Background: The prognosis of malignant mesothelioma (MM) remains dismal and effective treatment of MM patients represents a high un-met medical need. We have recently reported promising clinical activity of the anti-CTLA4 monoclonal antibody (mAb) tremelimumab in pre-treated MM patients: disease control rate (DCR) was 31%, and survival rate at 1- and 2-years was 48.3% and 36.7%, respectively (Calabrò et al., Lancet Oncol, 2013). These initial findings were corroborated by a second study in which, based on retrospective pharmacokinetic analyses, an intensified schedule of tremelimumab was utilized. Fifty-two % of patients achieved a DCR (median duration 10.9 months) (Calabrò et al., Lancet Respir Med, 2015). These intriguing clinical results and the emerging efficacy of immunomodulatory mAb targeting the PD1/PD-L1 axis in different tumor types, prompted us to design the NIBIT-MESO-1 study aimed to investigate the efficacy of tremelimumab combined with the anti-PD-L1 durvalumab in MM patients.

Trial design: The NIBIT-MESO-1 trial is a phase II, open-label, study that will enroll 40 first- or second-line pleural or peritoneal MM patients with ECOG performance status 0 or 1. Patients will receive tremelimumab at 1 mg/Kg i.v. every 4 weeks (Q4W) for 4 doses, and durvalumab at 20 mg/Kg i.v. Q4W for 12 months. Patients with progressive disease during the first 12 months of treatment or in the follow-up phase may be retreated with the combination of the two drugs. Modified RECIST (Byrne et al., Ann Oncol, 2004) and RECIST 1.1 will be utilized to assess tumor responses in pleural and peritoneal MM, respectively. Primary objective is immune-related (ir)-objective response rate; secondary objectives are ir-DCR, ir-progression free-survival (PFS), overall survival, DCR, PFS, and safety. Efficacy secondary endpoints will be explored per PD-L1 expression on tumor tissues. Clinical results will be correlated with extensive phenotypic, functional and humoral studies.

Disclosure: M. Maio: Consultant, advisor, or both, to Bristol-Myers Squibb, Merck Sharp and Dohme, Roche-Genetech, and Medimmune-AstraZeneca. All other authors have declared no conflicts of interest.