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# GU CONNECT

## ADVANCED RCC UPDATE FROM ESMO 2025

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**OCTOBER 2025**

RCC, renal cell carcinoma

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# CLINICAL TAKEAWAYS

- **LenCabo**: demonstrates the efficacy of lenvatinib + everolimus for ICI pre-treated RCC patients with improved PFS & ORR compared with cabozantinib, although with higher toxicity. This combination should be considered for patients needing rapid or high tumour response for whom the higher toxicity rate is acceptable
- **CLEAR**: Lenvatinib + pembrolizumab demonstrated improved efficacy versus sunitinib in advanced RCC, regardless of the presence or absence of bone metastases and continues to be a standard of care treatment in this population
- **KEYMAKER-U03**: Among various combinations tested, adding belzutifan (a HIF-2α inhibitor) to lenvatinib and pembrolizumab was the only regimen with improved PFS, response durability, and OS—supporting advancement to phase 3 trials as a promising new triplet for 1st-line RCC
- **CAIX PET/CT**: Ga-DPI PET provides high-resolution, tumour-specific imaging in clear cell RCC, enhancing distinction between oligometastatic and widespread disease and enabling more precise selection for multimodality treatments

CAIX, carbonic anhydrase IX; CT, computed tomography; Ga-DPI, [$^{68}$Ga]Ga-DPI-4452; ICI, immune checkpoint inhibitors; ORR, overall response rate; OS, overall survival; PET, positron emission tomography; PFS, progression-free survival; RCC, renal cell carcinoma

# EDUCATIONAL OBJECTIVES

- Understand the latest **clinical trial data** in advanced RCC and potential implications for patient management
- Recognise and determine the **appropriate placement and combination of therapies** for the treatment of advanced RCC

RCC, renal cell carcinoma

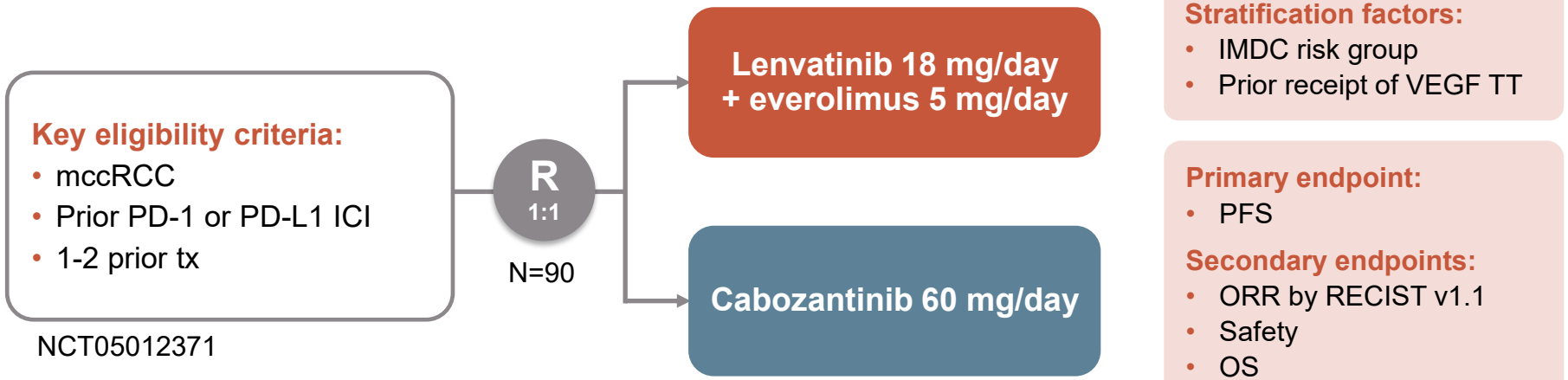
# LenCabo: A RANDOMISED, PHASE 2, MULTICENTRE TRIAL OF LENVATINIB PLUS EVEROLIMUS VS CABOZANTINIB IN PATIENTS WITH METASTATIC ccRCC THAT PROGRESSED ON PD-1 IMMUNE CHECKPOINT INHIBITION

**Hahn A, et al. Abstract LBA94, ESMO 2025**

ccRCC, clear cell renal cell carcinoma; PD-1, programmed cell death protein 1

# LenCabo: BACKGROUND AND STUDY DESIGN

- First-line treatment for metastatic ccRCC consists of PD-1 ICI plus either a CTLA-4 ICI or angiogenesis targeted therapy. Upon progression, many patients receive cabozantinib or lenvatinib/everolimus if cabozantinib or lenvatinib was not incorporated in 1st line treatment
- Cabozantinib and lenvatinib share many kinase targets, however lenvatinib also blocks FGFR and is paired with the mTOR inhibitor everolimus, potentially overcoming additional resistance pathways
- **LenCabo** is a multicentre, phase 2 randomised trial investigating lenvatinib plus everolimus vs cabozantinib after 1-2 prior lines of treatment (including a PD-1 ICI) in patients with metastatic ccRCC




**Stratification factors:**
- IMDC risk group
- Prior receipt of VEGF TT

**Primary endpoint:**
- PFS

**Secondary endpoints:**
- ORR by RECIST v1.1
- Safety
- OS

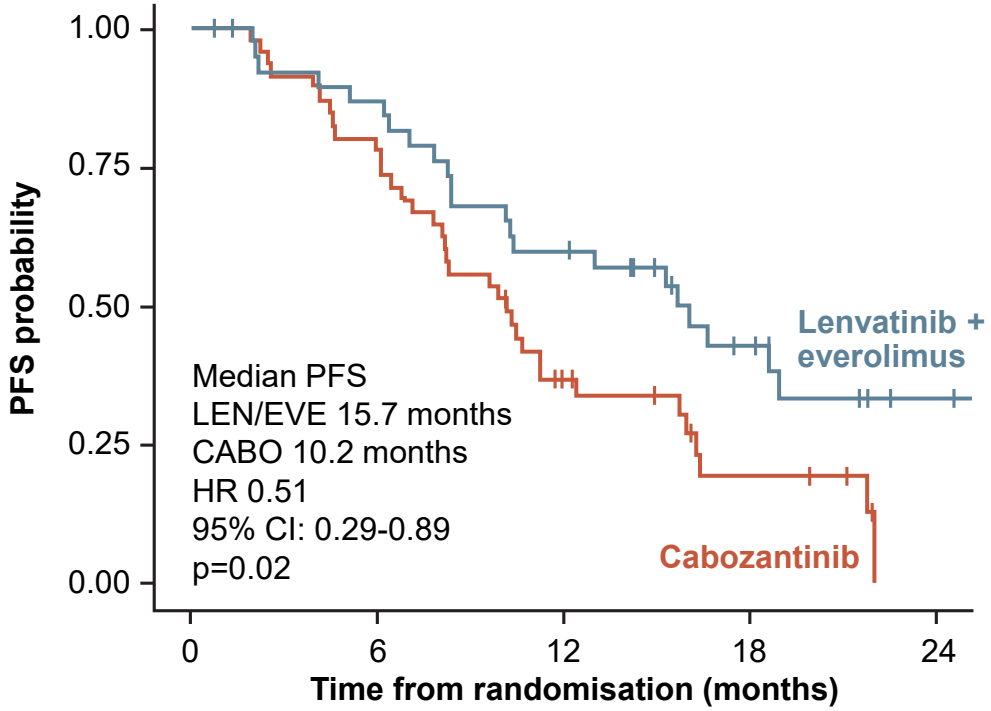
ccRCC, clear cell renal cell carcinoma; CTLA-4, cytotoxic T-lymphocyte associated protein 4; FGFR, fibroblast growth factor receptor; ICI, immune checkpoint inhibitor; IMDC, International Metastatic RCC Database Consortium; mccRCC, metastatic ccRCC; mTOR, mammalian target of rapamycin; ORR, objective response rate; OS, overall survival; PD-1, programmed cell death protein 1; PD-L1, programmed death-ligand 1; PFS, progression-free survival; R, randomised; RECIST, Response Evaluation Criteria in Solid Tumours; tx, treatments; VEGF TT, vascular endothelial growth factor-targeted therapy

Hahn A, et al. Abstract LBA94, ESMO 2025 (Oral presentation)

# LenCabo: EFFICACY RESULTS

- 90 patients were randomised, and 86 patients received at least 1 dose of assigned LEN/EVE (n=40) or CABO (n=46)

## PROGRESSION-FREE SURVIVAL




**Number at risk (number censored)**

| | | | | | |
|---|---|---|---|---|---|
| CABO | 46 (0) | 35 (1) | 13 (5) | 5 (8) | 0 (11) |
| LEN/EVE | 40 (0) | 33 (2) | 22 (3) | 11 (9) | 4 (14) |

## OBJECTIVE RESPONSE (RECIST V1.1)

| n (%) | LEN + EVE (N=40) | CABO (N=46) |
|---|---|---|
| Objective response<br>Complete response<br>Partial response | 20 (52.6)<br>0 (0)<br>20 (52.6) | 17 (38.6)<br>0 (0)<br>17 (38.6) |
| Stable disease | 15 (39.5) | 24 (54.5) |
| Progressive disease | 3 (7.9) | 3 (6.8) |
| Not evaluable | 2 | 2 |

**1-year OS probability (immature):**

- CABO: 84.6%, LEN/EVE: 87.0%
- HR 1.05 (95% CI: 0.47-2.38)
- p=0.86

CABO, cabozantinib; CI, confidence interval; EVE, everolimus; HR, hazard ratio; LEN, lenvatinib; OS, overall survival; PFS, progression-free survival; RECIST, Response Evaluation Criteria In Solid Tumours

Hahn A, et al. Abstract LBA94, ESMO 2025 (Oral presentation)

# LenCabo: SAFETY RESULTS

## TREATMENT-RELATED SAFETY SUMMARY

| n (%) | LEN + EVE (N=40) | CABO (N=46) | Odds ratio (95% CI) |
|---|---|---|---|
| Serious adverse events | 11 (27.5) | 9 (19.6) | 1.56 (0.57-4.24) |
| Grade 3/4 adverse events | 27 (67.5) | 23 (50) | 2.08 (0.86-5.02) |
| Dose interruptions | 28 (70) | 36 (78.3) | 0.65 (0.24-1.73) |
| Dose reductions | 23 (57) | 28 (60.9) | 0.80 (0.33-1.93) |
| Treatment discontinuation | 8 (20) | 5 (10.9) | 2.05 (0.61-6.91) |

## ANY GRADE TRAEs OF INTEREST

| Adverse event, n (%) | LEN + EVE (N=40) | CABO (N=46) |
|---|---|---|
| Diarrhoea | 28 (70) | 34 (73.9) |
| Fatigue | 29 (72.5) | 28 (60.9) |
| Proteinuria | 26 (65) | 17 (37) |
| Hypertension | 23 (57.5) | 18 (39.1) |
| Nausea | 16 (40) | 18 (39.1) |
| Palmar-plantar erythrodysesthesia syndrome | 8 (20) | 24 (52.2) |
| Vomiting | 13 (32.5) | 16 (34.8) |
| Mucositis oral | 6 (15) | 20 (43.5) |

CABO, cabozantinib; CI, confidence interval; EVE, everolimus; LEN, lenvatinib; TRAE, treatment-related adverse event

Hahn A, et al. Abstract LBA94, ESMO 2025 (Oral presentation)

# LenCabo: SUMMARY

- Among patients with metastatic ccRCC that progressed on prior PD-1 ICIs, lenvatinib/everolimus significantly prolonged PFS over cabozantinib
- As the first head-to-head randomised comparison of contemporary 2nd line treatments after ICI, these results are relevant to treatment sequencing and inform oncology practice

**Clinical perspective**

- LenCabo demonstrates the efficacy of lenvatinib + everolimus for ICI pre-treated patients with improved PFS & ORR compared with cabozantinib, although with higher toxicity. This combination should be considered for patients needing rapid or high tumour response for whom the higher toxicity rate is acceptable

ccRCC, clear cell renal cell carcinoma; ICI, immune checkpoint inhibitor; PD-1, programmed cell death protein 1; PFS, progression-free survival

Hahn A, et al. Abstract LBA94, ESMO 2025 (Oral presentation); Pickering L. Invited Discussant, ESMO 2025 (Oral presentation)

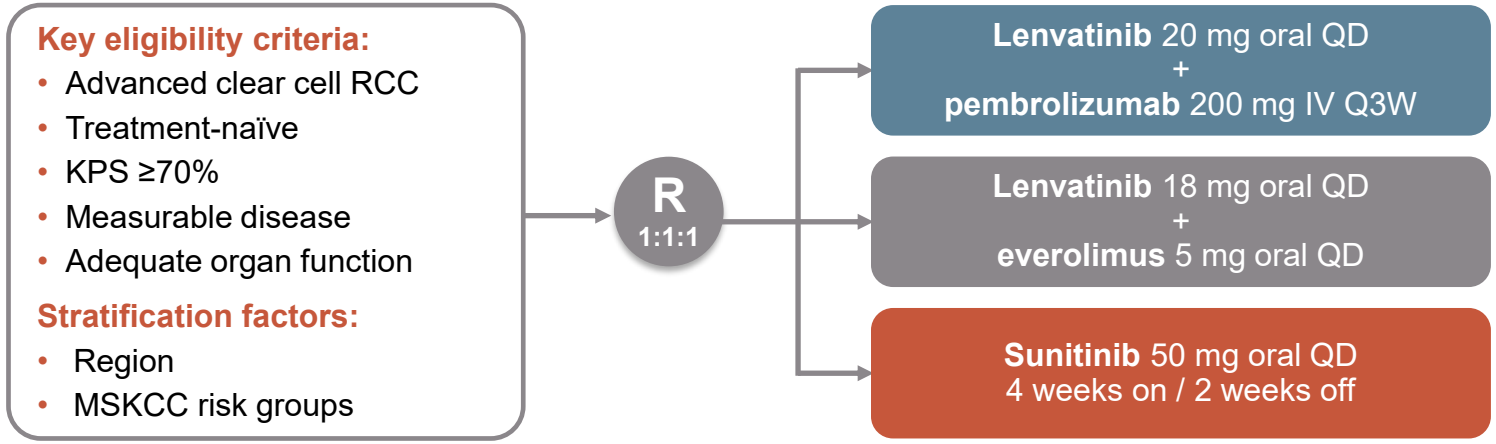
# FINAL ANALYSIS OF LENVATINIB + PEMBROLIZUMAB VS SUNITINIB IN PATIENTS WITH ADVANCED RCC WITH OR WITHOUT BONE METASTASES IN CLEAR

**Porta CG, et al. Abstract 2603P, ESMO 2025**

RCC, renal cell carcinoma

# CLEAR: BACKGROUND AND STUDY DESIGN

- Bone metastases occur in approximately one third of patients with advanced renal cell carcinoma (RCC) and are associated with a poor prognosis[1,2]
- Alteration of the FGF/FGFR axis is associated with the development of bone metastases in various cancers, including RCC[3]. Lenvatinib is a tyrosine kinase inhibitor with various targets, including: VEGFR, FGFR1-4, PDGFRα, KIT and RET[4]
- The phase 3 CLEAR study demonstrated that lenvatinib plus pembrolizumab significantly improved efficacy versus sunitinib as 1st line treatment for patients with advanced RCC[5]
- Additional results from the CLEAR study in patients with aRCC with and without bone metastases after ~4 years of follow up are reported[6]




(a)RCC, (advanced) renal call carcinoma; FGF(R), fibroblast growth factor (receptor); IV, intravenous; KPS, Karnofsky performance status; MSKCC, Memorial Sloan Kettering Cancer Center; PDGFRα, platelet-derived growth factor receptor-alpha; Q3W, once every 3 weeks; QD, once daily; R, randomisation; VEGFR, vascular endothelial growth factor receptor

1. Brown J, et al. Cancer Treat Rev. 2024;129:102792; 2. Grunwald V, et al. Nat Rev Urol. 2018;15(8):511-21; 3. Labanca E, et al. Endocr Relat Cancer. 2020; 27(7): R255-65; 4. Capozzi M, et al. Cancer Manag Res. 2019;11:3847-60; 5. Motzer R, et al. N Engl J Med. 2021;384:1289-1300; 6. Porta CG, et al. Abstract 2603P, ESMO 2025 (Poster presentation)

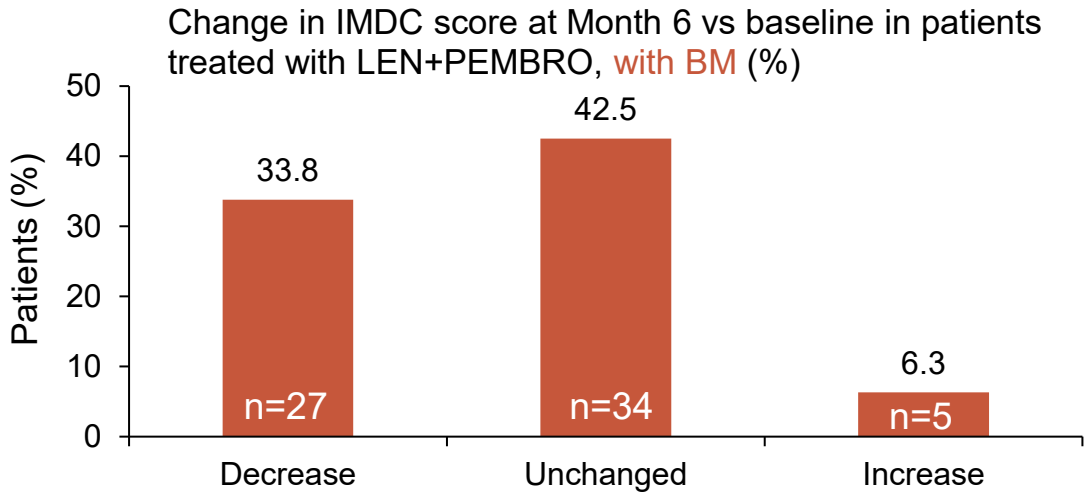
# CLEAR: EFFICACY RESULTS

## BASELINE CHARACTERISTICS

- Generally balanced across arms, with some exceptions in patients with **bone metastases (BM):**
  - for LEN+PEMBRO (vs SUN), **fewer** pts with **IMDC favourable risk** (17.5% vs 28.1%) and **prior nephrectomy** (62.5% vs 73.2%)
  - for LEN+PEMBRO (vs SUN), **more** pts with **≥3 metastatic sites** (65.0% vs 56.2%)

## SHIFT IN BASELINE IMDC SCORE

- IMDC scores in patients treated with LEN+PEMBRO generally improved or remained constant over 6 months, both in patients with/without BM




## TUMOUR RESPONSE

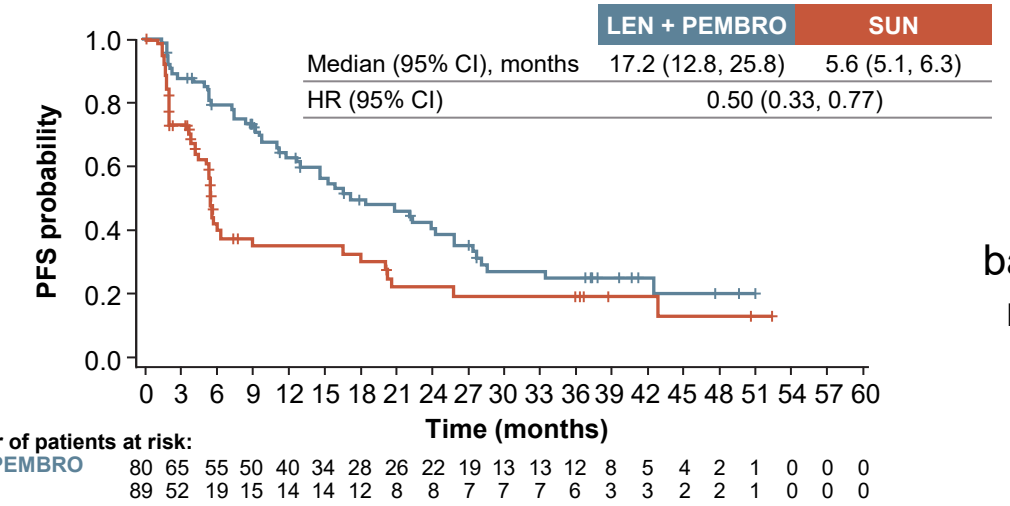
| | Bone metastases | | No bone metastases | |
|---|---|---|---|---|
| | LEN + PEMBRO (N=80) | SUN (N=89) | LEN + PEMBRO (N=275) | SUN (N=267) |
| Best overall response, n (%) | | | | |
| CR | 4 (5.0) | 1 (1.1) | 61 (22.2) | 16 (6.0) |
| PR | 44 (55.0) | 23 (25.8) | 144 (52.4) | 91 (34.1) |
| SD | 18 (22.5) | 34 (38.2) | 49 (17.8) | 100 (37.5) |
| PD | 9 (11.3) | 21 (23.6) | 10 (3.6) | 29 (10.9) |
| Unknown/not evaluable | 5 (6.3) | 10 (11.2) | 11 (4.0) | 31 (11.6) |
| ORR, n (%) | 48 (60.0) | 24 (27.0) | 205 (74.5) | 107 (40.1) |
| 95% CI | 49.3-70.7 | 17.8-36.2 | 69.4-79.7 | 34.2-46.0 |
| Clinical benefit rate, n (%) | 62 (77.5) | 41 (46.1) | 237 (86.2) | 171 (64.0) |
| 95% CI | 68.4-86.7 | 35.7-56.4 | 82.1-90.3 | 58.3-69.8 |
| Median time to first objective response (range), months | 1.87 (1.45-11.04) | 2.00 (1.64-16.62) | 1.94 (1.41-22.60) | 1.97 (1.61-34.96) |
| Median duration of objective response (95% CI), months | 22.0 (12.5-27.2) | 16.6 (3.7-35.5) | 30.5 (24.1-36.6) | 13.1 (9.3-18.4) |

CI, confidence interval; CR, complete response; IMDC, International Metastatic Renal Cell Carcinoma Database Consortium; LEN, lenvatinib; ORR, objective response rate; PD, progressive disease; PEMBRO, pembrolizumab; PR, partial response; pt, patient; SD, stable disease; SUN, sunitinib

Porta CG, et al. Abstract 2603P, ESMO 2025 (Poster presentation)

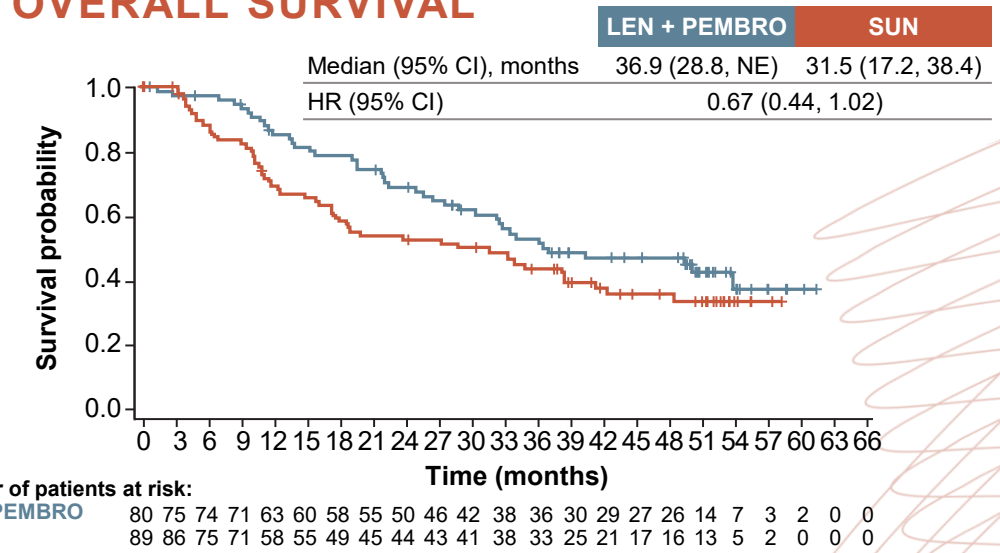
# CLEAR: EFFICACY RESULTS

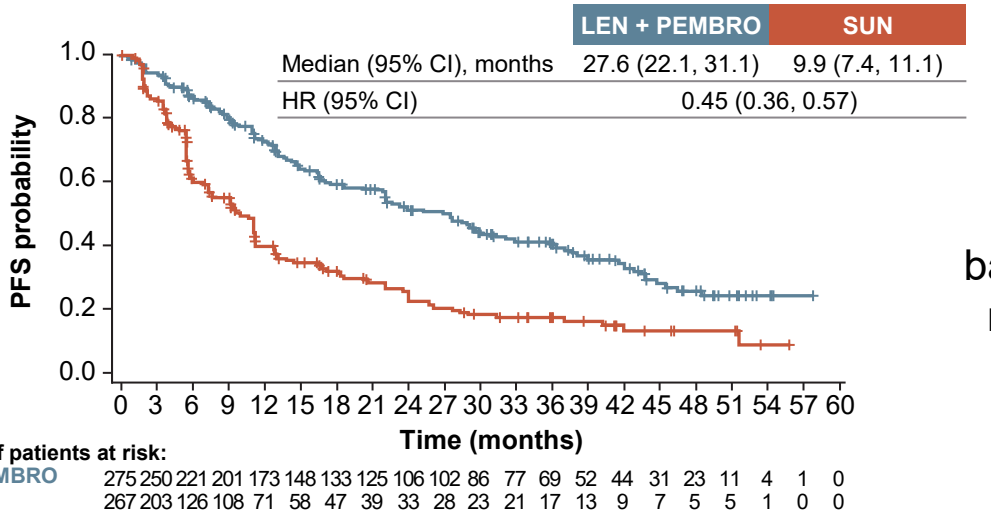
## PROGRESSION-FREE SURVIVAL



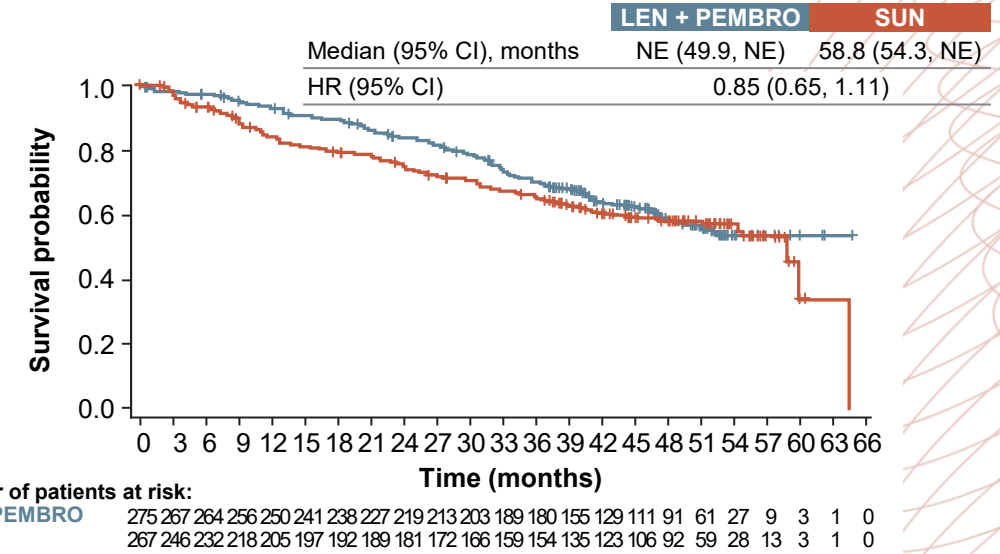

With baseline bone metastases

## OVERALL SURVIVAL




Without baseline bone metastases




CI, confidence interval; HR, hazard ratio; LEN, lenvatinib; NE, not evaluable; PEMBRO, pembrolizumab; PFS, progression-free survival; SUN, sunitinib

Porta CG, et al. Abstract 2603P, ESMO 2025 (Poster presentation)

# CLEAR: SUMMARY

- Despite worse baseline prognostic factors, LEN+PEMBRO improved OS, PFS and ORR vs SUN in advanced RCC patients with and without bone metastases
- In patients treated with LEN+PEMBRO, IMDC scores generally improved or remained constant over 6 months in patients with and without bone metastasis
- These results continue to support LEN+PEMBRO as a standard of care treatment for patients with advanced RCC regardless of the presence or absence of bone metastases at baseline

**Clinical perspective**

- Lenvatinib + pembrolizumab demonstrated improved efficacy versus sunitinib in advanced RCC, regardless of the presence or absence of bone metastases and continues to be a standard of care treatment in this population

IMDC, International Metastatic Renal Cell Carcinoma Database Consortium; LEN, lenvatinib; ORR, overall response rate; OS, overall survival; PEMBRO, pembrolizumab; PFS, progression-free survival; RCC, renal cell carcinoma; SUN, sunitinib

Porta CG, et al. Abstract 2603P, ESMO 2025 (Poster presentation)

# FIRST-LINE PEMBROLIZUMAB-BASED REGIMENS FOR ADVANCED ccRCC: KEYMAKER-U03 SUBSTUDY 03A

**Suarez Rodriguez C, et al. Abstract LBA96, ESMO 2025**

ccRCC, clear cell renal cell carcinoma

# KEYMAKER-U03: BACKGROUND AND STUDY DESIGN

- First-line triplet regimens adding novel mechanism of action to standard doublet therapy may be a promising approach for advanced ccRCC
- Substudy 03A (NCT04626479) of the umbrella phase 1/2 KEYMAKER-U03 trial evaluates novel pembrolizumab-based regimens in the 1st line for patients with advanced ccRCC

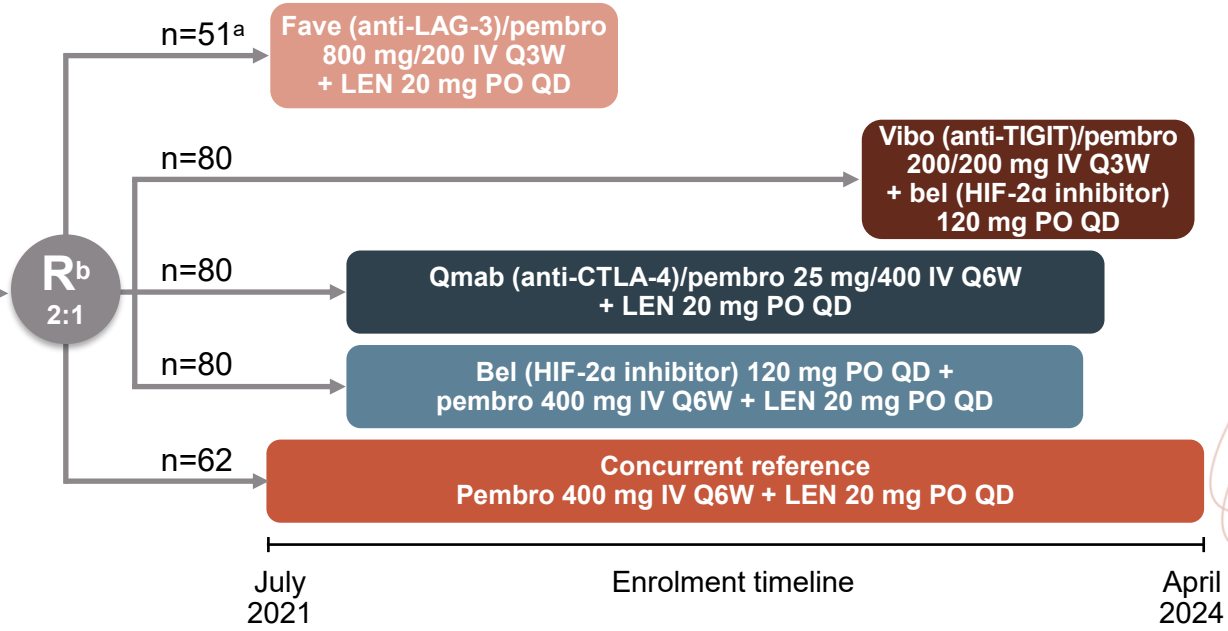
**Key eligibility criteria:**

- Histologically confirmed locally advanced or metastatic ccRCC measurable per RECIST v1.1
- No prior systemic therapy for advanced RCC
- KPS score of ≥70%

**Stratification factor:**

- IMDC risk group (favourable vs intermediate vs poor

**Safety lead-in phase:**
N=40
(10 patients per experimental arm)




**Endpoints:**
**Primary:** ORR per RECIST v1.1 by BICR and safety
**Secondary:** DoR and PFS per RECIST v1.1 by BICR and OS

[a] Enrolment ended early in Jan 2023 per data monitoring committee recommendation
[b] For each new investigational arm, additional patients were enrolled to the reference arm as needed to maintain the 2:1 randomisation ratio

bel, belzutifan; BICR, blinded independent central review; ccRCC, clear cell RCC; CTLA-4, cytotoxic T-lymphocyte associated protein 4; DoR, duration of response; fave, coformulated favezelimab; IMDC, International Metastatic RCC Database Consortium; IV, intravenous; KPS, Karnofsky performance status; LEN, lenvatinib; ORR, objective response rate; OS, overall survival; pembro, pembrolizumab; PFS, progression-free survival; PO, orally; QD, once a day; Q3/6W, every 3 or every 6 weeks; qmab, coformulated quavonlimab; R, randomisation; RCC, renal cell carcinoma; RECIST, Response Evaluation Criteria in Solid Tumours; TIGIT, T cell immunoreceptor with Ig and ITIM domains (ITIM, immunoreceptor tyrosine-based inhibitory motif); vibo, coformulated vibostolimab

Suarez Rodriguez C, et al. Abstract LBA96, ESMO 2025 (Oral presentation)

# KEYMAKER-U03: EFFICACY RESULTS

- Substudy 03A enrolled 393 patients (353 in the efficacy phase). Median follow-up for randomised patients across arms ranged from 16 to 39 months

| | Fave (anti-LAG-3)/ pembro + LEN N=51 | Vibo (anti-TIGIT)/ pembro + bel (HIF-2α inhibitor) N=80 | Qmab (anti-CTLA-4)/ pembro + LEN N=80 | Bel (HIF-2α inhibitor) + pembro + LEN N=80 | Reference: pembro + LEN N=62 |
|---|---|---|---|---|---|
| Median follow-up (range), mo | 39.2 (28.8-44.6) | 16.4 (11.8-23.4) | 22.1 (13.5-40.6) | 23.4 (14.1-41.0) | 21.2 (11.9-44.4) |
| ORR (95% CI), % | 63 (48-76) | 42 (32-54) | 71 (60-81) | 78 (67-86) | 81 (69-90) |
| CR (95% CI), % | 10 (3-21) | 5 (1-12) | 6 (2-14) | 12 (6-22) | 6 (2-16) |
| Median DoR (range), mo | 26.3 (1.4+-34.4+) | 14.0 (2.7+-18.2+) | 25.0 (2.4-37.1+) | 33.4 (2.6-37.6+) | 25.6 (1.4+-41.2+) |
| Median PFS (95% CI), mo | 26.0 (8.2-31.8) | 15.2 (12.4-NR) | 18.0 (11.6-34.3) | 31.8 (26.3-NR) | 26.3 (15.3-39.8) |
| PFS HR (95% CI) | 1.26 (0.65-2.42) | 1.42 (0.75-2.67) | 0.96 (0.57-1.61) | 0.45 (0.25-0.83) | – |
| PFS 24-mo rate (95% CI), % | 53 (38-67) | NR (NR-NR) | 46 (33-58) | 67 (53-78) | 53 (37-67) |
| OS 24-mo rate (95% CI), % | 76 (62-86) | NR (NR-NR) | 73 (60-83) | 86 (73-92) | 77 (60-87) |

Data cut-off: 31 March 2025

bel, belzutifan; CI, confidence interval; CR, complete response; CTLA-4, cytotoxic T-lymphocyte associated protein 4; DoR, duration of response; fave, coformulated favezelimab; HR, hazard ratio; LEN, lenvatinib; mo, months; NR, not reached; ORR, objective response rate; OS, overall survival; pembro, pembrolizumab; PFS, progression-free survival; qmab, coformulated quavonlimab; TIGIT, T cell immunoreceptor with Ig and ITIM domains (ITIM, immunoreceptor tyrosine-based inhibitory motif); vibo, coformulated vibostolimab

Suarez Rodriguez C, et al. Abstract LBA96, ESMO 2025 (Oral presentation)

# KEYMAKER-U03: SAFETY RESULTS

- Grade ≥3 TRAEs occurred in 66/90 patients (73%) with qmab/pembro + LEN, 53/61 (87%) with fave/pembro + LEN, 63/90 (70%) with pembro + bel + LEN, 62/90 (69%) with vibo/pembro + bel, and 44/62 (71%) in the reference arm

## MOST COMMON GRADE ≥3 TRAEs (≥5% IN ANY ARM)

| Participants, n (%) | Fave (anti-LAG-3)/ pembro + LEN N=61 | Vibo (anti-TIGIT)/ pembro + bel (HIF-2α inhibitor) N=90 | Qmab (anti-CTLA-4)/ pembro + LEN N=90 | Bel (HIF-2α inhibitor) + pembro + LEN N=90 | Reference: pembro + LEN N=62 |
|---|---|---|---|---|---|
| Hypertension | 19 (31.1) | 0 (0.0) | 25 (27.8) | 24 (26.7) | 21 (33.9) |
| Aspartate aminotransferase increased | 7 (11.5) | 6 (6.7) | 3 (3.3) | 5 (5.6) | 2 (3.2) |
| Alanine aminotransferase increased | 6 (9.8) | 9 (10.0) | 6 (6.7) | 7 (7.8) | 2 (3.2) |
| Diarrhoea | 6 (9.8) | 3 (3.3) | 6 (6.7) | 4 (4.4) | 2 (3.2) |
| Proteinuria | 6 (9.8) | 0 (0.0) | 5 (5.6) | 6 (6.7) | 1 (1.6) |
| Lipase increased | 5 (8.2) | 2 (2.2) | 4 (4.4) | 2 (2.2) | 2 (3.2) |
| Anaemia | 1 (1.6) | 30 (33.3) | 0 (0.0) | 22 (24.4) | 1 (1.6) |
| Weight increased | 1 (1.6) | 1 (1.1) | 4 (4.4) | 1 (1.1) | 4 (6.5) |
| Hypoxia | 0 (0.0) | 9 (10.0) | 0 (0.0) | 8 (8.9) | 0 (0.0) |

bel, belzutifan; CTLA-4, cytotoxic T-lymphocyte associated protein 4; fave, coformulated favezelimab; LEN, lenvatinib; pembro, pembrolizumab; qmab, coformulated quavonlimab; TIGIT, T cell immunoreceptor with Ig and ITIM domains (ITIM, immunoreceptor tyrosine-based inhibitory motif); TRAE, treatment emergent adverse event; vibo, coformulated vibostolimab

Suarez Rodriguez C, et al. Abstract LBA96, ESMO 2025 (Oral presentation)

# KEYMAKER-U03: SUMMARY

- Pembrolizumab + lenvatinib + belzutifan showed promising early efficacy and is being explored in the randomised phase 3 LITESPARK-012 study
- Other regimens did not show improved ORR and PFS compared with pembrolizumab + lenvatinib, but the duration of follow-up was insufficient to detect long-term contributions to OS
- Safety profiles were consistent with the profiles of the individual drugs in each regimen

**Clinical perspective**

- Among various combinations tested, adding belzutifan (an HIF-2α inhibitor) to lenvatinib and pembrolizumab was the only regimen with improved PFS, response durability, and OS—supporting advancement to phase 3 trials as a promising new triplet for 1st-line RCC

ORR, objective response rate; OS, overall survival; PFS, progression–free survival; RCC, renal cell carcinoma

Suarez Rodriguez C, et al. Abstract LBA96, ESMO 2025 (Oral presentation)

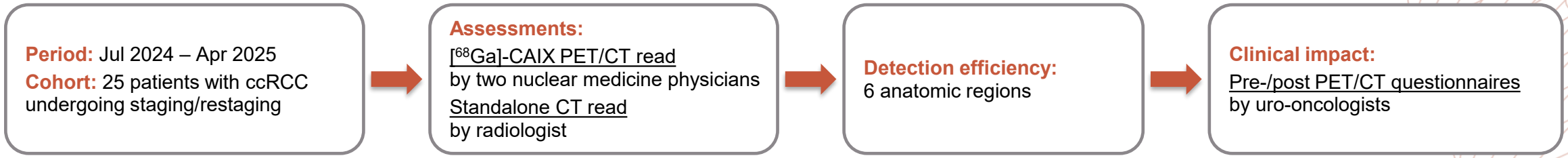
# [68GA]GA-DPI-4452 (CAIX) PET/CT FOR STAGING OF PATIENTS WITH ccRCC

**Küper AT, et al. Abstract 2597MO, ESMO 2025**

ccRCC, clear cell renal cell carcinoma; CT, computed tomography; PET, positron emission tomography

# CAIX PET/CT: BACKGROUND AND STUDY DESIGN

- One third of clear cell renal cell carcinoma (ccRCC) patients present with or develop metastases, with poor prognosis.[1,2] Despite major advances in treatment for RCC, the 5-year relative survival rate for distant metastatic disease remains low[1,2]
- CAIX is a cell-surface glycoprotein that plays a crucial role in acid-base regulation within cells and tissues.[1,3] CAIX is overexpressed in > 90% of cases of ccRCC[1,3]
- Aim of this study was to evaluate diagnostic accuracy and impact on management of carbonic anhydrase IX imaging by [$^{68}$Ga]Ga-DPI-4452 (CAIX) PET/CT vs conventional CT scans in patients with ccRCC[4]




CAIX, carbonic anhydrase IX; (cc)RCC, (clear cell) renal cell carcinoma; CT, computed tomography; PET, positron emission tomography

1. Hofman MS, et al. J Nucl Med. 2024;65(5):740-43; 2. Jonasch E, et al. Nat Rev Nephrol 2021; 17: 245-261; 3. Pastorekova S and Gillies RJ. Cancer Metastasis Rev. 2019;38:65-77; 4. Küper AT, et al. Abstract 2597MO, ESMO 2025 (Oral presentation)

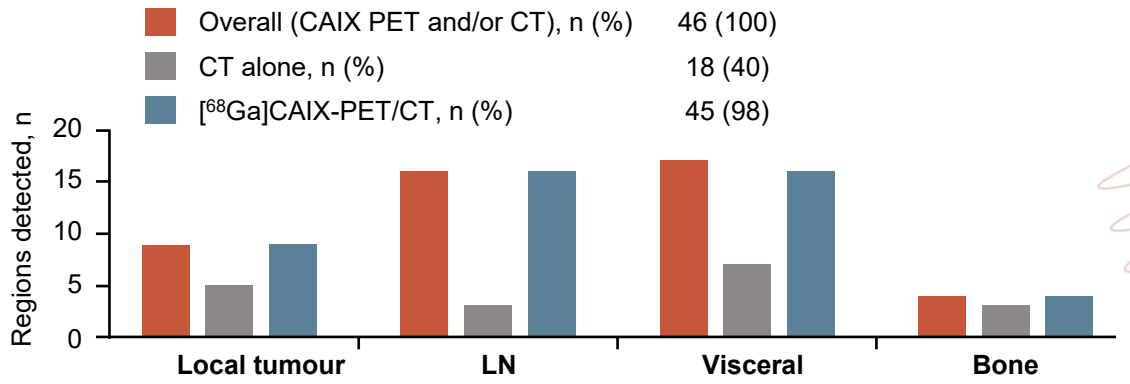
# CAIX PET/CT: EFFICACY RESULTS

## PATIENT CHARACTERISTICS

| Characteristic | Value |
|---|---|
| [68Ga]-CAIX PET | |
| Patients, N | 25 |
| Restaging, n | 24 |
| Mean activity (range), (Mbq) | 104 (41-155) |
| Mean uptake (range), (min) | 60 (30-150) |
| M1 at time of staging, n | 22 |
| Age (IQR) | 63 (12) |
| TNM score (initially), n | |
| 1 | 7 |
| 2 | 3 |
| 3 | 8 |
| 4 | 1 |
| Unknown | 5 |
| Grade, n | |
| 1 | 2 |
| 2 | 11 |
| 3 | 4 |
| 4 | 1 |
| Unknown | 6 |
| IMDC, n | |
| Favourable | 5 |
| Intermediate | 4 |
| Poor | 3 |
| Unknown | 13 |
| Previous therapy, n | |
| Nephrectomy | 21 |
| Metastasectomy | 18 |
| Systemic therapy | 17 |
| Treatment ongoing | 9 |

n = number of patients; N= total number of patients

## DETECTION RESULTS




**Inter-reader reproducibility of [68Ga]CAIX-PET/CT**

| CAIX-positive region | Local tumour | Lymph nodes | Bone | Other |
|---|---|---|---|---|
| Cohen's Kappa | 0.91 | 0.75 | 0.87 | 1.0 |

**Histological confirmation available in 19/45 CAIX-positive regions (42%)**

| | | | | Visceral metastases | |
|---|---|---|---|---|---|
| Local tumour | LN | Bone | Lung | Soft tissue | Other |
| 5 | 3 | 1 | 5 | 3 | 2 |

**Uptake:**

**Regional [68Ga]CAIX-Uptake (SUVmax)**

| Local tumour | LN | Bone | Visceral |
|---|---|---|---|
| 49.9 (±35.8) | 46.1 (±48.2) | 139.2 (±126.9) | 63.9 (±55.9) |

- Treatment modality changes occurred in 11 patients following CAIX-PET/CT imaging and 1 case shifted to palliative intent
- Highest uptake was found in bone metastases (mean SUVmax 139.2 ± 126.9)

CAIX, carbonic anhydrase IX; CT, computed tomography; IMDC, International Metastatic RCC Database Consortium; IQR, interquartile range; LN, lymph nodes; M1, metastatic disease; PET, positron emission tomography; SUVmax, maximised standardised uptake value; TNM, Tumour, Node, Metastasis

Küper AT, et al. Abstract 2597MO, ESMO 2025 (Oral presentation)

# CAIX PET/CT: SUMMARY

- [$^{68}$Ga]Ga-DPI-4452 (CAIX) PET/CT is a promising imaging tool for ccRCC with superior detection compared to CT, high inter-reader reproducibility and substantial clinical impact
- High SUV values indicate potential for a theranostic application

**Clinical perspective**

- Ga-DPI PET provides high-resolution, tumour-specific imaging in ccRCC, enhancing distinction between oligometastatic and widespread disease and enabling more precise selection for multimodality treatments

CAIX, carbonic anhydrase IX; ccRCC, clear cell renal cell carcinoma; CT, computed tomography; Ga-DPI, [$^{68}$Ga]Ga-DPI-4452; PET, positron emission tomography; SUV, standardised uptake value

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