Hemithoracic Irradiation with Proton Therapy in Malignant Pleural Mesothelioma

Sponsor: University College London
Funder: Asthma + Lung UK
Mesothelioma UK (participant travel expenses)
References: IRAS: 322732
EDGE: 148232
Clinicaltrials.gov: NCT05655078

Target accrual: 148 patients (1:1 randomisation)
Number of sites: 18-20 UK sites, including 2 PBT centres (UCLH, London & the Christie, Manchester)
Recruitment period: 3 years (Q4 2023-Q4 2026)

Overall aim:

- To determine if delivering proton beam therapy (PBT) to the involved hemithorax can improve progression-free survival and overall survival
- To determine if hemithoracic radiotherapy with PBT affects the quality of life of patients with MPM over 2 years
- To determine the relative cost-effectiveness of hemithoracic radiotherapy with PBT in MPM compared with current standard of care therapy over 2 years

Co-primary endpoints:

i. Progression-free survival (PFS) defined as the time from randomisation to the date of progression, using mesothelioma-modified RECIST v1.1, or date of death from any cause
ii. Overall survival (OS) defined as the time from randomisation to the date of death from any cause

Secondary endpoints: Time to first subsequent therapy, local-failure-free survival, distant-metastases-free survival, safety and toxicity, health related Quality of Life (QoL), health and social care resource use and costs, incremental cost-effectiveness

Exploratory biological endpoints: Archival tissue FFPE from biopsies, longitudinal blood and pleural effusion samples, and FFPE tissue from progression rebiopsy (if clinically indicated) are collected to identify if there are any blood based or imaging biomarkers that can predict which patients will benefit most from PBT for MPM.

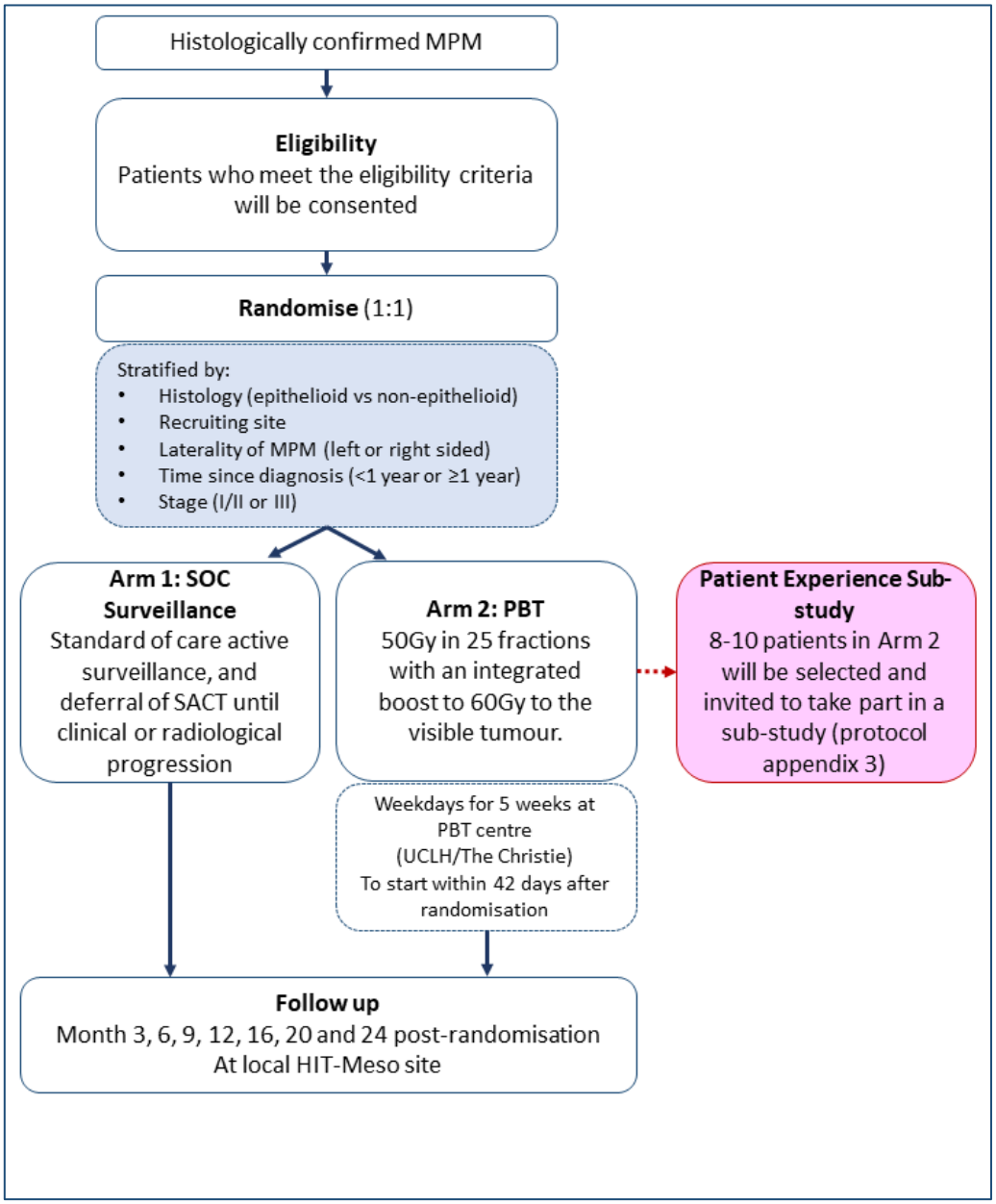
Qualitative sub-study: Investigating patient expectations prior to PBT, experiences of receiving PBT, and how/if expectations of the trial were met
8-10 consenting patients on arm 2 (PBT) will be invited to complete an online questionnaire pre-treatment and have a semi-structured interview 3 months post-treatment with research staff from the University of Sheffield

Treatment arms:

Arm 1 (control)
Active surveillance and deferral of systemic anti-cancer therapy (SACT) until clinical or radiological progression.

Arm 2 (interventional)
Proton Beam Therapy 50Gy in 25 fractions with an integrated boost to 60Gy to the visible tumour if organs at risk constraints are not exceeded.
Follow up at local referring centre.

Schema



Inclusion criteria:

- Patients ≥18 years of age, with histologically (Biopsy) confirmed MPM
- N0 or N1 and M0 disease
- Patient and responsible clinician opt for active surveillance, and deferral of SACT until clinical or radiological progression
- Written informed consent
- WHO Performance Status 0-1
- Disease confined to one hemithorax based on CT assessment
- Adequate pulmonary function:
  ≥ 40% predicted post-FEV1;
  ≥ 40% predicted DLCO/TLCO
- Agreement to travel to the PBT site for PBT treatment if randomised to arm 2
- Agreement to be followed up at a local HIT-Meso site

Exclusion criteria:

- Presence of metastatic or contralateral disease
- Prior thoracic radiotherapy, chemotherapy, immunotherapy for MPM
- Prior radical surgery for MPM (Extrapleural pneumonectomy or extended pleurectomy decortication or pleurectomy decortication)
- Initial systemic therapy or surgery is required and the patient and responsible clinician do not opt for active surveillance
- Involvement of contralateral or supraclavicular lymph nodes
- T4 disease with clear invasion of the myocardium
- N2 and/or M1 disease
- Presence of new effusion that is not amenable to drainage
- WHO Performance Status ≥ 2
- Women who are pregnant or breast feeding
- History of other malignancy; Exception: (a) Subjects who have been successfully treated and are disease-free for 3 years, (b) a history of treated non-melanoma skin cancer, (c) successfully treated in situ carcinoma, (d) CLL in stable remission, or (e) indolent prostate cancer requiring no or only anti-hormonal therapy.

Study contact:

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