Treatment of advanced/metastatic renal cell carcinoma (RCC)

Local therapy of advanced/metastatic RCC

1. Cytoreductive nephrectomy

Tumour resection is potentially curative only if all tumour deposits are excised (including primary tumour in place with single/oligometastatic resectable disease).

For most metastatic patients, cytoreductive nephrectomy (CN) is palliative and systemic therapy is needed; earlier signals with CN plus interferon (IFN) are no longer relevant.

CARMENA showed sunitinib alone was not inferior to immediate CN followed by sunitinib for overall survival (OS), and many patients later had secondary CN.

Recommendations	Strength rating
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

SURTIME found no progression-free survival (PFS) difference by sequence but suggested an OS benefit with deferred CN; surgery after sunitinib appears feasible and safe.

CN is not recommended in poor performance status (PS) or International Metastatic RCC Database Consortium (IMDC) poor risk, with small primaries and high metastatic burden, and/or sarcomatoid tumours.

First-line treatment with the primary tumour in place has shifted to immune checkpoint inhibitor (ICI) combinations, reserving tyrosine kinase inhibitor (TKI) monotherapy for those who cannot receive ICI. Patients needing systemic therapy should start drugs upfront; in IMDC intermediate/poor risk, use immuno-oncology (IO)-based combinations and consider CN only if there is a clinical response. Long-term outcomes are pending; randomised trials are ongoing.

2. Embolisation of the primary tumour

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

3. Local therapy of metastases in metastatic RCC

- **Evidence base:**

A systematic review (SR) of local treatments in RCC found only non-randomised comparative studies across metastasectomy, radiotherapy (RT) modalities, or no local therapy; data were heterogeneous and not suitable for meta-analysis, and a later SR did not improve evidence quality.

- **Complete vs. no/incomplete metastasectomy:**

Most studies reported longer overall/cancer-specific survival (CSS) with complete metastasectomy versus incomplete or none (median ~41 vs. ~15 months), though one study showed no difference and another lacked a p-value; in one series, only 45% achieved complete resection.

- **Local therapies for bone metastases:**

Single-dose image-guided radiotherapy (IGRT) >24 Gy improved 3-year local control versus hypofractionated IGRT. Metastasectomy/curettage with stabilisation yielded higher 5-year CSS than no surgery. Single-dose stereotactic body radiotherapy (SBRT) achieved pain outcomes similar to conventional RT.

- **Local therapies for brain metastases:**

Stereotactic radiosurgery (SRS) alone or SRS + whole-brain RT (WBRT) outperformed WBRT alone for 2-year survival and intracranial control; a tiny recursive partitioning analysis (RPA) class I subgroup suggested SRS+WBRT superiority. Fractionated SRT (FSRT) showed non-significant survival advantages versus surgery±RT. Stereotactic radiotherapy (SRT) (median 20 Gy; BED10 ~63) was safe with immune/targeted therapy, with ~75% 1-year local control and no grade IV–V toxicity.

- **Embolisation:**

Pre-resection embolisation of hypervascular bone/spinal metastases can reduce intra-operative blood loss and, in selected painful lesions, relieve symptoms.

- **SRT in oligo-recurrent/oligo-progressive disease:**

Single-arm series show high local control (~78–93% at 2 years), delayed need for systemic therapy (~12–14 months), and low ≥grade III toxicity; randomised trials are ongoing.

Recommendations	Strength rating
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

- **Adjuvant after metastasectomy (cM0 / M1-NED):**

Adjuvant tyrosine-kinase inhibitors did not improve disease-free survival (DFS) or overall survival. A small M1-NED signal with pembrolizumab is difficult to interpret; routine metastasectomy plus adjuvant pembrolizumab within the first year after primary surgery is not encouraged. Careful reassessment is advised; observation of limited recurrences can be prolonged before starting systemic therapy.