The creation of this resource has been fully funded by MSD and is an adaptation of a previous iteration. It has been developed in collaboration with Dr. Ricky Frazer, Medical Oncology Consultant at Velindre Cancer Centre and Honorary Clinical Lecturer at Cardiff University; and Mr Ben Challacombe, Consultant Urological Surgeon at Guy's & St Thomas' Hospitals and at King's College London who have received an honorarium for their services. Their views are their own, based upon their clinical experience and are not necessarily representative of their institutions.

Purpose of this resource

This resource has been developed to aid decision making within pre- and post-operative multidisciplinary team (MDT) meetings to identify suitable treatment choices for patients with renal cell carcinoma (RCC). The flow chart and content reflect key considerations based on the consulted clinicians experience and available evidence related to the RCC pathway in the UK of licensed and funded treatment options only. Responsibility for treatment decisions ultimately remains with the treating healthcare professional(s).

RENAL CELL CARCINOMA (RCC) PRE-OPERATIVE CONSIDERATIONS & POST-OPERATIVE MDT DECISION AID

MSD

KEY: CONSIDERATIONS DECISION AID

TNM CLASSIFICATION[1]

Tumour

T0, no evidence of disease;
T1a, tumour is 4cm or less in greatest dimension, limited to the kidney;
T1b, tumour is more than 4cm but less than or equal to 7cm in greatest dimension, limited to the kidney;
T2a, tumour is more than 7cm but less than or equal to 10cm in greatest dimension, limited to the kidney;
T2b, tumour is more than 10cm in greatest dimension, limited to the kidney;
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's 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's fascia (including contiguous extension into the ipsilateral adrenal gland).

Node

NX, regional lymph nodes cannot be accessed;
N0, no regional lymph node metastasis;
N1, metastasis in regional lymph node(s).

Metastasis

M0, no distant metastasis;
M1, with distant metastasis.

RCC Grade Classification[1]

The World Health Organisation - International Society of Urological Pathology (WHO/ISUP) and Fuhrman are grading systems based on nucleolar prominence. They are used to ensure potentially eligible patients are not excluded from follow-up care.

Reminder: Pre-book CT/MRI[3]

Urologist/MDT to pre-book CT/MRI for restaging post-surgery within timelines where there is an increased risk of disease recurrence following surgery and potential for commencing any additional treatment.

Adult patients with RCC

Pre-surgery

CLINICAL STAGING

Current clinical radiological staging[1,2]
- T classification (T0; T1a; T1b; T2a; T2b; T3a; T3b; T3c; T4)
- N classification (cNx/N0; cN+)
- M classification (cM0/M1)
- Tumour size (<10 cm; ≥10 cm)
- Tumour necrosis (absent; present)

HISTOLOGY AND PATHOLOGY

Histological diagnosis (i.e. biopsy results) if available

Includes: RCC cell type; evaluation of nuclear grade, sarcomatoid features, vascular invasion, tumour necrosis.[1]
- WHO/ISUP/Fuhrman grade (1-4)

PATIENT ELIGIBILITY

Does the patient have clear cell RCC?

YES

Has the patient received prior treatment with a checkpoint inhibitor, immunotherapy, or with any other systemic therapy for RCC?

YES

Review current evidence for routine post-operative surveillance and alternative approaches.

NO

If patient is likely to be at increased risk of disease recurrence following surgery, **introduce the concept of adjuvant treatment** management in pre-surgical patient consultation where suitable. Patient will require post-surgery CT/MRI scan prior to initiating adjuvant therapy.

NO

Post-surgery
(Following radical nephrectomy or partial nephrectomy +/- resection of metastatic lesions / lymph nodes)

What has been discussed with the patient?
- Has there been a previous discussion with the patient of potential for adjuvant treatment management (if eligible)?
- Have patient preferences and circumstances been considered?

Resection status
Patient's resection status is R0 (negative surgical margins).

NO

Review current evidence and alternatives to routine post operative surveillance.

YES

- What is the size and grade of the tumour?
- What is the TNM staging?

Does the patient have clear cell RCC?

NO

YES

Management pathway considerations based on risk categorisation
Defined by the risk categorisation process within your Trust.

Low risk of recurrence
Defined by the risk categorisation process within your MDT/Trust.

Intermediate-high or high risk of recurrence or M1 no evidence of disease (NED)
Consider KEYNOTE-564†: Prespecified increased disease risk categories.[3,4]

	Intermediate-high		High		M1 NED
Tumour	pT2	pT3	pT4	Any pT	Any pT
Grade	4 or sarcomatoid	Any	Any	Any	NED after resection
Node	N0	N0	N0	Positive	Any
Metastasis	M0	M0	M0	M0	M1

NO

Performance status (PS) of 0 or 1

YES

Post-surgery surveillance considerations‡
- Assess patient risk for recurrence and frequency of CT/MRI follow-up

Other
- Review current evidence and alternatives to routine post operative surveillance

Post-surgery adjuvant therapy indicated*
- Evaluate adjuvant treatment in eligible RCC patients within 12 weeks of nephrectomy, or within 12 weeks of nephrectomy and metastasectomy/resection of metastatic lesions[3,4]
- Patient will require radiological restaging ≤12 weeks post-surgery

Post-surgery patient discussion
- Have patient preferences and circumstances been considered?
- How and when will the patient be followed up?
- Has the patient received discussion on next steps and support information?

*Post-surgery considerations of adjuvant therapy with KEYTRUDA (pembrolizumab)[3-5]

Patient has not received prior treatment with a checkpoint inhibitor, immunotherapy, or with any other systemic therapy for RCC.

Pembrolizumab as monotherapy should be permanently discontinued for Grade 4 or recurrent Grade 3 immune-related adverse reactions, unless otherwise specified in the Summary of Product Characteristics (SmPC).

NICE Guideline Recommendation:
Pembrolizumab is recommended, within its marketing authorisation, as an option for the adjuvant treatment of renal cell carcinoma at increased risk of recurrence after nephrectomy, with or without metastatic lesion resection, in adults.

Refer to NHS England Blueteq criteria, or devolved nations local prescribing guidelines as appropriate.

Always refer to the SmPC and Risk Minimisation Materials before making prescribing decisions.

KEYTRUDA® (pembrolizumab) as monotherapy is indicated for the adjuvant treatment of adults with renal cell carcinoma at increased risk of recurrence following nephrectomy, or following nephrectomy and resection of metastatic lesions.[2]

Abbreviations: **mg**, milligram; **NED**, no evidence of disease; **Q3W**, once every three weeks.

†KEYNOTE-564: Randomised double-blinded phase 3 trial in patients with resected clear cell renal cell cancer with increased risk of recurrence. Patients were randomised 1:1 (N=994), KEYTRUDA 200 mg IV Q3W (n=496), placebo (saline solution) Q3W (n=498). Primary end point was investigator assessed disease free survival (DFS). Risk categories in KEYNOTE-564 were defined by pathological TNM and Fuhrman grading status.[3,4]

‡For all risk recurrence profiles, functional follow-up, mainly monitoring renal and cardiovascular function, may continue according to specific clinical needs irrespective of the length of oncological follow-up.[1]

Click the link to access **MSD Connect**, an MSD promotional website, which includes information and resources on the KEYNOTE-564 trial and management of RCC patients.

Click the link to access the **UK Prescribing Information**.

References: 1. EAU Guidelines on Renal Cell Carcinoma. 2023. Available at: https://uroweb.org/guidelines/renal-cell-carcinoma. Last accessed July 2025. **2.** Leibovich BC et al. Cancer. 2003;97(7):1663–1671. **3.**Choueiri TK et al. N Engl J Med. 2021;385(8):683–694. **4.** KEYTRUDA® Summary of Product Characteristics. **5.** NICE. Pembrolizumab for adjuvant treatment of renal cell carcinoma. Available at: https://www.nice.org.uk/guidance/ta830/chapter/1-Recommendations. Last accessed July 2025.

Adverse events should be reported. Reporting forms and information can be found at **https://yellowcard.mhra.gov.uk** or search for MHRA Yellow Card in the Google Play or Apple App Store.

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KEYTRUDA® (pembrolizumab)

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