<table>
<thead>
<tr>
<th>Title</th>
<th>Type</th>
<th>Phase</th>
<th>Description</th>
<th>Exclusion criteria</th>
</tr>
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<tr>
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<td>Real</td>
<td>II/III</td>
<td>A randomised, parallel group, phase II/III trial to compare the efficacy and safety of Pembrolizumab (Pemb) versus standard chemotherapy in the treatment of patients with locally advanced or metastatic malignant pleural mesothelioma (MPM).</td>
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## Malignant Pleural Mesothelioma

### Study Title
A Phase I/IIA Study to Assess Safety, Tolerability and Preliminary Activity of the Combination of FAK (Defactinib) and PD-1 (Pembrolizumab) inhibition in patients with advanced solid malignancies

### Description
To compare the effectiveness and safety of a new treatment approach versus standard care for patients with Malignant Pleural Mesothelioma (MPM). The study aims to assess whether a new combination of FAK and PD-1 inhibitors can improve outcomes for patients with MPM.

### Eligibility Criteria
- **Inclusion Criteria**
  - Histological diagnosis of unresectable Malignant Pleural Mesothelioma (MPM);
  - Patients with, at least, a performance status of 0, 1, 2, or 3 (ECOG);
  - The last platinum chemotherapy dose was administered at least 4 weeks prior to the start of the study.

- **Exclusion Criteria**
  - Patients with previous participation in an interventional clinical trial, including Co-enrolment in another interventional clinical trial.
  - Clinically active cancer other than mesothelioma.
  - Leptomeningeal metastases.
  - Central nervous system (CNS) metastases.
  - Hypersensitivity to defactinib (VS-6063), pembrolizumab (MK-3475) or excipients (including L-histidine, glucose, sucrose, sorbitol, acetic acid, sodium metabsulphite).
  - Replacement therapy (e.g. physiologic corticosteroid replacement therapy for adrenal or pituitary dysfunction).

### Treatment Route
IV pembrolizumab

### Sponsor
Royal Brompton and Harefield NHS Foundation Trust

### Contact
Anna Bibby (PI) - anna.bibby@bristol.ac.uk

### Other protocol defined inclusion criteria
- Other severe or uncontrolled systemic diseases (e.g. uncontrolled hypertension, recent myocardial infarction, active brain metastases).
- Prior radiotherapy to more than 50% of the bone marrow.
- Patients with prior non-platinum based systemic antineoplastic therapy, including systemic cytokines or vaccines.

### Other protocol defined exclusion criteria
- Centrally located tumours with radiographic evidence of extracapsular extension.
- Clinically active cancer other than mesothelioma.

### Recruitment
Royal Brompton and Harefield NHS Foundation Trust

### Phase
Phase I/IIA

### Allocation
Randomised to either:
- (extended) pleurectomy versus no (extended) pleurectomy
- VAT-PD versus IPC

### Randomisation
1:1 randomised trial comparing (extended) pleurectomy decortication - Beatson, Leeds, Leicester, Manchester, North Bristol Trust, and Wythenshaw.

### Comparator

### Treatment/study schedule
- 2 cycles chemotherapy followed by surgery/ no surgery,
- 2 cycles chemotherapy alone with respect to overall survival.

### Treatment units
- Beatson West我相信, Leeds, Leicester, Sheffield, St. Bartholomews.
- Mount Vernon (Northwood)
- Queen Elizabeth University Hospital (Glasgow)
- GOSH (London)
- St. James’s (Leeds)
- Royal Papworth (Cambridge)

### Trial duration
18 months

### Study assessments visits
- At routine visit/ phone call/ postal.

### Quality of life
- We will also investigate the feasibility of undertaking a cost-utility analysis of any symptom improvements.

### Symptom management
- We will also investigate the feasibility of developing the symptom questionnaire and self-care module.

### Therapies
- Aims to evaluate activity in terms of progression-free survival (PFS) and overall survival (OS) for patients with unresectable Malignant Pleural Mesothelioma (MPM).

### Side Effects
- Patients may experience side effects such as fatigue, nausea, and insomnia.

### Patient information
- To collect information about patients and their experience of using the system.

### Landmark
- To evaluate the feasibility of undertaking a cost-utility analysis of any symptom improvements.