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19-23 MARCH 2018 | LONDON, UK | HILTON LONDON CANARY WHARF

CAMBRIDGE HEALTHTECH INSTITUTE’S THIRD ANNUAL

Immuno-Oncology Summit Europe

INDUSTRY AND ACADEMIC ADVANCES IN THIS EXCITING AND RAPIDLY DEVELOPING FIELD

2018 CONFERENCES

19-20 MARCH
Adoptive T-Cell Therapy
SUCCESS FROM BENCH TO BEDSIDE WITH IMPROVED APPROACHES

20-21 MARCH
Combination Immunotherapy
STRATEGIES AND NEW APPROACHES FOR BETTER RESULTS IN THE CLINIC

22-23 MARCH
Immunomodulatory Antibodies
HARNESSING THE IMMUNE RESPONSE AND OVERCOMING INHIBITORY FACTORS

3 DINNER SHORT COURSES

20 MARCH
T-Cell Therapies: Current Field, Challenges and Future Directions

22 MARCH
Preclinical Models for Cancer Immunotherapy
The Tumour Microenvironment and Response to Cancer Immunotherapy

FEATURED PRESENTERS

Bent Jakobsen, PhD
CSO, Immunocore

K. Dane Wittrup, PhD
Carbon P. Dubbs Professor, Chemical Engineering and Biological Engineering, Massachusetts Institute of Technology

Roy D. Baynes, MD, PhD
Senior Vice President & Head, Global Clinical Development, CMO, Merck, Sharpe & Dohme

Immuno-OncologyEurope.com

Organized by: Cambridge Healthtech Institute
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Dear Colleague,

Cambridge Healthtech Institute's Third Annual Immuno-Oncology Summit Europe returns to the heart of London's Canary Wharf for a full week of cutting-edge science and discussion. Through three back-to-back conference tracks, delegates will hear from the research teams at the forefront of the rapidly developing field of cancer biotherapeutics.

In Adoptive T-Cell Therapy, leaders in the field from academia, industry and the clinic present advances in TCRs, CAR-Ts, TILs, and "unconventional" T cells. Investigators focus on increasing the range of potential targets, overcoming immune evasion mechanisms, affinity optimization, enhancement of efficacy, avoidance of tox and alloreactive occurrences, and on advancing T cell stimulation and T cell homing.

In Combination Immunotherapy, investigators are applying knowledge of the tumour environment by developing new combination approaches with new modes of action. In this track, attendees will discover how investigators are improving on the limitations of monotherapies with the application of clever combination strategies.

Immunomodulatory Antibodies examines the mechanisms behind checkpoint inhibition and presents advances with checkpoint blockers, agonists, CD3 targeting bispecifics and with targeting Fc receptors. It presents novel approaches to overcome resistance and boost the immune-stimulatory response as well as means of limiting toxicity, PK issues and auto-immune side effects.

Cambridge Healthtech Institute (CHI) brings you the highest standard of scientific content and collaboration with more than 130 conferences across the globe, including the industry leading PEPTalk, PEGS Protein & Antibody Engineering Summits and Immuno-Oncology Summits held each year in North America, Europe and Asia.

We look forward to seeing you at what promises to be another successful knowledge-sharing event.

Nicole Lyscom, PhD
Senior Conference Director
Cambridge Healthtech Institute

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SC1: T-Cell Therapies: Current Field, Challenges and Future Directions
Fiona Thistlethwaite, MB, PhD, Consultant, Medical Oncology, The Christie NHS Foundation Trust, and Honorary Senior Lecturer, Cancer Sciences, Biology Medicine & Health, University of Manchester
Reno Debets, PhD, Associate Professor, Tumor Immunology, Medical Oncology, Erasmus MC Cancer Institute
The field of Adoptive T cell (ACT) therapy is advancing rapidly, and with the FDA approval of a T cell product expressing CD19-specific Chimeric Antigen Receptor (CAR) to treat B cell leukemias (tisagenlecleucel), it has entered a new era. However, significant challenges remain, including safety assessment of target antigen and corresponding CARs or T cell receptors (TCRs), optimisation of T cell fitness, and the search for combinatorial approaches to enable T cells to target solid tumors. In the clinical setting, challenges include the manufacture and testing of clinical grade vector, development of efficient and reliable manufacturing methods, and delivering the therapies to patients safely, effectively, and at a cost that is considered reasonable. This workshop will explore these important issues.
- Selecting safe antigens and receptors for ACT
- Strategies to enhance therapeutic efficacy
- Clinical trial design to incorporate combining ACT with standard treatments or other immunotherapies such as checkpoint inhibitors and vaccines
- Establishing best practice for delivery of ACT in a hospital setting, including monitoring and managing toxicities from ACT
- Challenges of scale-up as we move beyond single-site investigator-led clinical trials
- Establishing links between the pharmaceutical industry and clinical centres to deliver ACT

SC3: Preclinical Models for Cancer Immunotherapy
Linda Martensson, Senior Research Scientist, Preclinical Research, Bioinvent
Valeria G. Nicolini, PhD, Principal Scientist, Pharmacology, Roche Innovation Centre
Part One: Preclinical Mouse Models in the Development and Selection of Therapeutic Immuno-Modulating Antibodies
This session will examine the pros and cons of the different types of animal model, the challenge of finding an antibody that cross reacts with mouse targets, and the need for surrogate antibodies or a humanized mouse model.
This session will examine different types of animal models for
A. Proof of Concept of new targets.
B. Choosing the optimal lead candidate.
- Surrogate antibodies in immunocompetent models
- Transgenic models expressing human targets
- Fcγ-receptor humanized models
- Patient-derived xenograft models
Part Two: Humanized Mouse Models: Technology and Applications in Preclinical Assessment of Cancer Immunotherapy
The course will describe different types of humanized mouse models, their immune characterization, and specific examples of their application in the field of cancer immunotherapy. The course will highlight advantages and pitfalls of currently available humanized mouse models and review next generation improved humanized models designed to better address specific immunological questions.
- Selection of humanized mouse model for specific immunotherapeutic applications
- Immunopharmacodynamic analyses in humanized mice: Impact of immunotherapeutic treatments on the immune cell contexture
- Humanized mouse models: In-house generation or outsourcing?

SC4: The Tumour Microenvironment and Response to Cancer Immunotherapy
Mark Cragg, PhD, Professor, Experimental Cancer Biology, Antibody & Vaccine Group, Cancer Sciences Unit, University of Southampton
Ann White, PhD, Senior Principal Scientist, New Medicines, UCB
The tumour microenvironment (TME) is a complex, dynamic environment in which extracellular matrix (ECM), soluble factors, immune cells, stromal cells and tumour cells interact. Each of these components is key to the establishment and growth of the tumour, as well as impacting tumour cell behaviour and response to treatment. In this short course, we will discuss the nature of the TME, how the tumour promotes an immunosuppressive environment, and what opportunities this presents for reversing immune suppression to deliver effective immunotherapy.
During the course, we will discuss:
- The constituents of the tumour microenvironment
- Factors in the TME that may influence therapeutic response
- Immune cell frequencies and phenotypes
- Cross-talk between tumour and stromal cells – suppressive cytokines, influence on characteristics of tumour cells and ability to metastasise
- Extracellular matrix components
- Vascularity, barriers to T-cell entry
- Opportunities to overcome some of these factors
- A conceptual framework for how immunomodulatory mAb might best function
- How therapeutic success is likely to require combination approaches
- The importance of relevant model systems
*Separate Registration Required
**TUMOUR INFILTRATING LYMPHOCYTES AND UNCONVENTIONAL T CELLS**

**11:40 Next Generation Products Based on Tumour Infiltrating Lymphocytes**
Robert Hawkins, MB BS, MRCP PhD, FRCP, Cancer Research UK Professor, Medical Oncology, University of Manchester & Honorary Consultant, Medical Oncology, Christie Hospital

Tumour Infiltrating Lymphocytes (TIL) are a prognostic biomarker in many tumours and have therapeutic efficacy in many tumour types. They can be used in a variety of ways to evolve next generations products, e.g. to enhance efficacy and to improve survival and proliferation by introducing novel genes. TILs can provide a rich source of tumour specific TCRs which can be cloned for conventional TCR based gene therapy or TCR libraries to produce synthetic TIL.

**12:10 The Advantages of Targeting Cancer with Unconventional T-Cells and T-Cell Receptors**
Andrew Sewell, PhD, Distinguished Research Professor and Wellcome Trust Senior Investigator, Infection and Immunity, Cardiff University School of Medicine

The major subsets of human T-cells target processed protein antigens presented as peptides bound to HLA at the cell surface. Our dissection of successful cancer immunotherapy and other pipelines has identified various broadly tumoricidal T-cell clones that are not HLA-restricted. These unconventional T-cells can kill most cancer types from all patients and thereby offer hope for pan-population, pan-cancer diagnostics and therapeutics.

**12:40 Automated Manufacture of CAR-T Cell Products in a Closed System**
Ian Johnston, PhD, Industrial and Academic Cooperations Manager, Research & Development, Miltenyi Biotec GmbH

Using closed system manufacturing reduces the risks of contamination and the requirements for in process controls and clean room infrastructure. Using the example of CAR T cell-based immunotherapies, I will demonstrate how production of cell products can be fully automated in a single-use closed system, the CliniMACS Prodigy®. Use of closed systems and automation will allow an easy establishment of robust processes at academic institutes and an effective scaling out of these procedures for commercialization.

**13:10 Luncheon Presentation (Sponsorship Opportunity Available) or Enjoy Lunch on Your Own**

**13:40 Session Break**

**BENEFITS OF PREDICTIVE BIOMARKERS, CHARACTERIZATION, AND AFFINITY OPTIMISATION**

**14:00 Chairperson’s Remarks**
Boris Engels, PhD, Senior Investigator, Exploratory Immunology, Novartis, Inc.

**14:05 Advances in CAR-T Therapy for Chronic Lymphocytic Leukemia (CLL)**
J. Joseph Melenhorst, PhD, Director, Product Development & Correlative Sciences, Center for Cellular Immunotherapies, University of Pennsylvania

We have shown that CD19-specific chimeric antigen receptor (CAR) T cell therapy can induce durable remission in most patients with acute but not chronic lymphocytic leukemia (ALL and CLL). We have now identified markers predictive of response and identified key mechanisms of response in CLL. Our preclinical studies have informed next-generation CAR-T based therapies for CLL. Our current trial in CLL has trumped our highest expectations in terms of response rate.
To accelerate progress and rapidly characterize emerging toxicities of CAR-T cell therapies, systems that permit the repeated and non-invasive assessment of CAR T-cell bio-distribution would be invaluable. An ideal solution would entail the use of a non-immunogenic reporter that mediates specific uptake of an inexpensive, non-toxic and clinically established imaging tracer by CAR T-cells.

14:35 Analytical Characterization Studies for CAR-T Cell Therapy
David G. Kugler, PhD, Senior Scientist, Team-Lead, T Cell Profiling, Juno Therapeutics, Inc.
Chimeric antigen receptor (CAR)-T cells are a promising new modality for cancer immunotherapy, and many variants are rapidly being developed across the immuno-oncology space for haematological and solid tumor malignancies. The field has displayed enormous promise; however, the rules governing which attributes drive efficacy are still being learned. Here, we present early insights from transcriptomic and epigenetic profiling of CAR-T cells describing how cell state may play an important role.

15:05 Taking TCR-Engineered Cells to the Clinic
Tom Holdich, MBBS, Head, Global Medical Affairs & EU Clinical Development, Clinical Research, Adapimmune
Adaptive T-cell therapy is a novel approach to treatment that has demonstrated promising results but also presents unique challenges in development. Adapimmune has developed Specific Peptide Engineered Antigen Receptor (SPEAR) T-cells with affinity-optimized TCRs that recognize intracellular cancer-expressed antigens. This requires target selection, TCR development, non-clinical safety testing and scalable manufacture. SPEAR T-cells targeting MAGE-A10, MAGE-A4, and AFP are in clinical trials in several solid tumor indications.

15:35 Networking Refreshment Break

INNOVATIVE APPROACHES

16:05 Small Molecule Control of CAR-T Cells
Simon Thomas, PhD, MBioch, Associate Director, Immunobiology, R&D, Autolus Ltd.
CAR-T cells are autonomous and after infusion they engraft and expand; hence, unlike small molecular or protein therapeutics, they have no half-life. Toxicity can therefore be progressive and fulminant. We have developed a number of different strategies for “remote control” of CAR-T cell activity whereby CAR-T cells are engineered to respond to small molecule drugs. These different approaches will be described and contrasted.

16:35 Best CAR Vehicle: Peripheral Versus Tumour Infiltrating Lymphocytes
Milena Kalaitsidou, PhD, Postdoctoral Research Fellow, Cell & Gene Therapy/Immunology, GSK/University of Manchester
Great successes have led to the FDA approval of CD19 CAR-T cells in haematological malignancies, however, obtaining similar results for solid tumours has been challenging. This could be attributed to lower tumour homing and infiltration of peripheral T cells, therefore a comparison of CEA expressing CAR-T cells and CAR-TILs was performed to determine whether CAR-TILs possess enhanced potential to infiltrate tumour sites and eradicate malignant cells.

17:05 Problem Solving Roundtable Breakout Discussions
See website for details

18:00 Welcome Reception in the Exhibit Hall with Poster Viewing
19:00 End of Day

TUESDAY, 20 MARCH

ADVANCING ADOPTIVE T-CELL THERAPY IN THE CLINIC

08:00 Registration & Morning Coffee

08:30 Chairperson's Remarks
John Maher, FRCPath, PhD, Consultant & Senior Lecturer, Immunology, Cancer Studies, King's College London

08:35 Seeing is Believing: Translational CAR T-Cell Imaging
Sophie Papa, MA(Oxon), MBBS, MRCP, PhD, Senior Lecturer and Honorary Consultant, Medical Oncologist, Cancer Studies, King's College London
To accelerate progress and rapidly characterize emerging toxicities of CAR T-cell therapies, systems that permit the repeated and non-invasive

09:05 TCR-Engineered T Cells Combined with T Cell Co-Stimulation to Treat Solid Tumors
Reno Debets, PhD, Associate Professor, Tumor Immunology, Medical Oncology, Erasmus MC Cancer Institute
To ensure further clinical development of TCR gene therapy, it is necessary to accurately select TCRs and, at the same time, include strategies that restore or enhance accumulation and activation of T cells in tumor tissues. Here, we present our recent preclinical and translational studies to enhance TCR-engineered T cell therapy, its combination with T-cell co-stimulation, and preparations towards a clinical T cell therapy trial to treat patients with melanoma and head-and-neck cancer in 2018 Q2.

09:35 Design of a Highly Efficacious CAR Targeting Mesothelin in Solid Tumors
Bons Engels, PhD, Senior Investigator, Exploratory Immunooncology, Novartis, Inc.
Following clinical experience with a murine scFv based CAR (SS1) targeting mesothelin (MSLN), we pursued the generation of a fully human MSLN-targeting CAR with increased potency against solid tumors. The strong anti-tumor activity of the lead CAR was confirmed in a unique primary pancreatic cancer xenograft mouse “clinical trial”. The lead candidate is now being evaluated in a Phase I clinical study in patients with malignant mesothelioma, ovarian, and lung cancer.

10:05 Advancing Non-Viral T-Cell Engineering Using Therapeutically Relevant Strategies
Jessica Carmen, PhD, Director, Marketing, Cell Therapy, MaxCyte, Inc.
Non-viral methods of engineering CAR-T cells and delivering gene editing tools have advanced to clinic, but how will they progress from here? In this presentation, we describe a key non-viral, enabling technology and the path to the clinic for the treatment of various cancers. Additionally, we discuss strategies for augmenting your current CART programs or developing your next-generation therapy using non-viral cell engineering.

10:35 Coffee Break in the Exhibit Hall with Poster Viewing

ADVANCES IN THE CLINIC WITH SOLID TUMOURS

11:15 Challenges of Targeting Solid Tumours with CAR-T Cells in the Clinical Setting
Fiona Thistlethwaite, MB, PhD, Consultant, Medical Oncology, The Christie NHS Foundation Trust
For solid malignancies, significant hurdles still need to be overcome if CAR-T cell therapy is to become a valid strategy in the clinical setting. These challenges include the identification of appropriate tumour antigens that avoid off-target/off-tissue toxicities, achieving adequate T-cell homing, and overcoming the immune suppressive tumour micro-environment. These aspects will be discussed in the context of CEA targeted CAR-T cell therapy for solid malignancies.

11:45 ErbB Targeted CAR-T Cell Immunotherapy of Head and Neck Cancer: T4 Immunotherapy
John Maher, FRCPath, PhD, Consultant & Senior Lecturer, Immunology, Cancer Studies, King's College London
T4 immunotherapy consists of a CD28+CD3z-based chimeric antigen receptor (CAR), targeted against the extended ErbB network, and which is co-expressed with an IL-4 responsive chimeric cytokine receptor. Preclinical efficacy and safety has been demonstrated in models of head and neck, ovarian, breast cancer and mesothelioma. Phase I clinical evaluation is now ongoing in patients with locally advanced or recurrent head and neck cancer, employing intra-tumoural delivery to minimize toxicity.

12:15 Luncheon Presentation (Sponsorship Opportunity Available) or Enjoy Lunch on Your Own
12:45 Close of Adaptive T-Cell Therapy
Significant advances have taken place in our understanding of the interplay between cancer and the immune system, and intervention points for immune modulatory antibodies and combinations that may enable immune stimulation. Contributions to synergistic innate and adaptive immunity have emerged from many such efforts, including monoclonal antibodies (mAbs) against tumor-associated antigens (TAAs) that are capable of profoundly synergizing with T cell-directed immunotherapies such as checkpoint blockade and adoptive cell therapy. Two key components account for this synergy: (i) a self-vaccinal effect mediated by dendritic cells (DCs); and (ii) an inflammatory repolarization of the tumor microenvironment. Efficient exploitation of these mechanisms has tremendous therapeutic potential.

In recent years, a number of publications have demonstrated the essential role that the tumour microenvironment and Fc receptors play for the development of immune modulatory antibodies and combinations that may enable immune stimulation. Contributions to synergistic innate and adaptive immunity have emerged from many such efforts, including monoclonal antibodies (mAbs) against tumor-associated antigens (TAAs) that are capable of profoundly synergizing with T cell-directed immunotherapies such as checkpoint blockade and adoptive cell therapy. Two key components account for this synergy: (i) a self-vaccinal effect mediated by dendritic cells (DCs); and (ii) an inflammatory repolarization of the tumor microenvironment. Efficient exploitation of these mechanisms has tremendous therapeutic potential.

We present two aspects of our work: First, we address the need for more extensive exploration of the design space for bi/multi-targeting by automating the production and screening of very large panels of such candidate molecules. Second, we apply machine learning methods to automating the production and screening of very large panels of such candidate molecules.

We reasoned that a bispecific antibody against two checkpoints would be more effective than single inhibitors, but also cause greater immune-related toxicities. Combinations of checkpoint-blocking antibodies are more efficacious than single inhibitors, but also cause greater immune-related toxicities. We generated several dual-checkpoint inhibitors including XmnAb20717 (anti-PD1 x anti-CTLA4) that are more efficacious in vivo relative to combinations of monospecific checkpoint blockers, suggesting that such bispecifics may have clinical advantages over combination therapy for the treatment of cancer.

significant advances have taken place in our understanding of the interplay between cancer and the immune system, and intervention points for immune modulatory antibodies and combinations that may enable immune stimulation. Contributions to synergistic innate and adaptive immunity have emerged from many such efforts, including monoclonal antibodies (mAbs) against tumor-associated antigens (TAAs) that are capable of profoundly synergizing with T cell-directed immunotherapies such as checkpoint blockade and adoptive cell therapy. Two key components account for this synergy: (i) a self-vaccinal effect mediated by dendritic cells (DCs); and (ii) an inflammatory repolarization of the tumor microenvironment. Efficient exploitation of these mechanisms has tremendous therapeutic potential.
CD3 bispecific antibodies induce rapid activation of T cells leading to degranulation of cytolytic vesicles and apoptosis of target expressing cancer cells. Both CD8 and CD4 cells can kill tumor cells in vitro although with distinct kinetics. T cell activation results also in feedback inhibition. PD1 up regulation has been described with multiple molecules and shown to inhibit activity of CD3 bispecific antibodies. The role of other co-inhibitory molecules is less clear. Our goal is to systematically characterize the induction and functional role of key co-inhibitory and co-stimulatory molecules upon treatment with CD3 bispecific antibodies to identify optimal combination strategies.

CHECKPOINT INHIBITORS

13:30 Dessert Break in the Exhibit Hall with Poster Viewing

13:15 Session Break

Lunch on Your Own

12:45 Luncheon Presentation (Sponsorship Opportunity Available) or Enjoy Lunch on Your Own

13:15 Session Break

13:30 Dessert Break in the Exhibit Hall with Poster Viewing

ADVANTAGES OF BISPECIFICS FOR TARGETING CHECKPOINT INHIBITORS

14:00 Chairperson's Remarks

14:05 Novel Combination Approaches for Cancer Immunotherapy

Christian Klein, PhD, Distinguished Scientist, Head, Oncology Programs, Cancer Immunotherapy Discovery, Roche Pharmaceutical Research and Early Development, Roche Innovation Center Zurich

This presentation will cover the experience with T cell bispecific antibodies, checkpoint inhibitors and immunomodulators as well as novel approaches to enhance their activity by combination therapy.

14:35 Rational Combination Strategies to Augment Activity of CD3 Bispecific Antibodies

Teemu Juntila, PhD, Senior Scientist, Translational Oncology, Genentech, Inc.

CD3 bispecific antibodies induce rapid activation of T cells leading to...
Melanoma are ongoing and a summary of preclinical and clinical data trials combining bemcentinib with pembrolizumab in NSCLC, TNBC and of immune checkpoint blockade, targeted- and chemotherapy. Three clinical development as combination therapy to enhance the efficacy Bemcentinib is a first-in-class, highly selective, oral AXL inhibitor in PhII evasion through tumour intrinsic and immune suppressive mechanisms. "brake") will be presented. Pembrolizumab in metastatic melanoma ("pushing the gas, releasing the paclitaxel in metastatic breast cancer (chemo-immunotherapy) or with CD8 T cells. Results from clinical studies with LAG-3Ig combined with agonist to activate antigen presenting cells (APC) and then effector resistance is currently in clinical phase testing. The potential of targeting FcgRIIB to improve cancer immunotherapy in its broadest sense will be discussed. LAG-3: Identification & Validation of the Next Generation Checkpoint Pathway Frederic Triebel, MD, PhD, CSO & CMO, Immutep S.A. LAG-3 is a well-known target with many checkpoint-blocking antibodies competing in the clinic. What is less known is the use of the soluble LAG-3 receptor (LAG-3Ig or etfligamod alpha) as a MHC class II agonist to activate antigen presenting cells (APC) and then effector CD8 T cells. Results from clinical studies with LAG-3Ig combined with paclitaxel in metastatic breast cancer (chemo-immunotherapy) or with pembrolizumab in metastatic melanoma ("pushing the gas, releasing the brake") will be presented. KEYNOTE: PD-1 Antibody Is a Broad Spectrum Anticancer Therapy Both as Monotherapy and in Combination Roy D. Baynes, MD, PhD, Senior Vice President & Head, Global Clinical Development, CMD, Merck, Sharpe & Dohme (MSD) PD-1 antibody has shown broad activity across a number of tumor types as a monotherapy. Precision medicine enriches for those most likely to respond to monotherapy and identify those for whom alternatives such as combination therapies should be explored. Combinations with PD-1 antibodies being explored include standard therapies (chemotherapy, radiation therapy), targeted therapies, other immunologic modulators, tumor vaccines and oncolytic viruses. The goal of combination therapy is enhanced efficacy without compounded toxicity. AXL Inhibition as a Potential Cornerstone of Combination Cancer Therapy Richard Godfrey, CEO, BerGenBio ASA AXL is a recognised target driving drug resistance and immune evasion through tumour intrinsic and immune suppressive mechanisms. Bemcentinib is a first-in-class, highly selective, oral AXL inhibitor in PhII clinical development as combination therapy to enhance the efficacy of immune checkpoint blockade, targeted- and chemotherapy. Three trials combining bemcentinib with pembrolizumab in NSCLC, TNBC and melanoma are ongoing and a summary of preclinical and clinical data supporting the potential for this combination will be discussed.
Cancer Immunotherapy

SC4: The Tumour Microenvironment and Response to Partnering

The potential of bispecific T cell-engaging antibodies is hindered by antibody with tumor-directed activity and augmented Treg depletion. ATOR-1015 is thought to be a combination of regulatory T cell (Treg) depletion and OX40, a receptor notorious for requiring alternative cross-linking strategies to achieve activity. Here, we demonstrate soluble bispecific antibodies can serve as potent agonists in NFkB activation and primary T-cell biology to deliver immune stimulation and immunotherapy.

16:05 OX40: The Agonist and the Ecstasy
Lucas Bailey, PhD, Principal Scientist, Protein Engineering, Invenra

The promise of combination immunotherapy has been tempered by a number of clinical setbacks and is awaiting novel approaches. We describe our B-Body™ multi-specific antibody platform screening strategy for the discovery of an array of agonistic molecules to targets simultaneously, promoting cell-cell interactions expected to develop for tumor-directed immunotherapy. ATOR-1015 binds both CTLA-4 x OX40 bispecific immune activating antibody to achieve activity. Here, we demonstrate soluble bispecific antibodies can serve as potent agonists in NFkB activation and primary T-cell biology.

16:35 Problem Solving Roundtable Breakout Discussions
See website for details

FRIDAY, 23 MARCH

08:00 Morning Coffee

NEXT GENERATION APPROACHES

08:30 Chairperson’s Remarks
Frederic Triebel, MD, PhD, CSO & CMO, Immutep S.A.

08:35 The CTLA-4 x OX40 Bispecific Antibody ATOR-1015 Induces Anti-Tumor Effects Through Tumor-Directed Immune Activation
Anne Månsson Kvarnhemmar, Ph.D. Senior Scientist, Alligator Bioscience

ATOR-1015 is a CTLA-4 x OX40 bispecific immune activating antibody developed for tumor-directed immunotherapy. ATOR-1015 binds both targets simultaneously, promoting cell-cell interactions expected to enhance the immune-stimulating effects. The mode of action of ATOR-1015 is thought to be a combination of regulatory T cell (Treg) depletion and effector T cell activation. It can be seen as a next generation CTLA-4 antibody with tumor-directed activity and augmented Treg depletion.

09:05 Elimination of Solid Tumors in Mice by mRNA-Encoded Bispecific Antibodies
Hayat Bahr-Mahmud, PhD, Deputy Head, Bispecific Antibodies, BioNTech AG

The potential of bispecific T cell-engaging antibodies is hindered by manufacturing challenges and short serum half-life. We circumvented these limitations by treating mice with in vitro-transcribed pharmacologically optimized, nucleoside-modified mRNA encoding the antibody. We achieved sustained endogenous synthesis of the antibody, which eliminated advanced tumors as effectively as the corresponding purified bispecific antibody. Because manufacturing of pharmaceutical mRNA is fast, this approach could accelerate the clinical development of novel bispecific antibodies.

10:05 Next Generation Approaches for Stimulatory Agonists Using Modified Antibodies
Shravan Madireddi, PhD, Senior Scientific Researcher, Cancer Immunology, Genentech

10:35 Networking Coffee Break

ENHANCEMENT OF PRODUCT PROPERTIES

11:05 Mode of Action, Enhancement of Stability, and Determination of Specific Delivery for Immuno-Oncology Products Targeting Agonists and/or Cytokines
Yan Qu, PhD, Senior Principal Scientist, Rinat Pfizer

Kurt R. Gehlsen, PhD, Vice President and CSO, Therapeutics, Research Corporation Technologies, Inc.

We have engineered a novel antibody-like scaffold platform (Abdurins) that is small in size (12-15kDa) and retains a long serum half-life through FcRn binding. Abdurin libraries can be used to generate highly specific binders to I/O targets, made into monospecific or multifunctional constructs and used to significantly increase drug concentration into tumors or other targeted tissues which should lead to increased efficacy and better safety compared to full-length antibodies.

12:05 Bispecific Antibodies for Selective Blockade of CD47 on Mesothelin-Positive Tumors
Krzysztof Masternak, PhD, Head, Biology, Research, Novimmune SA

We have developed bispecific antibodies (biAbs) pairing high affinity anti-mesothelin arms to a low affinity anti-CD47 arm. Such design restraints CD47 neutralization to mesothelin-positive cells, limiting toxicity and pharmacokinetic issues related to ubiquitous CD47 expression. Compared to anti-mesothelin mAbs, mesothelin/CD47 biAbs induce superior ADCC and phagocytosis in vitro, and enhanced anti-tumor responses in vivo. Mesothelin/CD47 biAbs represent a means to deliver potent efficacy safely, laying the clinical foundation for future combination therapies.

12:35 Close of Conference
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**HOTEL & TRAVEL INFORMATION**

**CONFERENCE VENUE & HOTEL:** Hilton London Canary Wharf  
Marsh Wall, South Quay, London, E14 9SH, UK, T: 44 (0) 203-002-2300  
Discounted Room Rate: £209 s/d ($285 USD) (includes breakfast and Wi-Fi)  
Discounted Room Rate Cut-off Date: 13 February 2018  
To make your hotel reservation & for additional travel information, please visit the travel page of Immuno-OncologyEurope.com.