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Renal Adjuvant Multiple Arm Randomised Trial (RAMPART)

Submission date 22/09/2017	**Recruitment status** No longer recruiting	[X] Prospectively registered [X] Protocol [_] Statistical analysis plan [_] Results [_] Individual participant data [X] Record updated in last year
Registration date 02/10/2017	**Overall study status** Ongoing	
Last Edited 11/02/2026	**Condition category** Cancer	

Plain English summary of protocol
https://www.cancerresearchuk.org/about-cancer/find-a-clinical-trial/a-trial-looking-at-durvalumab-and-tremelimumab-for-kidney-cancer-rampart#undefined (added 13/08/2020)

Background and study aims
Renal cell carcinoma is a type of kidney cancer that starts from the kidneys. It is the 8th most common cancer in the UK and an increase of new cases of 2% has been seen in the last 20 years. About half of the new cases of kidney cancer are among people aged 70 and over. Patients whose disease has not spread outside the kidneys typically have surgery to remove a part or all of their kidney (called a partial or radical nephrectomy). After surgery, patients are seen by their doctor with regular check-ups to look for signs of the cancer coming back or spreading to other parts of the body. This is generally called ‘active monitoring’ or ‘active surveillance’. Unfortunately, it is estimated that the cancer will return in 30-40% of the patients who have undergone surgery. Many studies have been carried out to find if a new treatment after surgery might slow the cancer coming back or prevent it from coming back altogether. However, to date no treatment is available. Immunotherapy is a type of cancer treatment that ‘wakes up’ the patient’s own immune system so it can fight the cancer. New drugs which act in this way have worked well in patients with skin cancer (melanoma), lung cancer and in patients witch kidney cancer that has spread outside the kidney. This study is looking at two new immunotherapy treatments. The aim is to find out whether taking one drug (durvalumab) or a combination of two drugs (durvalumab and tremelimumab) for one year can prevent or delay kidney cancer from coming back compared to the current standard of care (active monitoring after surgery). Durvalumab is currently being tested (alone or in combination with other drugs) in many types of cancer. Tremelimumab is also being tested in different types of cancer.

Who can participate?
Patients aged 18 and over with renal cell carcinoma

What does the study involve?
Participants are randomly allocated to one of three groups. Group A is actively monitored for 1 year after nephrectomy. Group B is treated with durvalumab (1500 mg) administered 4 weekly for 1 year (13 cycles maximum) by intravenous infusion (into a vein). Group C is treated with durvalumab administered as per group B (13 cycles maximum) and tremelimumab on day 1 and

week 4 visits (2 cycles) by intravenous infusion. The treatment duration is 1 year maximum. Once treatment is completed, participants are seen at week 52, then 3 monthly up to the end of year 3, 6-monthly up to year 5 and annually thereafter.

What are the possible benefits and risks of participating?
If positive, the results of the study will change the current standard of care for the treatment of kidney cancer after surgery. Like all drugs, these treatments have side effects and participants have regular blood tests and scans and appointments with their study doctor and nurse.

Where is the study run from?
Participating centres are being confirmed, list of centres to be updated in due course (Australia, France, UK and USA)

When is the study starting and how long is it expected to run for?
October 2018 to June 2030

Who is funding the study?
1. Kidney Cancer UK
2. AstraZeneca (UK)
3. Medical Research Council (UK)

Who is the main contact?
1. Mr Ben Smith
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2. Ms Hanna Bryant
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Contact information

Type(s)
Public

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Type(s)
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Contact name
Ms Hanna Bryant

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Additional identifiers

Clinical Trials Information System (CTIS)
2017-002329-39

ClinicalTrials.gov (NCT)
NCT03288532

Protocol serial number
RE06

Study information

Scientific Title
An international investigator-led phase III multi-arm multi-stage multi-centre randomised controlled platform trial of adjuvant therapy in patients with resected primary renal cell carcinoma (RCC) at high or intermediate risk of relapse

Acronym
RAMPART

Study objectives
Durvalumab is able to prevent tumour relapse by the inhibition of the programmed cell death 1 (PD-1)/ programmed death ligand 1 (PD-L1) pathway, which plays a critical role in tumour immune evasion.
Combination treatment with anti-CTLA4 agent tremelimumab increases immune response and anti-tumour activity.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 07/01/2018, London Riverside Ethics Committee (Level 3 Block B, Whitefriars, Lewins Mead, Bristol BS1 2NT; +44 (0)207 1048340, riverside.rec@hra.nhs.uk), ref 17/LO/1875

Study design
Multi-centre multi-arm multi-stage unblinded randomised controlled platform trial

Primary study design
Interventional

Study type(s)

Treatment

Health condition(s) or problem(s) studied
Resected primary renal cell carcinoma

Interventions
The trial will initially open with 3 research arms. The allocation ratio will be 3:2:2 with patients assigned centrally through block randomisation with a small number of clinically important stratification factors.

Arm A: The control arm is active monitoring after nephrectomy (observation through radiological means) for 1 year
Arm B: Durvalumab (1500 mg) administered 4 weekly for 1 year (13 cycles maximum) via intravenous infusion
Arm C: Durvalumab (1500 mg) administered as per arm B (13 cycles maximum) and tremelimumab (75 mg) on day 1 and week 4 visits (2 cycles) via intravenous infusion

The treatment duration is 1 year maximum. Once treatment is completed, patients will be seen at week 52, then 3 monthly up to the end of year 3, 6-monthly up to year 5 and annually thereafter.

Intervention Type
Drug

Phase
Phase III

Drug/device/biological/vaccine name(s)
Durvalumab, tremelimumab

Primary outcome(s)
1. Disease Free Survival (DFS), defined as the interval from randomisation to first evidence of local recurrence, new primary RCC, distant metastases, or death from any cause, whichever occurs first, measured using data collected from Case Report Forms (CRFs) at one timepoint

Updated 11/02/2026. Previous primary outcome:
1. Disease-Free Survival (DFS) will be assessed via radiological assessments through CT scans. DFS is defined as the interval from randomisation to first evidence of local recurrence, new primary RCC, distant metastases or death from any cause, whichever occurs first. All CT scans received will be further assessed by an independent review panel to ensure that progression has been reported correctly. Primary analysis for DFS will be carried out when:
Arm C vs Arm A
276 control arm events (approx 6.25 years) have occurred
Arm B vs Arm A
416 control arm events (approx 10.75 years) have occurred
DFS Interim analysis will be carried out at the following timepoints:
Arm B vs Arm A
Interim analysis 1 (overwhelming and lack-of-benefit) when 197 control arm events have occurred (approx 4.75 years)
Interim analysis 2 (overwhelming and lack-of-benefit) when 277 control arm events have occurred (approx 6.25 years)

Interim analysis 3 (overwhelming benefit) when 332 control arm events have occurred (approx 8 years)
Arm C vs Arm A:
Interim analysis 1 (overwhelming benefit and lack-of-benefit) when 198 control arm events have occurred (approx 4.75 years)

2. Overall Survival (OS) is another co-primary endpoint. OS is defined as all cause mortality, the time from randomisation to death from any cause (including RCC). For UK sites, survival status will also be collected against national mortality registers. Comparison of overall survival for Arm B vs Arm A will be carried out at approximately 20.5 years after trial commencement (triggered by 344 control arm OS events). For Arm C vs Arm A, overall survival will be assessed at approximately 13.25 years after trial commences (triggered by 238 control arm OS events)

Key secondary outcome(s))

1. Overall Survival (OS), defined as all-cause mortality, is the time from randomisation to death from any cause (including RCC) measured using data collected from Case Report Forms (CRFs) at one time point

2. Metastasis-free survival (MFS), defined as the interval from randomisation to first evidence of metastasis or death from RCC, via radiological means (CT scan with contrast) measured using data collected from CRFs at one time point

3. RCC-specific survival time, defined as the time from randomisation to death from RCC, measured using data collected from trial-specific CRFs at one time point

4. Quality of life measured using quality of life questionnaires (EQ-5D and QLQ-C30 CRFs) at baseline, week 16, month 15, month 36 visits and at progression (if progression occurs before month 36)

5. Toxicity measured using data collected from the trial-specific CRFs at one time point

6. Patient preferences for adjuvant immunotherapy information measured using the optional PAIR questionnaire at baseline, at the week 12 visit and the month 15 visit, or approximately 3 months after the last treatment visit if the patient stops treatment early

Updated 11/02/2026. Previous secondary outcomes:
Assessment of all secondary outcomes will take place at each follow-up visit at week 52, then 3 monthly up to the end of year 3, 6-monthly up to year 5 and annually thereafter.
1. Metastasis-free survival (MFS), defined as the interval from randomisation to first evidence of metastasis or death from RCC, measured via radiological means (CT scan with contrast)
2. RCC-specific survival time, defined as the time from randomisation to death from RCC, reported on trial-specific CRF
3. Quality of life, measured using quality of life questionnaires (EQ-5D and QLQ-C30 CRFs) at baseline, week 16, month 15, month 36 visits and at progression (if progression occurs before month 36)
4. Toxicity, reported on trial-specific CRF
5. Patient preferences for adjuvant immunotherapy information collected through the optional PAIR questionnaire completed at baseline, at the week 12 visit and the month 15 visit, or approximately 3 months after the last treatment visit if patient stops treatment early

Secondary outcome measures will be assessed after the primary analysis and therefore will be confirmed at a later date

Completion date
30/06/2030

Eligibility

Key inclusion criteria
Current key inclusion criteria as of 11/02/2026:
1. Histologically proven RCC (all cell types of RCC 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
2. At the start of recruitment, patients with a Leibovich score of 3-11 will be eligible for randomisation. MRC CTU at UCL will monitor accrual and stop recruiting intermediate risk patients (Leibovich Score 3-5) once agreed by the RAMPART TMG. Intermediate risk patients will contribute up to 25% of the total accrual target. Recruitment of patients with Leibovich Score 6-11 will continue until the accrual target is reached.
3. Patients with synchronous ipsilateral adrenal metastases will be eligible, provided they are fully resected (adrenal metastectomy) at the time of nephrectomy and there is no evidence of residual macroscopic disease on post-operative CT scans
4. Patients with a single soft tissue metastasis developing at any organ site will be eligible, provided they are fully resected (metastectomy) between 6-24 months after nephrectomy and there is no evidence of residual macroscopic disease on post-metastectomy CT scans
5. Patients should have had surgery (nephrectomy or metastectomy) at least 28 days but no more than 91 days prior to their randomisation date
6. Post-operative scans should be performed within 28 days prior to randomisation
7. Patients with microscopically positive resection margins after radical nephrectomy at the nephrectomy bed, renal vein or inferior vena cava are eligible, provided the post-operative CT scan shows no evidence of residual macroscopic disease
8. WHO Performance Status 0 or 1
9. Patient has archival FFPE pathology tissue available, and agrees to provide at least one sample (FFPE tumour block from nephrectomy and, where applicable, the adrenal metastectomy, or a minimum of 10 unstained slides), as well as baseline CPDA and PAXgene blood samples for future translational research (this is separate to providing consent for TransRAMPART)
10. Adequate normal organ and marrow function
11. Subjects must be ≥18 years of age
12. Written informed consent obtained from the patient
13. Both men and women enrolled in this trial must be in agreement with the trial policy on contraception during the treatment phase of the study and 6 months afterwards. Egg donation, sperm donation and breastfeeding must be avoided.
14. Evidence of post-menopausal status or a negative serum HCG pregnancy test for female pre-menopausal patients. Women will be considered post-menopausal if they have been amenorrhoeic for 12 months without an alternative medical cause. The following age-specific requirements apply:
14.1. Women <50 years of age will be considered post-menopausal if they have been amenorrhoeic for 12 months or more following cessation of exogenous hormonal treatments and if they have luteinising hormone and follicle-stimulating hormone levels in the post-menopausal range for the institution or underwent surgical sterilisation (bilateral oophorectomy or hysterectomy)
14.2. Women ≥50 years of age will be considered post-menopausal if they have been amenorrhoeic 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)

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Previous inclusion criteria as of 17/07/2020:
1. Histologically proven RCC (all cell types of RCC 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
2. At the start of recruitment patients with Leibovich score 3-11 will be eligible for randomisation . MRC CTU at UCL 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
3. Patients should have had surgery at least 28 days but no more than 91 days prior to their randomisation date
4. Post-operative scans should be performed within 28 days prior to randomisation
5. Patients with microscopically positive resection margins after radical nephrectomy at the nephrectomy bed, renal vein or inferior vena cava are eligible provided the post-operative CT scan shows no evidence of residual macroscopic disease
6. WHO Performance Status 0 or 1
7. 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)
8. Adequate normal organ and marrow function
8.1. Haemoglobin ≥ 9.0g/dl (transfusions will be allowed within 2 weeks prior to randomisation in order to achieve the entry criteria)
8.2. Absolute neutrophil count (ANC) ≥ 1.5 x 109/l (≥ 1,500 per mm3)
8.3. Platelet count ≥ 100 x 10^9 (≥ 100,000 per mm3)
8.4. 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)
8.5. AST/ALT ≤2.5 x ULN
8.6. Calculated Creatinine Clearance level >40mL/min by Cockcroft Gault formula (using actual body weight)
9. 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
10. Subjects must be ≥ 18 y of age
11. Written informed consent obtained from the patient
12. Both men and women enrolled in this trial must be in agreement with trial policy on contraception (Section 5.8.4) during the treatment phase of the study and 6 months afterwards. Egg donation, sperm donation and breastfeeding must be avoided
13. Evidence of post-menopausal status or negative serum HCG pregnancy test for female pre-menopausal patients. Women will be considered post-menopausal if they have been amenorrhoeic for 12 months without an alternative medical cause. The following age-specific requirements apply:
13.1. Women < 50 y of age will be considered post-menopausal if they have been amenorrhoeic

for 12 months or more following cessation of exogenous hormonal treatments and if they have luteinising hormone and follicle-stimulating hormone levels in the post-menopausal range for the institution or underwent surgical sterilisation (bilateral oophorectomy or hysterectomy)
13.2. Women ≥ 50 y of age will be considered post-menopausal if they have been amenorrhoeic for 12 months or more following cessation of all exogenous hormonal treatments, had radiation-induced menopause with last menses > 1 y ago, had chemotherapy-induced menopause with last menses > 1 y ago, or underwent surgical sterilisation (bilateral oophorectomy, bilateral salpingectomy, or hysterectomy)

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Previous inclusion criteria:
1. Histologically proven RCC (all cell types of RCC 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
2. At the start of recruitment patients with Leibovich score 3-11 will be eligible for randomisation. MRC CTU at UCL 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
3. Patients should have had surgery at least 28 days but no more than 91 days prior to randomisation date
4. Post-operative scans should be performed within 28 days prior to randomisation
5. WHO Performance Status 0 or 1
6. Patient has archival FFPE pathology tissue (FFPE tumour block from nephrectomy, or a minimum of 10 unstained slides) available as well as a baseline EDTA blood sample and agrees to provide a sample for future biomarker testing
7. Adequate normal organ and marrow function:
7.1. Haemoglobin ≥9.0g/dL (transfusions will be allowed within 2 weeks prior to randomisation in order to achieve the entry criteria).
7.2. Absolute neutrophil count (ANC) ≥1.5 x 109/L (≥1500 per mm3)
7.3. Platelet count ≥100 x 109 (≥100,000 per mm3)
7.4. 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)
7.5. AST/ALT ≤2.5 x ULN.
7.6. Calculated Creatinine Clearance level >40mL/min by Cockcroft Gault formula (using actual body weight)
8. 12-lead ECG on which QTcF must be <470 ms. In case of clinically significant ECG abnormalities, including a QTcF value >470 ms, two additional 12-lead ECGs should be obtained over a brief period (e.g., 30 minutes) to confirm the finding
9. Current weight ≥ 40kg
10. Subjects must be ≥18 years of age
11. Written informed consent obtained from the patient
12. 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 9 months afterwards. Egg donation, sperm donation and breastfeeding must be avoided
13. 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 amenorrhoeic for 12 months without an alternative medical cause. The following age specific requirements apply:

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

Participant type(s)
Employee, Health professional, Patient

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
18 years

Upper age limit
99 years

Sex
All

Total final enrolment
790

Key exclusion criteria
Current key exclusion criteria as of 11/02/2026:
1. Previous diagnosis of RCC
2. Metastatic disease except:
2.1. Synchronous ipsilateral adrenal metastases, which are fully resected at the time of nephrectomy
2.2. A single soft tissue metastasis developing at any organ site that has been fully resected between 6-24 months after radical nephrectomy
3. Macroscopic residual disease following nephrectomy
4. Patients with positive resection margins after partial nephrectomy. If multiple resection margins are taken, the patient will be considered eligible as long as the last margin is negative.
5. Patients with a single pulmonary nodule ≥5mm in 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.
6. Prior anticancer treatment (other than nephrectomy) for RCC
7. Any unresolved toxicity NCI CTCAE Grade ≥2 from previous anticancer therapy with the exception of alopecia, vitiligo, and the laboratory values defined in the inclusion criteria
7.1. Patients with Grade ≥2 neuropathy will be evaluated on a case-by-case basis after consultation with the Study Physician.

7.2. 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
8. Previous invasive or non-invasive malignancy except:
8.1. Basal cell carcinoma, where treatment consisted of resection alone or radiotherapy.
8.2. Low-grade non-muscle-invasive bladder carcinoma where treatment consisted of endoscopic resection alone or with a single installation of intravesical chemotherapy or with BCG treatment.
8.3. Ductal carcinoma in situ of the breast, where treatment consisted of resection alone.
8.4. Cervical carcinoma in situ where treatment consisted of resection alone.
8.5. Previously treated clinically localized low- or intermediate-risk prostate cancer with undetectable PSA after surgery or stable PSA for radiation therapy
8.6. Malignancy treated with curative intent and with no known active disease > 5 years before the first dose of IP and of low potential risk of recurrence
8.7. Other cancers with very low potential of recurrence can be discussed with MRC CTU at UCL, where eligibility will be considered on an individual basis
9. History of leptomeningeal carcinomatosis
10. 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
11. 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
12. 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 10 mg/day of prednisone, or an equivalent corticosteroid
13. 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 exceptions to this criterion:
13.1. Patients with vitiligo or alopecia
13.2. Patients with hypothyroidism (e.g., following Hashimoto syndrome), stable on hormone replacement
13.3. Any chronic skin condition that does not require systemic therapy
13.4. Patients without active disease in the last 5 years may be included, but only after consultation with the RAMPART Trial Management Team
13.5. Patients with coeliac disease controlled by diet alone
14. A history of immunodeficiency syndrome. Please consult the MRC CTU at UCL on an individual basis if there is any uncertainty.
15. History of allogeneic organ transplant.
16. Uncontrolled intercurrent illness including, but not limited to:
16.1. Ongoing or active infection of any kind (patients who are exhibiting symptoms consistent with COVID-19, or who have tested positive, should not be randomised into the study until they are asymptomatic and at least 14 days after a positive test)
16.2. Symptomatic congestive heart failure
16.3. Uncontrolled hypertension
16.4. Unstable angina pectoris
16.5. Uncontrolled cardiac arrhythmia
16.6. Active peptic ulcer disease or gastritis
16.7. Active bleeding diatheses
16.8. Psychiatric illness or social situations that would limit compliance with study requirements or compromise the ability of the subject to give written informed consent
17. Active infection, including:

17.1. Tuberculosis (clinical evaluation that includes clinical history, physical examination and radiographic findings, and TB testing in line with local practice)
17.2. Hepatitis B (known positive HBV surface antigen (HBsAg) result). 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.
17.3. Hepatitis C
17.4. Human immunodeficiency virus (positive HIV 1/2 antibodies).
Note: Patients positive for hepatitis C (HCV) antibody are eligible only if the polymerase chain reaction is negative for HCV RNA.
18. Receipt of live attenuated vaccine within 30 days prior to the start of treatment. Note: Patients, if enrolled, should not receive live vaccines while receiving investigational medicinal product and up to 30 days after the last dose of investigational medicinal product.
19. Pregnant or breastfeeding patients.
20. Any condition that, in the opinion of the investigator, would interfere with evaluation of study treatment or interpretation of patient safety or study results.
21. Known allergy or hypersensitivity to durvalumab or tremelimumab, or any of their excipients.
22. Previous investigational medicinal product assignment in the present study.
23. Clinically significant pneumonitis or fibrosis

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Previous exclusion criteria as of 17/07/2020:
1. Previous diagnosis of RCC
2. Metastatic or macroscopic residual disease
3. Patients with positive resection margins after partial nephrectomy
4. 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.
5. Prior anticancer treatment (other than nephrectomy) for RCC
6. Any unresolved toxicity NCI CTCAE Grade ≥ 2 from previous anticancer therapy with the exception of alopecia, vitiligo, and the laboratory values defined in the inclusion criteria:
6.1. Patients with Grade ≥ 2 neuropathy will be evaluated on a case-by-case basis after consultation with the Study Physician
6.2. 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
7. History of another primary malignancy except for:
7.1. Malignancy treated with curative intent and with no known active disease ≥ 5 y before the first dose of IP and of low potential risk for recurrence
7.2. Adequately treated non-melanoma skin cancer or lentigo maligna without evidence of disease
7.3. Adequately treated carcinoma in situ without evidence of disease
8. History of leptomeningeal carcinomatosis
9. 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
10. 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
11. 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 10 mg/day of prednisone, or an equivalent corticosteroid
12. Active or prior documented autoimmune or inflammatory disorders (including inflammatory

bowel disease [e.g., colitis or Crohn's disease], diverticulitis [with the exception of diverticulitis], systemic lupus erythematosus, Sarcoidosis syndrome, or Wegener syndrome [granulomatosis with polyangiitis, Graves' disease, rheumatoid arthritis, hypophysitis, uveitis, etc]). The following are exceptions to this criterion:
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12.2. Patients with hypothyroidism (e.g., following Hashimoto syndrome) stable on hormone replacement
12.3. Any chronic skin condition that does not require systemic therapy
12.4. Patients without active disease in the last 5 years may be included but only after consultation with the RAMPART Trial Management Team
12.5. Patients with coeliac disease controlled by diet alone
13. A history of immunodeficiency syndrome. Please consult the MRC CTU at UCL on an individual basis if there is any uncertainty
14. History of allogeneic organ transplant
15. Uncontrolled intercurrent illness including, but not limited to:
15.1. Ongoing or active infection of any kind (patients who are exhibiting symptoms consistent with COVID-19, or who have tested positive, should not be randomised into the study until they are asymptomatic and at least 14 days after a positive test)
15.2. Symptomatic congestive heart failure
15.3. Uncontrolled hypertension
15.4. Unstable angina pectoris
15.5. Uncontrolled cardiac arrhythmia
15.6. Active peptic ulcer disease or gastritis
15.7. Active bleeding diatheses
15.8. Psychiatric illness or social situations that would limit compliance with study requirements or compromise the ability of the subject to give written informed consent
16. Active infection including:
16.1. Tuberculosis (clinical evaluation that includes clinical history, physical examination and radiographic findings, and TB testing in line with local practice)
16.2. Hepatitis B (known positive HBV surface antigen (HBsAg) result). 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
16.3. Hepatitis C
16.4. Human immunodeficiency virus (positive HIV 1/2 antibodies). Note: Patients positive for hepatitis C (HCV) antibody are eligible only if polymerase chain reaction is negative for HCV RNA
17. 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 medicinal product and up to 30 days after the last dose of investigational medicinal product
18. Pregnant or breastfeeding patients
19. Any condition that, in the opinion of the investigator, would interfere with evaluation of study treatment or interpretation of patient safety or study results
20. Known allergy or hypersensitivity to durvalumab or tremelimumab, or any of their excipients
21. Previous investigational medicinal product assignment in the present study
22. Clinically significant pneumonitis or fibrosis

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1. Previous diagnosis of RCC
2. Metastatic or macroscopic residual disease
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eligible if nodules have been shown to be radiologically stable for at least 8 weeks
4. Prior anticancer treatment (other than nephrectomy) for RCC
5. Any unresolved toxicity NCI CTCAE Grade ≥2 from previous anticancer therapy with the exception of alopecia, vitiligo, and the laboratory values defined in the inclusion criteria:
5.1. Patients with Grade ≥2 neuropathy will be evaluated on a case-by-case basis after consultation with the Study Physician.
5.2. 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. Prior malignancy which in the opinion of the investigator has an estimated risk of recurrence in 5 years greater than 5%
7. History of leptomeningeal carcinomatosis
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
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
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 10 mg/day of prednisone, or an equivalent corticosteroid
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 exceptions to this criterion:
11.1. Patients with vitiligo or alopecia
11.2. Patients with hypothyroidism (e.g., following Hashimoto syndrome) stable on hormone replacement
11.3. Any chronic skin condition that does not require systemic therapy
11.4. Patients without active disease in the last 5 years may be included but only after consultation with the RAMPART Trial Management Team
11.5. Patients with coeliac disease controlled by diet alone
12. A history of immunodeficiency syndrome. Please consult the MRC CTU at UCL on an individual basis if there is any uncertainty.
13. History of allogeneic organ transplant.
14. Uncontrolled intercurrent illness including, but not limited to:
14.1. Ongoing or active infection
14.2. Symptomatic congestive heart failure
14.3. Uncontrolled hypertension
14.4. Unstable angina pectoris
14.5. Uncontrolled cardiac arrhythmia
14.6. Active peptic ulcer disease or gastritis
14.7. Active bleeding diatheses
14.8. 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:
15.1. Tuberculosis (clinical evaluation that includes clinical history, physical examination and radiographic findings, and TB testing in line with local practice)
15.2. Hepatitis B (known positive HBV surface antigen (HBsAg) result)
15.3. Hepatitis C
15.4. 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 medicinal product and up to 30 days after the last dose of investigational medicinal product.
17. Pregnant or breastfeeding patients
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
19. Known allergy or hypersensitivity to durvalumab or tremelimumab, or any of their excipients
20. Previous investigational medicinal product assignment in the present study

Date of first enrolment
15/10/2018

Date of final enrolment
30/03/2023

Locations

Countries of recruitment
United Kingdom

England

Scotland

Wales

Australia

France

Spain

Study participating centre
The Royal Marsden Hospital (Surrey)
Downs Road
Sutton
England
SM2 5PT

Study participating centre
Aberdeen Royal Infirmary
Intensive Care Unit

Aberdeen
Scotland
AB25 2ZN

Study participating centre
Addenbrooke's Hospital
Hills Road
Cambridge
England
CB2 0QQ

Study participating centre
Beatson West of Scotland Cancer Centre
1053 Great Western Road
Glasgow
Scotland
G12 0YN

Study participating centre
Bristol Haematology and Oncology Centre
Horfield Road
Bristol
England
BS2 8ED

Study participating centre
Broomfield Hospital
Court Road
Chelmsford
England
CM1 7ET

Study participating centre
Castle Hill Hospital
Castle Road
Cottingham
England
HU16 5JQ

Study participating centre
Charing Cross Hospital
Imperial College Healthcare NHS Trust
Fulham Palace Rd
Hammersmith
London
England
W6 8RF

Study participating centre
Cheltenham General Hospital
Sandford Road
Cheltenham
England
GL53 7AN

Study participating centre
The Christie
Wilmslow Road
Manchester
England
M20 4BX

Study participating centre
Churchill Hospital
Oxford University Hospitals NHS Foundation Trust
Old Road
Headington
Oxford
England
OX3 7LE

Study participating centre
Clatterbridge Cancer Centre
Clatterbridge Road
Bebington
Wirral
England
CH63 4JY

Study participating centre

Colchester General Hospital
Turner Road
Colchester
England
CO4 5JL

Study participating centre
Glan Clwyd Hospital
Rhuddlan Rd
Rhyl
Wales
LL18 5UJ

Study participating centre
Guy's Hospital
Great Maze Pond
London
England
SE1 9RT

Study participating centre
Leicester Royal Infirmary
Infirmary Square
Leicester
England
LE1 5WW

Study participating centre
Mount Vernon Hospital
Rickmansworth Road
Northwood
England
HA6 2RN

Study participating centre
Nottingham University Hospital
Hucknall Road
Nottingham
England
NG5 1PB

Study participating centre
Queen Alexandra Hospital
Southwick Hill Road
Cosham
England
PO6 3LY

Study participating centre
Raigmore Hospital
Old Perth Rd
Inverness
Scotland
IV2 3UJ

Study participating centre
Royal Bournemouth Hospital
Castle Lane
Bournemouth
England
BH7 7DW

Study participating centre
Royal Free Hospital
Pond Street
London
England
NW3 2QG

Study participating centre
Scunthorpe General Hospital
Cliff Gardens
Scunthorpe
England
DN15 7BH

Study participating centre
Southend University Hospital
Prittlewell Chase
Southend-on-Sea

England
SS0 0RY

Study participating centre
South Tyneside District Hospital
Harton Ln
South Shields
England
NE34 0PL

Study participating centre
St Bart's Hospital
West Smithfield
London
England
EC1A 7BE

Study participating centre
St James University Hospital
Beckett Street
Leeds
England
LS9 7TF

Study participating centre
Sunderland Royal Hospital
Kayll Rd
Sunderland
England
SR4 7TP

Study participating centre
Torbay District Hospital
Lowes Bridge
Torquay
England
TQ2 7AA

Study participating centre

Velindre Cancer Centre
Velindre Road
Cardiff
Wales
CF14 2TL

Study participating centre
Western General Hospital
Crewe Road South
Edinburgh
Scotland
EH4 2XU

Study participating centre
Weston Park Hospital
Whitham Road
Sheffield
England
S10 2SJ

Study participating centre
Ysbyty Gwynedd
Penrhosgarnedd
Bangor
Wales
LL57 2PW

Sponsor information

Organisation
University College London

ROR
https://ror.org/02jx3x895

Funder(s)

Funder type
Industry

Funder Name
Kidney Cancer UK

Funder Name
AstraZeneca

Alternative Name(s)
AstraZeneca PLC, Pearl Therapeutics, AZ

Funding Body Type
Government organisation

Funding Body Subtype
For-profit companies (industry)

Location
United Kingdom

Funder Name
Medical Research Council

Alternative Name(s)
Medical Research Council (United Kingdom), UK Medical Research Council, Medical Research Committee and Advisory Council, MRC

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan
The RAMPART Trial Management Team should be contacted in the first instance with any data release requests (mrcctu.rampart@ucl.ac.uk). Review of the request will be then escalated to the Trial Management Group and TSC for final approval. MRC CTU SOP on Data Sharing will be followed for the review and release process. Requests to release control arm data will be considered at any point during the trial but data release requests for the entire dataset (including treatment arms) will not be granted until the primary end-points have been reached

and published. Consent will be obtained by patients prospectively and data release is subject to successful execution of the relevant contract.

IPD sharing plan summary

Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol article		01/09/2021	21/09/2021	Yes	No
Protocol article		01/09/2021	21/09/2021	Yes	No
HRA research summary			28/06/2023	No	No
Study website	Study website	11/11/2025	11/11/2025	No	Yes