<table>
<thead>
<tr>
<th>Title</th>
<th>Type</th>
<th>Sponsor</th>
<th>Drug companies involved</th>
<th>Principal investigator</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>PROMISE-Meso</td>
<td>Biostudy</td>
<td>Phase III</td>
<td>Phase III</td>
<td>Dr. Kevin Blyth</td>
<td>N/A – not a drug trial but analogous to a phase I/II drug study.</td>
</tr>
</tbody>
</table>

**Inclusion criteria**

- Age >18 years
- Known alcohol or drug abuse.
- Known to be serologically positive for hepatitis B virus or hepatitis C virus indicating acute or chronic infection.
- History of severe hypersensitivity reactions to other monoclonal antibodies.
- Prior treatment with first-line standard platinum-based chemotherapy for metastatic malignant pleural mesothelioma.
- Patients who have received superficial photon or electron beam radiotherapy and where there is concern that the dose of radiotherapy is more effective for pain than traditional methods of radiotherapy delivery which limit the dose delivered to the heart, lung and bone marrow.
- Women of child-bearing potential must use an effective method of contraception for 30 days prior to randomisation and throughout the trial.
- Patients with a life expectancy of at least 2 years prior to study entry AND no additional therapy is required during the study period. To have an expected life of at least 2 years.
- Prior maintenance therapy (e.g. avastin) is allowed and will not count as a line of therapy.
- Known alcohol or drug abuse.

**Exclusion criteria**

- Patients with known or suspected allergy to pembrolizumab, any other monoclonal antibodies, corticosteroids or immunosuppressive agents.
- Patients with active interstitial lung disease or confirmed pleural or pericardial effusions.
- Active or previous malignancy other than melanoma or breast carcinoma of the skin or superficial soft tissue (fibrosarcoma, liposarcoma, angiosarcoma).
- Women of child-bearing potential who are pregnant or breast feeding.
- Patients with a history of severe hypersensitivity reactions to other monoclonal antibodies.
- Patients with active interstitial lung disease or confirmed pleural or pericardial effusions.
- Patients with a history of severe hypersensitivity reactions to other monoclonal antibodies.

**Treatment arm:**

- **Control arm – standard chest drain insertion and talc slurry pleurodesis following current standard practice.**
- **Intervention arm – large volume pleural aspiration with concurrent digital pleural aspiration MRI scans to address additional secondary research questions.**

**Methods of radiotherapy delivery which limit the dose delivered to the heart, lung and bone marrow.**

- Patients will be randomised 3:1 to standard chest drain insertion and talc slurry pleurodesis following current standard practice or large volume pleural aspiration with concurrent digital pleural aspiration MRI scans to address additional secondary research questions.

**Randomisation and stratification criteria:**

- Randomisation will be stratified to disease stage (stage I vs stage II).
- Intervention arm – large volume pleural aspiration with concurrent digital pleural aspiration MRI scans to address additional secondary research questions.

**Follow-up visits:**

- Visit 1: Baseline visit (up to 1 week before radiotherapy)
- Visit 2: Baseline visit (up to 1 week before radiotherapy)
- Visit 3: Final day of radiotherapy
- Visit 4: 5 weeks post-discharge
- Visit 5: Week 9 after the start of radiotherapy
- Visit 6: 3 months post-discharge
- Visit 7: 6 months post-discharge
- Visit 8: 1 year post-discharge
- Visit 9: 2 years post-discharge

**Intervention:**

- Large volume pleural aspiration with concurrent digital pleural aspiration MRI scans to address additional secondary research questions.

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**Intervention:**

- Large volume pleural aspiration with concurrent digital pleural aspiration MRI scans to address additional secondary research questions.
<table>
<thead>
<tr>
<th><strong>Study Title</strong></th>
<th><strong>Clinical Trial Phase</strong></th>
<th><strong>Sponsor</strong></th>
<th><strong>Centres Opening</strong></th>
<th><strong>Participants</strong></th>
<th><strong>Major Inclusion Criteria</strong></th>
<th><strong>Major Exclusion Criteria</strong></th>
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</thead>
<tbody>
<tr>
<td>ASyMS-meso</td>
<td>Phase 2</td>
<td>Boehringer Ingelheim</td>
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<td>Weekly until cycle 2 then three weekly (Both Phases)</td>
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<td></td>
<td>Boehringer Ingelheim</td>
<td>FAK-PD1</td>
</tr>
</tbody>
</table>

**Major Inclusion Criteria**

- Patient willing to receive either VAT-PD or IPC and attend the follow-up assessment.
- Patient lacks capacity to consent.
- Liver failure (e.g. encephalopathy and/or coagulation end organ failure).
- ECOG status ≥ 2, pre-operative chemotherapy or other treatments, or to live longer.
- Patient willing to receive either VAT-PD or IPC, and therefore eligible for treatment.
- Considered by the clinical team to be suitable and fit enough to undergo (extended) pleurectomy.
- Pleural effusion present (following re-accumulation).
- Lung re-expands fully following pleural fluid drainage i.e. no pleural fluid remaining.
- No evidence of active infection.
- No previous history of infection on the date of randomisation.
- No evidence of Severe acute respiratory syndrome.
- No evidence of active infection in patients with solid organ malignancy.
- Age ≥ 18 years.
- Expected survival of at least 4 months, as assessed by managing physician.
- Other protocol defined inclusion criteria.

**Major Exclusion Criteria**

- Age <18 years old.
- Females: pregnant or lactating.
- Pregnancy or lactation.
- Previous severe or life-threatening skin adverse reaction with other immune-stimulatory anticancer treatment.
- Active autoimmune disease that has required systemic treatment in the past 2 years (i.e. with use of replacement therapy (e.g. physiologic corticosteroid replacement therapy for adrenal or pituitary insufficiency).