RAMPART

Eligibility Criteria CRF - Form 02

Version 1.0 25 June 2018

Patient Initials | Date of Birth (dd/mm/yyyy) | Trial Number R

Date Of Randomisation (dd/mm/yyyy)

This CRF should be completed prior to randomisation. For inclusion criteria, tick yes to confirm patient meets the inclusion criteria and for exclusion criteria, tick no to confirm patient does not meet exclusion criteria.

A. Inclusion Criteria

1 **Histologically proven RCC (all cell types are eligible, except for pure oncocytoma, collecting duct, medullary and transitional cell cancer (TCC); no evidence of residual macroscopic disease on post-operative CT scan after resection of RCC. Patients with treated bilateral synchronous RCCs are eligible.....** ☐ No ☐ Yes

2 **At the start of recruitment patients with Leibovich score 3-11 will be eligible for randomisation. MRC CTU will monitor accrual and stop recruiting intermediate risk patients (Leibovich Score 3-5) after three years or when intermediate risk patients contribute 25% of the total accrual target, whichever is earlier. Recruitment of patients with Leibovich Score 6-11 will continue until the accrual target is reached.....** ☐ No ☐ Yes

3 **Patients should have had surgery at least 28 days but no more than 91 days prior to randomisation date...** ☐ No ☐ Yes

4 **Post-operative scans should be performed within 28 days prior to randomisation.....** ☐ No ☐ Yes

5 **WHO Performance Status 0 or 1.....** ☐ No ☐ Yes

6 **Patient has archival FFPE pathology tissue available, and agrees to provide at least one sample (FFPE tumour block from nephrectomy, or a minimum of 10 unstained slides), as well as a baseline EDTA blood sample for future translational research (this is separate to providing consent for TransRAMPART).....** ☐ No ☐ Yes

7 **Adequate normal organ and marrow function**

a) Haemoglobin ≥9.0g/dL (transfusions will be allowed within 2 weeks of randomisation in order to achieve the entry criteria)..... ☐ No ☐ Yes

b) Absolute neutrophil count (ANC) ≥1.5 x 10^9/L (≥1500 per mm^3)..... ☐ No ☐ Yes

c) Platelet count ≥100 x 10^9 (≥100,000 per mm^3)..... ☐ No ☐ Yes

d) Bilirubin ≤1.5 x ULN (this will not apply to subjects with confirmed Gilbert's syndrome (i.e., persistent or recurrent hyperbilirubinemia that is predominantly unconjugated in the absence of haemolysis or hepatic pathology), who will be allowed only in consultation with their physician)..... ☐ No ☐ Yes

e) AST/ALT ≤2.5 x ULN..... ☐ No ☐ Yes

f) Calculated Creatinine Clearance level >40mL/min by Cockcroft Gault formula (using actual body weight)..... ☐ No ☐ Yes

8 **12-lead ECG on which QTcF must be <450 ms. In case of clinically significant ECG abnormalities, including a QTcF value ≥450 ms, two additional 12-lead ECGs should be obtained over a brief period (e.g., 30 minutes) to confirm the finding. Patients are only eligible if a QTcF of <450ms is confirmed.....** ☐ No ☐ Yes

9 **Subjects must be ≥18 years of age.....** ☐ No ☐ Yes

10 **Written informed consent obtained from the patient.....** ☐ No ☐ Yes

11 **Both men and women enrolled in this trial must be in agreement with trial policy on contraception during the treatment phase of the study and for 6 months afterwards. Egg donation, sperm donation and breastfeeding must be avoided.....** ☐ No ☐ Yes

12 **Evidence of post-menopausal status or negative urinary or serum pregnancy test for female pre-menopausal patients. Women will be considered post-menopausal if they have been amenorrheic for 12 months without an alternative medical cause. The following age-specific requirements apply:.....** ☐ No ☐ Yes ☐ N/A

a) Women <50 years of age will be considered post-menopausal if they have been amenorrheic for 12 months or more following cessation of exogenous hormonal treatments and if they have luteinizing hormone and follicle-stimulating hormone levels in the post-menopausal range for the institution or underwent surgical sterilisation (bilateral oophorectomy or hysterectomy)

b) Women ≥50 years of age will be considered post-menopausal if they have been amenorrheic for 12 months or more following cessation of all exogenous hormonal treatments, had radiation-induced menopause with last menses >1 year ago, had chemotherapy-induced menopause with last menses >1 year ago, or underwent surgical sterilisation (bilateral oophorectomy, bilateral salpingectomy, or hysterectomy)

Signature | Printed Name | Date Completed (dd/mmm/yyyy)

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B. Exclusion Criteria

1 **Previous diagnosis of RCC**..... ☐ No ☐ Yes

2 **Metastatic or macroscopic residual disease**..... ☐ No ☐ Yes

3 **Patients with a single pulmonary nodule ≥5mm diameter are not eligible unless the nodule has had a definite benign diagnosis. Patients with multiple small, less than 5 mm nodules may be eligible if nodules have been shown to be radiologically stable for at least 8 weeks**..... ☐ No ☐ Yes

4 **Prior anticancer treatment (other than nephrectomy) for RCC**..... ☐ No ☐ Yes

5 **Any unresolved toxicity of NCI CTCAE Grade ≥2 from previous anticancer therapy with the exception of alopecia, vitiligo, and the laboratory values defined in the inclusion criteria**..... ☐ No ☐ Yes
   a) Patients with Grade ≥2 neuropathy will be evaluated on a case-by-case basis after consultation with the Study Physician
   b) Patients with irreversible toxicity not reasonably expected to be exacerbated by treatment with durvalumab or tremelimumab may be included only after consultation with the Study Physician

6 **History of another primary malignancy except for:**..... ☐ No ☐ Yes
   a) Malignancy treated with curative intent and with no known active disease ≥5 years before the first dose of IP and of low potential risk for recurrence
   b) Adequately treated non-melanoma skin cancer or lentigo maligna without evidence of disease.
   c) Adequately treated carcinoma in situ without evidence of disease

7 **History of leptomeningeal carcinomatosis**..... ☐ No ☐ Yes

8 **Concurrent enrolment in another clinical study, unless it is an observational (non-interventional) clinical study or during the follow-up period of an interventional study**..... ☐ No ☐ Yes

9 **Major surgical procedure (as defined by the investigator) within 28 days prior to the start of treatment. Local surgery of isolated lesions for palliative intent is acceptable**..... ☐ No ☐ Yes

10 **Current or prior use of immunosuppressive medication within 14 days before the first dose of durvalumab or tremelimumab, with the exceptions of intranasal and inhaled corticosteroids or systemic corticosteroids at physiological doses, which are not to exceed 10mg/day of prednisone, or an equivalent corticosteroid**..... ☐ No ☐ Yes

11 **Active or prior documented autoimmune or inflammatory disorders (including inflammatory bowel disease [e.g., colitis or Crohn's disease], diverticulitis [with the exception of diverticulosis), systemic lupus erythematosus, Sarcoidosis syndrome, or Wegener syndrome [granulomatosis with polyangiitis, Graves' disease, rheumatoid arthritis, hypophysitis, uveitis, etc.]). The following are <u>exceptions</u> to this criterion:**..... ☐ No ☐ Yes
   a) Patients with vitiligo or alopecia
   b) Patients with hypothyroidism (e.g., following Hashimoto syndrome) stable on hormone replacement
   c) Any chronic skin condition that does not require systemic therapy
   d) Patients without active disease in the last 5 years may be included but only after consultation with the RAMPART Trial Management Team.
   e) Patients with coeliac disease controlled by diet alone

12 **A history of immunodeficiency syndrome. Please consult the MRC CTU on an individual basis if there is any uncertainty**..... ☐ No ☐ Yes

13 **History of allogeneic organ transplant**..... ☐ No ☐ Yes

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B. Exclusion Criteria - continued

14 **Uncontrolled intercurrent illness including, but not limited to:** ☐ No ☐ Yes
a) Ongoing or active infection
b) Symptomatic congestive heart failure
c) Uncontrolled hypertension
d) Unstable angina pectoris
e) Uncontrolled cardiac arrhythmia
f) Active peptic ulcer disease or gastritis
g) Active bleeding diatheses
h) Psychiatric illness or social situations that would limit compliance with study requirements or compromise the ability of the subject to give written informed consent

15 **Active infection including:** ☐ No ☐ Yes
a) Tuberculosis (clinical evaluation that includes clinical history, physical examination and radiographic findings, and TB testing in line with local practice)
b) Hepatitis B (known positive HBV surface antigen [HBsAg] result)
c) Hepatitis C
d) Human immunodeficiency virus (positive HIV 1/2 antibodies). Patients with a past or resolved HBV infection (defined as the presence of hepatitis B core antibody [anti-HBc] and absence of HBsAg) are eligible.
Note: Patients positive for hepatitis C (HCV) antibody are eligible only if polymerase chain reaction is negative for HCV RNA

16 **Receipt of live attenuated vaccine within 30 days prior to the start of treatment.** *Note. Patients, if enrolled, should not receive live vaccine while receiving investigational product and up to 30 days after the last dose of investigational product* ☐ No ☐ Yes

17 **Pregnant or breast feeding patients** ☐ No ☐ Yes

18 **Any condition that, in the opinion of the investigator, would interfere with evaluation of study treatment or interpretation of patient safety or study results** ☐ No ☐ Yes

19 **Known allergy or hypersensitivity to durvalumab or tremelimumab, or any of their excipients** ☐ No ☐ Yes

20 **Previous investigational product assignment in the present study** ☐ No ☐ Yes

C. Patient Information

1 ☐☐☐/☐☐☐ mmHg **Blood pressure**
systolic *diastolic*

2 ☐☐☐ cm **Height**

3 ☐☐☐.☐ kg **Weight**

4 **Gender**
☐ Female
☐ Male
☐ Other, please specify: .....

5 **Race**
☐ American Indian or Alaska Native
☐ Asian
☐ Black or African American
☐ Native Hawaiian or Other Pacific Islander
☐ White

6 **Ethnicity**
☐ Hispanic or Latino
☐ Not Hispanic or Latino

ⓘ Race must be self reported by the patient. If applicable, the patient can belong to more than one race group.

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Date Of Randomisation [d][d]/[m][m][m]/[y][y][y][y]

D. Risk Factors

1 **Has the patient ever smoked?**
- ☐ No — ☞ *go to question D6*
- ☐ Yes, currently a smoker
- ☐ Yes, previously a smoker

2 [ ][ ] **At what age did the patient start smoking?**

3 [ ][ ] **At what age did the patient stop smoking?**

4 **Method(s) of smoking** (please indicate yes or no for each)
- ☐ No ☐ Yes Cigarettes
- ☐ No ☐ Yes Cigars
- ☐ No ☐ Yes Pipes
- ☐ No ☐ Yes e-Cigarettes/Vaping

5 [ ][ ][ ] **Average number smoked daily**

6 [ ][ ][ ] units **Average weekly alcohol consumption**

E. Primary Tumour

1 [d][d]/[m][m][m]/[y][y][y][y] **Date of renal cell carcinoma (RCC)**

2 **Clinical presentation**
- ☐ Incidental finding (no symptoms referable to the primary renal tumour)
- ☐ Symptoms considered related to the primary renal tumour
- ☐ Systemic symptoms considered related to RCC
- ☐ Systemic and local symptoms considered related to RCC
- ☐ Other clinical presentation, please specify:

F. Leibovich Score Components

1 **Pathological T category**
- ☐ pT1a
- ☐ pT1b
- ☐ pT2
- ☐ pT3/pT4

2 **Regional lymph node status**
- ☐ pNx/pN0
- ☐ pN1/pN2

3 [ ][ ][ ] mm **Maximum diameter of tumour**

4 **Tumour size**
- ☐ < 10 cm
- ☐ ≥ 10 cm

5 **Nuclear grade**
- ☐ 1
- ☐ 2
- ☐ 3
- ☐ 4

6 **Is there histological tumour necrosis?**
- ☐ No
- ☐ Yes

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G. Inpatient & Outpatient Visits (please record all visits from the 4 weeks prior to randomisation, if no visits write "00")

ⓘ **Non-Trial Visits** (only include visits related to patient's renal cell carcinoma)

✔ **Report:**
GP visits, outpatient visits, any hospital visits or admissions related to patient's RCC.

✕ **Do not report:**
Any GP visits, outpatient visits, hospital visits or admissions that do not relate to patient's RCC.
Any visits where patients are prepared or receive non-trial treatment for RCC.

How many **nights** has the patient spent in:

1 **Intensive therapy/care units**

2 **HDU department**

3 **General/medical/surgical ward**

4 **Medical oncology**

How many **days** has the patient spent in:

5 **An outpatient clinic**

6 **Surgical day unit**

7 **Accident & emergency**

8 **Investigation or treatment as a day patient**

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