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MESOTHELIOMA UK

Supporting People With This Asbestos Cancer

January 2018 Issue

Last Updated: 3rd January 2018

	ATOMIC-meso	LUME-MESO	CheckMate 743	pre-EDIT	VIM	PROMISE-meso
Trial title	Ph 2/3 Study in patients with malignant pleural mesothelioma (MPM) w/low ASS 1 expression to assess ADI-PEG 20 with Pemetrexed and Cisplatin (ATOMIC)	Double blind, randomised, multicentre, phase II/III study of Nintedanib in combination with Pemetrexed / Cisplatin followed by continuing Nintedanib monotherapy versus placebo in combination with Pemetrexed / Cisplatin followed by continuing placebo monotherapy for the treatment of patients with unresectable malignant pleural mesothelioma	A phase III, randomized, open label trial of Nivolumab in combination with Ipilimumab versus Pemetrexed with Cisplatin or Carboplatin as first line therapy in unresectable pleural mesothelioma	A randomised, feasibility trial of Elastance-Directed Intra-pleural catheter or Talc Pleurodesis (EDIT) in the management of symptomatic malignant pleural effusion without obvious non-expansile lung.	A randomised phase II trial of oral Vinorelbine as second line therapy for patients with malignant pleural mesothelioma	PembROlizuMab immunotherapy versus standard chemotherapy for advanced pre-treated malignant pleural mesothelioma
Type	First line	First Line	First Line	First line in patients with symptomatic malignant pleural effusion (including mesothelioma)	Second Line	International, multi-centre, randomised, phase III, pre-treated patients (2nd+ line)
Treatment/study focus	Non-epithelioid MPM	This is a Phase II/III confirmatory study designed to evaluate the safety and efficacy of Nintedanib (BIBF 1120) in combination + (Pemetrexed / Cisplatin) followed by Nintedanib (BIBF 1120) versus placebo + Pemetrexed / cisplatin followed by placebo for the treatment of patients with unresectable malignant pleural mesothelioma	Drug	Pleural procedures	Drug treatment	Trial to demonstrate superiority of Pembrolizumab versus standard chemotherapy
Phase	Phase II/III	Phase III	Phase III	N/A – not a drug trial but analogous to a phase I/II drug study	Phase II	Phase III
Sponsor	Polaris Pharma	Boehringer Ingelheim	Bristol-Myers Squibb	NHS Greater Glasgow & Clyde	Academic Institution: University of Leicester	ETOP
Drug companies involved	Polaris Pharma	Boehringer Ingelheim	Bristol-Myers Squibb	Rocket Medical (UK)	Pierre Fabre	Merck Sharp & Dohme Corp
Principal investigator	Peter Szlosarek	Dr Sanjay Popat (Royal Marsden Hospital)	Prof Dean Fennell	Dr Kevin Blyth	Professor Dean Fennell	Trial Chairs: Sanjay Popat (UK), Alessandra Curioni-Fontecedro (Switzerland) Trial Co-Chair: Solange Peters (Switzerland)
Contact	peter.szlosarek@bartshealth.nhs.uk	Clinical Operations Department, Boehringer Ingelheim	medical.information@bms.com	Dr Geoff Martin geoffreymartin@nhs.net	Georgina Gardner,Trial Manager Gardnerg@Cardiff.ac.uk 029 20687950	Mark Finlayson (Project Manager ETOP) mark.finlayson@etop-eu.org
Description	This is a phase 2/3, randomised, double-blind trial. Weekly ADI-PEG 20 at 36 mg/m2 (or placebo) will be combined with pemetrexed 500 mg/m2 and cisplatin 75 mg/m2 both given every 3 weeks as first-line chemotherapy to non-epithelioid (biphasic and sarcomatoid) MPM. Eligible subjects will be randomised in a 1:1 ratio to ADIPemCis or PlaceboPemCis. The randomisation will be stratified by histology (biphasic or sarcomatoid). Subjects may receive a maximum of 6, 3-week cycles of ADIPemCis or PlaceboPemCis for a total of 18 weeks of treatment. Those subjects completing ADIPemCis or PlaceboPemCis treatment may continue on ADI-PEG 20 or Placebo monotherapy if they have SD or better. Subjects who do not tolerate cisplatin may be switched to carboplatin.	Double Blind, Randomised, Multicentre, Phase II/III Study of Nintedanib in Combination With Pemetrexed / Cisplatin Followed by Continuing Nintedanib Monotherapy Versus Placebo in Combination With Pemetrexed / Cisplatin Followed by Continuing Placebo Monotherapy for the Treatment of Patients With Unresectable Malignant Pleural Mesothelioma	The PD-1 inhibitor nivolumab (Opdivo) is approved in the EU for the treatment of patients with advanced melanoma, locally advanced or metastatic non-small cell lung cancer, and advanced renal cell carcinoma. It is also in development for a range of other cancers. The combination of nivolumab and ipilimumab has also been approved for the treatment of previously untreated metastatic melanoma. Nivolumab in combination with ipilimumab is being tested in this study to determine whether it can improve outcomes in patients with unresectable pleural mesothelioma undergoing treatment for the first time. Following a screening period, suitable patients will be randomly assigned to one of two treatment arms. Patients will receive either: Arm A: nivolumab in combination with ipilimumab Arm B: pemetrexed plus cisplatin or carboplatin chemotherapy Approximately 600 patients will be treated in this study. Approximately 36 of these patients will be from the UK.	Malignant Pleural Effusion (MPE) is a collection of fluid inside the chest caused by a variety of cancers including mesothelioma. It is a common medical problem and often causes severe breathlessness. Standard treatment for MPE involves an admission to hospital to drain the fluid and then attempt to prevent the fluid from returning by sticking the lung to the inside of the rib cage with medical talc powder which acts like glue. This is called talc pleurodesis (TP) but unfortunately it fails in about 30% of patients. This is usually because the lung has not fully re-expanded and has not made contact with the inside of the ribs. When this happens, the fluid can be effectively treated with a different type of drainage tube called an indwelling pleural catheter (IPC) which tunnels under the skin and is drained at home by the district nurses. It is thought that pressure measurements taken from the fluid as it is drained may be able to show doctors whether or not the lung will re-expand before patients are committed to either TP or an IPC. In this research we wish to test if these measurements can be used to choose which is the best first treatment option (TP or IPC) for patients with MPE. We have called this 'EDIT management'. Since it is uncertain whether this new approach will work, patients will be randomised to have either standard treatment or EDIT management. We will compare the two groups to assess whether the patients who had EDIT management had to have fewer repeat procedures over the following 3 months.	Patients will be randomised (1:2) to receive either active symptom control (ASC) or ASC with vinorelbine. Patients will continue vinorelbine treatment until evidence of disease progression (or unacceptable toxicity to the drug or patient withdrawal). If vinorelbine activity is demonstrated.	Randomised phase III multicentre clinical trial to demonstrate superiority of pembrolizumab versus standard, institutional-choice chemotherapy (gemcitabine or vinorelbine) in patients progressing after previous platinum-based chemotherapy. Patients randomised to chemotherapy will be allowed to cross over to receive pembrolizumab at progression.
Randomised? Y/N	Yes	Yes	Yes	Yes	Yes	Yes
Treatment Schedule	Standard Pem/CIS + Weekly ADI-PEG20 or placebo	Variable	This is dependent on treatment arm.	Screening visit followed by admission to hospital for fluid drainage procedures (between 1 and 4 night stay). Follow-up clinic visits at 1 and 4 weeks post-discharge and 2 and 3 months post-discharge.	3 weekly cycles until progression	Frequency of visits: 3-weekly. Pembrolizumab administered up to a maximum of 2 years.
Treatment route	Standard Pem/CIS + Weekly ADI-PEG20 or placebo	Oral nintedanib with IV Cisplatin/Pemtrexed	IV	N/A – pleural procedures	Oral	Pembrolizumab: IV Standard chemotherapy: oral/IV (institutional-choice)
Drugs used	Standard Pem/CIS + Weekly ADI-PEG20 or placebo	Placebo Comparator: Placebo + pemetrexed/cisplatin Experimental: Nintedanib 200mg + pemetrexed/cisplastin Experimental arm	Control arm: pemetrexed plus cisplatin or carboplatin chemotherapy Treatment arm: nivolumab in combination with ipilimumab	N/A – pleural procedures: Control arm – standard chest drain insertion and talc slurry pleurodesis following current BTS guidelines Intervention arm – large volume pleural aspiration with concurrent digital pleural manometry followed by either chest drain / talc slurry or first-line indwelling pleural catheter insertion. Patients within the intervention arm will also undergo pre- and post-aspiration MRI scans to address additional secondary research questions.	Treatment arm: Vinorelbine + active symptom control Control arm: Active symptom control	Treatment Arm: pembrolizumab Control Arm: (institutional-choice): gemcitabine (IV) or vinorelbine (IV/oral)
Entry criteria	1. Histologically proven advanced MPM of biphasic or sarcomatoid histology. 2. Naïve to prior chemotherapy or immunotherapy (i.e. this is a first-line systemic therapy study). 3. MPM tumor sample for determination of ASS1 status. ASS1-deficiency is not required for study entry at study start, but tumor sample for ASS1 status is required. 4. Measurable disease as assessed by modified RECIST or RECIST 1.1 5. ECOG performance status of 0 - 1 6. Predicted life expectancy of at least 12 weeks.	1. Age – 18 years and older 2. Histologically confirmed malignant pleural mesothelioma (MPM) (Epithelioid or biphasic subtype for Phase II patients; epithelioid subtype only for Phase III patients) 3. Life expectancy of at least 3 months in the opinion of the investigator 4. Eastern Cooperative Oncology Group (ECOG) score of 0 or 1 5. Measurable disease according to modified RECIST (Response Evaluation Criteria In Solid Tumours) criteria	1. Males and Females at least 18 years of age 2. Histologically confirmed pleural malignant mesothelioma not eligible for curative surgery 3. ECOG Performance status of 0 or 1 4. Available tumour sample for testing 5. Acceptable blood work 6. Other protocol defined inclusion criteria may apply	1. Clinically confident diagnosis of MPE, defined as any of the following: a) Pleural effusion with histocytologically proven pleural malignancy OR b) Pleural effusion in the context of histocytologically proven malignancy elsewhere, without a clear alternative cause for fluid OR c) Pleural effusion with typical features of malignancy with pleural involvement on cross-sectional imaging (CT/MRI) 2. Degree of breathlessness for which therapeutic pleural intervention would be offered 3. Age >18 years 4. Expected survival > 3 months 5. Written Informed Consent	1. Histological diagnosis of malignant pleural mesothelioma 2. Prior treatment with first-line standard platinum doublet based chemotherapy. Patients who will have received re-challenge with 1st line platinum based therapy, and/or maintenance therapy in the front line setting are allowed. 3. Expected survival ≥ 3 months 4. ECOG performance status 0-1 5. Adequate haematological and liver function 6. Willing to consent to provide diagnostic tissue for translational research 7. Disease which is measurable using modified RECIST. 8. Radiological evidence of disease progression	(selection) 1. Histologically confirmed malignant pleural mesothelioma (all subtypes) 2. Progressing after or on previous platinum based chemotherapy 3. Availability of tumour tissue for translational research 4. Older than 18 years 5. ECOG performance status 0-1 6. Life expectancy of at least 3 months 7. Measurable or evaluable disease according to RECIST 1.1 criteria 8. Adequate haematological, renal, and liver function
Exclusion criteria	1. Radiotherapy (except for palliative reasons) the previous two weeks before. 2. Ongoing toxic manifestations of previous treatments. 3. Symptomatic brain or spinal cord metastases. 4. Major thoracic or abdominal surgery from which the patient has not yet recovered. 5. Serious infection requiring treatment with intravenous antibiotics at the time of study entrance or 7 days prior. 6. Known to be serologically positive for human immunodeficiency virus (HIV).	1. Previous systemic chemotherapy for MPM 2. Prior treatment with nintedanib or any other prior line of therapy 3. Patients with biphasic or sarcomatoid subtype MPM 4. Patients with symptomatic neuropathy 5. Radiotherapy (except extremities) within 3 months prior to baseline imaging 6. Active brain metastases (e.g. stable for < 4 weeks) 7. Radiographic evidence of cavitary or necrotic tumours or local invasion of major blood vessels by MPM 8. Significant cardiovascular diseases 9. Inadequate hematologic, renal, or hepatic function	1. Primitive peritoneal, pericardial and tunica vaginalis testis mesotheliomas 2. Prior chemotherapy for pleural mesothelioma 3. Prior treatment with an anti-PD-1, anti-PD-L1, anti-PD-L2 or anti-CTLA-4 antibody 4. History of other malignancy unless the subject has been disease-free for at least 3 years 5. Active, untreated central nervous system (CNS) metastasis 6. Other protocol defined exclusion criteria may apply	1. Females who are pregnant or lactating 2. Clinical suspicion of NEL for which TP would not be offered 3. Patient preference for 1st-line IPC insertion 4. Previous ipsilateral failed TP 5. Estimated pleural fluid volume ≤ 1 litre, as defined by TUS 6. Any contraindication to chest drain or IPC insertion, including: 7. Irreversible coagulopathy 8. Inaccessible pleural collection, including lack of suitable IPC tunnel site 9. Any contraindication to MRI scanning, including: 10. Claustrophobia 11. Cardiac pacemaker 12. Ferrous metal implants or retained ferrous metal foreign body 13. Previously documented reaction to Gadolinium-containing intravenous contrast agent 14. Significant renal impairment (eGFR<30 ml/min)	1. Uncontrolled CNS disease 2. Diagnosis of a second malignancy except prostate or cervical cancer in remission, patients with a diagnosis of basal cell carcinoma of the skin or superficial bladder cancer. 3. Any live vaccine within 30 days of consent 4. Severe hepatic insufficiency 5. Patients on long term oxygen therapy	(selection) 1. Prior therapy with an anti-PD-1, anti-PD-L1/L2, anti-CD137, or anti-CTLA-4 antibody 2. Prior therapy with gemcitabine or vinorelbine 3. Known active central nervous system metastases and/or carcinomatous meningitis. 4. Active autoimmune disease that has required systemic treatment in past 2 years (i.e. with use of disease modifying agents, corticosteroids or immunosuppressive drugs).
Performance status criteria	0-1	0 or 1	0-1	Not specified	0-1	0-1
Participants required	386	537	36 in UK	30 participants within 12 months	200	142
No. of participants to date	plee@polarispharma.com	Confidential information not in public domain	21 (in UK)	Recruitment commenced 28th August 2017 To date (9th November 2017), 6 patients have been recruited	68	0
Centres opening & recruiting	Open in US & Taiwan; due to open UK in June (15 sites); Europe (France, Italy, Belgium, Germany, Austria); Australia (Perth + 4 other sites)	Recruiting: Beatson Hospital West of Scotland Cancer Centre, Glasgow Guys Hospital, London Leicester Royal Infirmary Royal Marsden Hospital Wythenshawe Hospital, Manchester	Barts Cancer Institute, Queen Mary University of London Edinburgh Cancer Centre, Western General Hospital Leicester Royal Infirmary Royal Cornwall Hospital, Truro Southampton General Hospital	Single centre – Glasgow Pleural Disease Unit, Queen Elizabeth University Hospital, Glasgow, UK	Aberdeen Royal Infirmary Churchill Hospital, Oxford Leicester Royal Infirmary Velindre Cancer Centre, Cardiff Weston Park Hospital, Sheffield	Recruiting: Addenbrooke's Hospital, Cambridge Clatterbridge Cancer Centre, Liverpool Guy's and St Thomas' Hospital, London Kent Oncology Centre, Maidstone Plymouth Hospitals NHS Trust, Plymouth Royal Marsden Hospital, London Weston Park Hospital, Sheffield
Where can patients get more information?	plee@polarispharma.com	www.clinicaltrials.gov ClinicalTrials.gov Identifier: NCT01907100	Patients/carers should contact their doctor to get further information.	As a single centre feasibility study, Pre-EDIT is only open to recruit patients from within NHS Greater Glasgow & Clyde. Patients interested in participation within this catchment area should discuss this with their chest physician who may contact the trial team.	http://www.cardiff.ac.uk/centre-for-trials-research	PROMISE-meso@etop-eu.org
Where can healthcare professionals get more information?	p.w.szlosarek@qmul.ac.uk	Clinical Operations Department, Boehringer Ingelheim	medical.information@bms.com	Study research fellow Dr Geoff Martin geoffreymartin@nhs.net	NIHR Website and Clinicaltrial.gov websites	PROMISE-meso@etop-eu.org
Trial/Study website	https://clinicaltrials.gov/ct2/show/NCT02709512	www.clinicaltrials.gov ClinicalTrials.gov Identifier: NCT01907100	https://clinicaltrials.gov/ct2/show/record/NCT02899299?term=CA209-743&rank=1	N/A	http://www.cardiff.ac.uk/centre-for-trials-research	www.etop-eu.org

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	CONFIRM	SYSTEMS-2	MARS 2	ASyMS-meso	MesoTRAP	ASSESS-MESO
Trial title	CONFIRM: Checkpoint blockade for inhibition of relapsed mesothelioma	SYSTEMS-2: A Randomised Phase II trial of standard versus dose escalated radiotherapy in the treatment of pain in malignant pleural mesothelioma	A pilot study to determine if it is feasible to recruit into a randomised trial comparing (ex-tended) pleurectomy decortication versus no pleurectomy decortication in the multimo-dality management of patients with malignant pleural mesothelioma	Real-Time Symptom Assessment using the Advanced Symptom Management System (ASyMS) for Patients with Malignant Pleural Mesothelioma (MPM): a Feasibility Study	A pilot clinical trial and feasibility study comparing video-assisted thoracoscopic partial pleurectomy/decortication (VAT-PD) with indwelling pleural catheter (IPC) in patients with trapped lung.	A prospective observational cohort study collecting data on demographics, symptoms and biomarkers in people with meso-thelioma that will provide a resource for future trials
Type	Third line	Radiotherapy	Surgery vs No surgery. All patients receive standard of care chemotherapy	Test of a medical device	Surgery versus insertion of indwelling pleural catheter	Non-interventional, observational
Treatment/study focus	Drug	Radiotherapy for pain control	Surgery, patient experience and quality of life	Symptom Management and Quality of Life	Symptom management for patients with trapped lung	To collect information about mesothelioma and the people who develop it, their symptoms, and how things change over time, whilst also screening partici-pants for clinical trial participation.
Phase	Phase III	Phase II	Phase II (Pilot study)	N/A	Feasibility, pre-Phase III	N/A
Sponsor	Academic institution: University of Southampton	Sponsor: Beatson Cancer Charity and June Hancock Mesothelioma Research Fund Academic Institution: University of Glasgow	Sponsor: Royal Brompton and Harefield NHS Foundation Trust Co-ordination and Management: Papworth Hospital NHS Foundation Trust Funding: Cancer Research UK (Grant number: CRUK/12/030)	Academic institution: University of Strathclyde	Papworth Hospital NHS Foundation Trust	North Bristol NHS Trust
Drug companies involved	Bristol Myers Squibb (BMS)	None	None	None	N/A	None
Principal investigator	Prof Dean Fennell	Professor Anthony Chalmers	Mr Eric Lim, Consultant Thoracic Surgeon, Royal Brompton and Harefield NHS Foundation Trust	Prof Roma Maguire	Dr Robert Rintoul	Dr Anna Bibby
Contact	Emma Kirkpatrick - confirmtrial@soton.ac.uk - 023 8120 3785	Dr Miranda Ashton (Clinical Research Fellow) Miranda.ashton @glasgow.ac.uk	MARS 2 study team (phn-tr.mars2@nhs.net)	Dr Anne Arber (a.arber@surrey.ac.uk) or Dr Naomi Klepacz (n.klepacz@surrey.ac.uk)	Carol Freeman (carolfreeman@nhs.net)	Anna.bibby@bristol.ac.uk (PI) Natalie.Zahan-Evans@nbt.nhs.uk (Study nurse)
Description	A double blind, placebo controlled randomised phase III trial comparing nivolumab (anti PD-1 antibody) monotherapy 240mg Q2W versus placebo until disease progression, for a maximum of 12 months. The treatment allocation ratio will be 2:1 in favour of nivolumab.	A randomised, multicentre trial of radiotherapy dose escalation for pain control in malignant pleural mesothelioma. Patients will be randomised to receive either standard dose radiotherapy (20Gy in 5 treatments) over 1 week, or a higher dose (36Gy in 6 treatments) over 2 weeks. The aim of the trial is to assess whether the higher dose of radiotherapy is more effective for pain 5 weeks after the start of treatment. Methods of radiotherapy delivery which limit the dose received by normal tissues will be used to minimise side effects.	The objective of the trial is to determine if it is feasible to recruit patients with malignant pleural mesothelio-ma with disease amenable to surgical resection into a trial of (extended) pleurectomy decortication (lung sparing surgery) versus no surgery. All patients will receive standard of care. The pilot component will also assess if there is any evidence of harm associated with (extended) pleurec-tomy decortication.	ASyMS-meso is a 'real-time' symptom monitoring system for people with Mesothelioma. Patients using ASyMS-meso will complete a symptom questionnaire once daily and at any time they feel unwell. This information will be sent via the mobile phone to a computer server which will determine whether any of the reported symptoms are a cause for concern and will trigger an alert at the patient's hospital if they require attention. Patients will receive self-care advice and additional information through the mobile phone. This study is being conducted in two parts. In part one we will work with patients, carers and clinical staff to develop the symptom questionnaire and self-care advice to be provided through ASyMS-meso. In part two, patients will use ASyMS-meso for a period of 3-months and will be asked to provide us with feedback regarding their experience of using the system.	The overarching aim of our research programme is to determine the best treatment for managing trapped lung in patients with malignant pleural mesothelioma (MPM) and pleural effusion Prior to undertaking a full Phase III randomised controlled trial of VAT-PD versus IPC to determine the best method of controlling/ palliating dyspnoea and chest pain, there are some uncertainties that need to be addressed to inform the best design of a study. These are: 1) How prevalent is trapped lung in MPM? 2) Will patients accept randomisation to IPC or VAT-PD? iii) What is the standard deviation of Visual Analogue Scale scores for dyspnoea and chest pain in each treatment group? (This will be used to estimate parameters that will be included in the sample size estimates for a phase III trial) We will also investigate the feasibility of undertaking a cost-effectiveness analysis from the perspective of the NHS.	We want to learn more about mesothelioma, specifically whether there are any patient characteristics, factors relating to the tumour, or blood tests that will allow us to predict which patients might respond better to chemotherapy or other treatments, or to live longer. We also want to know about people's symptoms and how these may change over time. ASSESS-meso is a 'real-life' study that will collect information from patients at their routine clinic appointments. This information includes symptom scores, imaging such as x-rays, ultrasounds and CT scans, and blood tests and collection of pleural fluid (if present). We will also screen participants to see if there are any clinical trials they may be eligible for. If you are not having regular appointments in hospital, there is an option to undergo telephone study assessments.
Randomised? Y/N	Yes	Yes	Yes	No	Yes	No
Treatment Schedule	Fortnightly	• Visit 1: Screening visit (up to 1 month before radiotherapy) • Visit 2: Baseline visit (up to 1 week before radio-therapy) • Visit 3: Final day of radiotherapy • Visit 4: Week 5 after the start of radiotherapy • Visit 5: Week 9 after the start of radiotherapy • Visit 6: Week 26 after the start of the radiotherapy	Patients will be reviewed at their routine clinical follow up visits (6 weeks, 3, 6, 9, 12, 18 and 24 months and annually thereafter for 5 years).	Patients will be required to use the device once daily and complete some questionnaire measures at three time points during the study.	Follow-up visits at 6 weeks, 3, 6 and 12 months post-randomisa-tion are planned to coincide with clinical care visits.	Study assessment visits will be co-ordinated with routine clinic appointments
Treatment route	IV	External beam radiotherapy	All patients will receive standard of care chemotherapy	All patients will continue to receive usual care while using the medical device.	N/A	All participants will continue to receive treatment as usual whilst participating in this study.
Drugs used	Treatment arm: Nivolumab Control arm: placebo	No drugs used (radiotherapy trial) Treatment arm: 36Gy in 6 fractions delivered over 2 weeks Control arm: 20Gy in 5 fractions delivered over 1 week	All patients will receive the usual standard of care chemotherapy (eg Platinum / Pemetrexed). After 2 cycles, participants will be re-assessed by CT to screen for progressive disease. Patients with no evidence of disease progression beyond the limits of surgical resection will be randomised to either: a) (Extended) pleurectomy decortication OR b) No surgery All patients will then receive the remaining 4 cycles of chemotherapy.	None	N/A	All participants will continue to receive treatment as usual whilst participating in this study.
Entry criteria	1. Histological confirmation of mesothelioma (pleural or peritoneal). 2. At least two prior lines of chemotherapy. Prior maintenance therapy (e.g. avastin) will not count as a line of therapy. Patients enrolled into theCRUK VIM trial as second line therapy who are randomised to best supportive care, will be eligible upon progression. 3. ECOG PS 0-1. 4. CT scan and radiologically assessable disease by modified RECIST or RECIST 1.1 within 28 days of first dose of study treatment. 5. Prior palliative radiotherapy completed at least 14 days prior to first dose of study treatment. 6. Consent to provide issue and blood samples for research. 7. Age≥18 years. 8. Screening laboratory values must meet the following criteria in section 4.2 of the protocol within 48 hours prior to commencement of treatment 9. For women of child-bearing potential, negative serum or urine pregnancy test (minimum sensitivity 25 IU/L or equivalent units of HCG) at enrolment and within 24 hours prior to the start of study drug. 10. Women must not be breastfeeding. 11. Agreement to use suitable methods of contraception as outlined in protocol section 4.6. 12. Expected survival of at least 12 weeks.	1. Malignant pleural mesothelioma (histological or MDT diagnosis) 2. Predicted life expectancy >12 weeks 3. CT scan within 8 weeks of starting radiotherapy 4. Worst pain score ≥ 4/10 after analgesia optimisation 5. Radiotherapy plan compatible with treatment arm (36Gy/6 fractions or 30Gy in 5 fractions) prior to randomisation	1. Histological confirmation of pleural mesothelioma 2. Disease confined to one hemi-thorax.	Malignant Pleural Mesothelioma	1. Confirmed MPM 2. Trapped lung, defined as a "clinically significant trapped lung requiring intervention in the opinion of the clinical team" 3. Pleural effusion present (following re-accumulation) 4. Considered by the clinical team to be suitable and fit enough to undergo VAT-PD 5. Considered by the clinical team to be equally suitable for treatment with VAT-PD or IPC, and therefore eligible for treatment allocation by randomisation. 6. Patient willing to receive either VAT-PD or IPC and attend the respective designated centre for their treatment 7. Community services or patient/carer able to drain IPC at least twice weekly 8. Expected survival of at least 4 months, as assessed by managing clinician 9. Age ≥ 18 years 10. Able to provide informed consent	Any patient with mesothelioma, whose diagnosis has been confirmed at multidisciplinary team meeting, and who is willing (and able) to attend study follow up assessments.
Exclusion criteria	1. Patients with untreated, symptomatic CNS metastases unless adequately treated & neurologically returned to baseline for 2 wks before randomisation. 2. Patients with carcinomatous meningitis 3. Patients with active, known or suspected autoimmune disease, excluding: Type I diabetes mellitus, residual hypothyroidism due to an auto-immune condition requiring HRT, psoriasis not requiring systemic treatment, or conditions not expected to recur in the absence of an external trigger. 4. Patients with a condition requiring systemic treatment with either corticosteroids (> 10 mg daily prednisone equivalent)/immunosuppressive medications within 14 days of the first dose of study drug. 5. Patients with previous malignancies (except non-melanoma skin cancers, and the following in situ cancers: bladder, gastric, colon, endometrial, cervical/dysplasia, melanoma or breast) unless complete remission achieved at least 2 years prior to study entry AND no additional therapy is required during the study period. 6. Serious or uncontrolled medical disorder or active infection that may increase the risk of participation, or impair patient's ability to receive protocol therapy. 7. Toxicities attributed to prior any cancer therapy other than alopecia and fatigue not resolved to CTCAE Grade 1 or baseline before first dose of study treatment. 8. Patients who have not recovered from the effects of major surgery or significant traumatic injury at least 14 days before the first dose of study treatment. 9. Known alcohol or drug abuse. 10. Patients who have received prior therapy with anti-PD 1, anti PD L1, anti-PDL2, anti-CD137, or anti-CTLA 4 antibody. 11. Known history of testing positive for HIV or known AIDS. 12. Positive test for hepatitis B virus or hepatitis C virus indicating acute or chronic infection. 13. History of severe hypersensitivity reactions to other monoclonal antibodies.	1. Anticancer therapy 4 weeks prior to study entry or 6 weeks after radiotherapy 2. Patients who have previously received palliative radiotherapy and where there is concern that the proposed treatment volume would overlap with the previously irradiated area. This does not include patients who have received superficial photon or electron therapy to drain sites 3. Coexisting lung tumours at the time of study entry	1. Unable to give informed consent 2. Patients unwilling to be randomised 3. Extent of disease not deemed to be surgically resectable 4. ECOG status 2 or more 5. Patients with predicted pre-operative FEV1 or TLco less than 20% 6. Patients with severe heart failure (EF less than 30%) 7. Patients with end stage kidney failure requiring dialysis 8. Patients with liver failure 9. Patients who are participating in another interventional clinical trial in mesothelioma.	Patients with brain metastases or for which the participation is deemed inappropriate by their clinician	1. Lung re-expands fully following pleural fluid drainage i.e. no entrapment 2. Previous attempt at pleurodesis on ipsilateral side 3. Evidence of active pleural infection 4. IPC in situ for more than 28 days 5. Current participation in an RCT or receiving a CTIMP 6. Females: pregnant or lactating	1. Age <18 years old 2. Unable to give written informed consent 3. Declines ongoing hospital follow up
Performance status criteria	0-1	0-2	0-1	N/A [although the patient must be expected to live for the 3-month study period, and 1-month follow-up]	0 - 1	All
Participants required	336	112	n=50 patients in the Pilot phase (n=327 in full-study)	45 patients are needed to test the ASyMS-meso system	38	700
No. of participants	52	23	n=57 patients	3	4	2
Centres opening & recruiting	Aberdeen Royal Infirmary Beatson Hospital West of Scotland Cancer Centre, Glasgow Royal Bournemouth Hospital Harrogate District Hospital Leicester Royal Infirmary Royal Lancaster Infirmary Southend Hospital Southampton General Hospital Velindre Cancer Centre Wythenshawe Hospital	Beatson Hospital West of Scotland Cancer Centre Glasgow, Forth Valley Royal Hospital, Larbert The Royal Marsden University Hospital Southampton Weston Park Hospital, Sheffield	<u>Medical</u> Cardiff, Clatterbridge, Colchester, Derby, Glasgow - Beatson, Leeds, Leicester, Papworth, Peterborough, Royal Gwent, Royal Marsden, Sheffield, South Tees (James Cook), South Tyneside, St. Bartholemews, Wolverhampton, Wythenshawe <u>Surgical & Medical</u> Leicester, Sheffield, St. Bartholemews <u>Surgical</u> Glasgow Golden Jubillee	Ashford & St Peter's Hospitals, Surrey Glasgow Hairmyres Hospital, Lanarkshire Queen Alexandra's Hospital, Portsmouth Queen Elizabeth University Hospital	Blackpool; Barts; Bristol; Cambridge; Golden Jubilee Glasgow; Greater Glasgow; Oxford; Papworth; Peterborough; Preston; Sheffield. Sites in set up: Coventry, Leicester, North Midlands, Nottingham, Wythenshawe and Pennine Acute Hospitals.	Churchill Hospital, Oxford Southmead Hospital, Bristol 8-10 further sites planned across the UK, TBC later this year.
Where can patients get more information?	http://www.cancerresearchuk.org/about-cancer/find-a-clinical-trial/a-trial-looking-at-nivolumab-for-mesothelioma-confirm	Their local clinical oncologist Miranda.ashton @glagsow.ac.uk www.systems-2.co.uk	mars2-trial@bristol.ac.uk	ASyMSmeso@Surrey.ac.uk	Please email papworth.mesotraptrial@nhs.net or telephone 01480 830541 and ask for Dr Rintoul or Kate Slaven	Anna.bibby@bristol.ac.uk (PI) Natalie.Zahan-Evans@nbt.nhs.uk (Study nurse)
Where can healthcare professionals get more information?	Email trial team confirmtrial@soton.ac.uk	Laura.alexander @glasgow.ac.uk Miranda.ashton @glasgow.ac.uk www.systems-2.co.uk	mars2-trial@bristol.ac.uk	ASyMSmeso@Surrey.ac.uk or Dr Naomi Klepacz on n.klepacz@surrey.ac.uk	Please email papworth.mesotraptrial@nhs.net or telephone 01480 830541 and ask for Dr Rintoul or Carol Freeman	Anna.Bibby@bristol.ac.uk
Trial/Study website	N/A	www.systems-2.co.uk	http://mars2.org.uk/		This is currently in set up	N/A