

Recommendations from the EAU RCC Guideline Panel applicable during the COVID-19 pandemic

Diagnosis				
Priority category	Low Priority	Intermediate Priority	High priority	Emergency
Definition	Clinical harm (progression, metastasis, loss of renal function) very unlikely if postponed 6 months	Clinical harm (progression, metastasis, loss of renal function) possible if postponed 3 months but unlikely	Clinical harm (progression, metastasis) and (cancer related) deaths very likely if postponed > 6 weeks	Life-threatening situation or opioid-dependent pain
Level of evidence	1	3	3	3
COVID-recommendation	Defer by 6 months	Diagnose before end of 3 months	Diagnose within < 6 weeks	Diagnose within < 24 h
	<ul style="list-style-type: none"> • Cross-sectional diagnostic and staging imaging for all renal tumours < 4 cm suspected on ultrasound • Renal mass biopsy for all cT1a tumours (small renal masses < 4 cm) cN0 cM0 • Cross sectional imaging for complex cysts irrespective of size on ultrasound 	Cross-sectional diagnostic and staging imaging for all renal tumours > 4 - < 7 cm suspected on ultrasound	<ul style="list-style-type: none"> • Staging for clinically advanced or suspected metastatic renal cancer • Renal mass biopsy to establish subtype for systemic therapy in metastatic IMDC intermediate- and poor-risk patients • Adequate cross-sectional imaging to diagnose thrombus level in suspected advanced RCC with IVC thrombi[§] 	<ul style="list-style-type: none"> • Visible (macroscopic) haematuria with clot retention • Suspected bowel obstruction in conjunction with a known history of renal mass • Excruciating pain in conjunction with a known history of renal mass • Spinal cord compression in conjunction with a known history of renal mass
<p>* Some patients with kidney cancer are octogenarians and older. They may require ITU support based on frailty and comorbidity. In case of low resources but competing high-priority cases preference should be given to younger patients not requiring ITU support. In addition old age and frailty are risk factors for community or hospital acquired COVID-19.</p> <p>§ Some patients with IVC thrombi (level 3-4) may require cardiovascular bypass and ITU support. In case of low resources but competing high-priority cases preference should be given to patients not requiring ITU support.</p>				
Treatment of locally confined or advanced but non-metastatic RCC				
Priority category	Low Priority	Intermediate Priority	High priority	Emergency

Definition	Clinical harm (progression, metastasis, loss of renal function) very unlikely if postponed 6 months	Clinical harm (progression, metastasis, loss of renal function) possible if postponed 3 months but unlikely	Clinical harm (progression, metastasis) and (cancer related) deaths very likely if postponed > 6 weeks	Life-threatening situation or opioid-dependent pain
Level of evidence	1	3	3	3
COVID-recommendation	Defer by 6 months	Treat before end of 3 months	Treat within < 6 weeks	Treat within < 24 h
	<ul style="list-style-type: none"> All cT1a tumours (small renal masses < 4 cm) cN0 cM0 Bosniak III cysts irrespective of size¹ Treatment of AML (embolisation, ablation) > 4 cm^{2,3} Participation in neoadjuvant or adjuvant trials 	All cT1b-cT2a cN0 cM0 asymptomatic RCC*	<ul style="list-style-type: none"> Clinically advanced RCC, cT2b-4, cN0-cN1 cM0* Advanced RCC with IVC thrombi Novick level 1-4[§] Or other, if symptomatic 	Actively bleeding <i>symptomatic</i> renal mass: <ul style="list-style-type: none"> Try embolisation first. Surgical intervention only if embolisation not successful or not available

* Some patients with kidney cancer are octogenarians and older. They may require ITU support based on frailty and comorbidity. In case of low resources but competing high-priority cases preference should be given to younger patients not requiring ITU support. In addition old age and frailty are risk factors for community or hospital acquired COVID-19.

§ Some patients with IVC thrombi (level 3-4) may require cardiovascular bypass and ITU support. In case of low resources but competing high-priority cases preference should be given to patients not requiring ITU support.

References

1. Chandrasekar T, et al. Urol. 2018 Mar;199(3):633-640. Natural History of Complex Renal Cysts: Clinical Evidence Supporting Active Surveillance.
2. Bhatt JR, et al. Eur Urol. 2016 Jul;70(1):85-90. Natural History of Renal Angiomyolipoma (AML): Most Patients with Large AMLs >4cm Can Be Offered Active Surveillance as an Initial Management Strategy.
3. Fernández-Pello S, et al. Eur Urol Oncol. 2020 Feb;3(1):57-72. Management of Sporadic Renal Angiomyolipomas: A Systematic Review of Available Evidence to Guide Recommendations from the European Association of Urology Renal Cell Carcinoma Guidelines Panel.

Treatment of metastatic RCC

Priority category	Low Priority	Intermediate Priority	High priority	Emergency
Definition	Clinical harm (progression, metastasis, loss of renal	Clinical harm (progression, metastasis, loss of renal function)	Clinical harm (progression, metastasis) and (cancer	Life-threatening situation or opioid-dependent pain

	function) very unlikely if postponed 6 months	possible if postponed 3 months but unlikely	related) deaths very likely if postponed > 6 weeks	
Level of evidence	3	1-3	3	3
COVID-recommendation	Defer by 6 months***	Treat before end of 3 months*	Treat within < 6 weeks**	Treat within < 24 h
	<p><u>Synchronous mRCC:</u> Cytoreductive nephrectomy and in <i>asymptomatic</i> patients with oligometastatic disease and IMDC favourable risk, metastasectomy or other forms of focal therapy</p> <p><u>Metachronous mRCC:</u> Oligometastatic <i>asymptomatic</i> metastases in IMDC favourable risk*</p>	<p><u>Non-progressing <i>asymptomatic</i> metastatic RCC in IMDC favourable and intermediate risk</u></p> <p>[Consider surveillance rather than VEGF-targeted therapy for some*]</p>	<p><u>Progressive metastatic RCC irrespective of IMDC risk</u></p> <p>[Consider starting on VEGFR-TKI rather than immune checkpoint inhibitor therapy**]</p>	<ul style="list-style-type: none"> Actively bleeding renal mass with <i>symptoms</i>: Try embolisation first. Surgical intervention only if embolisation not successful or not available. Spinal cord compression in conjunction with mRCC Central or peripheral nervous system disorders suggestive of symptomatic brain metastases Serious adverse events related to systemic treatment
<p>* An initial “wait and see” strategy with re-imaging in 3 months is feasible in favourable- and intermediate- IMDC risk patients with asymptomatic mRCC. Reference: Rini BI, et al. Lancet Oncol. 2016 Sep;17(9):1317-24. Active surveillance in metastatic renal-cell carcinoma: a prospective, phase 2 trial.</p> <p>** Treatment with systemic therapy will be dependent on the stage of the pandemic within a particular region and the state/functionality of healthcare resources. Starting immune combination therapy has a significant chance of admission and/or steroid use¹. Therefore there is uncertainty around increased complications of COVID-19 infection in this population. Starting treatment with VEGF-targeted therapy appears attractive as an alternative in some situations. It also negates the risk associated with IV infusions which are hospital based. Patients established on immune therapy may interrupt doses if the risk of breaking self-isolation is high. Patients on VEGF and immune combinations may have the immune therapy withheld for short periods during periods where the pandemic is not well controlled. Reference: Motzer RJ, et al; CheckMate 214 Investigators. N Engl J Med. 2018 Apr 5;378(14):1277-1290. Nivolumab plus Ipilimumab versus Sunitinib in Advanced Renal-Cell Carcinoma.</p> <p>*** Surgery for asymptomatic metastatic disease is controversial irrespective of the COVID-19 pandemic. There needs to be clear justification for this to</p>				

occur. during the pandemic. Multidisciplinary team discussion is essential. Risk-benefit ratio is high without randomised data.

Follow-up of RCC

Priority category	Low Priority	Intermediate Priority	High priority	Emergency
Definition	Clinical harm (progression, metastasis, loss of renal function) very unlikely if postponed 6 months	Clinical harm (progression, metastasis, loss of renal function) possible if postponed 3 months but unlikely	Clinical harm (progression, metastasis) and (cancer related) deaths very likely if postponed > 6 weeks	Life-threatening situation or opioid-dependent pain
Level of evidence	1	3	3	3
COVID-recommendation	Defer by 6 months	Follow-up before end of 3 months	Follow-up within < 6 weeks	Follow-up within < 24 h
	All non-metastatic low- and intermediate risk RCC patients following radical nephrectomy, partial nephrectomy, thermal ablation or active surveillance ^{*,1,2}	<ul style="list-style-type: none"> All non-metastatic high-risk RCC patients following radical nephrectomy and partial nephrectomy All <i>asymptomatic</i> metastatic RCC patients who stopped medical therapy or those that have been on therapy for > 1 year³ Patients on systemic therapy/ or in adjuvant trials, preferably according to protocol 	<i>Asymptomatic</i> metastatic RCC patients on systemic treatment	<ul style="list-style-type: none"> Actively bleeding renal mass with <i>symptoms</i> after embolisation. Any emergency treatment as above <i>Symptomatic</i> metastatic RCC

*Prospective active surveillance studies and RECUR database analyses suggest that deferring follow-up in this group by 6 months is safe¹.

References

1. Dabestani S, et al. Eur Urol Focus. 2019 Sep;5(5):857-866. Long-term Outcomes of Follow-up for Initially Localised Clear Cell Renal Cell Carcinoma: RECUR Database Analysis.
2. Finelli A, et al. J Clin Oncol. 2017 Feb 20;35(6):668-680. Erratum in: J Clin Oncol. 2017 Apr 1;35(10):1141. Management of Small Renal Masses: American Society of Clinical Oncology Clinical Practice Guideline.
3. A retrospective study in 2012 suggests that 61% of patients who achieved a CR after VEGFR-TKI therapy and stopped medication were still in CR after a median follow-up of 255 days: Albiges L, et al. J Clin Oncol. 2012 Feb 10;30(5):482-7. Complete remission with tyrosine kinase inhibitors in renal cell carcinoma.

Abbreviations

AML = Angiomyolipoma; IMDC = International Metastatic RCC Database Consortium; ITU = intensive care Unit; LE = Oxford level of evidence; LE 1 = based on several prospective studies; LE 3 = based on retrospective cohort studies; mRCC = metastatic renal cell carcinoma; URS = ureterorenoscopy; IVC = inferior vena cava; TKI = tyrosine kinase inhibitors; VEGF = vascular endothelial growth factor.