McGill

Centre universitaire de santé McGill
McGill University Health Centre

DDTP Symposium

Biological Therapeutics

"Do's and Don'ts and Points to Consider"

Thursday, May 17, 2012

8:30 AM to 12:30 PM

Faculty Club, McGill University

presented by

McGill-CIHR

Drug Development

Training Program

CIHR IRSC

Canadian Institutes of Health Research | Instituts de recherche en santé du Canada

Schedule

8:30 - 9:00 — **Coffee/Registration**

9:00 -10:00 — **Dr. Nicki Panoskaltsis**

Lessons from TGN1412: What really happened at Northwick Park?

10:00 -10:15 — **Coffee**

10:15 -11:15 — **Dr. Mario Filion**

Digging deeper to identify new therapeutic targets for targeted therapies

11:15 –12:15 — **Dr. Brian Booth**

Safe & Effective: The regulatory issues with the development of biologic products.

Chair: **Dr. Phil Oldfield**

Co-Chair: **Dr. John Di Battista**

Dr. Nicki Panoskaltsis, MD PhD FRCP

Assistant Professor, Imperial College London
Head of Clinical Haematology, Northwick Park Hospital
Harrow, United Kingdom

Lessons from TGN1412: What really happened at Northwick Park?

In 2006, 6 healthy volunteers simultaneously received TGN1412, an investigational drug in a Phase I first-into-man (FIM) clinical trial. TGN1412 was a first-in-class anti-CD28 IgG_4 humanised monoclonal antibody designed to stimulate T_{reg} cells without the usual requirement for co-stimulation – a "super-agonist". The study was sponsored by TeGenero, a new biopharmaceutical company, and conducted by a Contract Research Organisation (CRO), Parexel International, at their research unit housed in leased space at Northwick Park Hospital (NPH), London. Although an expansion of T-cells without cytokine release was expected based on pre-clinical studies, the opposite was observed. All 6 individuals suffered a life-threatening cytokine storm starting with TNF-alpha release within an hour as well as severe lymphopenia, monocytopenia and pulmonary compromise within 6 hours of drug infusion. By 16-20 hours after infusion, all volunteers suffered multi-organ failure and were transferred to the intensive care unit at NPH for aggressive support with ventilation, haemo-filtration, ionotropes and high-dose methylprednisolone to suppress the cytokine storm. All 6 patients survived - one required amputation of digits due to necrosis of tissue. Despite intensive efforts, the immunologic mechanism and aetiology of the serious adverse event due to TGN1412 is still unclear and there is an ongoing requirement for monitoring of all patients. The event changed the conduct of FIM studies and stimulated discussion and change in policy regarding the safe and ethical conduct of trials in general within, and between, the pharmaceutical industry, CROs and academia to ensure the safety of trial volunteers and continued progress in drug discovery.

Dr. Mario Filion, PhD

Executive Vice-President and Chief Scientific Officer
Alethia Biotherapeutics
Montreal, QC

Digging deeper to identify new therapeutic targets for targeted therapies.

We have witnessed the approval and prescription of an increasing number of targeted therapeutics in the last decade which has translated into a shift of paradigm for the care of patients with diseases that are difficult to treat. The advent of genomics, transcriptomics and proteomics has undoubtedly contributed to our understanding of disease mechanisms. Current advances in personalized medicine represent the culmination of decades of basic and applied research. Interestingly, very few novel therapeutic targets have emerged from this enormous amount of research. Consequently, the majority of approved therapeutic monoclonal antibodies or small molecules developed in oncology indications and inflammatory disorders hit relatively few therapeutic targets.

To face the challenge of developing more specific and potentially safer therapeutics, we have designed a discovery approach based on a highly sensitive transcriptomics technology which permits the identification of novel targets for engineering therapeutic monoclonal antibodies. Our approach was successfully applied for the development of more specific therapies for the treatment of ovarian cancer as well as for severe bone loss in acute disorders. We are focusing our efforts on new therapeutic targets with improved specificity to diseased tissues that are functionally relevant to the disease process.

Dr. Brian Booth, PhD

Deputy Director of the Division of Clinical Pharmacology 5
U.S. Food & Drug Administration
Silverspring, MD

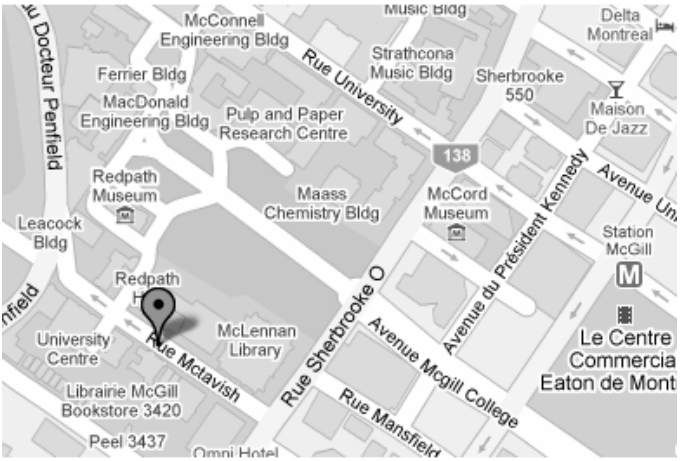
Safe & Effective: The regulatory issues with the development of biologic products.

New drugs and biologics must meet the minimum requirements that they are safe and effective before they can be approved for marketing in the US. The types of issues that need to be addressed range from the chemical nature of the product (stability, sterility, shelf-life, etc) to the clinical effects and the adverse events that can occur after treating the patient. The timeframe and settings over which the clinical data are generated to support the approval of the product will be discussed with particular emphasis on the clinical pharmacology aspects of these products.

Directions

The symposium will take place in the ballroom at the Faculty Club of McGill University located at 3450 McTavish Street, Montreal, QC, H3A 1X9.
(Tel.: 514.398.6660)

Faculty Club



Drug Development Training Program

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