This section presents full abstract summaries for the ten kidney cancer abstracts selected by the Editor-in-Chief as the most clinically significant presentations from GU ASCO 2026. Each entry includes background, methods, key results, safety profile, and editorial perspective. Abstracts are ordered by assigned rank from the editorial selection. Primary data are drawn from presentations, published JCO supplement abstracts, press releases, and peer-reviewed commentary.

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☐ Abstract 1 — LBA418

LITESPARK-022: Pembrolizumab Plus Belzutifan Versus Pembrolizumab Plus Placebo as Adjuvant Therapy for Clear Cell Renal Cell Carcinoma

Investigators: Choueiri TK et al. | Session: Genitourinary Cancer — Kidney and Bladder Oral Abstract Session

Background

Adjuvant pembrolizumab became a standard of care option for high-risk clear cell RCC following nephrectomy based on the KEYNOTE-564 trial, which demonstrated a significant improvement in disease-free survival (DFS) versus placebo. However, approximately 40% of patients treated with pembrolizumab alone still experience disease recurrence within five years, representing a substantial unmet need. Belzutifan, a first-in-class oral HIF-2α inhibitor, has demonstrated single-agent activity in advanced ccRCC and preclinical data suggest complementary mechanisms with PD-1 blockade. LITESPARK-022 was designed to determine whether adding belzutifan to pembrolizumab could further improve outcomes in the adjuvant setting.

Methods

LITESPARK-022 (NCT05239728) was a randomized, double-blind, placebo-controlled phase 3 trial enrolling 1,841 patients with resected clear cell RCC at increased risk of recurrence, defined as pathologic T3 or T4 disease, regional lymph node involvement, or M1 no evidence of disease (NED) status. Patients were randomized 1:1 to pembrolizumab 400 mg IV every 6 weeks plus belzutifan 120 mg orally daily, or pembrolizumab plus placebo, for up to 54 weeks. The primary endpoint was investigator-assessed DFS; overall survival (OS) was a key secondary endpoint. Stratification factors included disease stage, geographic region, and PD-L1 expression.

Key Results

At a median follow-up of 28.4 months:

- Disease-Free Survival: HR 0.72 (95% CI, 0.59–0.87; P=0.0003), representing a 28% reduction in the risk of recurrence or death
- 2-year DFS rate: 81.1% (combination) vs 70.2% (pembrolizumab alone) — an absolute difference of approximately 11 percentage points
- Median DFS: Not reached in either arm
- Overall Survival: Immature at this analysis; follow-up ongoing
- Subgroup analyses: Benefit was consistent across disease stage, PD-L1 expression, and geographic region
- Safety: Grade ≥3 treatment-emergent adverse events occurred in 52% vs 30% of patients; the most common higher-grade events in the combination arm were anemia (12%), elevated ALT (6%), and hypoxia (5%), all manageable with dose modification; discontinuation rates were higher in the combination arm but did not substantially affect efficacy outcomes

Editorial Perspective

LITESPARK-022 represents a watershed moment in adjuvant RCC therapy — the first phase 3 trial in this setting to demonstrate a statistically significant and clinically meaningful benefit over an active immunotherapy comparator. The 11 percentage-point absolute improvement in 2-year DFS is a clinically substantial gain for a patient population in which recurrence carries significant morbidity and mortality consequences. The biologic rationale is compelling: HIF-2α inhibition and PD-1 blockade target non-overlapping tumor-promoting pathways, and their combination appears to produce additive, if not synergistic, anti-tumor activity.

Practical considerations for clinicians include the management of belzutifan-associated anemia and hypoxia, which require proactive monitoring and may necessitate erythropoiesis-stimulating agent support or dose adjustment in a subset of patients. The higher rate of grade ≥3 adverse events in the combination arm warrants careful patient selection and informed consent.

OS data remain immature and will be critical to confirm the durability of the DFS benefit. Nevertheless, regulatory filings are anticipated, and pembrolizumab plus belzutifan is positioned to become the new standard of care in adjuvant ccRCC for high-risk patients who can tolerate combination therapy.

☐ Abstract 2 — LBA417

LITESPARK-011: Belzutifan Plus Lenvatinib Versus Cabozantinib in Previously Treated Advanced Clear Cell Renal Cell Carcinoma

Investigators: Motzer RJ et al. | Session: Genitourinary Cancer — Kidney and Bladder Oral Abstract Session

Background

For patients with advanced clear cell RCC whose disease has progressed following immune checkpoint inhibitor (ICI)-based therapy, VEGFR-targeted kinase inhibitors — particularly cabozantinib — have been widely used, though this practice was established largely in the pre-IO era. No phase 3 trial had previously evaluated a novel combination against a contemporary VEGFR-TKI in the post-IO setting. Belzutifan inhibits the HIF-2α transcription factor, a central driver of ccRCC biology that regulates VEGF expression, erythropoiesis, and tumor cell proliferation. Lenvatinib is a multi-kinase inhibitor with potent anti-angiogenic activity. LITESPARK-011 was the first phase 3 trial designed to directly evaluate HIF-2α inhibition combined with VEGFR-TKI therapy versus a standard-of-care VEGFR-TKI in this population.

Methods

LITESPARK-011 (NCT04586231) enrolled 747 patients with locally advanced or metastatic ccRCC who had received one or two prior systemic therapies, including at least one anti-PD-(L)1 agent. Patients were randomized 1:1 to belzutifan 120 mg plus lenvatinib 20 mg orally daily (n=371) versus cabozantinib 60 mg orally daily (n=376). Co-primary endpoints were progression-free survival (PFS) and overall survival (OS), both assessed by blinded independent central review (BICR). Key secondary endpoints included objective response rate (ORR), duration of response (DoR), and patient-reported outcomes.

Key Results

At the second interim analysis (data cutoff April 2025):

- Median PFS: 14.8 months vs 10.7 months (HR

0.70; 95% CI, 0.59–0.84; P<0.001)

- 24-month PFS rate: 35.6% vs 19.1%
- ORR: 52.6% vs 40.2%; complete responses in 20 vs 4 patients
- Median Duration of Response: 23.0 vs 12.3 months — a near doubling
- Median OS: 34.9 vs 27.6 months (HR 0.85; 95% CI, 0.68–1.05) — trending in favor of the combination; final OS analysis pending
- Patient-reported outcomes: Time to deterioration in disease-specific symptoms was similar between arms, suggesting the PFS benefit was not achieved at the cost of quality of life
- Safety: Most common grade ≥3 adverse events were anemia (belzutifan/lenvatinib arm) and diarrhea (cabozantinib arm); no unexpected toxicity signals identified; the investigator noted that patients with significant cardiac disease, baseline anemia, or prior pulmonary toxicity were excluded from enrollment

Editorial Perspective

LITESPARK-011 fills a critical evidence gap in the management of advanced ccRCC in the post-IO setting. The superiority of belzutifan plus lenvatinib over cabozantinib — a regimen that itself demonstrated survival benefit in the post-IO setting in CheckMate 9ER and METEOR — is both statistically convincing and clinically meaningful. The near doubling of median duration of response (23.0 vs 12.3 months) is particularly noteworthy and suggests that HIF-2α inhibition adds depth and durability to the anti-tumor response beyond what VEGFR inhibition alone can achieve.

From a practical standpoint, anemia management will be the defining challenge as this combination enters broader clinical use. Clinicians should be prepared to utilize erythropoiesis-stimulating agents and monitor hemoglobin levels proactively. The exclusion of patients with significant comorbidities from the trial also warrants attention: real-world RCC populations often include patients with baseline anemia, cardiac disease, or prior ICI-related pulmonary toxicity, and outcomes in these subgroups remain to be characterized.

The FDA accepted the supplemental NDA for belzutifan plus lenvatinib in May 2026 for priority review. Pending OS maturation and regulatory approval, this combination is positioned to displace cabozantinib as the preferred second-line regimen in advanced ccRCC following IO-based first-line therapy.

☐ Abstract 3 — LBA4511

RAMPART: Adjuvant Durvalumab Monotherapy and Durvalumab Plus Tremelimumab Versus Active Monitoring in Resected Renal Cell Carcinoma

Investigators: Larkin J et al. | Session: Genitourinary Cancer Oral Abstract Session

Background

The RAMPART trial is the largest investigator-initiated adjuvant immunotherapy study conducted in RCC to date. Designed prior to the availability of KEYNOTE-564 data, RAMPART sought to evaluate whether adjuvant PD-L1 blockade with durvalumab, alone or in combination with the CTLA-4 inhibitor tremelimumab, could reduce disease recurrence following nephrectomy in patients with intermediate- and high-risk RCC. The trial's active monitoring control arm — rather than placebo — reflects its real-world design philosophy and its origin in the pre-adjuvant-IO era.

Methods

RAMPART (NCT03288532) enrolled 790 patients with resected RCC at intermediate or high risk of recurrence in a 3:2:2 ratio: active monitoring (n=340), durvalumab monotherapy for 12 months (n=225), or durvalumab plus tremelimumab for 12 months (n=225). The primary endpoint was DFS; a pre-specified analysis in the high-risk and M1 NED subpopulation was included. Quality of life was assessed as a key secondary endpoint using validated patient-reported outcome instruments.

Key Results

- Durvalumab monotherapy vs active monitoring: HR 0.74 (95% CI, 0.53–1.04; P=0.041) — a 26% relative risk reduction in recurrence or death; did not cross the pre-specified significance threshold
- 3-year DFS: 78% (durvalumab) vs 72% (active monitoring)
- Durvalumab + tremelimumab vs active monitoring: HR 0.65 (95% CI, 0.45–0.93; P=0.009) — statistically significant
- High-risk/M1 NED subgroup: HR 0.77 (durvalumab mono) and HR 0.52 (combination) — the combination benefit was most pronounced in this higher-risk population, with a 2-year DFS of 81% vs 67%
- Quality of Life: The combination arm was associated with clinically meaningful deterioration in overall health status, role functioning, fatigue, and sleep at week 16; most effects improved by month 15
- Overall Survival: Immature; follow-up ongoing

Editorial Perspective

RAMPART adds important and nuanced evidence to the adjuvant RCC landscape. The durvalumab monotherapy arm fell just short of its pre-specified significance threshold — a finding that underscores the importance of rigorous statistical design in adjuvant trials and the challenge of powering studies in this heterogeneous population. The combination arm, however, achieved statistical significance with a notably strong signal in the high-risk subgroup, where a 48% relative risk reduction in recurrence or death is a clinically compelling result.

The quality of life data deserve careful attention. The meaningful deterioration in role functioning and fatigue in the combination arm at week 16 is a real clinical cost that must be weighed against the DFS benefit, particularly for patients who are otherwise asymptomatic following nephrectomy. The fact that most QoL effects attenuated by month 15 is reassuring but does not eliminate the relevance of early-treatment burden.

The regulatory path for durvalumab plus tremelimumab in the adjuvant RCC setting remains unclear, particularly given the concurrent availability of KEYNOTE-564 data and the emerging LITESPARK-022 results. Nevertheless, RAMPART provides meaningful biological validation of adjuvant dual checkpoint blockade in RCC and will inform the design of future biomarker-stratified adjuvant studies.

☐ Abstract 4 — Oral Abstract

Phase 1b/2 Study of First-Line Cadonilimab Plus Axitinib in Advanced Non-Clear Cell Renal Cell Carcinoma

Investigators: Hu X et al. | Session: Genitourinary Cancer Oral Abstract Session

Background

Non-clear cell RCC histologies — including papillary, chromophobe, collecting duct, medullary, and

translocation-associated subtypes — collectively account for 15–25% of all RCC diagnoses but have been consistently underrepresented in pivotal clinical trials. No globally approved first-line standard of care exists specifically for these patients, and many are treated empirically with regimens developed for clear cell disease. Cadonilimab is a novel bispecific antibody that simultaneously targets PD-1 and CTLA-4, offering integrated dual checkpoint blockade through a single agent. Combined with axitinib, a potent VEGFR inhibitor, this regimen offers a mechanistically rational TKI-plus-immunotherapy approach tailored to the non-clear cell population.

Methods

This prospective, multi-center phase 1b/2 trial enrolled patients with treatment-naïve advanced non-clear cell RCC across multiple histologic subtypes. The phase 1b portion established the recommended phase 2 dose; the phase 2 expansion evaluated safety and efficacy as co-primary endpoints. Key efficacy measures included ORR by RECIST v1.1, duration of response (DoR), progression-free survival, and overall survival. Biomarker analyses including PD-L1 expression and histology-specific correlates were exploratory.

Key Results

- Safety: The combination demonstrated a manageable and consistent safety profile across non-clear cell histologic subtypes; no unexpected toxicity signals were identified relative to known profiles of each agent
- ORR and DoR: Objective response rates and duration of response were reported as comparable to TKI plus IO doublet regimens previously evaluated in this setting
- Histologic subtype activity: Responses were observed across multiple non-clear cell subtypes, suggesting broad applicability of the PD-1/CTLA-4 bispecific plus VEGFR inhibitor approach
- Biomarker correlates: Exploratory analyses ongoing; PD-L1 expression did not appear to be a strict prerequisite for response

Editorial Perspective

This trial addresses one of the most persistent gaps in the RCC field: the absence of prospective, histology-specific efficacy data for non-clear cell patients. The signal of activity across multiple non-clear cell subtypes is encouraging and biologically coherent — the dual PD-1/CTLA-4 blockade offered by cadonilimab, combined with VEGFR inhibition through axitinib, recapitulates the mechanistic rationale that has driven IO/TKI combinations in clear cell disease.

What is particularly notable is the use of a bispecific antibody rather than a combination of two separate checkpoint inhibitors, which offers potential advantages in terms of dosing convenience, pharmacokinetic predictability, and potentially differentiated immune activation at the tumor microenvironment level. Whether this translates into a clinical advantage over conventional PD-1 plus CTLA-4 combinations remains to be established in comparative studies.

Phase 3 data will be required before this regimen can be considered a standard of care. However, for a patient population that has long been treated without dedicated evidence, the cadonilimab plus axitinib data represent a meaningful and welcome step forward.

☐ Abstract 5 — Biomarker Substudy

ctDNA Analysis from KEYNOTE-564: Circulating Tumor DNA as a Predictive Biomarker for Adjuvant Pembrolizumab Benefit in Clear Cell RCC

Investigators: Choueiri TK et al. | Session: Genitourinary Cancer — Translational Science

Background

KEYNOTE-564 established adjuvant pembrolizumab as a standard of care for high-risk clear cell RCC following nephrectomy, based on significant improvement in DFS versus placebo. However, a persistent clinical challenge has been the identification of which patients truly benefit from adjuvant immunotherapy — and which patients might be safely spared treatment and its associated toxicity, cost, and quality-of-life impact. Circulating tumor DNA (ctDNA), detected and quantified using tumor-informed liquid biopsy assays, offers a potential window into the presence and burden of residual microscopic disease following surgical resection. This biomarker substudy evaluated whether ctDNA status at baseline could predict pembrolizumab benefit in KEYNOTE-564.

Methods

Plasma samples from KEYNOTE-564 participants were analyzed using the Natera Signatera tumor-informed ctDNA assay, which tracks patient-specific somatic variants to detect molecular residual disease with high sensitivity. Patients were stratified by ctDNA status at baseline (ctDNA-positive vs ctDNA-negative) and DFS outcomes were analyzed within each stratum across treatment arms. Additional analyses examined ctDNA dynamics on treatment and their association with clinical outcomes.

Key Results

- ctDNA-positive patients: Demonstrated the greatest absolute benefit from adjuvant pembrolizumab versus placebo; the DFS hazard ratio in ctDNA-positive patients was substantially more favorable than in the overall trial population
- ctDNA-negative patients: Showed high event-free rates regardless of treatment assignment; the DFS benefit of pembrolizumab in this group was markedly attenuated, raising the question of whether these patients derive meaningful benefit from adjuvant therapy
- ctDNA dynamics: Clearance of ctDNA during treatment was associated with favorable outcomes; persistent or rising ctDNA on therapy was associated with higher recurrence risk
- Clinical implication: A meaningful proportion of patients receiving adjuvant pembrolizumab today — those who are ctDNA-negative — may be deriving little benefit while being exposed to immunotherapy-related adverse events and substantial treatment cost

Editorial Perspective

This is among the most clinically consequential biomarker presentations in the recent history of kidney cancer research. The KEYNOTE-564 ctDNA analysis provides the clearest evidence yet that adjuvant immunotherapy benefit in RCC is not uniformly distributed across the treated population — it is concentrated in patients with detectable molecular residual disease at baseline.

The implications are profound on multiple levels. At the individual patient level, ctDNA testing could enable more personalized adjuvant decision-making: treating ctDNA-positive patients more aggressively, while offering ctDNA-negative patients the option of active surveillance with serial monitoring. At the health system level, avoiding unnecessary adjuvant immunotherapy in a low-risk molecular subgroup would have significant

cost and toxicity reduction implications.

It must be acknowledged that this analysis is retrospective and hypothesis-generating; prospective validation in a ctDNA-stratified adjuvant trial is essential before clinical adoption can be recommended. Nevertheless, the data are sufficiently compelling that ctDNA assessment should now be considered a priority endpoint in all future adjuvant RCC trial designs. The field appears to be converging on a future in which molecular residual disease detection — rather than pathologic staging alone — defines who receives adjuvant therapy, for how long, and at what intensity.

☐ Abstract 6 — Abstract 534

Kidney Injury Molecule-1 (KIM-1) as a Prognostic and Predictive Biomarker in Metastatic RCC Receiving Immune Checkpoint Inhibitor-Based Therapy

Investigators: Presented at ASCO 2026 Genitourinary Biomarker Session

Background

Despite major therapeutic advances in metastatic RCC, reliable blood-based biomarkers for treatment selection and monitoring remain elusive. Kidney Injury Molecule-1 (KIM-1) — also known as TIM-1 or HAVCR1 — is a type I transmembrane glycoprotein expressed on proximal tubular cells and overexpressed in clear cell RCC. Soluble KIM-1 is detectable in plasma and has been associated with RCC diagnosis and prognosis in prior studies. Whether circulating KIM-1 levels at baseline or during treatment carry predictive value for response to contemporary ICI-based regimens was the central question of this investigation.

Methods

Circulating KIM-1 levels were measured in plasma samples from metastatic RCC patients receiving ICI-based therapy in prospective cohorts. Analyses evaluated associations between baseline KIM-1 levels, on-treatment KIM-1 dynamics, objective response rate, progression-free survival, and overall survival. Multivariable models adjusted for IMDC risk score and treatment regimen. A separate analysis explored KIM-1 in the context of the K-COMPASS prognostic model (Abstract 537), which integrated KIM-1 with ctDNA data in oligometastatic ccRCC.

Key Results

- Baseline KIM-1: Higher baseline circulating KIM-1 levels were associated with worse treatment outcomes including lower ORR, shorter PFS, and shorter OS in patients receiving ICI-based therapy
- Dynamic KIM-1: Early on-treatment reductions in KIM-1 were associated with favorable response and improved survival outcomes, suggesting potential utility as an early pharmacodynamic biomarker
- K-COMPASS integration (Abstract 537): The combination of KIM-1 and ctDNA into an integrated prognostic model demonstrated superior risk stratification in oligometastatic ccRCC compared to either biomarker alone, supporting the complementary nature of these two blood-based tools
- Non-clear cell applicability (Abstract 538, CAN-I): KIM-1 demonstrated prognostic relevance across divergent RCC histologies, broadening its potential clinical applicability
- Papillary RCC (Abstract 557, CALYPSO): KIM-1 showed independent prognostic value in papillary RCC, representing one of the first validated blood-based biomarkers in this non-clear cell

subtype

Editorial Perspective

The KIM-1 data presented across multiple ASCO 2026 abstracts collectively represent one of the most coherent and promising biomarker stories in kidney cancer in recent years. The convergence of evidence across clear cell and non-clear cell histologies, across treatment settings, and in both prognostic and predictive contexts suggests that KIM-1 is not a niche biomarker but a broadly relevant molecular signal in RCC biology.

What makes the KIM-1 story particularly compelling is its complementarity with ctDNA. Where ctDNA captures the presence and burden of residual or circulating tumor-derived DNA — a measure of tumor shedding — KIM-1 appears to reflect tumor-specific biological activity and potentially the functional state of the tumor microenvironment. Together, as the K-COMPASS model suggests, they may offer a more complete picture of disease biology than either marker alone.

The critical next step is prospective validation in biomarker-stratified clinical trials. The RCC field has a long history of promising biomarkers that have not survived rigorous prospective testing; KIM-1 must be held to the same evidentiary standard. However, the breadth and consistency of the ASCO 2026 KIM-1 data make a compelling case for its prioritization in the next generation of RCC trial design — both as a stratification factor and as a dynamic efficacy endpoint.