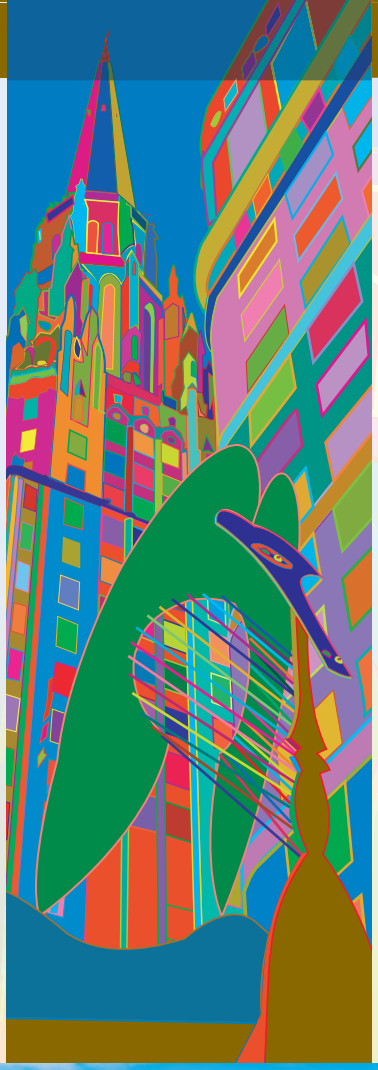

Sixteenth International Kidney Cancer Symposium

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Results: 142 patients with CC (N=98), NCC (N=43), or brain metastases (N=1) received nivolumab. Most CC patients (77%) had 1 prior systemic therapy for advanced/metastatic disease; most NCC patients (65%) were treatment-naïve. Median follow-up was 8.0 months. The types and frequencies of IMAEs were generally consistent between CC and NCC patients. Among the total population, G3-4 IMAE rates were very low and consisted of hepatitis (overall 2.1%; increased ALT, AST, or blood bilirubin, or hyperbilirubinemia [0.7% each]) starting within 47-119 days, with all cases resolved within 8-33 days; endocrine events (diabetic ketoacidosis [1.4%], acute adrenocortical insufficiency [0.7%]) starting within 46-132 days; and nephritis (0.7%) starting at day 43 and resolving in 22 days. There were no G3-4 pneumonitis, rash, hyperthyroidism, hypophysitis, or hypersensitivity IMAEs. Rates of treatment-related AEs were similar to/compared favorably with previous nivolumab studies in advanced/metastatic RCC. No G5 events occurred. Efficacy outcomes will be reported when data mature.

Conclusions: A 240-mg flat dose of nivolumab showed acceptable safety, with similarly low rates of grade 3-4 IMAEs in patients with CC or NCC RCC.

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Savolitinib versus sunitinib in patients with MET-driven, unresectable and locally advanced or metastatic papillary renal cell carcinoma: SAVOIR, a randomised, phase III trial

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Background: Papillary renal cell carcinoma (PRCC) is the most common of the non-clear cell renal cell carcinomas (RCCs), accounting for 10–15% of RCCs. However, there are no therapies approved specifically for patients with PRCC, who currently receive treatments approved for clear cell RCC, such as sunitinib. PRCC is often MET-driven (defined as MET kinase domain mutations, MET amplification, chromosome 7 gain and/or HGF amplification). Savolitinib (AZD6094, HMPL-504, volitinib) is a highly selective MET tyrosine kinase inhibitor which demonstrated anti-tumour activity for patients with MET-driven PRCC in a phase II trial.

Trial design: SAVOIR (NCT03091192) is a global, phase III, open-label, randomised, controlled trial evaluating the efficacy and safety of savolitinib, compared with sunitinib, in patients with MET-driven, unresectable, locally advanced or metastatic PRCC. Approximately 180 patients will be randomised at ~50–75 sites across 5–10 countries. Eligible patients (aged ≥18 with MET-driven PRCC confirmed by a novel, sponsor designated, validated, targeted next generation sequencing assay; a Karnofsky performance status ≥80; and measurable disease at baseline) will be randomised in a 1:1 ratio to receive either continuous savolitinib 600 mg (400 mg if <50 kg) orally, once daily (QD), or sunitinib 50 mg orally QD (4 weeks on/2 weeks off).

The primary objective is to determine the efficacy of savolitinib compared with sunitinib in terms of progression free survival (PFS) as assessed by blinded independent central review [BICR]. Tumour assessments (RECIST 1.1) will be performed at screening and the end of every 6-week cycle until 12 months, and every 12 weeks thereafter until disease progression. Secondary endpoints include overall survival, objective response rate, duration of response, best percentage change in tumour size, disease control rate at 6 and 12 months, safety and tolerability, pharmacokinetics and biomarkers. The impact of savolitinib compared with sunitinib on disease symptoms and quality of life will also be assessed.

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Second-Line Treatment of Metastatic Renal Cell Carcinoma: Systematic Review and Network Meta-Analysis

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Introduction: Several agents have been approved for patients with mRCC who have failed to a first-line VEGF-targeted therapy. No direct comparisons have been performed between those agents. We have performed a systematic review and network meta-analysis to compare and rank the regimens available for second-line treatment in terms of its efficacy and toxicity.

Methods: A systematic search was carried out in MEDLINE, Cochrane Central Register of Controlled Trials and EMBASE. Our primary objective was overall survival (OS). Secondary endpoints include progression free survival (PFS) and toxicity. Inclusion criteria were: phase II or III randomized clinical trials comparing any second-line treatment regimen in patients who had progressed to first-line VEGF-targeted therapy. Biomarkers studies or trials using other immunotherapies rather than immune checkpoint inhibitors were excluded from this analysis. Network meta-analysis [multiple treatment comparison (MTC)] was performed using a Bayesian methodology. MTC estimates use direct and indirect evidence across studies to yield relative comparisons among all included arms for the outcomes of interest. Based on their relative comparisons [relative risks (RR) or hazard ratios (HR)] with their associated credibility intervals (CrI), treatments were ranked, showing the probability of each arm being the best (or the worst) for each outcome.

Results: Literature search retrieved 1410 studies. Of these, only 7 clinical trials met inclusion criteria. Ten treatment arms were identified: axitinib, levatinib, lenvatinib + everolimus (LEV+EVE), everolimus, temsirolimus, sorafenib, nivolumab, cabozantinib, apitolisib and placebo. Temsirolimus and everolimus were arbitrarily considered as a single arm called "mTOR inhibitor". Overall, the network analysis included 3034 patients. HRs are described in table 1. No significant differences in OS were observed across cabozantinib, LEV+EVE and nivolumab arms. However, in terms of PFS nivolumab was found to be inferior when compared to LEV+EVE and cabozantinib. In the ranking for OS and PFS, LEV+EVE had the highest probability of being the most effective second-line treatment (68.56% and 86.49%, respectively). Nivolumab was ranked as the safest regimen with 100% probability with a relative risk reductions of 62% and 56% in relation to LEV+EVE (RR 0.38; 95% CrI 0.23-0.55) and cabozantinib (RR 0.44; 95% CrI 0.32-0.56), respectively.

Conclusions: In this indirect comparison, no significant differences in OS were observed between agents. Nivolumab was the less toxic treatment strategy in this clinical scenario.

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Systemic therapy for oligo-progressive, metastatic renal cell carcinoma (mRCC) treated with stereotactic radiosurgery (SBRT): to switch or not to switch?

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Introduction: There are limited data regarding the role of changing systemic therapy upon receiving SBRT for oligo-progression (O-PD).

Methods: We reviewed our experience comparing switching *vs.* maintaining systemic therapy in mRCC patients receiving SBRT to brain or osseous metastases for O-PD. Patients who were off systemic therapy for more than 8 weeks before or after SBRT date were excluded.

The treatment response outside SBRT site was evaluated according to RECIST criteria for extra-osseous disease and incorporated clinical (symptoms) and radiographic criteria (new lesions in scans) for bone metastases. O-PD included patients who had all progressive lesions treated with SBRT and no other sites of PD outside SBRT site(s).

Based on the timing of systemic therapy switch after SBRT, two groups were identified: (STAY) patients remained on the same systemic treatment; (SWITCH) patients changed systemic therapy after the completion of SBRT. Systemic therapy change or not was made at the treating physician discretion. Treatment duration was defined as the time interval between SBRT date and last day of systemic therapy