<table>
<thead>
<tr>
<th>Study Title</th>
<th>ATOMIC scaffold</th>
<th>Meso</th>
<th>ATOMIC HTT</th>
<th>CONFIRM</th>
<th>C3</th>
<th>BEAT-Meso</th>
<th>MiST</th>
<th>MiST3</th>
<th>MiST4</th>
</tr>
</thead>
<tbody>
<tr>
<td>A multicenter, randomised, double-blind, placebo-controlled phase III study comparing the efficacy and safety of ADI-PEG 20 (a pegylated lipid nanoparticle) with the combination of pemetrexed and cisplatin in subjects with malignant pleural mesothelioma who have not previously received treatment for malignant pleural mesothelioma</td>
<td>Non-randomised</td>
<td>MPM</td>
<td>No</td>
<td>Non-randomised</td>
<td>NCT03610360</td>
<td>NCT02609931</td>
<td>NCT01916620</td>
<td>NCT00537967</td>
<td>NCT00539791</td>
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<tr>
<td>A multicenter, randomized, phase III study of ADI-PEG 20 in combination with pemetrexed for the treatment of patients with previously untreated malignant pleural mesothelioma</td>
<td>Randomised</td>
<td>MPM</td>
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<td>Randomised</td>
<td>NCT03654833</td>
<td>NCT02609931</td>
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<td>NCT00537967</td>
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<tr>
<td>A phase II study of the safety, tolerability and pharmacokinetics of Bemcentinib 400mg loading dose and 200mg maintenance dose in combination with pemetrexed and cisplatin in subjects with untreated malignant pleural mesothelioma</td>
<td>Randomised</td>
<td>MPM</td>
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<td>Randomised</td>
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<tr>
<td>A multicenter, phase II study of pembrolizumab in combination with ADI-PEG 20 for the treatment of previously untreated malignant pleural mesothelioma</td>
<td>Randomised</td>
<td>MPM</td>
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<td>NCT00537967</td>
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**Eligibility Criteria:***

1. Histologically confirmed malignant pleural mesothelioma (PM) with measurable lesions.
2. Patients must have a histological diagnosis of malignant pleural mesothelioma confirmed by a qualified pathologist.
3. Patients must have histologically confirmed malignant pleural mesothelioma (PM) with measurable lesions.
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11. Patients must have histologically confirmed malignant pleural mesothelioma (PM) with measurable lesions.
12. Patients must have histologically confirmed malignant pleural mesothelioma (PM) with measurable lesions.

**Exclusions:***

1. Patients with a history of hematologic malignancy.
2. Patients with a history of non-hematologic malignancy that has been diagnosed in the past 5 years or is currently being treated or previously treated.
3. Patients with a history of non-hematologic malignancy that has been diagnosed in the past 5 years or is currently being treated or previously treated.
4. Patients with a history of non-hematologic malignancy that has been diagnosed in the past 5 years or is currently being treated or previously treated.
5. Patients with a history of non-hematologic malignancy that has been diagnosed in the past 5 years or is currently being treated or previously treated.
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**Treatment Arms:***

1. ADI-PEG 20 + pemetrexed + cisplatin (control arm)
2. Pembrolizumab + ADI-PEG 20 + pemetrexed + cisplatin (experimental arm)

**Randomisation:**

The randomisation will be stratified by histology (epithelial vs. non-epithelial) and by mesothelioma stage (early vs. advanced).

**Study Duration:**

This is a multicenter, randomized, phase III study comparing the combination of ADI-PEG 20 + pemetrexed + cisplatin with pembrolizumab + ADI-PEG 20 + pemetrexed + cisplatin for the treatment of patients with untreated malignant pleural mesothelioma. The primary endpoint is overall survival.

**Data Collection:**

Data will be collected at baseline and at the end of each cycle of treatment, as well as at follow-up visits. The study will be conducted in accordance with the CONSORT (Consolidated Standards of Reporting Trials) guidelines.

**Study Endpoints:**

- Overall survival
- Progression-free survival
- Safety and tolerability
- Pharmacodynamic and pharmacokinetic assessments
- Quality of life
- Other relevant endpoints as determined by the sponsor.

**Trial Management:**

The study is managed by a steering committee, which includes the principal investigator, co-investigators, and a data safety monitoring board (DSMB).

**Patient Recruitment:**

Recruitment is on-going until the target number of patients is reached.

**Recruitment Status:**

The study is currently recruiting in the UK at Addenbrooke's Hospital and Royal Papworth Hospital, as well as in other centers in Europe.

**Contact Information:**

For more information, please contact info@mesothelioma.uk.com.
# Recruitment

<table>
<thead>
<tr>
<th>Site</th>
<th>Contact</th>
<th>廢棄</th>
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<tbody>
<tr>
<td>Bristol University Hospitals NHS Foundation Trust</td>
<td><a href="mailto:mars2-trial@bristol.ac.uk">mars2-trial@bristol.ac.uk</a></td>
<td>N/A</td>
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<tr>
<td>University Hospitals of Leicester</td>
<td><a href="mailto:Natalie.Zahan-Evans@nbt.nhs.uk">Natalie.Zahan-Evans@nbt.nhs.uk</a></td>
<td>N/A</td>
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<tr>
<td>The Christie NHS Foundation Trust</td>
<td><a href="mailto:Anna.bibby@bristol.ac.uk">Anna.bibby@bristol.ac.uk</a> (PI)</td>
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<tr>
<td>The Royal Marsden NHS Foundation Trust</td>
<td><a href="mailto:rintoul.r@rmh.nhs.uk">rintoul.r@rmh.nhs.uk</a></td>
<td>N/A</td>
</tr>
<tr>
<td>St James’s University Hospital, Leeds Teaching Hospitals NHS Trust</td>
<td>St James’s University Hospital, Leeds Teaching Hospitals NHS Trust</td>
<td>N/A</td>
</tr>
</tbody>
</table>

# Logistics


# Recruitment

**Inclusion criteria:**

1. **Age:** 16 years of age or over
2. **Histological diagnosis of unresectable Malignant Pleural Mesothelioma (MPM) who have failed a minimum of first line platinum-based doublet chemotherapy, including frontline rAd IFN, when administered with combination drugs.
3. **Performance status (PS):**
   - ECOG (Eastern Cooperative Oncology Group) 0-2
4. **ECOG performance status:**
   - ECOG PS 0-2
5. **Karnofsky performance status:**
   - Karnofsky PS 60-100
6. **ECOG performance status:**
   - ECOG PS 0-2
7. **Other protocol defined inclusion criteria:**
   - Other protocol defined inclusion criteria

# Exclusion criteria:

- **Other protocol defined exclusion criteria:**
  - Other protocol defined exclusion criteria

# Study

1. **Primary objective:**
   - The primary objective of this study is to compare the overall survival (OS) associated with rAd IFN, when administered with combination drugs.
2. **Secondary objectives:**
   - To compare the effectiveness of the combination of Gemcitabine and Celecoxib in the treatment of patients with malignant pleural mesothelioma.
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# Consent

- **Consent:**
   - Consent will be obtained from all participants before they are included in the study.

# Study design

- **Study duration:**
   - Study duration: 2 years

# Study groups

- **Drug A:**
  - Gemcitabine
  - Celecoxib
- **Drug B:**
  - Gemcitabine
  - Celecoxib

# Study visits

- **Visit 1:**
  - Baseline assessment
- **Visit 2:**
  - Baseline assessment
- **Visit 3:**
  - Final day
- **Visit 4:**
  - Week 5 after the start of radiotherapy
- **Visit 5:**
  - Week 26 after the start of radiotherapy
- **Visit 6:**
  - Week 26 after the start of radiotherapy

# Study outcomes

- **Outcomes:**
  - Overall survival (OS)
  - Progression-free survival
  - Quality of life
  - Resource use

# Study procedure

- **Procedure:**
  - Participants will be randomized to receive the combination of Gemcitabine and Celecoxib.
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# Summary

- **Summary:**
  - A randomised, multicentre trial of Gemcitabine in combination with Celecoxib in patients with malignant pleural mesothelioma who have failed first line platinum-based chemotherapy.
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# Conclusion

- **Conclusion:**
  - The study results will provide insights into the effectiveness of the combination of Gemcitabine and Celecoxib in the treatment of patients with malignant pleural mesothelioma.
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# References

- [2] A randomised, multicentre trial of Gemcitabine in combination with Celecoxib in patients with malignant pleural mesothelioma who have failed first line platinum-based chemotherapy.

# New trial

- **New trial:**
  - Recruitment
  - New site
  - New drugs
  - New design
  - New funding
  - New participants
  - New outcomes