Experimental Medicine Training Initiative

Cancer Drug Discovery and Development

TUESDAY, 5TH MARCH 2019

TRINITY HALL, TRINITY LANE, CAMBRIDGE CB2 1TJ

UNIVERSITY OF CAMBRIDGE

Cambridge University Hospitals NHS Foundation Trust

Cambridge Biomedical Research Centre

NHS National Institute for Health Research

AstraZeneca

MedImmune

gsk GlaxoSmithKline

LEARNING OBJECTIVES

To understand cancer drug discovery and development through an introduction to cancer biology and target identification and validation. Understand components of the pharmacological audit trail (PhAT) and application to cancer drug development. Give practical example(s) of PhAT in drug development

To explore pre-clinical development through pharmacokinetic and pharmacodynamic modelling, predictive biomarkers and adaptive trial design

To explore early phase clinical trials in cancer and understand regulatory considerations in cancer drug development from an industry perspective

To understand how imaging biomarkers for treatment response are developed and validated

To learn about a range of imaging biomarkers from morphological to functional and molecular approaches

To explore markers of anti-tumour efficacy and review a clinical development Case study with panel discussion

ROYAL COLLEGE OF PHYSICIANS CPD

ACCREDITATION UNDER APPLICATION

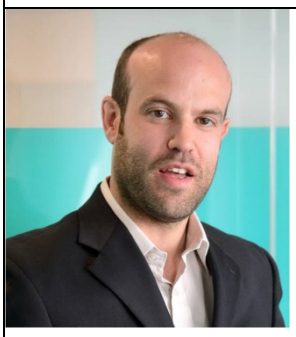
SCHEDULE		SPEAKERS
09.30-10.00	**Registration and Refreshments**	
10.00-10.05	**Welcome**	**Professor Duncan Jodrell** Professor of Cancer Therapeutics Director Cambridge Cancer Trials Centre (CCTC), Department of Oncology, University of Cambridge
10.05-10.30	**Introduction to the drug development paradigm**	**Andrew Foxley** Senior Director Scientific Project Management Oncology Translational Medicine Unit, Early Clinical Development Innovative Medicines, AstraZeneca
10.30-10.55	**Cell Therapy Target Validation and "Hit ID" in Oncology**	**Dr Mark Creighton-Gutteridge** Director, Head of Discovery and New Technologies, Oncology Cell Therapy Unit, Oncology R&D, GlaxoSmithKline
10.55-11.20	**Pre-clinical development (toxicology/PK/PD)**	**Dr James Yates** Principal Scientist applying Quantitative Systems Pharmacology at AstraZeneca
11.20-11.45	**Pharmacological Audit Trail in Cancer Drug Development ++**	**Dr Simon Pacey** Clinical Senior Research Associate Honorary Consultant Medical Oncologist Early Phase and Urology trials teams, University of Cambridge
11.45-12.15	**Panel Discussion**	
12.15 – 1.30	**Lunch & student posters**	
1.30-2.00	**Adaptive Trial Design**	**Dr Steven Fox** Principal Statistician, ECD Biometrics Oncology, AstraZeneca
2.00-2.30	**Drug combinations**	**Professor Duncan Jodrell** Professor of Cancer Therapeutics Director Cambridge Cancer Trials Centre (CCTC), Department of Oncology, University of Cambridge
2.30-2.50	**Imaging biomarkers of treatment response: from RECIST to functional and molecular imaging +**	**Dr Ferdia Gallagher** Cancer Research UK Clinician Scientist Fellow, Reader in Molecular Imaging, Department of Radiology, University of Cambridge
2.50-3.15	**Panel Discussion**	
3.15-3.45	**Break**	
3.45-4.05	**The immuno-oncology revolution - A clinical overview**	**Dr Lewis Au** Clinical Research Fellow, Skin and Renal Units, The Royal Marsden Hospital & Translational Research Scientist, The Francis Crick Institute
4.05-4.25	**A Case Study: Durvalumab +++**	**Dr Robert Wilkinson** Director, Oncology Research, AstraZeneca
4.25-4.45	**Immuno-oncology Combinations**	**Dr Simon Dovedi** Group Leader Immuno-oncology, AstraZeneca & Honorary Senior Visiting Fellow in the Department of Oncology, University of Cambridge.
4.45- 5.30	**Panel Discussion and Closing Remarks**	
5.30-7.00	**Drinks reception followed by Dinner at 7pm**	

BIOGRAPHIES

Dr Lewis Au (FRACP, MBBS, BMedSci)

Dual appointed Clinical Research Fellow of the Skin and Renal Units at The Royal Marsden Hospital, and as a Translational Research Scientist at The Francis Crick Institute (FCI).

Lewis completed his undergraduate training at The University of Melbourne, Australia, and obtained his Medical Oncology specialist qualification in 2017. He is currently a Clinical Research Fellow of the Skin and Renal Units at The Royal Marsden Hospital, and a Translational Research Scientist at The Francis Crick Institute (FCI).
Lewis divides his time between the clinic and the Cancer Evolution and Genome Instability Laboratory at FCI. He is involved in a number clinical and translational studies in melanoma and kidney cancer, with a research focus on improving our understanding of cancer biology, particularly why current treatments are effective for some patients but not others. His other research interests include developing novel techniques to monitor and predict cancer behaviour through blood tests (termed 'liquid biopsies').



Dr Mark Creighton-Gutteridge

Director, Head of Discovery and New Technologies, Oncology Cell Therapy Unit, Oncology R&D, GlaxoSmithKline, UK

Mark heads the Discovery and New Technologies team for the Oncology Cell Therapy Research Unit at GSK Mark has a principal role in identifying and implementing cutting-edge targets and technologies, transitioning these into research and development programmes for immune-receptor engineered immune-cells.
GSK are developing differentiated and innovative immunotherapies for treatment of cancer patients with high unmet medical needs. In his talk, Mark will detail some of the GSK-wide efforts behind Cell Therapies, the challenges faced by the Cell therapy unit and some relevant examples to highlight innovation and learnings.

Dr Simon Dovedi

Group Leader Immuno-oncology, AstraZeneca

Simon Dovedi is a Group Leader at AstraZeneca. Based in Cambridge his group focus on immuno-oncology drug discovery. In addition to this Simon is an Honorary Senior Visiting Fellow in the Department of Oncology, University of Cambridge.
Previous to this he was a Fellow at the University of Manchester where he investigated the impact of radiotherapy on the immune system and explored how to utilise radiotherapy as an immune-modulator. Simon continues to undertake research in the field of radiotherapy and holds an honorary lectureship at the University of Manchester. Simon received his Ph.D in cancer immunology at Newcastle University studying immunotherapy combinations in models of bladder cancer.

Dr Steven Fox

Principal Statistician, ECD Biometrics Oncology, AstraZeneca

Steven competed his master's degree at Leicester University in Medical Statistics, before joining GlaxoSmithKline in 2006. Steven provided broad statistical consultancy across a range of science units, including pre-clinical toxicity, target identification from high-through screening, transcriptomic /proteomic analysis and investigative statistical techniques for siRNA, gene knock-down assays. He transitioned into clinical trials in 2012, where he has worked in various areas including immuno-inflammatory: Lupus, Idiopathic thrombocytopenic purpura (ITP), Respiratory: COPD, Transplant: Kidney. He also served, as the lead international statistician for the GSK ECLIPSE observational study, designed to find predictors of COPD progression. In 2015, Steven joined PPD to take on the compound lead role supporting one of AstraZeneca's late phase assets for Asthma. Steven subsequently joined AstraZeneca in 2016, as a Principal Statistician to support the design and analysis of early stage

Oncology studies. In particular, he has developed an extensive knowledge in the design and analysis of Platform studies, where multiple treatment combinations are available within one study.

Andrew Foxley BA (Hons) MFPM (Hon)

Senior Director Scientific Project Management Oncology Translational Medicine Unit, Early Clinical Development Innovative Medicines, AstraZeneca

Andrew is a pharmaceutical research professional with expertise in drug development in oncology and cardiovascular therapeutic areas across all phases of development in CRO (to board level) and pharma.

Awarded Honorary Membership of the Faculty of Pharmaceutical Medicine of the Royal College of Physicians, UK (July 2016); nominated for numerous achievement awards including recipient of an annual Individual Special Recognition Award (2013) Andrew has experience of organising and chairing successful company/academic steering boards and designing clinical development programme. He has worked internationally to deliver drug development programmes to cost, time and quality targets. Andrew is the Acting Global Medicines Leader for the AKT inhibitor capivasertib and holds a number of other positions including: AstraZeneca representative and Chair of the ABPI Experimental Medicine Expert Network, ,
Chair, Executive Steering Team, AstraZeneca-Sarah Cannon Alliance, Co-Chair, Clinical Pharmacology Skills Alliance, Chair of the Clinical Pharmacology Trailblazer Apprenticeship Group.

Dr Ferdia Gallagher

Cancer Research UK Clinician Scientist Fellow, Reader in Molecular Imaging, Department of Radiology, University of Cambridge

Ferdia studied medicine at both the Universities of Cambridge and Oxford before training as a radiologist at Addenbrooke's Hospital. He undertook a PhD in Biochemistry in Cambridge as part of a CRUK Clinical Research Training Fellowship; this work focused on a new form of imaging termed hyperpolarized carbon-13 MRI that allows tumour metabolism to be imaged non-invasively in realtime.

Ferdia is currently a CRUK Clinician Scientist, University Reader in Molecular Imaging and an Honorary Consultant Radiologist in the Department of Radiology in the University of Cambridge. His main interest is developing new molecular imaging methods to study fundamental biological processes in tumours that can be translated into patient care. These techniques include MRI and PET. Part of this research has involved the translation of hyperpolarized carbon-13 MRI into humans and this has involved creating a bespoke pharmacy facility to assembly the consumables for the clinical hyperpolarizer. In addition, he is currently developing methods to study tumour aggressiveness using diffusional weighted imaging and to probe tissue structure and function using sodium MRI. Ferdia is also interested in new PET tracers, such as labelled sodium fluoride to more accurately stage tumours, and cell labelling methods using 89Zr-PET. The group is also interested in the application of novel trial designs to imaging studies. He sits on the CRUK Clinical Research Committee and the CRUK New Investigators Committee. He is the Chair of the MR of Cancer Study Group within the International Society of Magnetic Resonance in Medicine 2017-18. Dr Gallagher also directs the local Academic Research Training Programme in Radiology.

Professor Duncan Jodrell

Professor of Cancer Therapeutics, Department of Oncology
Director of the Cambridge Cancer Trials Centre, University of Cambridge

In addition to his role as the Director of the Cambridge Cancer Trials Centre, Duncan leads the Pharmacology & Drug Development Group (PDDG) which aims to optimise preclinical development and science-led clinical application of novel therapeutics and therapeutic strategies, focussing in particular on drug combination strategies for pancreatic cancer. In the lab he utilises model systems representing pancreatic cancer and compares the data generated with results from the analysis of samples from patients in clinical trials. The PDDG is closely linked to the Early Phase Cancer Clinical Trials Team (EPCTT), clinical researchers at Cambridge University Hospitals Trust. This allows him to rapidly translate laboratory discoveries into the clinic.

Dr Simon Pacey

Clinical Senior Research Associate & Honorary Consultant Medical Oncologist Early Phase and Urology trials teams, University of Cambridge

Simon's research interests are early phase clinical trials (phase I/II) and Urological malignancy (prostate cancers), centered around the transition of new drugs into humans and exploring and proposing new treatments paradigms for men with early/ localised prostate cancer.

Current projects include: Chief Investigator Cambridge Neoadjuvant Carcinoma of the Prostate (CANCAP) studies: Clinical studies of investigational drugs prior to radical prostatectomy, clinicatrials.gov identifiers NCT02064608 (AZD2014), see GU ASCO 2017 and NCT02324998 (Olaparib); Pre-clinical studies to investigate effect of mTOR inhibition in early, hormone sensitive prostate cancer; Phase 1/ early phase trials in patients with advanced solid tumours (local investigator led, Cancer Research UK and industry collaborations both as CI and PI).

Dr Robert Wilkinson

Director of Oncology Research, R&D Oncology Unit, AstraZeneca

Robert leads an Oncology Research department (Granta Park, Cambridge) and oversees pre-clinical oncology biologics research ranging from target identification to candidate drug selection and IND enabling support. Activities focus on utilising the latest biotherapeutic technologies incl. mono- and bispecific antibodies, antibody-drug conjugates (ADCs), novel protein mimetics, oncolytic virotherapy and oligonucleotides. Robert has made significant contributions in the discovery of several novel immuno-oncology (IO) therapies including recently FDA-approved Imfinzi® (durvalumab), an anti-PD-L1 antibody used in the treatment of NSCLC and bladder cancer. Other IO molecules discovered and or developed by his department include: MEDI1873, a GITRL agonist; MEDI9197 (in partnership with 3M), a TLR7/8 agonist; MEDI1191, IL-12 mRNA (in partnership with Moderna); MEDI5752, a PD-1/CTLA-4 bispecific antibody and MEDI5395, oncolytic virotherapy.

From 2001-2012, Robert was based at Alderley Park (AstraZeneca) and held several leadership roles. He made significant contributions to the discovery and delivery of several small molecules into the clinic incl. Barasertib (AZD1152), an Aurora B kinase inhibitor and AZD538, a CDK2 inhibitor. Robert received a PhD in Experimental Immunology from The University of Birmingham Medical School and then spent several years within Cancer Research Technology (the drug discovery arm of CRUK), where he established a tumour immunotherapy group. Robert has co-authored over 60 peer reviewed scientific papers, and is an Executive Committee member for the British Association of Cancer Research (BACR) and Industrial Committee member for the Society for Immunotherapy of Cancer (SITC).

Professor Ian Wilkinson

Professor of Therapeutics, Director of Cambridge Clinical Trials' Unit, Director of the Office of Translational Research, University of Cambridge, Director of the Experimental Medicine Training Initiative

Ian has a long track record in clinical pharmacology and arterial haemodynamics. His research interest is in clinical/experimental studies designed to understand the mechanisms underlying arteriosclerosis and cardiovascular disease, and to understand the importance of novel biomarkers of arterial function in risk prediction. He directs the Cambridge Clinical Trials' Unit and is also a director of the Office of Translational Research in Cambridge and the Experimental Medicine Initiative. He has considerable experience of translational research, and in forming academic collaborations with Industry.

Dr James Yates

Principal Scientist applying Quantitative Systems Pharmacology at AstraZeneca

James' role at AstraZeneca is to support drug discovery and development projects with regard to PKPD and efficacy data analysis as well as predicting human PK using physiologically based models. He has experience writing regulatory quality documents on PKPD modelling and simulation analyses and have contributed to a number of IB and IND submissions. James' role also involves development of scientific strategy with respect to model based drug discovery and act as a discipline lead in this area. This includes working with other modelling groups, such as Discovery Statistics, Computational Biology and the Pharmacometrics Group in Clinical at AstraZeneca as well as the various experimental functions such as oncology bioscience. James also provides training and support to colleagues and members of other functions.

James is interested in the development of mechanistic disease models, particularly for oncology, to enable translation from pre-clinical data to the clinic.

READING LIST

* Gottschalk et al. Cancer J. 2014; 20(2): 151–155. doi:10.1097/PPO.0000000000000032

\+ Imaging biomarker roadmap for cancer studies. Nat Rev Clin Oncol. 2017 Mar;14(3):169-186

++ Critical parameters in targeted drug development: the pharmacological audit trail. Banerji and Workman. Semin Oncol 2016 https://www.ncbi.nlm.nih.gov/pubmed/27663475

+++ Identification and Characterization of MEDI4736, an Antagonistic Anti–PD-L1 Monoclonal Antibody.
Ross Stewart1, Michelle Morrow1, Scott A. Hammond2, Kathy Mulgrew2, Danielle Marcus1, Edmund Poon1, Amanda Watkins1, Stefanie Mullins1, Matthieu Chodorge1, John Andrews1, David Bannister1, Emily Dick1, Nicola Crawford1, Julie Parmentier3, Marat Alimzhanov4, John S. Babcook5, Ian N. Foltz6, Andrew Buchanan1,Vahe Bedian7, Robert W.Wilkinson1, and Matthew McCourt8

RESOURCES

HTTP://WWW.EMI-TRAINING.ORG/