

Project title: A platform trial to improve the Management of immUne reLated advErse evenTs (AMULET Study)

Project Summary:

Immune Related Adverse events (irAEs) are a major cause of morbidity and mortality in patients with cancer undergoing Checkpoint Inhibitor (CPI) immunotherapy. There is currently a limited understanding of why irAEs affect some patients but not others. For those patients who develop irAEs, the cessation of CPIs and the current, empirical management of irAEs with high dose steroids adversely affect cancer outcomes. Understanding and optimising the management of irAEs is expected to improve cancer outcomes, in addition to improving overall health and minimising patient hospital stays. We have developed a phase III, randomised, multi-arm, multi-basket platform trial to optimise the management of irAEs and to gain a deeper understanding of the biology of irAEs, through the collection of serial translational samples (clinical trial led by Dr Kate Young & Prof James Larkin, RMH/ICR). Current irAE treatment choices are largely empirical, although a molecular understanding of irAEs is moving quickly. Efforts to identify predictive biomarkers for the different biological targets of immune suppression, to treat irAEs, are underway. To this end, MANIFEST is a major MRC/UK Life Science/ Industry initiative with a translational platform based at the Francis Crick Institute (led by Prof Samra Turajlic). Serial samples from patients enrolled on our platform study will be analysed as part of MANIFEST. The basket approach allows for comparisons of efficacy (incorporating evolving predictive biomarkers) across organ cohorts, in collaboration with the MRC Centre of Research Excellence in clinical trial design and methodology at UCL (led by Dr Duncan Gilbert). The CRUK Fellow would support the running of the clinical trial, working with the teams at RMH and at UCL, have the opportunity to conduct translational work within the MANIFEST study at the Crick and complete interim analyses for the 3 initial baskets within the platform study (hepatitis, myocarditis and colitis).

Supervisory Team:

Dr Kate Young, Consultant Medical Oncologist, Royal Marsden Hospital, ICR Associate Honorary Faculty

Dr Duncan Gilbert, Consultant Clinical Oncologist and Associate Professor in Cancer and Clinical Trials, MRC Clinical Trials Unit at UCL

Prof Samra Turajlic, Group Leader Cancer Dynamics Laboratory, Crick

Prof James Larkin, Consultant Medical Oncologist, Head of Skin Unit, Royal Marsden Hospital, ICR Honorary Faculty

Clinical Specialities: Oncology, Immunology