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MRC Clinical Trials Unit at UCL

Smarter Studies
Global Impact
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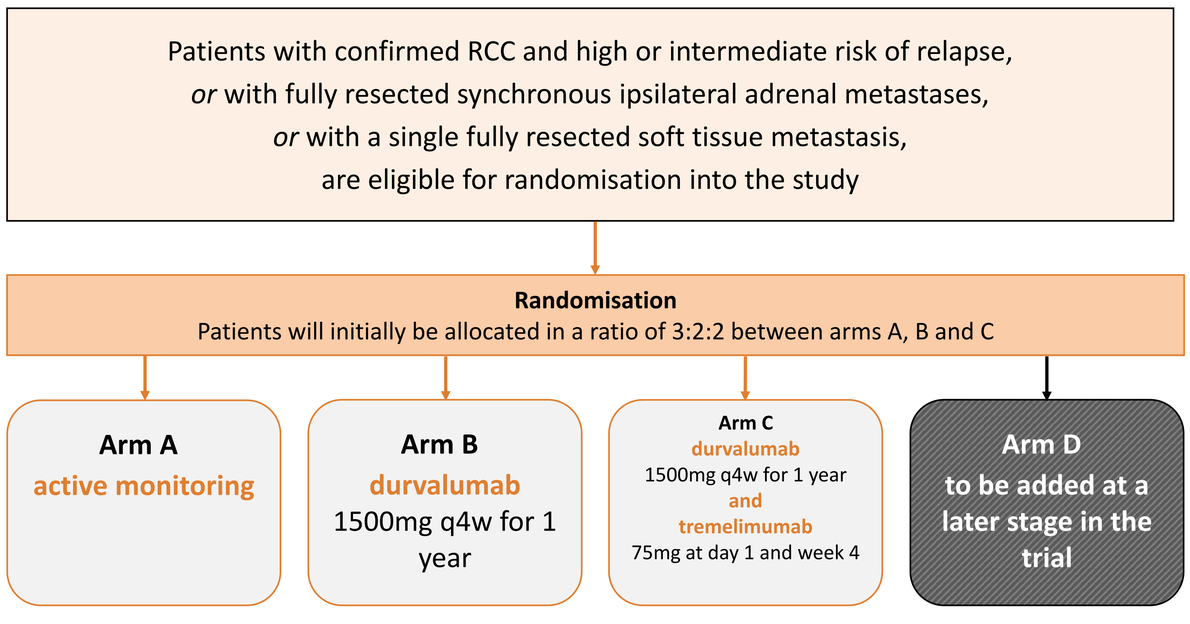
Adopt to Adapt: Keeping the RAMPART Trial on Track in the COVID-19 Era

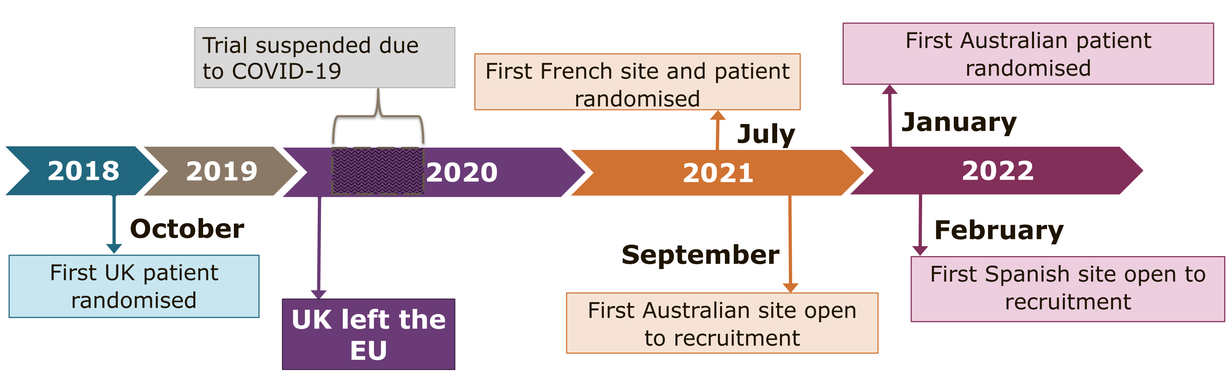
Introduction

RAMPART is an international, UCL-led, MAMS platform trial investigating the efficacy of immune checkpoint inhibitors after nephrectomy in patients with renal cancer.



Challenges caused by COVID-19

- Trial suspension at a time when many UK sites just coming on board
- Slow re-start of recruitment in UK and slower launch of international sites (also affected by the UK leaving the EU)
- Potential concern about sites' ability to comply with treatment and outcome assessment
- Consequent delays to timing of interim and final analyses



Methods

Steps to get the trial back on track

- Clear communication with sites
- E-consent and remote assessments (where possible)
- Collection of critical data, related to the primary outcome (CT scans): refined CRFs to only collect necessary data

Re-Randomisation of Arm A Patients

Arm A patients with a single metastasis within 6-24 months of their initial surgery may wish to be re-considered for randomisation. There is no restriction on what treatment RAMPART participants can have once they have experienced a DFS event, and many may go on to receive immunotherapy off trial. These patients are effectively no different to patients who decide not to take part in RAMPART after nephrectomy, but subsequently develop a single metastasis and then decide to take part.

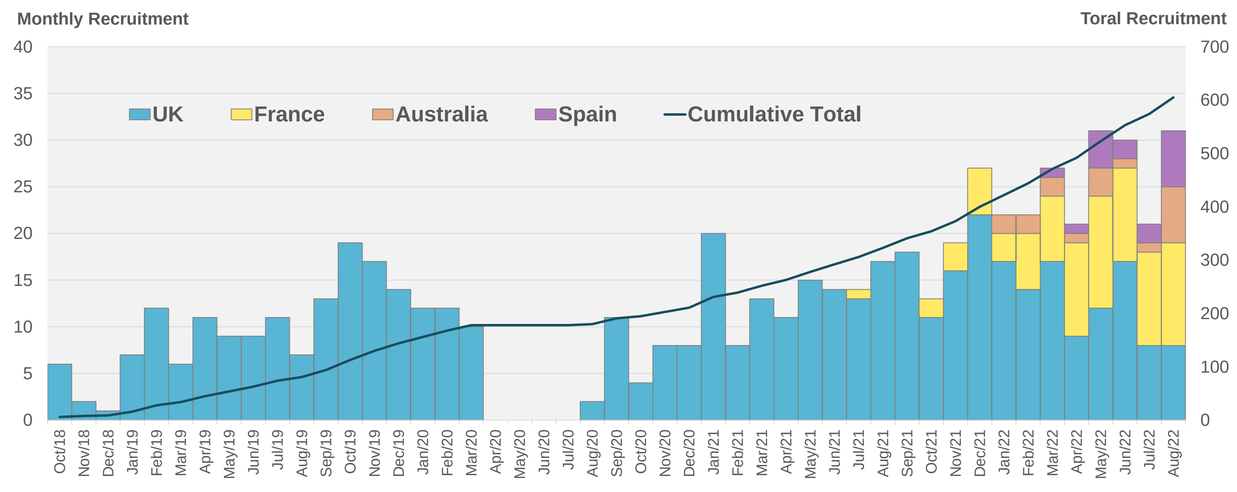
Three conditions suggested for re-randomisation to be valid:

1. Patients are only eligible for re-randomisation when the follow-up period from their previous randomisation is complete – met in RAMPART for DFS
2. Randomisations for the same patient are performed independently for each randomisation period – met in RAMPART
3. The treatment effect is constant across all randomisation periods. This implies a patient should expect the same treatment effect each time they are randomised – sufficiently met in RAMPART

Despite some support, the RAMPART TMG decided against allowing second randomisation (June 2022).

Results

Patient recruitment



External Data: Pembrolizumab (similar agent to Durvalumab)
KEYNOTE-564, testing pembrolizumab against placebo, reported beneficial results on DFS (HR = 0.63 95% C.I. (0.50, 0.80), The Lancet Oncology Vol.23, September 2022)

Next challenge: NICE decision on reimbursement of pembrolizumab in England and Wales - expected on 28th September 2022

Updated Analysis timelines

Accrual Rate (patients per month)	Target HR	Primary Analysis B vs A	Primary Analysis C vs A
	HR_{BvsA} = 0.75, HR_{CvsA} = 0.70	Apr2029 (Protocol)[1] Dec2035 (Revised)[2]	Dec2024 (Protocol) Oct2026 (Revised)
Calculations based on actual accrual rates, realistic projections and updated target effect sizes			
20	HR_{BvsA} = 0.70, HR_{CvsA} = 0.65	Sep2027	Mar2026
	HR_{BvsA} = 0.70, HR_{CvsA} = 0.60	Sep2027	Dec2024
30	HR_{BvsA} = 0.70, HR_{CvsA} = 0.65	Dec2027	Jun2025
	HR_{BvsA} = 0.70, HR_{CvsA} = 0.60	Jun2026	Jun2024
40	HR_{BvsA} = 0.70, HR_{CvsA} = 0.65	Jun2026	Dec2024
	HR_{BvsA} = 0.70, HR_{CvsA} = 0.60	Jun2026	Mar2024

1: Original timelines, prior to starting the trial; 2: Updated timelines based on original target effect sizes and actual RAMPART accrual rates

We updated timeline projections with the observed recruitment figures and more realistic future projections. We used nstage and artpep in Stata to obtain the required control arm events for each analysis and the timings of analyses respectively. The "updated" timelines raise concerns about timeliness of reporting / potential relevance of results.

Based on other adjuvant RCC trials we investigated different targeted effect sizes for each comparison and their impact on analysis timelines. Next steps for RAMPART are under discussion.

- ❑ **Impact of COVID-19 has been substantial and recovery in the UK has been slow**
- ❑ **Adaptations such as remote assessments and re-randomisation were implemented or considered to aid the trial's recovery**
- ❑ **Changes to targeted effect sizes are being considered to aid the timeliness of reporting**