The creation of this resource has been fully funded by MSD and developed in collaboration with Miss. Maxine Tran, Honorary Consultant Urological Surgeon at Royal Free Hospital London and Professor of Urology at UCL; and Dr. Ricky Frazer, Medical Oncology Consultant at Velindre Cancer Centre (VCC) and Honorary Clinical Lecturer at Cardiff University 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**

In recognition of the evolving renal cell carcinoma (RCC) treatment pathway, this resource has been developed to aid decision making within pre- and post-operative MDT meetings to assist in identifying the suitable treatment choices for patients with RCC. The flow chart and content reflect key considerations based on the consulted clinicians experience and available evidence related to the current 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

KEY: CONSIDERATIONS | DECISION AID

**ADULT PATIENTS WITH RCC**

## PRE-SURGERY

### CLINICAL STAGING

**CURRENT CLINICAL STAGING**
- 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 type; evaluation of nuclear grade, sarcomatoid features, vascular invasion, tumour necrosis[1]
- Grade (low grade/high grade)

**Does the patient have clear cell RCC?**

YES

NO → Review current evidence and alternatives to routine post operative surveillance

### PATIENT ELIGIBILITY

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

YES → Review current evidence and alternatives to routine post operative surveillance

NO → If patient is likely to be at increased risk of disease recurrence following surgery, **consider discussion of adjuvant treatment** management in pre-surgical patient consultation*

## POST-SURGERY

(Following radical nephrectomy or partial nephrectomy +/- resection of metastatic lesions)

### CLINICAL STAGING

**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?

### HISTOLOGY AND PATHOLOGY

**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 → Review current evidence and alternatives to routine post operative surveillance

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**

Consider KEYNOTE-564: Prespecified increased disease risk categories[4]

**INTERMEDIATE-HIGH RISK:†**
- pT2 with Grade 4 or sarcomatoid, N0, M0
- pT3, any grade, N0, M0

**HIGH-RISK:†**
- pT4, any grade, N0, M0
- Any pT, any grade with node positive, M0

**M1 NO EVIDENCE OF DISEASE:†**
- Any pT, any N, M1 with no evidence of disease (NED) after resection of both loco-regional and all metastatic lesion(s). Resection had taken place within 1 year of nephrectomy

**ECOG performance status (PS) of 0 or 1**

NO → **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

YES → **CONSIDER POST-SURGERY ADJUVANT THERAPY****
- Consider adjuvant treatment in eligible RCC patients following surgery with an increased risk of recurrence
- 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?

**Abbreviations:** ECOG, Eastern Cooperative Oncology Group; mg, milligram; M0, without distant metastases; M1, with distant metastases; NX, nodes cannot be accessed; N1, nodal involvement; N0, without nodal involvement; NED, no evidence of disease; Q3W, once every three weeks; T0, no evidence of disease; T1a, tumour in kidney <4cm in the greatest dimension; T1b, tumour in kidney is between 4-7cm in the greatest dimension; T2a, tumour in kidney is between 7-10cm in the greatest dimension; T2b, tumour in kidney >10cm in the greatest dimension; T3a, metastases to nearby tissues or veins; T3b, metastases into vena cava but below the diaphragm; T3c, metastases to vena cava above the diaphragm; T4, metastases outside the kidney

***Pre-surgery considerations of adjuvant therapy with KEYTRUDA (pembrolizumab)**
- Initiation is necessary within 12 weeks from the date of nephrectomy or metastasectomy[2,4]
- Urologist and/or MDT member to book CT/MRI scan for restaging post-surgery within timelines for commencing any additional treatment

****Post-surgery considerations of adjuvant therapy with KEYTRUDA (pembrolizumab)**
- Patient has not received prior treatment with a checkpoint inhibitor, immunotherapy, or with any other systemic therapy for RCC
- Always refer to the Summary of Product Characteristics before prescribing decisions and evaluate contraindications or comorbidities to immunotherapy
- Pembrolizumab as monotherapy should be permanently discontinued for Grade 4 or recurrent Grade 3 immune-related adverse reactions, unless otherwise specified in the SmPC[2]
- Consider if initiation is within 12 weeks from the date of nephrectomy or metastasectomy[2,4]
- Refer to NHS England blueteq criteria, or devolved nations local prescribing guidelines appropriately

**Always refer to the Summary of Product Characteristics 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]

Click the link below to access the MSD Connect website which includes promotional information and resources on the KEYNOTE-564 trial and management of RCC patients: Training and resources RCC | KEYTRUDA® (pembrolizumab) | MSD Connect UK

†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.[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]

**References:**

1. EAU Guidelines on Renal Cell Carcinoma. 2023. Available at: https://uroweb.org/guidelines/renal-cell-carcinoma. Last accessed June 2023.
2. KEYTRUDA® Summary of Product Characteristics.
3. Leibovich BC *et al.* Cancer. 2003;97(7):1663-1671.
4. Choueiri TK *et al.* N Engl J Med. 2021;385(8):683–694.

**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. Adverse events should also be reported to Merck Sharp & Dohme (UK) Limited (Tel: 0208 154 8000).**

Access the GB Prescribing Information here

Access the NI Prescribing Information here

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