

SELECTmeso1 trial: A phase II trial of the MTA-cooperative PRMT5 inhibitor BMS-986504 in patients with MTAP-deficient relapsed mesothelioma

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INTRODUCTION

Precision medicine for mesothelioma, particularly in the relapsed setting, is lacking.

The genomic landscape of mesothelioma has revealed frequent homozygous deletion of 9p21 which encompasses methylthioadenosine phosphorylase (MTAP), a tumour suppressor involved in methionine salvage and polyamine metabolism. MTAP deletion confers tumour aggressiveness and shorter survival, but confers a vulnerability resulting from binding of its elevated substrate (methylthioadenosine or MTA) to protein arginine methyltransferase 5 (PRMT5).

BMS-986504 (Navlimetostat) is an oral potent inhibitor of the PRMT5:MTA complex and targets MTAP-deleted cells while sparing wild-type cells to achieve synthetic lethality. It has demonstrated tolerability and promising signals of activity in a phase I clinical trial of MTAP-deficient advanced solid tumours.

AIMS

To determine the efficacy of BMS-986504 in MTAP-deficient relapsed mesothelioma and to decipher correlates of *de novo* and acquired resistance.

METHODS

The SELECTmeso trial platform, is a UK, multicentre, multi-candidate, adaptive, phase II platform trial to determine the activity and safety of multiple targeted therapies for the treatment of patients with relapsed malignant mesothelioma in molecularly stratified cohorts.

Patients must have received prior standard of care systemic therapy (with at least one prior line).

THE PLATFORM

PLATFORM PRIMARY OBJECTIVE

To determine the molecular subtype of mesothelioma to determine eligibility for SELECTmeso trial candidates which are open to recruitment.

A virtual pathology platform in a cloud based trusted research environment will be used to determine MTAP protein expression loss.

PLATFORM SECONDARY OBJECTIVE

To conduct in-depth molecular profiling of tumour blocks to enable exploration of the molecular determinants of sensitivity, acquired drug resistance, and further associated translational investigations.

PRIMARY OBJECTIVE (FOR EACH ARM)

To determine the Disease Control Rate (DCR) at 12 weeks.

SECONDARY OBJECTIVES (FOR EACH ARM)

To determine DCR at 24 weeks, response rate, progression-free and overall survival (up to 24 weeks), safety and tolerability.

The **SELECTmeso1 arm** of the platform opened in Q2 2026 investigating the MTA-cooperative PRMT5 inhibitor BMS-986504 in patients with MTAP-deficient relapsed mesothelioma.

EXPLORATORY OBJECTIVES

Whole genome and transcriptome analyses will be used to identify predictors of exceptional response and acquired resistance. Ensemble machine learning will be used to distil significant, predictive features. Responding patients will have re-biopsies with multiomic analysis at the time of disease progression.

Deep learning based volumetric tumour analysis will be conducted to support multiomics correlation analysis.

SELECTmeso1 TRIAL SCHEMA



SELECTmeso1 is a single-arm phase II trial of BMS-986504 in patients with MTAP-deficient relapsed mesothelioma using a Bayesian Optimal Phase II (BOP2) design, which is currently open to recruitment.

Eligible patients have confirmed histological diagnosis of mesothelioma (any histology) with evidence of MTAP deficient status on immunohistochemistry, and evidence of disease progression following prior standard systemic therapy on CT scan.

A total of 30 participants will be administered BMS-986504 orally at a dose of 600mg QD (once daily) continuously in 3-weekly cycles for up to 24 weeks.

The primary endpoint is DCR at 12 weeks measured by mRECIST1.1.

Secondary endpoints include DCR at 24 weeks, response rate, progression-free and overall survival, safety and tolerability.



Trial information

For more information email: selectmeso@soton.ac.uk

ClinicalTrials.gov Identifier: NCT07602946

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