Production of investigational advanced therapy medicinal products for phase I clinical trials

Bart Vandekerckhove
Ghent University
CERTAIN TUMORS ARE IMMUNOGENIC

R.T. Prehn, J.M. Main
**Immunity to methylcholanthrene-induced sarcomas**
Adaptive immune resistance.

IMMUNOGENIC TUMORS ARE CURABLE BY IMMUNE ACTIVATION


©2016 by American Association for Cancer Research
MUTATIONS GENERATE IMMUNOGENIC TUMORS
CERTAIN TUMORS ARE IMMUNOGENIC

Number of somatic mutations in representative human cancers, detected by genome-wide sequencing studies.

B Vogelstein et al.
Science 2013;339:1546-1558
MIDRIX NEO: MPLA-Interferon-activated neoantigen-targeted dendritic cell vaccine
A truly personalized approach

Advanced therapies and their challenges

- Gene therapy medicinal products
- Somatic cell therapy medicinal products
- Tissue engineering products
- Genetically modified cells

www.heartandmetabolism.org
NAT Biotechnol 2005, 23(7)
www.biomed.brown.edu
ANNEX I

Manipulations referred to in the first indent of Article 2(1)(c)

— cutting,
— grinding,
— shaping,
— centrifugation,
— soaking in antibiotic or antimicrobial solutions,
— sterilization,
— irradiation,
— cell separation, concentration or purification,
— filtering,
— lyophilization,
— freezing,
— cryopreservation,
— vitrification.


**Good manufacturing practices**

**Starting materials**
- mRNA
- Apheresis product

**GMP environment:**
- Controlled environment
- Risk reduction

**Drug substance:**
- mRNA electroporated DC

**Drug products:**
- Frozen mRNA EP DC

**ATMP**

Full documentation in the Investigational Medicinal Product Dossier

GMP facility and production process audited and licensed by FAGG
Translation into a GMP compliant protocol

- Research
  - Open systems
  - Bovine serum

- GMP
  - Closed systems
  - No animal products
Clean room environment at GMP unit 3 Cell Therapy UZ Ghent

- Qualified personnel
- Controlled environment
- Strict clothing requirements
- Control of devices
Project info meetings

For SMEs, academic research centres, spin-offs and academic hospitals, the National Innovation Office foresees the possibility to present a specific clinical research project situated in a very early stage of development.

Project info meetings give innovators high level guidance on general regulatory requirements and procedural steps to follow when considering initiating a medicine development project and help identify any future scientific, technical and regulatory hurdles that may impact the project.

Project info meetings create awareness about particular uncertainties or the feasibility of the project which can facilitate further project planning, thereby increasing the chances for success. If needed the applicants will be advised to request a formal national and/or European scientific advice.

How to apply:

Applicants can request a project info meeting via innovationoffice@fagg-amphs.be. The request should contain a short summary of the project and motivation. The Innovation Office will then contact the applicant with information whether an project info meeting can be granted, depending on the eligibility of the request and availability of FAMHP experts, and to discuss further practicalities.

Last updated on 18/05/2017

In 2018, the following fees(*) apply to requests for national STA submitted to the FAMHP:

TYPE I: **Technical-regulatory advice** : € 2,217.91
TYPE II: **Scientific advice** : € 13,307.48
TYPE III: **Mixed advice** (i.e. scientific and technical-regulatory advice) :€ 17,743.32

(*) Fees for national STA are subject to indexation on a yearly basis. Indexation of the fees normally takes place at the beginning of each calendar year.

The same fees for national STA request will apply independently of the type of applicant by whom the STA request is submitted to the FAMHP: i.e. sponsors of clinical trials, pharmaceutical/biotech companies (eg. small biotech spin offs, SME's, global companies), research centres, etc.

The same fees for national STA request will apply regardless of the area of advice (eg. paediatrics, oncology, etc..) or timing of seeking advice at national level (eg. initial versus follow-up advice).
FUNDING: WHO WILL PAY FOR IT?
Principal investigators
Prof. Karim Vermaelen
Prof. Bart Vandekerckhove

GMP production
Prof. Bart Vandekerckhove
Pam Devreker
Saskia Desmet
Nele Lootens
Sarah Vanreenterghem

Bioinformatics
Prof. Bjorn Menten
Prof. Kathleen Claes
Laurenz De Cock

Immunology
Dr. Elisabeth Brabants
Joline Ingels
Kelly Heyns

Immunopeptidomics
Prof. Francis Impens
Dr. Rupert Mayer

Farmacy
Prof. Stefaan DE Smedt
Dr. Ine Lentacker
Dr. Heleen De witte

Sponsors
Kom op tegen Kanker
University of Ghent
Galsome technology

GALSOMES
Lipid nanoparticles
Nucleoside-modified mRNA
5meC, ψ

Glycolipid embedded in lipid nanoparticle
smart adjuvant

Delivery to antigen presenting cells (APC) after i.v. injection

NKT cells as driving force
Dual antigen signal

MHC-I (antigen-mRNA)

CD8+ T cell

Driving force

CD1d (glycolipid)

NKT cell

Synchronised & dose-controllable activation of APCs, CD8+ T cells & Natural killer T cells

Cancer immunotherapy
Turn cold into hot tumor

Broadening the message

Infiltrate of T cells, NK & NKT cells + Reduction of suppressive cells

IFN-γ + upregulation of PD-1/PD-L1

Tumor antigen

Synergy with checkpoint inhibition

Anti-PD-L1 antibodies

Broad antitumor immunity & synergistic efficacy with PD-L1 checkpoint inhibition