

# EAU GUIDELINES ON RENAL CELL CARCINOMA (RCC)

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A. Bex (Chair), Y. Abu-Ghanem, J. Bedke (Vice-Chair), D.J. Breen, U. Capitanio, S. Dabestani, M. Hora, T. Klatte, T. Kuusk, L. Lund, L. Marconi, G. Pignot, T. Powles, C. Saurez, M. Tran, P. Zondervan  
Patient Representative: S. Bonn, R. Woodward  
Guidelines Associates: R. Campi, C. Palumbo  
Guidelines Office: N. Schouten

## Introduction

### Epidemiology, aetiology and screening

The widespread use of imaging techniques such as ultrasound (US) and computed tomography (CT) has increased the detection of asymptomatic renal cell carcinoma (RCC). The peak incidence of RCC occurs between 60 and 70 years of age, with a 3:2 ratio of males to females. Aetiological factors include lifestyle factors, such as smoking, obesity and hypertension.

Having a first-degree relative with RCC is associated with a significantly increased risk of RCC.

There is no evidence to support primary screening of the general population. Genetic screening of subgroups of patients with a family history of RCC is recommended.

Recommendations for epidemiology, aetiology and screening	Strength rating
Increase physical activity, eliminate smoking and in patients with obesity reducing weight are the primary preventative measures to decrease the risk of RCC.	Strong
Do not routinely screen people for primary RCC.	Weak

### Staging system

The current Union for International Cancer Control (UICC) 2017 Tumour Node Metastasis (TNM) classification is recommended for the staging of RCC (Table 1).

**Table 1: 2017 TNM classification system**

<b>T - Primary tumour</b>	
TX	Primary tumour cannot be assessed
T0	No evidence of primary tumour
T1	Tumour $\leq$ 7 cm or less in greatest dimension, limited to the kidney
T1a	Tumour $\leq$ 4 cm or less
T1b	Tumour $>$ 4 cm but $\leq$ 7 cm
T2	Tumour $>$ 7 cm in greatest dimension, limited to the kidney
T2a	Tumour $>$ 7 cm but $\leq$ 10 cm
T2b	Tumours $>$ 10 cm, limited to the kidney
T3	Tumour extends into major veins or perinephric tissues but not into the ipsilateral adrenal gland and not beyond Gerota fascia

T3a	Tumour extends into the renal vein or its segmental branches, or invades the pelvicalyceal system or invades perirenal and/or renal sinus fat*, but not beyond Gerota fascia*		
T3b	Tumour grossly extends into the vena cava below diaphragm		
T3c	Tumour grossly extends into vena cava above the diaphragm or invades the wall of the vena cava		
T4	Tumour invades beyond Gerota fascia (including contiguous extension into the ipsilateral adrenal gland)		
<b>N - Regional in lymph nodes</b>			
NX	Regional lymph nodes cannot be assessed		
N0	No regional lymph node metastasis		
N1	Metastasis in regional lymph node(s)		
<b>M - Distant metastasis</b>			
M0	No distant metastasis		
M1	Distant metastasis		
<b>pTNM stage grouping</b>			
Stage I	T1	N0	M0
Stage II	T2	N0	M0
Stage III	T3	N0	M0
	T1, T2, T3	N1	M0
Stage IV	T4	Any N	M0
	Any T	Any N	M1

A help desk for specific questions about TNM classification is available at <http://www.uicc.org/tnm>.

\*Adapted based on the American Joint Committee on Cancer (AJCC), 8<sup>th</sup> Edn. 2017.

<b>Recommendations for the management of other renal tumours</b>	<b>Strength rating</b>
Manage Bosniak type III cysts the same as localised RCC, or offer active surveillance (AS).	Weak
Manage Bosniak type IV cysts the same as localised RCC.	Strong
Offer AS to patients with biopsy-proven oncocytoma or other oncocytic renal tumours as an acceptable alternative to surgery or ablation.	Weak
Treat angiomyolipoma (AML) with selective arterial embolisation or nephron-sparing surgery, in: <ul style="list-style-type: none"> <li>• large tumours (a recommended threshold of intervention does not exist);</li> <li>• females of childbearing age;</li> <li>• patients for whom follow-up or access to emergency care may be inadequate;</li> <li>• persistent pain or acute or repeated bleeding episodes.</li> </ul>	Weak
Offer systemic therapy (everolimus) to patients with surgically unresectable AMLs which are not amenable to embolisation and require therapy.	Weak

## Diagnostic evaluation

Many renal masses remain asymptomatic until late disease stages. The classic triad of flank pain, visible haematuria, and palpable abdominal mass is rare and correlates with aggressive histology and advanced disease.

Paraneoplastic syndromes are found in approximately 30% of patients with symptomatic RCCs. A few symptomatic patients present with symptoms caused by metastatic disease, such as bone pain or persistent cough.

## Imaging

Computed tomography imaging, unenhanced, and during the nephrographic phase after intravenous contrast, can verify the diagnosis and provide information on the function and morphology of the contralateral kidney and assess tumour extension, including extra-renal spread, venous involvement and enlargement of lymph nodes (LNs) and adrenals.

Abdominal US and magnetic resonance imaging (MRI) are supplementary to CT. Contrast-enhanced US can be helpful in specific cases (e.g., chronic renal failure with a relative contraindication for iodinated or gadolinium-based contrast media, complex cystic masses, and differential diagnosis of peripheral vascular disorders such as infarction and cortical necrosis).

Magnetic resonance imaging is an alternative to abdominal CT and is useful in patients with an allergy to intravenous contrast. It can also be used for the work-up of patients with possible venous involvement. Chest CT is the most accurate for chest staging and is recommended in the primary work-up of patients with suspected RCC.

In younger patients, MRI may be offered as alternative for follow-up imaging.

## Biopsy

Percutaneous renal tumour biopsies are used:

- to obtain histology of radiologically indeterminate renal masses;
- to select patients with small renal masses for active surveillance;

- to obtain histology before (advantageous), or simultaneously with ablative treatments;
- to select the most suitable form of medical and surgical strategy in the setting of metastatic disease.

In patients with any sign of impaired renal function, a renal scan and total renal function evaluation using estimated glomerular filtration rate should always be undertaken to optimise the treatment decision.

Renal biopsy is not indicated for comorbid and frail patients who can be considered only for conservative management regardless of biopsy results.

<b>Recommendations for the diagnosis of RCC</b>	<b>Strength rating</b>
Use multi-phasic contrast-enhanced computed tomography (CT) of the abdomen and chest for the diagnosis and staging of renal tumours.	Strong
Omit chest CT in patients with incidentally noted cT1a disease due to the low risk of lung metastases in this cohort.	Weak
Use magnetic resonance imaging (MRI) to better evaluate venous involvement, reduce radiation or avoid intravenous CT contrast medium.	Weak
Use non-ionising modalities, including MRI and contrast-enhanced ultrasound, for further characterisation of small renal masses, tumour thrombus and differentiation of unclear renal masses, in case the results of contrast-enhanced CT are indeterminate.	Strong

Offer brain CT/MRI in metastatic patients when systemic therapy or cytoreductive nephrectomy is considered.	Weak
Do not routinely use bone scan and/or fluorodeoxyglucose positron emission tomography (FDG-PET) CT for primary staging of RCC.	Weak
Perform a renal tumour biopsy before ablative therapy and systemic therapy without previous pathology.	Strong
Perform a percutaneous biopsy in select patients who are considering active surveillance.	Weak
Use a coaxial technique when performing a renal tumour biopsy.	Strong
Do not perform a renal tumour biopsy of cystic renal masses unless a significant solid component is visible at imaging.	Strong
Use a core biopsy technique rather than fine needle aspiration for histological characterisation of solid renal tumours.	Strong

<b>Recommendations for the genetic assessment of RCC</b>	<b>Strength rating</b>
Perform a genetic evaluation in patients aged $\leq 46$ years, with bilateral or multifocal tumours and/or a first- or second-degree relative with RCC and/or a close blood relative with a known pathogenic variant and/or specific histologic characteristics which suggest the presence of a hereditary form of RCC.	Strong

Refer patients to a cancer geneticist or to a comprehensive clinical care centre in case of suspected hereditary RCC.	Strong
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## Histological diagnosis

A variety of renal tumours exist and about 15% are benign. All kidney lesions require examination for malignant behaviour.

## Histopathological classification

The 2017 World Health Organisation (WHO)/International Society of Urological Pathology (ISUP) grade classification has replaced the Fuhrman nuclear grade system. The new WHO morphological classification combines both morphologic and molecular analysis. Still, the three most common RCC types, with genetic and histological differences, are: clear cell RCC (ccRCC) (70-85%), papillary RCC (pRCC) (10-15%), and chromophobe RCC (chRCC) (4-5%). The various RCC types have different clinical courses and responses to therapy.

Other, rarer RCC variants are addressed in the full RCC Guidelines document.

## Prognostic factors

In all RCC types, prognosis worsens with stage and histopathological grade. Histological factors include tumour grade, RCC subtype, sarcomatoid features, lymphovascular invasion, tumour necrosis and invasion of the peri-renal fat and collecting system. Clinical factors include performance status, local symptoms, cachexia, anaemia, platelet count, neutrophil/lymphocyte ratio, C-reactive protein and albumin (see Tables 6.3 and 6.4 in the 2026 RCC Guidelines publication).

## Frailty and comprehensive geriatric assessment

Frailty is a geriatric syndrome characterised by a decline in resilience and physiological functional reserve across

multiple body systems, resulting in increased vulnerability to external stressors. Frailty is an adverse prognostic factor in older patients with localized RCC, being associated with worse perioperative outcomes as well as poorer oncological outcomes across different stages (See Table 6.2 in the 2026 RCC Guidelines publication for Frailty and Geriatric Assessment factors).

<b>Recommendations for prognostic factors</b>	<b>Strength rating</b>
Use the current Tumour, Node, Metastasis classification system.	Strong
Use the World Health Organization (WHO)/International Society of Urological Pathology (ISUP) grading system and classify RCC type.	Strong
Use prognostic models in localised and metastatic disease.	Strong
Use the 2003 Leibovich scoring model for risk stratification of localised and locally advanced clear cell RCC.	Weak
Use the venous involvement, necrosis, size, stage and sarcomatoid differentiation (VENUSS) scoring model for risk stratification of localised and locally advanced papillary RCC.	Weak
Do not routinely use molecular markers to assess prognosis.	Strong
Screen elderly patients with a renal mass/ RCC with a validated geriatric frailty score to identify patients at risk for frailty.	Weak

Offer comprehensive geriatric assessment in elderly patients whose screening revealed a risk for frailty.	Weak
Offer pre-treatment nephrological consultation in selected patients with or at risk for impaired renal function (e.g., pre-existing chronic kidney disease or proteinuria; solitary kidney, known medical comorbidities affecting renal function; new baseline estimated glomerular filtration rate (eGFR) below 45 ml/min/1.73m <sup>2</sup> )	Weak

## Disease Management

### Patient involvement in kidney cancer treatment

Recommendation for prognostic factors	Strength rating
Employ a shared decision-making approach when deciding on appropriate treatment for RCC.	Strong

### Smoking cessation

Recommendation for prognostic factors	Strength rating
Counsel RCC patients to stop smoking.	Strong

### Treatment of localised RCC

Localised RCCs are best managed with partial nephrectomy (PN) rather than radical nephrectomy (RN), irrespective of the surgical approach. Partial nephrectomy is unsuitable in some patients with localised RCC due to:

- locally advanced tumour growth;
- unfavourable tumour location;
- significant health deterioration.

If pre-operative imaging and intra-operative findings are normal, routine adrenalectomy is not indicated.

Lymphadenectomy should be restricted to staging as the survival benefit of extended LN dissection (LND) is unclear in patients with localised disease. In patients who have RCCs with tumour thrombus and no metastatic spread, prognosis is improved after nephrectomy and complete thrombectomy.

### **Nephron-sparing surgery versus radical nephrectomy**

Based on current available oncological and quality of life (QoL) outcomes, localised RCC is best managed by nephron-sparing surgery (NSS) rather than RN, irrespective of the surgical approach. Before routine nephrectomy, tumour embolisation has no benefit.

<b>Recommendations for the treatment of localised RCC</b>	<b>Strength rating</b>
Offer surgery to achieve cure in localised RCC.	Strong
Offer partial nephrectomy (PN) to patients with T1 tumours.	Strong
Offer PN to patients with T2 tumours and a solitary kidney or chronic kidney disease, if technically feasible.	Weak
Do not perform ipsilateral adrenalectomy if there is no clinical evidence of invasion of the adrenal gland.	Strong
Do not routinely perform a lymph node dissection in patients with organ-confined disease.	Weak
Offer embolisation to patients unfit for surgery presenting with massive haematuria or flank pain.	Weak

<b>Recommendations for radical and partial nephrectomy techniques</b>	<b>Strength rating</b>
Offer laparoscopic or robotic radical nephrectomy (RN) to patients with T2 tumours and localised masses not treatable by partial nephrectomy (PN).	Strong
Do not perform minimally invasive RN in patients with T1 tumours for whom a PN is feasible by any approach, including open.	Strong
Do not perform minimally invasive surgery if this approach may compromise oncological- functional- and peri-operative outcomes.	Strong
Do not perform re-resection or RN in patients with a microscopic positive surgical margins.	Weak
Intensify follow-up in patients with a positive surgical margin, especially in upstaged pT3a patients.	Weak
Do not attempt off-clamp PN unless indicated.	Weak

### **Therapeutic approaches as alternatives to surgery**

Most population-based analyses show a significantly lower cancer-specific mortality in patients treated with surgery compared to non-surgical management.

### **Active surveillance and watchful waiting**

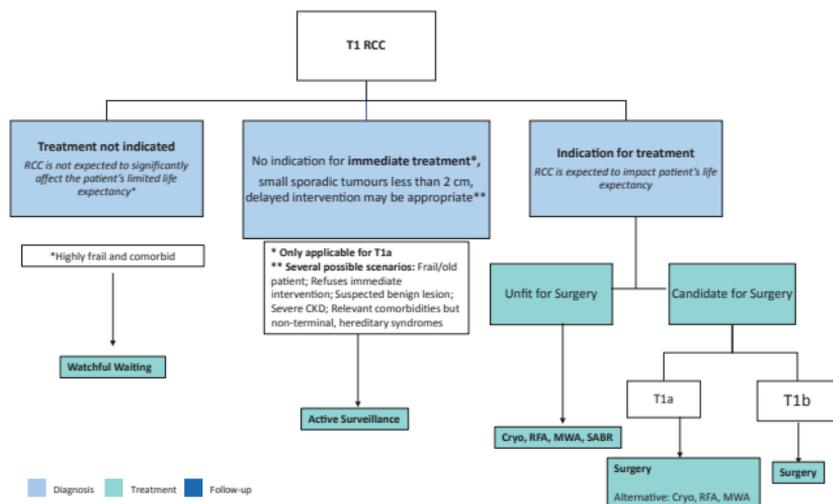
Elderly and comorbid patients with incidental small renal masses may have significant competing-cause mortality exceeding RCC-specific mortality. Therefore, in selected patients, initial monitoring through active surveillance (AS) of small renal masses, followed, if required, by treatment for progression, is appropriate. The concept of AS differs from the

concept of watchful waiting. Watchful waiting is reserved for patients whose comorbidities contra-indicate any subsequent active treatment and who do not require follow-up imaging, unless clinically indicated.

## Cryoablation and radiofrequency ablation

Cryoablation or radiofrequency ablation (RFA) techniques are associated with less morbidity as compared to PN, at the cost of higher recurrence rates.

**Figure 1: Alternatives to surgery**



CKD = chronic kidney disease; Cryo = cryoablation;  
MWA = microwave ablation; RCC = renal cell carcinoma;  
RFA = radiofrequency ablation; SABR = stereotactic ablative  
body radiotherapy

<b>Recommendations for therapeutic approaches as alternative to surgery</b>	<b>Strength rating</b>
Offer watchful waiting to highly frail and comorbid patients with reduced life expectancy.	Weak
Offer active surveillance (AS) to cT1a patients with no indication for immediate treatment and where delayed intervention may be appropriate.	Weak
Offer tumour ablation (TA) or stereotactic ablative radiotherapy in patients with cT1 lesions who have an indication for treatment but are unfit for surgery.	Weak
Perform a percutaneous renal mass biopsy prior to, and not concomitantly with, TA.	Strong
Discuss the limitations in the clinical evidence, with regards to oncological outcomes and complications when TA or AS is offered.	Strong
Do not routinely offer radiofrequency ablation for tumours > 3 cm and cryoablation for tumours > 4 cm.	Weak

## **Treatment of locally advanced RCC**

### **Management of clinically positive lymph nodes (cN+)**

In the presence of clinically positive LNs (cN+), LND is always justified but the extent of LND is still controversial.

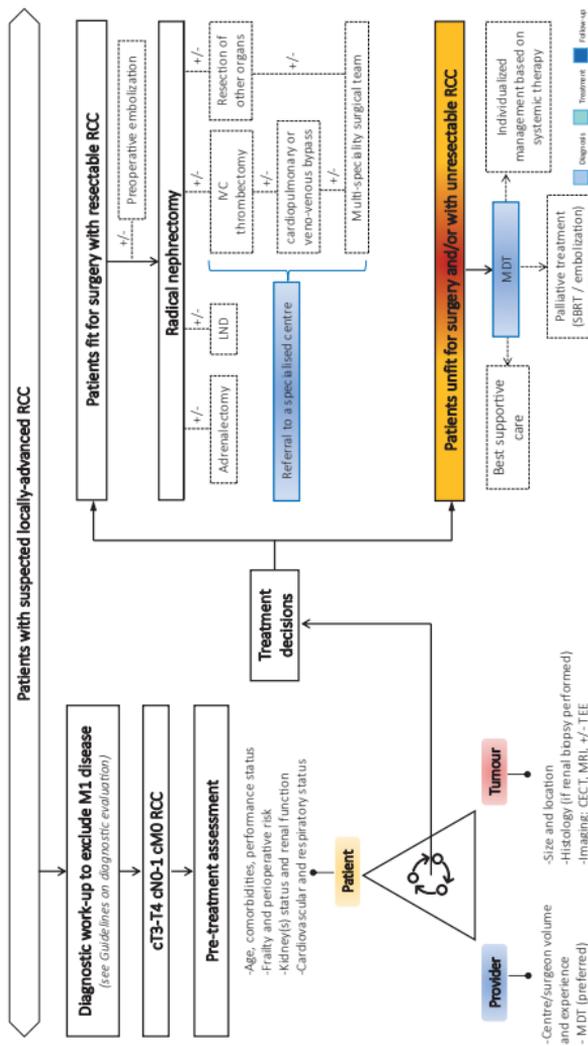
Low level data suggest that tumour thrombus in the setting of non-metastatic disease should be excised.

Adjunctive procedures such as tumour embolisation or inferior vena cava filter do not appear to offer any benefits in the treatment of tumour thrombus.

In patients unfit for surgery, or with non-resectable disease, embolisation can control symptoms, including visible haematuria or flank pain.

Immune checkpoint inhibitors (ICI), restoring immune activity, have shown impressive efficacy in advanced RCC. Previous tyrosine kinase inhibitor (TKI) adjuvant trials have failed to improve disease-free survival (DFS) except one with no effect on overall survival (OS). The Keynote-564 study with adjuvant pembrolizumab was the first ICI trial showing significantly improved DFS and OS (with longer follow-up) in ccRCC with a high risk of relapse. Primary DFS endpoints were not met in three adjuvant ICI studies (IMmotion010, CheckMate 914, PROSPER) while the updated follow-up of the Keynote-564 study remained significant. Differences in effect can be due to heterogeneity in patient selection and different ICIs studied. Pembrolizumab remains recommended in this setting. Treatment decisions should be made with caution and individual patient preference should be carefully considered including a discussion with the patient on the potential risk of overtreatment.

**Figure 2: Treatment of locally advanced RCC**



CECT = contrast-enhanced computed tomography;  
 IVC = inferior vena cava; LND = lymph node dissection;  
 MDT = multidisciplinary team; MRI = magnetic resonance  
 imaging; TEE = transoesophageal echocardiogram

<b>Recommendations for lymph node dissection, the management of RCC with venous tumour thrombus and unresectable tumours</b>	<b>Strength rating</b>
During nephrectomy, remove clinically enlarged lymph nodes for staging, prognosis and follow-up implications.	Weak
Remove the renal tumour and thrombus in case of venous involvement in non-metastatic disease.	Strong
Discuss treatment options in patients with locally-advanced unresectable RCC (biopsy and/or systemic therapy/deferred resection, or palliative management) within a multidisciplinary team to determine treatment goal.	Strong

## Neoadjuvant and adjuvant therapy

Recommendations for neoadjuvant and adjuvant therapy	Strength rating
Do not use neoadjuvant therapy outside a clinical trial setting.	Weak
<p>Offer adjuvant pembrolizumab to clear cell RCC (ccRCC) patients, preferably within 12 - 16 weeks post-nephrectomy, following restaging, with a recurrence risk as defined in the Keynote-564 trial:</p> <p>Intermediate-high risk:</p> <ul style="list-style-type: none"> <li>• pT2, grade 4 or sarcomatoid, N0 M0</li> <li>• pT3, any grade, N0, M0</li> </ul> <p>High risk:</p> <ul style="list-style-type: none"> <li>• pT4, any grade, N0, M0</li> <li>• any pT, any grade, N+, M0</li> </ul> <p>M1 no evidence of disease:</p> <ul style="list-style-type: none"> <li>• No evidence of disease after resection of oligometastatic sites within one year from nephrectomy.</li> </ul>	Strong
<p>If adjuvant therapy is planned:</p> <ul style="list-style-type: none"> <li>• Discuss the contradictory results of the available adjuvant immune checkpoint inhibitor (ICI) trials with the patient to facilitate shared decision-making.</li> <li>• Inform the patient about the potential risk of overtreatment and immune related side effects if adjuvant therapy is considered.</li> </ul>	Strong
Do not offer adjuvant sunitinib following surgically resected high-risk ccRCC.	Weak

Offer vascular endothelial growth factor receptor - tyrosine kinase inhibitor (VEGFR-TKI) to patients developing a recurrence while receiving pembrolizumab or within the first six months after stopping pembrolizumab given for one year.	weak
Do not offer ICI mono- or combination therapy in patients with recurrence during or within six months after adjuvant pembrolizumab.	weak

## Advanced/metastatic RCC

### Local therapy of advanced/metastatic RCC

#### Cytoreductive nephrectomy

Tumour nephrectomy is curative only if all tumour deposits are excised. This includes patients with the primary tumour in place and single- or oligometastatic resectable disease. For most patients with metastatic disease, cytoreductive nephrectomy (CN) is palliative and systemic treatments are necessary.

<b>Recommendations for local therapy of advanced/metastatic RCC</b>	<b>Strength rating</b>
Do not perform cytoreductive nephrectomy (CN) in IMDC/MSKCC poor-risk patients.	Strong
Do not perform immediate CN in intermediate-risk patients who have an asymptomatic synchronous primary tumour and require systemic therapy.	Weak
Start systemic therapy without CN in intermediate-risk patients who have an asymptomatic synchronous primary tumour and require systemic therapy.	Weak

Discuss delayed CN with patients who derive clinical benefit from systemic therapy.	Weak
Perform immediate CN in patients with a good performance status who do not require systemic therapy.	Weak
Perform immediate CN in patients with oligometastases when complete local treatment of the metastases can be achieved.	Weak

*IMDC = International Metastatic Renal Cell Carcinoma Database Consortium, MSKCC = Memorial Sloan Kettering Cancer Centre.*

### **Local therapy of metastases in metastatic RCC**

A systematic review of the local treatment of metastases from RCC in any organ was undertaken. The heterogeneity of the data will only allow for cautious recommendations.

<b>Recommendations for local therapy of metastases in metastatic RCC</b>	<b>Strength rating</b>
To control local symptoms, offer ablative therapy, including metastasectomy, to patients with metastatic disease and favourable disease factors and in whom complete resection is achievable.	Weak
Offer stereotactic radiotherapy for clinically relevant bone- or brain metastases for local control and symptom relief.	Weak
Do not offer tyrosine kinase inhibitor treatment to metastatic RCC patients after metastasectomy and no evidence of disease.	Strong

Perform a confirmatory axial scan of disease status prior to metastasectomy to rule out rapid progressive metastatic disease which requires systemic treatment.	Weak
Before initiating systemic therapy for oligometastases that cannot be resected, discuss with your patient a period of observation until progression is confirmed.	Weak

## Systemic therapy for advanced/metastatic RCC

Recommendation for systemic therapy in advanced/metastatic RCC	Strength rating
Do not offer chemotherapy to patients with metastatic RCC.	Strong

### Targeted therapies

At present, several targeting drugs have been approved for the treatment of clear cell metastatic renal carcinoma (cc-mRCC).

### Immunotherapy

Interferon- $\alpha$  monotherapy either alone or combined with bevacizumab, as well as single-agent TKI (except for IMDC favourable risk patients) have been superseded as standard treatment of treatment-naïve advanced cc-mRCC by ICI combinations and combinations with ICI and targeted therapies.

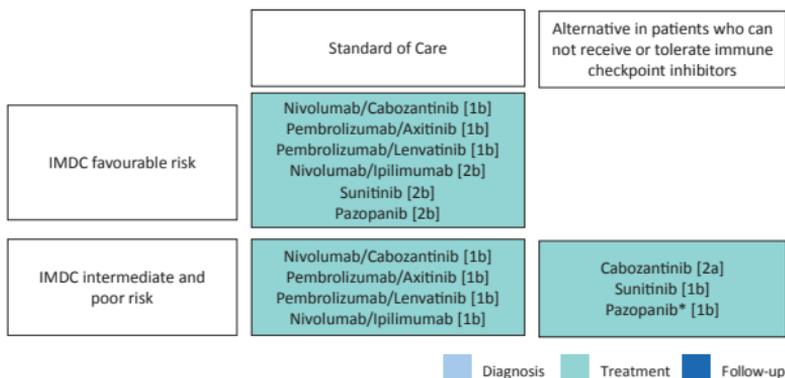
Recommendations for immunotherapy in cc-mRCC	Strength rating
<i>First-line Treatment for metastatic clear cell RCC patients</i>	
Offer nivolumab plus ipilimumab, pembrolizumab plus axitinib, lenvatinib plus pembrolizumab or nivolumab and cabozantinib to patients with International Metastatic Renal Cell Carcinoma Database Consortium (IMDC) intermediate- or poor risk-disease.	Strong
Offer pembrolizumab plus axitinib, lenvatinib plus pembrolizumab or nivolumab and cabozantinib or nivolumab plus ipilimumab or sunitinib or pazopanib for IMDC favourable risk disease.	Weak
Offer sunitinib or pazopanib to patients with any IMDC risk who cannot receive or tolerate immune checkpoint inhibitors (ICI).	Strong
Offer cabozantinib to patients with IMDC intermediate- and poor-risk clear cell metastatic renal carcinoma (cc-mRCC) who cannot receive or tolerate immune checkpoint inhibition.	Strong <sup>a</sup>
Patients who do not receive the full four doses of ipilimumab due to toxicity should continue on single-agent nivolumab, where safe and feasible. Re-challenge with combination therapy requires expert support after discontinuation for toxicity.	Weak
Offer ICI combination therapy for advanced cc-mRCC with sarcomatoid features.	Strong

Intermittent single agent vascular endothelial growth factor (VEGF)- tyrosine kinase inhibitor (TKI) can be offered in case of partial response or stable disease for more than six months.	Weak
<i>Sequencing systemic therapy for metastatic clear cell RCC</i>	
Do not offer ICI monotherapy or combination therapy to patients with recurrence during or within six months after adjuvant pembrolizumab.	Weak
Sequence systemic therapy in treating mRCC.	Strong
Offer cabozantinib or other VEGF-TKI as second-line therapy to patients refractory to nivolumab plus ipilimumab or axitinib plus pembrolizumab or cabozantinib plus nivolumab or lenvatinib plus pembrolizumab.	Strong
Sequence the agent not used as second-line therapy (nivolumab or cabozantinib) for third-line therapy is recommended.	Weak
Offer nivolumab or cabozantinib for those patients who received first line VEGF targeted therapy alone.	Strong
Treatment past progression can be justified but requires close scrutiny and the support of an expert multidisciplinary team.	Weak
Do not re-challenge patients who stopped ICI because of toxicity without expert guidance and support from a multidisciplinary team.	Strong

Do not offer programmed death-ligand 1 (PD-L1) combination therapy after progression after ICI combination.	Weak
Offer belzutifan as an alternative to everolimus in patients previously treated with second to fourth line therapy for clear cell RCC.	Weak

<sup>a</sup> While this is based on a randomised phase II trial, cabozantinib (weak) looks at least as good as sunitinib in this population. This justified the same recommendation under exceptional circumstances.

**Figure 3: EAU Guidelines recommendations for the first-line treatment of clear cell metastatic RCC**



IMDC = The International Metastatic Renal Cell Carcinoma Database Consortium.

\*pazopanib for intermediate-risk disease only.

[1b] = based on one randomised controlled phase III trial.

[2a] = based on a well-designed study without randomisation, or a subgroup analysis of a randomised controlled trial.

**Figure 4: EAU Guidelines recommendations for later-line therapy**

	Standard of Care	Alternative
Prior TKI+IO Prior IO+IO	Cabozantinib [3] Any VEGF-targeted therapy that has not been used previously in combination with IO [4]	
Prior TKI	Nivolumab [1b] Cabozantinib [1b]	Axitinib [2b]
Several prior lines including IO and TKI	Belzutifan [1b]	

■ Diagnosis  
■ Treatment  
■ Follow-up

IO = immunotherapy; TKI = tyrosine kinase inhibitors;  
VEGF = vascular endothelial growth factor.

[1b] = based on one randomised controlled phase III trial.

[2b] = subgroup analysis of a randomised controlled phase III trial.

[4] = expert opinion.

### Therapy for renal tumours with sarcomatoid features

Immune checkpoint inhibitor-combination therapy was superior to sunitinib in terms of PFS and OS in a subset analysis of a trial including patients with ccRCC and sarcomatoid differentiation.

Recommendation for targeted therapy in RCC with sarcomatoid features	Strength rating
Offer immune checkpoint inhibitor combination therapy for advanced clear cell metastatic RCC with sarcomatoid features.	Weak

## Treatment of patients with papillary metastatic RCC

<b>Recommendations for systemic therapy in papillary metastatic RCC</b>	<b>Strength rating</b>
Offer cabozantinib to patients with papillary RCC (pRCC) based on a positive randomised controlled trial.	Weak
Offer lenvatinib plus pembrolizumab or nivolumab plus cabozantinib to patients with pRCC based on small single-arm trials.	Weak

## Treatment of patients with metastatic non-clear cell RCC other than papillary RCC

The evidence surrounding systemic therapy for non-ccRCC tumours other than pRCC is especially weak and has relied on subset analysis of randomised phase II trials as well as expanded access programmes.

<b>Recommendations for systemic therapy in chromophobe and unclassified RCC</b>	<b>Strength rating</b>
Offer sunitinib to patients with other non-clear cell renal cell carcinoma (cc-RCC) subtypes than papillary RCC.	Weak
Offer lenvatinib plus pembrolizumab to patients with non-ccRCC subtypes.	Weak
Offer cabozantinib and nivolumab to patients with non-ccRCC subtypes other than chromophobe RCC.	weak
Offer nivolumab plus ipilimumab to patients with non-ccRCC.	Weak

## Recurrent RCC

Locally recurrent disease in the treated kidney can occur either after PN, or ablative therapy. After RN or nephron-sparing treatment approaches, recurrence may occur in the renal fossa or regional, for example, venous tumour thrombi or retroperitoneal LN metastases. Isolated local recurrence in the true renal fossa after RN is rare.

Patients can benefit from a complete surgical resection of local recurrent disease. In cases where complete surgical removal is not feasible due to advanced tumour growth and pain, palliative treatments including radiation treatment can be considered as well as systemic therapy.

<b>Recommendation on locally-recurrent RCC after treatment of localised disease</b>	<b>Strength rating</b>
Offer local treatment of locally-recurrent disease when technically possible and after balancing adverse prognostic features, comorbidities and life expectancy.	Weak

## Hereditary and syndrome specific RCC

Five to eight percent of RCCs are hereditary; this proportion could be underestimated due to the limitations of available studies. (See Table 8.1 in the 2026 RCC Guidelines publication for syndrome-specific RCC histotypes and extra-renal organ involvement patterns).

Recommendations on hereditary and syndrome specific RCC	Strength rating
Suspect hereditary or syndrome-specific RCC in patients with positive family history, young onset and bilateral or multiple tumours.	Strong
Offer germline testing to patients < 46 years.	Weak
Offer surveillance in von Hippel-Lindau (VHL) until the largest tumour reaches 3 cm in diameter.	Strong
Offer belzutifan to patients with VHL related renal and other tumours who are not surgical candidates.	Weak

### Follow-up in RCC

The aim of surveillance is to detect either local recurrence or metastatic disease while the patient is still surgically curable. Surveillance after treatment for RCC allows the urologist to assess:

- post-operative complications;
- renal function;
- local recurrence;
- recurrence in the contralateral kidney;
- development of metastases.

Depending on the availability of new effective treatments, more intensive follow-up schedules may be required, particularly as there is a higher local recurrence rate after cryotherapy and radiofrequency ablation (RFA). At present there is no evidence-based standard for the follow-up of patients with RCC, or for the optimal duration of follow-up. An example of a surveillance algorithm monitoring patients after treatment for RCC that recognises not only the patient's risk

profile but also treatment efficacy is provided in Table 2. For patients with metastatic disease, individualised follow-up is indicated.

In younger patients who are worried about the radiation exposure of frequent CT scans, MRI may be offered as alternative for follow-up imaging.

**Table 2: Proposed follow-up schedule following treatment for localised RCC, taking into account patient risk of recurrence profile and treatment efficacy**

Risk profile (*)	Oncological follow-up after date of surgery								
	3 mo	6 mo	12 mo	18 mo	24 mo	30 mo	36 mo	> 3 yr (**) (***)	> 5 yr (**) (***)
<b>Low risk of recurrence</b> For ccRCC: Leibovich Score 0-2  For non-ccRCC: pT1a-T1b pNx-0 M0 and histological grade 1 or 2.	-	CT	-	CT	-	CT	-	CT once every two yrs	-
<b>Intermediate risk of recurrence</b> For ccRCC: Leibovich Score 3-5  For non-ccRCC: pT1b pNx-0 and/or histological grade 3 or 4.	-	CT	CT	-	CT	-	CT	CT once yr	CT once every two yrs

<b>High risk of recurrence</b> <u>For ccRCC:</u> Leibovich Score $\geq 6$  <u>For non-ccRCC:</u> pT2-pT4 with any histological grade or pT any, pN1 cM0 with any histological grade	CT	CT	CT	CT	CT	-	CT	CT once yr	CT once every two yrs
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ccRCC = clear cell renal cell carcinoma; CT = computed tomography; mo = months; non-ccRCC = non clear cell renal cell carcinoma; yr = years.

The table above provides recommendations on follow-up strategies for low, intermediate and high risk of recurrence in patients curatively treated for localised RCC either with NSS or RN. Computed tomography in the table refers to imaging of both chest and abdomen. Alternatively, MRI of the abdomen can be performed instead of a CT-scan.

- \* Risk of recurrence profiles should be based on validated prognostic models. The EAU RCC Guidelines Panel recommends the 2003 Leibovich model for ccRCC. However, other validated models can be used by physicians based on their own national/regional recommendations. In a similar fashion, for curatively treated localised non-ccRCC, the Panel recommends the use of the University of California Los Angeles integrated staging system (UISS) to determine risk of recurrence.
- \*\* For all risk of recurrence profiles, functional follow-up, mainly monitoring renal and cardiovascular function, may continue according to specific clinical needs irrespective of the length of the oncological follow-up.

\*\*\* For low-risk profiles at > three years and intermediate-risk at > five years of follow-up respectively, consider counselling patients about terminating oncological follow-up imaging based on assessment of comorbidities, age, life expectancy and/or patient wishes.

<b>Recommendations for surveillance following radical nephrectomy or partial nephrectomy or ablative therapies in RCC</b>	<b>Strength rating</b>
Base follow-up after treatment of localised RCC on the risk of recurrence.	Strong
Base risk of recurrence stratification on validated subtype-specific models such as the Leibovich Score for clear cell RCC (ccRCC), or the University of California Los Angeles integrated staging system for non-ccRCC.	Weak
Intensify follow-up in patients after nephron-sparing with a positive surgical margin.	Weak
Consider curtailing follow-up when the risk of dying from other causes is double that of the RCC recurrence risk.	Weak
Offer psychological evaluation for all patients diagnosed with RCC to provide timely support for distress, depression, or anxiety.	Weak

Seek nephrological consultation during follow-up in patients treated for RCC with one or more of the following conditions: <ul style="list-style-type: none"><li>- pre-existing chronic kidney disease</li><li>- treatment-induced chronic kidney disease (e.g. new baseline estimated glomerular filtration rate &lt; 45 mL/min)</li><li>- known comorbidities potentially affecting renal function.</li></ul>	Weak
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*This short booklet text is based on the more comprehensive EAU Guidelines accessible on the website:*  
<http://www.uroweb.org/guidelines/>.