

ESMO 2026 SNEAK PEEK

What Kidney Cancer Clinicians Should Watch in Madrid, October 23–27

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□ For kidney cancer, ESMO 2026 has one of its most concentrated programmes in years. Nearly all of the practice-relevant renal data come on a single day, Sunday, October 25. The morning Proffered Paper session puts both phase 3 belzutifan readouts, a randomized trial in oligometastatic disease and two first-in-class agents into 90 minutes. The afternoon Rapid Oral session covers the adjuvant setting, non-clear cell disease and a set of biomarker and imaging studies.

This preview is written from the final programme, before results are public. It does not report data. It sets out what each study was designed to answer, what we already know going in, and what would change practice if the results hold.

The HIF-2 α Chapter: Two LITESPARK Readouts in One Morning Proffered Paper 2, Sunday, October 25, 08:30–10:00

The session opens with two presentations that together will shape how belzutifan is used across lines of therapy.

LITESPARK-012 (3586O, Toni Choueiri) is the first detailed presentation of the three-arm, 1,688-patient first-line phase 3 trial. It compared pembrolizumab plus lenvatinib with or without belzutifan, and with the pembrolizumab/quavonlimab coformulation MK-1308A, against pembrolizumab plus lenvatinib. In April, Merck and Eisai announced that neither experimental arm met the dual primary endpoints of progression-free and overall survival. The questions for Madrid are therefore about explanation, not efficacy:

- Did any clinically defined subgroup benefit?
- Did adding a third agent cost dose intensity of the backbone?
- What do the data say about moving HIF-2 α inhibition into the first line through a triplet?

A negative trial presented in full is often more instructive than a positive topline. This one will anchor the field's thinking on first-line intensification for several years.

LITESPARK-011 final analysis (3587O, Daniel Heng) follows. The primary analysis, published in *The Lancet* in August, showed that belzutifan plus lenvatinib improved PFS over cabozantinib after anti-PD-(L)1 therapy:

- median PFS 14.6 vs 10.6 months (HR 0.74)
- ORR 53% vs 40%

Overall survival favored the combination numerically but did not reach statistical significance (HR 0.85). The FDA approved the regimen in late September. The final analysis is the moment of truth for overall survival, and with cabozantinib the long-standing reference in this setting, the result will shape how clinicians sequence therapy after immunotherapy. A companion rapid oral that afternoon (3595RO) examines the relationship between health-related quality of life and efficacy in the same trial. Given the anemia and hypoxia profile of HIF-2 α inhibition, that analysis deserves equal attention.

Together, the two LITESPARK readouts sharpen a picture that is already emerging: belzutifan has a secure role after progression on immunotherapy and in the adjuvant combination setting, while its role in the first line is now uncertain. Naomi Balzer-Haas's discussion of both trials should be required viewing.

Oligometastatic Disease Gets a Randomized Answer LBA88, PE-PE trial, Roberto Iacovelli

Metastasis-directed therapy for oligometastatic RCC has spread widely on the strength of retrospective series and single-arm studies. The randomized phase II PE-PE trial asks a question many clinicians answer by instinct: does adding perioperative pembrolizumab to surgery or stereotactic radiotherapy for limited metastases improve outcomes over local therapy alone?

Its late-breaking status suggests the result is noteworthy. It also connects directly to this issue's review of stereotactic body radiotherapy. If systemic therapy meaningfully extends the benefit

of ablative local treatment, the case for SBRT in carefully selected metastatic patients becomes considerably stronger.

New Mechanisms: Bispecifics and Cell Therapy

XmAb819 (3588O, Sumanta Pal) is a first-in-class ENPP3 × CD3 bispecific antibody. Its 2+1 format uses two tumor-binding arms to favor tumor over normal tissue. Pal will present the intravenous dose-expansion data that will set the recommended phase 3 dose, and Xencor has said it plans to begin a pivotal monotherapy trial in 2027. Clear cell RCC has so far been largely untouched by T-cell engagers, so this will be the first real look at whether that approach can work in kidney cancer.

Ivonescimab (3592O), the PD-1/VEGF bispecific, is presented as first-line therapy in IMDC favorable-risk disease from a Chinese phase Ib/II study. Favorable-risk patients are the group in which the added benefit of immunotherapy-based combinations over VEGF monotherapy has been hardest to demonstrate. A single molecule hitting both targets is a mechanistically tidy way to approach that question. With the global IVORY trial already under way in the post-checkpoint setting, these data will help define where ivonescimab fits.

UCL70802 (3615RO), an armored anti-CD70 CAR-T cell product, reports first-in-human results in metastatic clear cell RCC. CD70 is one of the most consistently overexpressed surface targets in ccRCC, and several cellular programmes are pursuing it. Any durable responses here will be watched closely.

Manuela Schmidinger discusses XmAb819 and ivonescimab. Sylvie Rottey discusses the CAR-T data alongside the non-clear cell presentations.

The Adjuvant Setting: Final Answers and Patient Voices. Rapid Oral 2, Sunday, October 25, 14:45–16:15

KEYNOTE-564 final protocol-prespecified analysis (3589RO, Toni Choueiri). KEYNOTE-564 became the first adjuvant trial in RCC to show an overall survival benefit (HR 0.62, NEJM 2024), establishing a year of pembrolizumab as standard after nephrectomy for high-risk disease. The final analysis will show whether that survival advantage holds with longer follow-up. It also gives the reference arm against which the newer LITESPARK-022 combination of belzutifan and

pembrolizumab will be judged. Our Journal Club this issue argues that the incremental benefit of that combination has to be weighed against its toxicity burden. Durable, mature data for single-agent pembrolizumab are central to that conversation.

RAMPART patient-reported outcomes (3590RO, Sophie Merrick). RAMPART is the UK-led adjuvant trial with an active-monitoring control arm. Its PRO analysis compares adjuvant durvalumab with active monitoring from the patient's perspective. Adjuvant therapy is given to many patients who would never have relapsed, so what treatment costs in quality of life matters as much as what it adds in disease-free survival.

Non-Clear Cell RCC: Data Where Evidence Is Thin Two presentations address histologies that make up about a quarter of RCC but have a small share of randomized evidence.

SWOG S2200 (3591RO, Benjamin Maughan) reports the first results of a randomized phase II comparison of cabozantinib with or without atezolizumab in metastatic papillary RCC. It follows SWOG S1500 (PAPMET), which established cabozantinib as the preferred agent in papillary disease. This trial tests whether adding a checkpoint inhibitor improves on that benchmark. It is the most direct randomized evidence to date on the combination question in papillary RCC.

REPRINT – MeetURO 4/25 (3612RO, Giuseppe Procopio) reports preliminary results from the first stage of a trial of enfortumab vedotin plus pembrolizumab in collecting duct and renal medullary carcinoma. These rare, aggressive cancers share biological features with urothelial carcinoma. Borrowing the regimen that transformed metastatic urothelial cancer is a logical test.

For readers in Madrid on Saturday, the educational session "Rare GU Cancers" includes talks on papillary RCC (Cristina Suárez) and unclassifiable RCC (Ramaprasad Srinivasan), which make useful background for both trials.

Biomarkers and Imaging: Toward Measurable Disease Biology

The final block of the afternoon session covers circulating markers, pathology and imaging. Readers of this issue's original research

on plasma proteomic and metabolomic biomarkers will find it especially relevant.

Plasma KIM-1 dynamics (3593RO, Wenxin Xu) during first-line immunotherapy with or without cabozantinib. KIM-1 has already shown prognostic value in the adjuvant setting. Its behavior on treatment could make it a practical, non-invasive measure of response.

CARE1 PD-L1 feasibility (3594RO, Ronan Flippot) comes from a phase III, biomarker-driven, pragmatic trial aiming to personalize first-line treatment. PD-L1 has had an uneven history as a biomarker in RCC. This analysis asks whether it can be measured reliably enough to guide decisions.

CAIX-targeted [⁶⁸Ga]Ga-DPI-4452 PET/CT (3604RO, Liangyou Gu) reports diagnostic and staging performance from a prospective trial. It joins zirconium-89 girentuximab in the growing field of molecular imaging directed at carbonic anhydrase IX, with implications for characterizing indeterminate renal masses and staging.

Multi-omics profiling of RCC metastasis (4241O, Yuanyuan Qu) is in [Monday's translational Proffered Paper session](#). It aims to define the drivers of organ-specific metastatic spread and build predictive models.

Beyond Kidney: Presidential Data With Crossover Relevance

Two Presidential Symposium presentations deserve attention from kidney cancer specialists.

VOLGA (LBA2), will be presented in Presidential Symposium I on Saturday evening, reports perioperative durvalumab with or without tremelimumab plus neoadjuvant enfortumab vedotin in muscle-invasive bladder cancer. It is the latest step in the perioperative ADC-plus-immunotherapy trend that began with KEYNOTE-905 and KEYNOTE-B15.

MOIO (LBA10, Gwenaëlle Gravis), in Presidential Symposium III on Monday, is a phase III non-inferiority trial of reduced-frequency immune checkpoint inhibitor dosing in patients responding to treatment for advanced cancer.

Many RCC patients now stay on immunotherapy for years. Evidence that less frequent dosing preserves benefit would affect toxicity, patient convenience and cost, which could make MOIO one of the most practically important presentations of the meeting for our field.

The rest of the GU programme is heavy on bladder cancer:

- the phase 3 KEYNOTE-866 trial of perioperative pembrolizumab with neoadjuvant chemotherapy
- a phase 3 trial of neoadjuvant chemotherapy with or without nivolumab
- a ctDNA analysis of KEYNOTE-B15
- long-term EV-103 follow-up

These will be covered in our GU section next quarter.

Sessions Worth the Walk

Beyond the abstracts, two sessions stand out for kidney cancer clinicians:

- **"Emerging New Systemic Therapies for RCC"** (Special Symposium, Sunday, 10:15). Laurence Albiges on next-generation HIF-2α agents and combinations, Koen Van Der Mijl on CAR-T, bispecifics and new checkpoint inhibitors, Yuji Miura on antibody–drug conjugates, and David Braun on vaccines. It is effectively a survey of the RCC pipeline in 90 minutes.
- **Response-Based Adaptive Strategies in Primary Metastatic Kidney Cancer** (Multidisciplinary Session, Monday, 10:15). Chaired by Axel Bex and Shankar Siva, it covers image-guided strategy, what to do with the primary tumor in exceptional responders, and the timing of local therapy. Paired with PE-PE, it may define the year's discussion of cytoreductive and metastasis-directed therapy.

Bernadett Szabados closes the renal and urothelial track with the Congress Highlights talk on Tuesday morning, October 27.