified (Figure 1, points 1–9). Additionally, preliminary interview results from two countries (five each country) revealed two additional drivers, highlighting trust in specific treatment options as a significant barrier to SDM.

To increase SDM, HCPs identified the need to inform and educate patients about both their condition and available treatment options before their consultation. HCPs expressed that a clear pathway including education could enhance SDM and lead to more meaningful discussions.

CONCLUSION This study highlights key drivers identified by HCPs involved in cancer care and confirms that SDM in SRM is complex, with implementation varying according to different drivers.

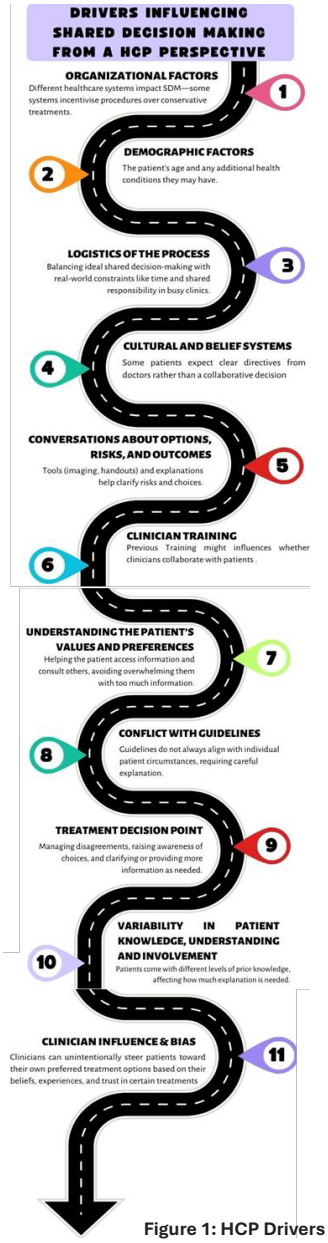

Figure 1: HCP Drivers

G1 • BASIC SCIENCE/TUMOR BIOLOGY/MICROENVIRONMENT

Unraveling the role of autophagy in RCC using spheroid cultures and patient-derived organoids

Renal cell carcinoma (RCC) is a complex disease composed of multiple subtypes with different histologies, genetic changes and responses to therapy. A major challenge is to predict which tumors will advance to metastatic disease and to identify optimal therapy for these patients. We found that autophagy is differentially activated in certain RCC subtypes compared to matched healthy kidney tissue. Using RCC cell line spheroid cultures and patient-derived organoids from RCC tumor and matched normal tissue we aim to unravel the molecular mechanism underlying the alterations in autophagy. Furthermore, we are performing drug screens in RCC spheroids and patient-derived organoids targeting autophagy and related pathways and aiming at identifying biomarkers and potential targets for further treatment. The long-term goal is to offer new inroads for the clinical management of RCC.

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G2 • BASIC SCIENCE/TUMOR BIOLOGY/MICROENVIRONMENT

Soluble CD163 and CD206 as potential biomarkers in metastatic Renal Cell Carcinoma Patients receiving Anti-Angiogenic Treatments

Despite improvements in the prognosis of patients with metastatic renal cell carcinoma (mRCC) by the introduction of immunotherapy and tyrosine kinase inhibitors (TKIs), a large group of patients do not respond to treatment. Based on the current predictive biomarkers, clinicians cannot identify non-responders upfront, and improved prognostication in mRCC is thus needed to guide both clinicians and patients.

In a phase IV prospective trial conducted at Aarhus University Hospital, Denmark, conducted from 2012-2017, blood samples were collected from mRCC patients. All patients received either a TKI (sunitinib or pazopanib) or a mTOR inhibitor (temsirolimus) as first-line treatment. Healthy donor serum (n=22) and patient serum (n=34) was analyzed for the macrophage-activation biomarkers soluble scavenger receptor CD163 (sCD163) and soluble macrophage mannose receptor (sCD206) using ELISA.

Results showed a median follow up time of 15.5months. Significantly impaired progression free survival was associated with elevated baseline levels of sCD206 (5.3months vs 13.1months, P=0.006). Significantly impaired overall survival was associated with both elevated baseline levels of sCD163 (6months vs. 14.3months, P=0.02) and sCD206 (5.5months vs 27.0months, P=0.002).

Based on these results, the patients were divided into three groups: elevated levels above the median of none, one, or both sCD163 and sCD206. When these groups were examined as a continuous variable from 0 to 2 elevated parameters, patients had an increasingly higher risk of worse overall survival in both univariate (HR 3.06 [95% CI 1.68; 5.57], P=0.0003) and multivariate cox regression analysis (HR 3.10 [95% CI 1.49; 6.46], P=0.002). The multivariable analysis was adjusted for IMDC criteria, first-line treatment, and nephrectomy status.

In conclusion, the macrophage markers sCD163 and sCD206 seem to have a strong prognostic potential in patients with mRCC. Further validation is needed in a larger cohort, which is planned for biomarker studies in the NORDIC SUN trial (NCT03977571).

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ORAL PRESENTATION

H1 • PATIENT-REPORTED OUTCOMES

Subgroup analyses of health-related quality of life (HRQoL) outcomes in the phase 3 CLEAR trial

BACKGROUND In CLEAR, lenvatinib+pembrolizumab (L+P) improved efficacy versus sunitinib (Su) in treatment-naive patients with advanced renal cell carcinoma. L+P demonstrated similar/favorable HRQoL versus Su. We present subgroup HRQoL analyses from CLEAR to explore QoL by metastatic sites.

METHODS Patients (N=1069) were randomized (1:1:1) to L 20mg PO QD + P 200mg IV Q3W; L+everolimus (not reported); or Su 50mg PO QD (4-wks-on/2-wks-off). HRQoL instruments were administered at baseline, on day-1 of each subsequent 3-week-cycle starting with cycle-2, and post-treatment. Analyses were conducted by baseline HRQoL and common baseline metastatic sites.

RESULTS Patients in the L+P (n=351) and Su (n=340) arms with HRQoL data who received ≥1 treatment dose were included.

Baseline HRQoL scores generally reflected no imbalance between arms across subgroups, including subgroups of patients with below/equal or above median baseline QoL scores (Table). Median VAS was 80.0 at baseline in most subgroups of patients with/without metastases; notably, patients with bone metastases had slightly worse QoL (VAS medians: 75.0 with L+P, 70.0 with Su).

Differences in least squares mean change (L+P vs Su) stratified by baseline scores are shown (Table). Patients with worse baseline symptom scores than the median trended toward greater improvement with L+P versus Su.

HRQoL was similar or trended toward improvements with L+P across metastatic sites (Table). Differences in least squares mean change for patients with bone metastases (limited by sample size) and for patients with baseline scores higher than the median favored L+P for pain.

CONCLUSIONS Metastatic sites (particularly presence of bone metastases) influenced baseline QoL and QoL changes with therapy; however, L+P demonstrated similar/better HRQoL scores versus Su, irrespective of baseline HRQoL or metastatic site, consistent with results from the overall trial population.

	Median baseline scores (Q1-Q3)				Differences in least squares mean change from baseline (95% CI): L+P versus Su									
	Pts with ≤median baseline QoL scores		Pts with >median baseline QoL scores		Baseline score ≤median[a]		Liver mets		Bone mets		Lymph node mets		Lung mets	
Scale	L+P	Su	L+P	Su	Y	N	Y	N	Y	N	Y	N	Y	N
n (L+P/Su)	–	–	–	–			62/67	289/273	77/86	274/254	159/145	192/195	249/216	102/124
FKSI-DRS	n=175	n=175	n=161	n=148										
Total score	29.0 (26.0–31.0)	29.0 (26.0–31.0)	35.0 (34.0–36.0)	35.0 (34.0–36.0)	0.6 (−0.3–1.45)	−0.3 (−1.0–0.4)	0.5 (−1.0–2.1)	0.1 (−0.5–0.7)	0.8 (−0.9–2.6)	0.02 (−0.6–0.6)	0.7 (−0.3–1.6)	−0.25 (−0.9–0.4)	0.1 (−0.6–0.9)	0.2 (−0.8–1.1)
EORTC QLQ-C30	n=172	n=186	n=164	n=141	–	–	–	–	–	–	–	–	–	–
GHS/QoL	58.3 (50.0–66.7)	62.5 (50.0–66.7)	83.3 (83.3–100.0)	83.3 (83.3–100.0)	0.2 (−3.0–3.4)	1.15 (−2.0–4.3)	−0.8 (−6.2–4.7)	1.1 (−1.4–3.5)	2.7 (−3.1–8.6)	0.4 (−2.0–2.8)	1.45 (−2.0–4.9)	0.01 (−2.9–3.0)	1.3 (−1.5–4.2)	−0.2 (−3.9–3.5)
Symptom scales														
	n=197	n=179	n=138	n=148	–	–	–	–	–	–	–	–	–	–
Fatigue	11.1 (0–22.2)	11.1 (0–22.2)	33.3 (33.3–55.6)	33.3 (33.3–55.6)	−2.2 (−5.6–1.2)	−4.0 (−8.4–0.5)	−6.9 (−13.2–−0.5)*	−2.0 (−5.0–1.0)	−2.2 (−9.3–5.0)	−3.0 (−5.9–−0.04)*	−3.0 (−7.2–1.3)	−2.6 (−6.2–0.9)	−2.9 (−6.4–0.5)	−2.3 (−6.8–2.3)
	n=244	n=211	n=92	n=116	–	–	–	–	–	–	–	–	–	–
Pain	0 (0–16.7)	0 (0–16.7)	33.3 (33.3–66.7)	33.3 (33.3–66.7)	1.7 (−1.05–4.45)	−7.9 (−13.7–−2.1)	−3.2 (−9.1–2.8)	−0.6 (−3.4–2.3)	−7.1 (−14.7–0.6)	0.5 (−2.2–3.1)	−0.4 (−4.7–3.8)	−1.2 (−4.4–2.0)	−1.2 (−4.4–2.1)	−0.5 (−4.9–3.9)
EQ-5D	n=178	n=183	n=158	n=136	–	–	–	–	–	–	–	–	–	–
Index	0.8 (0.7–0.8)	0.7 (0.7–0.8)	1.0 (1.0–1.0)	1.0 (1.0–1.0)	0.06 (0.02–0.1)*	−0.01 (−0.05–0.02)	0.1 (0.02–0.2)*	0.01 (−0.02–0.04)	0.09 (−0.01–0.2)	0.01 (−0.01–0.04)	0.04 (0.00–0.08)	0.02 (−0.02–0.05)	0.04 (0.00–0.08)*	0.01 (−0.03–0.06)
	n=201	n=208	n=137	n=113	–	–	–	–	–	–	–	–	–	–
VAS	70.0 (60.0–80.0)	70.0 (60.0–80.0)	90.0 (90.0–95.0)	90.0 (90.0–95.0)	2.7 (−0.5–5.8)	−0.2 (−3.9–3.4)	2.1 (−3.8–8.0)	1.8 (−0.9–4.4)	3.5 (−1.9–8.9)	1.3 (−1.4–3.9)	3.1 (−0.6–6.75)	0.5 (−2.7–3.7)	2.1 (−1.0–5.2)	0.8 (−3.0–4.5)

The overall differences in least squares mean change were estimated at the mean follow-up time during treatment within each subgroup. [a]Sample sizes for these columns might differ for each score and arm as data is stratified by median score at baseline. Further details will be presented.
L+P, lenvatinib plus pembrolizumab; Q1, first quartile; Q3, third quartile; Su, sunitinib; VAS, visual analog scale.
*$P<0.05$.

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POSTER AD

H2 • PATIENT-REPORTED OUTCOMES

A phase III study testing the role of PRoactivE coaching on PAtient REported outcome in advanced or metastatic renal cell carcinoma

BACKGROUND This study evaluated whether proactive onco-coaching (POC) could improve quality of life (QoL) in patients with metastatic renal cell carcinoma (mRCC) undergoing treatment with tyrosine kinase inhibitors (TKI) ± checkpoint inhibitors (CPI).

METHODS Adult, treatment-naïve mRCC patients eligible for sunitinib (SU), axitinib + avelumab (AA), or axitinib + pembrolizumab (AP) were 1:1 randomized to POC (nurse-led structured coaching) or standard of care (SOC). POC involved 8 sessions (24 weeks) of structured interviews, education, and follow-up on managing adverse events (AEs). The primary endpoint was QoL response (≥3-point improvement on FKSI-15). Secondary endpoints included patient-reported outcomes, time to QoL improvement, efficacy, survival, and safety. A total of 430 patients were planned; analyses used log-rank tests and Fisher exact tests.

RESULTS Of 113 patients enrolled, 89 were assessable for the primary endpoint. Median ages were 72 (POC) and 68 (SOC). Most had intermediate/poor MSKCC risk (73%) and clear cell histology (86%). Coaching completion rates were 80% (full) and 16% (partial) for POC. QoL response rates were similar: 43.6% (POC) vs. 41.5% (SOC; p=0.95). POC did not improve objective response rates (37.5% vs. 33.3%; p=0.96) or median PFS (11.1 vs. 9.2 months; p=0.21). However, overall survival (OS) trended higher in POC (49.6 vs. 25.4 months; p=0.11), particularly in patients with comorbidities (CCI ≥2; 52.4 vs. 15.7 months). Grade ≥3 AEs were more frequent with POC (52.7% vs. 36.4%).

CONCLUSIONS POC did not improve QoL or treatment efficacy but showed a potential OS benefit, especially in comorbid patients. Further studies are warranted despite early trial termination which limited the sample size.

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ORAL PRESENTATION

I1 • QUALITY OF CARE AND QUALITY IMPROVEMENT

The Top 10 Italian Priorities in Renal Cell Carcinoma (RCC): a people centered approach to cancer care for future research.

BACKGROUND The management of renal cell carcinoma (RCC) has advanced significantly in recent years, necessitating research priorities that integrate both clinician and patient-centered perspectives. Increasingly, individuals with cancer are recognized for their pivotal roles in the decision-making process regarding treatment pathways. In this context, our project facilitated a consensus-based priority-setting partnership between Italian patients with RCC and oncologists to identify the top 10 research priorities in RCC in Italy.

METHODS The study comprised three steps. In Step I (August-October 2024), two targeted surveys were distributed via the "Survio" online platform: one for oncologists, developed by the Italian Medical Research (IMR), consisting of 37 questions, and another for patients with RCC and their caregivers, created by the Italian Association of Kidney Cancer Patients (ANTURE), containing 27 questions. Both surveys addressed key aspects of RCC treatment, including guidelines, prognostic scores, adjuvant and first-line therapies, treatment personalization, cytoreductive nephrectomy, biomarkers, toxicity, bone metastases, quality of life (QoL), and home care. The responses included multiple-choice questions and a 5-point Likert scale to rank priorities, with some questions allowing for multiple answers to gather more comprehensive opinions. In Step II, a panel of Italian oncologists specializing in RCC convened on October 24-25, 2024, to evaluate the survey results and extract key themes. During Step III, the data from the patients' and oncologists' surveys were compared to identify areas of alignment and divergence. Finally, the expert panel established a definitive ranking of research priorities.

RESULTS Of the 467 oncologists invited, 156 (33.4%) completed the survey (53% male, 47% female). Similarly, 107 out of 312 (34.3%) individuals with RCC and caregivers (69% male, 31% female) completed the patient-directed survey. Both groups identified adjuvant therapy, personalized first-line treatment strategies—including both intensification and de-intensification—and biomarker development as their shared top three priorities for future research. However, notable divergences in priority rankings emerged: patients placed a greater emphasis on focusing on bone metastases (ranked 6th), QoL data in clinical trials (ranked 7th), and management of toxicities (ranked 10th), which were absent from the oncologists' top 10 priorities. In contrast, oncologists prioritized topics such as the unmet need for biological features of long-term responders to immuno-oncology combination therapy (ranked 5th), prognostic scores (ranked 8th), and the necessity for real-world evidence studies (ranked 10th), which were less prominent for patients.

CONCLUSIONS The top 10 research priorities project demonstrates the importance of actively listening to individuals with cancer to inform future research and treatment directions. This collaborative effort helps align the differing perspectives of clinicians and patients with RCC, resulting in a ranking that is recognized by both parties.

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The importance of multidisciplinary team meetings (MDMs) with focus on minimal surgery.

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INTRODUCTION Multidisciplinary team meetings (MDMs) have emerged as a crucial governance model for complex decision-making in Western healthcare systems. MDMs are known as multidisciplinary team conferences (MDT) in Denmark. They have become an essential corner stone in the cancer pathways, which was implemented during a national reorganization of cancer care in the late 2000s and early 2010s. In Denamrk, approximately 1,100 patients with renal cancer are diagnosed each year, of which about 70% are men. It is mandatory to have weekly MDM according to the national renal cancer guidelines.

PURPOSE The purpose of MDM is to secure the quality of diagnostics and treatment to the individual patient. While the clinical implications of MDMs remain, studies conducted by health care professionals suggest that MDMs improve care coordination and outcomes, reduce unexpected hospital admissions and shorten hospital stays. The purpose is to show whether our registration in our database really makes a difference.

MATERIAL AND METHOD All departments treating RCC must report data on all patients. Every Danish resident has a unique Civil Registration (CPR) number which is included in all registries and allow for linkage to the National Patient Register and the Pathology Register. These registers contains information about all examinations and treatments in Danish hospitals. DaRenCaData is based on these central data sources. A nationwide DMCG (Danish Multi-disciplinary Cancer Group) for RCC has selected different indicators for monitoring the quality of the treatment and outcome.

RESULTS The database was established 1 August 2010 and contains more than 13.000 new cases of RCC, including 1.035 from the current year (the period 1 August 2023 to 31 July 2024).

In the current period, 939 patients were treated surgically (operation or ablation), and of these, 54% underwent kidney-preserving interventions. For patients who underwent nephrectomy, total 85% were performed laparoscopically (including robot-assisted), and this is a significant increase over time. However, differences are still observed in two Regions having the lowest robotic/laparoscopic procedures, but all regions have shown increasing development. The Capital Region in particular has currently improved the result, which is moving upwards towards the development target of 80 % (Figure 1).

The proportion of patients with small (T1a) tumors who received nephrectomy rather than kidney-preserving treatment was 13%, slightly above the development target (10%) but with very positive development over time. The proportion of endoscopically or ablatively treated patients discharged within 3 days after the procedure was 89% with some departmental variation, with 2 Regions having a lower proportion than the rest of the country, and the steering group encourages this to be a focus area for the departments in collaboration with DaRenCa. Survival after renal cancer is increasing in Denmark with a current 1-year survival at 91% and 5-year survival was 71%.

Figure 1

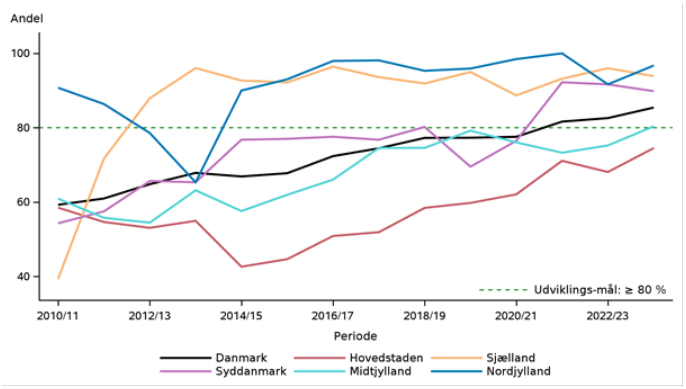

Figure 1: Proportion of nephrectomy patients who underwent Robotic/laparoscopic surgery

CONCLUSION Through systematic work with quality results, interdisciplinary collaboration and the introduction of new treatments, we have observed a uniform treatment and increased survival in patients with renal cancer.

J1 • THERAPEUTICS

Management Sequences and Clinical Outcomes in Advanced Clear Cell Renal Cell Carcinoma (ccRCC): A real world analysis

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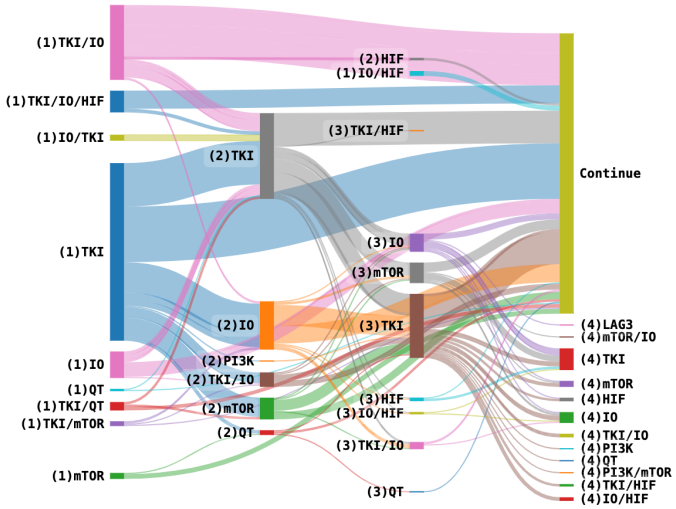
BACKGROUND Over the years, we have witnessed the advancement of treatments for patients with ccRCC. However, uncertainties remain regarding the optimal treatment sequence to follow in this context

METHODS A retrospective analysis of ccRCC patients treated at Vall d'Hebron Hospital from 2004 to 2024 their assessed clinical characteristics and outcomes. Descriptive and univariate analyses were performed, and PFS2 was estimated using the Kaplan-Meier method and compared with the log-rank test.

RESULTS 281 patients with advanced ccRCC were included. Mean age was 54 years (23-81). 63% were metastatic at diagnosis or had less than one year between diagnosis and the initiation of systemic therapy. First line treatment primarily consisted of Tyrosine kinase inhibitor (TKI) in 53%, TKI/PD1i in 6.1%, PD1 inhibitor(PD1i)/CTL4 inhibitor (CTL4i) in 5.4%, TKI/PD1/HIF inhibitor (HIFi) in 6.5%, TKI/PD1i/LAG3 inhibitor in 5.7%, and TKI/PD1i/CTL4i in 4.3%. A second-line treatment was administered to 141 patients (50%), third-line to 100 patients (35%), and fourth-line to 52 patients (18%). The most common treatment sequences were: TKI followed by another TKI (26%), TKI followed by immunotherapy (IO) (24%), TKI/IO followed by TKI (12%).

Median PFS2 for initiating treatment with an IO and switching to TKI upon progression was 23.5 months[15-NA,95%Confidence Interval(CI)]. When compared to other approaches, the only sequence that showed a significant difference was TKI/IO followed by TKI(PFS2 40.5 months[26-61,95%CI],HR=0.45[0.21-0.99,p=0.046]). Among others combinations, no significant differences were observed; however, a trend toward improved PFS2 was noted in certain sequences, including TKI/IO followed by HIFi(66 months;p=0.09), TKI followed by an mTOR inhibitor(29 months;p=0.34), TKI followed by TKI/IO(28 months;p=0.19), and TKI followed by IO(26 months;p=0.09).

CONCLUSIONS Despite TKIs being the most commonly used drugs since their approval in 2006, new combinations with checkpoint inhibitors have led to improved survival outcomes. Furthermore, we observed a trend toward improved PFS2 in patients who initially received combinations. Further analysis is required.



J2 • THERAPEUTICS

A phase II study of nivolumab combined with metformin in pre-treated metastatic renal cell carcinoma (mRCC) patients. NivoMet TWINS-GU002 Study

BACKGROUND Recent evidence suggests a potential synergistic antitumor effect of the combination of immune checkpoint inhibitors targeting PD-1/PD-L1 with the oral hypoglycemic agent metformin. We designed a prospective study to evaluate the activity of nivolumab plus metformin in pre-treated mRCC patients.

MATERIALS AND METHODS NivoMet TWINS-GU002 Study was a prospective, multicentre, single-arm, phase II trial involving pre-treated mRCC patients eligible for nivolumab without a diagnosis of diabetes mellitus. Patients received nivolumab (flat dose of 240 mg every 2 weeks) plus metformin (500 mg twice daily) until disease progression. Primary endpoint was the 9-month progression-free survival (PFS) rate. The study aimed to identify a 25% increase (from 30% to 55%), requiring 21 patients to show this difference. Secondary endpoints included median PFS, overall survival (OS), overall response rate (ORR) and safety.

RESULTS A total of 12 patients from 2 sites in Italy were enrolled between November 2020 and April 2023. The trial was terminated early due to slow accrual. The median PFS was 2.7 months (95% confidence interval [CI], 2.6-3.2 months). The 9-months PFS rate was 8%. Median OS was 14.9 months (95% CI, 2.5-27.4 months). The ORR in the overall population was 8% and the disease control rate was 25%. Adverse events (AEs) of any grade occurred in 9 patients (75%), with grade 3 or 4 occurring in only 1 patient (grade 3 fatigue), which was determined to be unrelated to treatment. No treatment-related deaths were reported.

CONCLUSIONS The concomitant use of nivolumab and metformin showed a marginal activity. Nevertheless, recent genomic and transcriptomic evidence confirms the key role of metabolic pathways in RCC pathogenesis, suggesting the need for further investigations to identify new therapeutic targets.

Table 1. Baseline characteristics of the patients

Baseline characteristics	Patients (N = 12)
Median age (range)	60 (42 - 84)
Male sex, n (%)	11 (91)
Karnofsky performance-status score, n (%)	
90 or 100	10 (83)
70 or 80	2 (17)
Histology, n (%)	
Clear cell RCC	9 (75)
Papillary RCC	3 (25)
IMDC prognostic risk categories, n (%)	
Favourable	2 (17)
Intermediate	8 (66)
Poor	2 (17)
Previous nephrectomy, n (%)	10 (83)
No. of previous therapies, n (%)	
1	10 (83)
2	2 (17)
N. of organs involved, n (%)	
1	2 (17)
≥ 2	10 (83)
Sites of metastasis, n (%)	
Lung	7 (58)
Lymph node	6 (50)
Bone	3 (25)
Liver	4 (33)
Adrenal gland	2 (17)

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J3 • THERAPEUTICS

PErioperative PEmbrolizumab in patients with resectable metastases from kidney cancer: the PE-PE study.

Radical metastasectomy and other local treatment strategies (including definitive radiotherapy, RT) can be employed as alternatives to systemic therapies for selected metastatic renal cell carcinoma (mRCC) patients (pts) with the aim of achieving patient healing, even in advanced stage. Recently, adjuvant pembrolizumab has shown significant efficacy in the M1 NED pts. Furthermore, the combination of RT with a short course of pembrolizumab has demonstrated activity in oligometastatic RCC pts. However, no randomised trial has investigated the concomitant use of pembrolizumab with radical metastasis directed therapy (MDT; metastasectomy or RT) in mRCC compared to local therapy alone.

The PE-PE study (NCT05578664) is a randomised, open-label, multicentre, phase 2 study evaluating the efficacy of pembrolizumab in delaying tumour progression in oligometastatic RCC patients who have undergone previous nephrectomy and have maximum three metastases in the same or in different site considered eligible for MDT. The study will include patients who have had recurrence of disease within 5 years from prior nephrectomy or metastasectomy. Participants will be randomly assigned to receive pembrolizumab at flat dose of 400 mg every six weeks for nine cycles, followed by MDT from day 21 to day 42 of cycle 1 (Arm A), or MDT alone within 42 days from randomisation (Arm B).

The primary endpoint is relapse-free survival (RFS), defined as the time from randomisation to the appearance of radiological progression of kidney cancer in patients who received pembrolizumab or not. Secondary endpoints include: distant relapsed free survival (dRFS), defined as the time from randomisation to the appearance of distant metastases outside those treated; overall survival (OS), defined as the time from randomisation to the patient's death or last contact; the overall incidence of adverse events and incidence of local progression in both arms.

The study is actively enrolling, until today (February 2025) 49 pts (60.5%).

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J4 • THERAPEUTICS

The AxIn study: Phase II study of axitinib intensification compared to nivolumab alone after induction with ipilimumab plus nivolumab in patients with mRCC without previous complete response.

BACKGROUND The CheckMate214 study demonstrated that nivolumab plus ipilimumab led to a significant increase in overall survival (OS), progression-free survival (PFS), and objective response rate (ORR) compared to sunitinib (SUN) in patients with metastatic renal cell carcinoma (mRCC) with intermediate or poor prognosis. Recently, a higher rate of partial responses was obtained with the combination Pembrolizumab-Axitinib (45.9%) compared with that reported with N+I (30.6%). Moreover, analysis of outcomes based on the depth of response strongly revealed a connection between response and survival. The aim of this study is to investigate the efficacy of an intensified strategy with axitinib added to nivolumab in patients with mRCC without complete response at the end of N+I induction. METHODS: The AxIn study (NCT05817903) is a randomized, open-label, multicenter, phase 2 trial evaluating whether the intensification of therapy by adding axitinib to the standard nivolumab can increase the response rate and improve survival compared with nivolumab alone in 118 mRCC pts ≥ 18 years old, with ECOG between 0-1, who completed induction with N+I without complete response or progressive disease and without any toxicity ≥ G2. Eligible patients, will be randomized 1:1 to intensification of therapy with axitinib in addition to nivolumab (Arm A) or nivolumab alone (Arm B). The primary endpoint is to assess the ORR of patients treated with the intensification of axitinib plus nivolumab compared to the standard of care of nivolumab monotherapy. Secondary endpoints include PFS, OS, depth of response, duration of response, quality of life, and safety. Exploratory biomarkers analysis will be performed. The trial is actively enrolling to date (31 patients as of February 2025).

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J5 • THERAPEUTICS

Optimizing Sunitinib Treatment in Metastatic Renal Cell Carcinoma: Integrating Therapeutic Drug Monitoring and Pharmacogenetics into Clinical Practice

BACKGROUND Sunitinib (SUN) is a key treatment for metastatic renal cell carcinoma (mRCC), yet its fixed dosing results in substantial interpatient variability in drug exposure and toxicity. Integrating Therapeutic Drug Monitoring (TDM), pharmacogenetic (PGx) profiling, and drug-drug interaction (DDI) assessments may enhance treatment personalization. This study evaluated the feasibility and clinical impact of pharmacological counseling in optimizing SUN therapy.

METHODS Patients enrolled in the CRO-2022-14 trial provided steady-state plasma samples for LC-MS/MS quantification of SUN levels (Cmin). Therapeutic target ranges were defined as 37.5–60/75 ng/mL (continuous dosing) and 50–80/87.5 ng/mL (intermittent dosing). Genetic polymorphisms affecting SUN metabolism and transport were analyzed, while potential DDIs were screened via UpToDate Lexi-Drug. Integrated pharmacological reports were provided to oncologists for treatment adjustments.

RESULTS Among 11 patients (median treatment duration: 34 months),, 10 were on reduced doses due to toxicity. Seven patients on 50 or 37.5 mg/day dose achieved therapeutic Cmin (53–70 ng/mL). Two female patients exhibited Cmin > 80 ng/mL despite dose reductions (25 mg/day), experiencing recurrent Grade 2/3 toxicities, suggesting further dose refinement. Conversely, two male patients on 25 mg/day had Cmin < 40 ng/mL, with none/mild toxicity, indicating a need for dose escalation. Females (n = 2) exhibited higher SUN exposure (82 ng/mL) than males (n = 8, 55 ng/mL). PGx analysis was limited by sample size, and no significant DDIs were detected.

CONCLUSIONS Toxicity-driven dose adjustments generally led to optimal SUN exposure. Females showed higher plasma levels, though sample size limits conclusions. Early TDM integration could refine dose individualization, enhancing tolerability, adherence, and therapeutic efficacy. Pharmacological counseling was feasible and clinically valuable, supporting its implementation in routine mRCC management.

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J6 • THERAPEUTICS

Newly Updated Data from the Tide-A Trial on Avelumab (Ave) Plus Intermittent Axitinib (Axi) in Previously Untreated Patients with Metastatic Renal Cell Carcinoma (mRCC)

The combination of VEGFR-TKI (TKI) and anti-PD1/PDL1 immunotherapy (IO) is the standard first-line treatment for metastatic renal cell carcinoma (mRCC). The Tide-A trial demonstrated the feasibility of interrupting TKI while continuing IO in patients who responded to the combination, meeting its primary endpoint. This study presents updated results with extended follow-up.

Patients (pts) who underwent surgery for primary tumors and had no symptomatic/bulky disease or liver metastasis received Ave 800 mg flat dose IV Q2W + Axi 5 mg PO BID for 36 weeks. At week 36, pts achieving partial response (PR) interrupted Axi and continued Ave until progression (PD) or unacceptable toxicity. If PD occurred on Ave, Axi was restarted and interrupted again in case of new PR. Pts without PR continued the combination until PD. The analysis focused on median progression-free survival (mPFS) and overall survival (mOS) in the overall population and those who interrupted Axi.

75 pts (40% favorable risk, 60% intermediate/poor risk) were included in the efficacy analysis. After a median follow-up of 31.7 months, mPFS was 27.9 months (95% CI, 23.0–32.8). mOS was not reached, with a 24-month OS rate of 85%. The median duration of 1st avelumab maintenance was 16 weeks. Among 29 pts who interrupted Axi at week 36, mPFS and mOS were not reached, and the 24-month PFS and OS rates were 68% and 82%, respectively. 5 pts remained on avelumab without evidence of PD, and 21 restarted Axi. In these 21 patients, after restarting Axi, the ORR was 50% (10 PR, 8 SD, 2 PD, 1 NA), and mPFS was 17.2 months (95% CI, 11.9–22.5).

Updated results confirmed that interrupting TKI therapy while maintaining IO is a feasible strategy for selected mRCC patients. Progression during IO maintenance does not affect the response to TKI reintroduction, supporting further investigation in randomized trials.

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POSTER AD

J7 • THERAPEUTICS

Two-stage estimation of overall survival (OS) in CheckMate 9ER (CM9ER), adjusting for the impact of subsequent therapy

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BACKGROUND In CM9ER (NCT03141177), first-line cabozantinib plus nivolumab (1L CaboNivo) demonstrated superiority over sunitinib in patients with advanced renal cell carcinoma (aRCC). Here, we report the outcomes of a secondary analysis using a two-stage estimation (TSE) approach to assess the efficacy of CaboNivo versus sunitinib after adjustment for the impact of subsequent treatment, which can confound cross-trial comparisons of OS. The 67.6-month median follow-up of CM9ER was used.

METHODS TSE was used to statistically estimate OS for patients who switched to any subsequent treatment after discontinuation of the randomized treatment, under the hypothetical scenario that they didn't switch to a subsequent treatment. The TSE recognises that randomisation holds until the point of treatment discontinuation, which is treated as a "secondary baseline", and beyond that the trial becomes an observational study. The analysis included patients who discontinued treatment for any reason. Starting from the secondary baseline, a parametric acceleration failure-time (AFT) model was fitted for each arm, controlling for prognostic covariates and a time-dependent covariate indicating treatment switching. The best fitting model was then used to estimate the expected survival deceleration factor which indicates how many times post-discontinuation survival is extended due to initiating subsequent treatment, and subsequently to estimate adjusted (i.e. reduced) post-discontinuation and overall survival times.

RESULTS Results are shown in the attached Table.

CONCLUSIONS Adjusting for the effect of subsequent therapy had a limited impact on OS for CaboNivo, but a larger impact for sunitinib. These results are consistent with clinical practice, further supporting 1L CaboNivo as a standard of care for aRCC.

	CaboNivo	Sunitinib
Discontinued CM9ER (N)	264	276
Subsequent treatment (n)	129	168
Deceleration factor	1.255	4.754
	p-value = 0.223	p-value = <0.001
Median OS (95% CI)		
Observed	46.5 (40.6, 53.7)	35.5 (29.2, 42.8)
	HR 0.79 (0.65, 0.96)	
Adjusted (without re-censoring)	42.7 (38.4, 49.1)	21.3 (18.1, 24.9)
	HR 0.53 (0.43, 0.65)	

K1 • TRANSLATIONAL RESEARCH

Circulating cytokine and outcomes in metastatic clear cell renal cell carcinoma treated with frontline immunotherapy combinations

INTRODUCTION Metastatic clear cell renal cell carcinoma (ccRCC) relies on immune checkpoint inhibitor (ICI)-based regimens including dual ICI and ICI plus tyrosine kinase inhibitor (TKI) combinations, but optimal patient selection remains challenging. Circulating cytokines may better reflect the broader tumor immune microenvironment than tissue biomarkers. We explored cytokine profiles at sequential timepoints in patients in metastatic ccRCC treated with ICI combinations.

METHODS Patients treated with first-line ICI combination for ccRCC were included (NCT04932525). Serum cytokine levels were measured at baseline (T0) and 12 weeks after treatment initiation (T1) using the Olink Target 96 Immuno-oncology platform. Main endpoints included overall response rate, overall survival (OS) and progression-free survival (PFS).

RESULTS Overall, 23 patients were included (10 dual ICI, 13 ICI-TKI). We identified an inflammatory cytokine cluster (CD5, IFN-γ, IL-13, NOS3, IL-4) associated with early resistance to ICI-TKI combinations at baseline. In the dual ICI subgroup, the CCL23 cytokine related to myeloid inflammation was significantly elevated in non-responders ($p = 0.02$); notably, CCL23 showed significant associations with both PFS ($p = 0.006$) and OS ($p = 0.028$). Longitudinal analysis demonstrated that responders had significant increases in CCL19, CCL3, CD27, CXCL13, and PDCD1, irrespective of the treatment regimen.

CONCLUSIONS These preliminary findings suggest that specific cytokine profiles may help predict benefit to first-line ICI combinations. Validation in larger cohorts is warranted.

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K2 • TRANSLATIONAL RESEARCH

Elaboration and clinical validation of an AI algorithm as decision support system in kidney cancer

BACKGROUND Clear cell renal cell cancer (ccRCC) is a lethal disease with significant knowledge gaps to be addressed. Although it is genetically homogeneous (90% of cases involve VHL mutations), treatment response and tolerability are highly variable. Additionally, the development of new drugs has stalled because the most successful therapies interact with the tumor microenvironment (antiangiogenics and immunotherapy), which is difficult to replicate in vitro. In this project, we aim to integrate complex clinical data with multiple omic platforms (genomics and transcriptomics) using an artificial intelligence algorithm (named Clin-ART), to predict response to treatments and select the best theraputic option for every patient.

METHDOLOGY Initally, clinic and RNA sequencing data (43893 transcripts) of 181 ccRCC patients treated with NIVOLUMAB , an immune checkpoint inhibitor, in the clinical trials Checkmate 009, 010 and 025 were recorded. After assessing different machine learning classifiers, logistic regression achieved the best results with an accuracy of 86.4%.

Currently, we have added 804 patients from the Javelin 101 trial and 305 additional cases from the IMMOTION 150 trial to train the model.

Finally we have started a prospective study, in 30 centers members of the GUARD consortium, aiming to recruit 500 real life cases (85 have been alredy included).

CONCLUSION The Clin-ART algorithms seems to be accurate when predicting response to treatments in ccRCC. Updated results will be presented at the symposium

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K4 • TRANSLATIONAL RESEARCH

Gut Microbiome Dynamics in Metastatic Renal Cell Carcinoma Patients Undergoing Dual Check-point Inhibition

BACKGROUND The gut microbiome is increasingly recognized as a key modulator of immune responses and may influence treatment outcomes in metastatic renal cell carcinoma (mRCC) patients receiving immune checkpoint inhibitors (ICIs). While previous studies suggest a link between microbial diversity and immunotherapy response, data from patients undergoing dual ICI treatment remain limited.

METHODS In this initial study, we performed shotgun metagenomic sequencing on fecal samples from 18 primary mRCC patients treated with Nivolumab and Ipilimumab in the NORDIC-SUN clinical trial (ClinicalGovTrials ID NCT03977571). Samples (n =31) were collected before treatment initiation and after three months of therapy. Microbial composition, diversity, and functional profiles were analyzed to assess changes in response to treatment and potential associations with clinical outcomes.

RESULTS Preliminary findings indicate inter-individual variability in baseline microbiome composition, with shifts in microbial diversity and taxonomic profiles observed during treatment. No significant associations were found between baseline microbiome composition and treatment response. However, patients who did not experience immune-related adverse events (n = 3) had significantly higher alpha diversity at baseline compared to those who developed adverse events. No other microbiome characteristics showed a significant correlation with clinical outcomes.

CONCLUSION While the study did not identify a strong link between microbiome composition and treatment response, the finding that patients without adverse events had higher microbial diversity warrants further investigation. Larger studies are needed to explore the potential role of gut microbiome diversity in predicting toxicity during dual ICI therapy.

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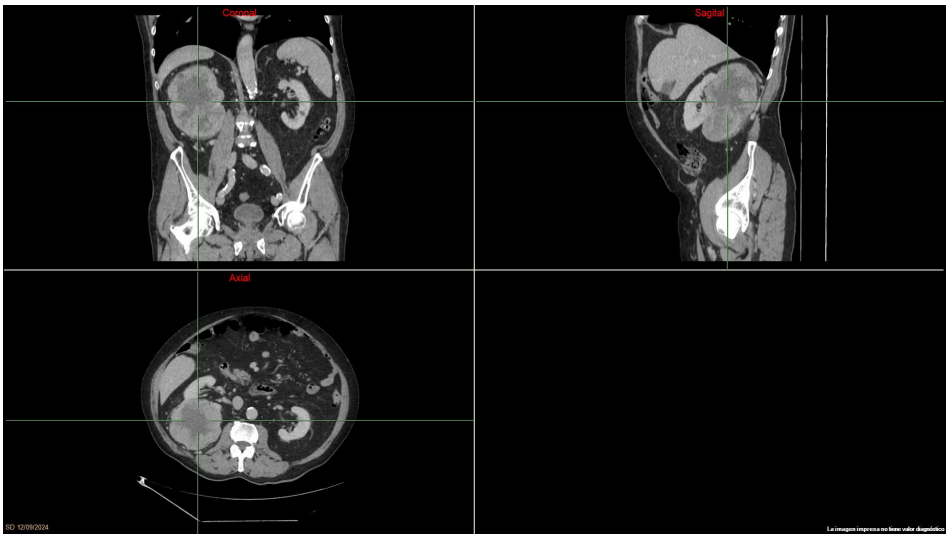
L1 • TREATMENT TOXICITIES AND SYMPTOM MANAGEMENT

Adjuvant Pembrolizumab in Renal Cell Carcinoma and Immune-Mediated Myositis and Myocarditis: How Much Does the Benefit Outweigh the Risk?

We present a 73-year-old male ex-smoker past medical history of hypertension, dyslipidemia, atrial fibrillation, severe aortic insufficiency, hypertensive cardiomyopathy and chronic ischemic leukoencephalopathy.

He was operated in August 2024 of a clear cell renal carcinoma of the right kidney, grade 3-4, pT3apNxcM0 (Figure 1). He started adjuvant treatment with pembrolizumab 200 mg every 3 weeks in January 2025. At his clinic visit prior to the second cycle, he reported proximal muscle pain, binocular diplopia, left ocular proptosis and dyspnea that worsens in decubitus. Laboratory tests showed elevated ALT 350 U/l, AST 596 U/l, LDH1382 U/l along with elevated CK 5047 U/l. Upon these findings troponins were determined and were elevated at 22372 ng/l (normal value under 40 ng/l). An urgent cranial CT scan ruled out acute intracranial pathology and echocardiogram and electrocardiogram showed no significant alterations. With suspicion of immune-mediated myositis with associated transaminitis and myocarditis, he was evaluated by Oncology, Neurology, and hospitalized in Cardiology for potential arrhythmia monitoring and treatment with methylprednisolone 1 g daily for 3 days followed by prednisone 60 mg daily. Myastheniform component was ruled out and despite initial improvement in limb strength, given the respiratory failure secondary to diaphragmatic weakness that required noninvasive mechanical ventilation and new onset of right bundle branch block in electrocardiogram, immunosuppressive treatment was escalated to intravenous gamma globulins for 5 days and prednisone 90 mg daily. Although he remains hospitalized a few weeks later due to the need for mechanical ventilation and physiotherapy, he is progressing favorably, with clinical and analytical improvement.

This case report highlights the importance of understanding acute and late immune-mediated toxicities and improving patient selection for adjuvant pembrolizumab in renal carcinoma to maximize clinical benefit while considering the risks of toxicity and relapse.



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