PreDiCT-TB

Model-based preclinical development of anti-tuberculosis drug combinations

The Objectives

The overall project objective is to tackle TB drug development bottlenecks and to answer patients' unmet needs by:

- improving/enhancing current pre-clinical models (to adopt a consistent decision making framework to optimize clinical trial design and identify likely effective drug combinations)
- To compare information from in vitro & in vivo assays and clinical trials for licensed and novel drug combinations in TB.
- To enhance predictive power of pre-clinical experimental models for future clinical efficacy by developing mathematical models, based on PK-PD relationships and model improvements using novel technologies.

The Organization

PreDiCT-TB is a consortium of 19 public and private scientific partners from seven EU members' states.

A specific PreDiCT-TB structure based on seven work packages (WP) has been deployed to ensure that objectives are maintained.

To secure deliverables, strong interactions have been established between the different WPs with efficient project management co-ordinating all activities.
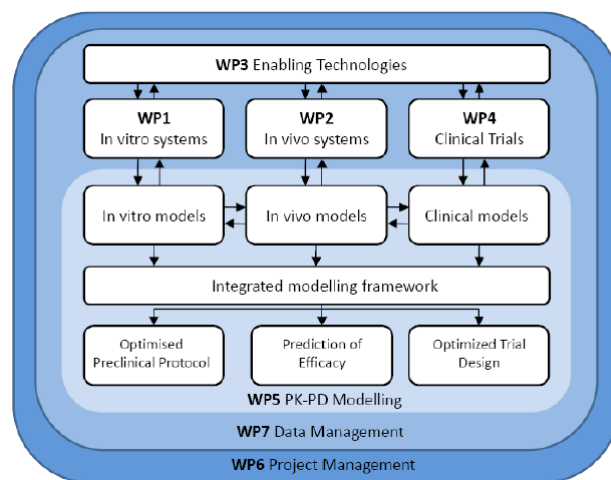

Structure of workpackages and their interactions within the PreDiCT-TB consortium. Integration of data from WPs 1-4 will be achieved in the modelling framework created in WP5 and data flow will be ensured by the data management activities in WP7. Effective co-ordination of activities will be ensured by project management provided by WP6.

The Background

Tuberculosis (TB) is a major global killer responsible for ~9 million new cases and 1-2 millions deaths per year. It remains the leading cause of death of young adults in developing countries. Rising drug resistance, HIV co-infection and long treatment times mean new regimens are urgently required.

However, the development of novel compounds for TB is hampered by inaccurate prediction of clinical effectiveness by currently available laboratory methods. New integrated methods should rapidly transition novel compounds within a new combination regimen in order both to shorten the duration of treatment and combat multi-drug resistance (MDR).

While a single TB drug development program might take 5-8 years, developing a drug regimen sequentially might take at least 20 years unless we adopt this new approach.

Therefore PreDiCT-TB aims to improve the predictive power of pre-clinical methods in order to hasten the delivery of new regimens. This truly translational project is critical if we are to bring new regimens to patients in a timely fashion.

The Approach

A sustained and iterative interaction between experimentalists and modellers during two main phases lasting approximately 24 months each, in which approved and then novel drugs will be evaluated.

Information from clinical studies will be used to inform *in vitro* and *in vivo* studies enabling modellers to construct mathematical models which aim to predict clinical efficacy of individual drugs and their combinations.
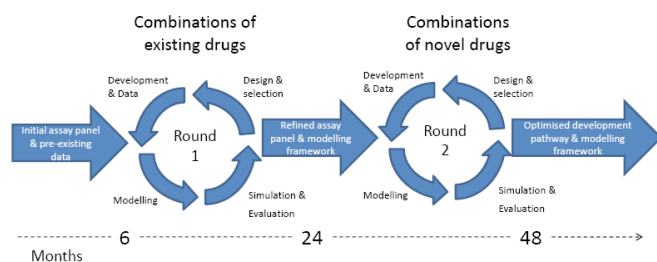
The Impact

Scientific:
This new model-based approach has the potential to shift the paradigm of drug discovery and development in the TB field.

External scientific partners:
Such a proposed approach has generated great interest among the TB and wider scientific community.

Findings will be disseminated through regular presentations, posters and papers at international scientific meetings and high impact factor journals to promote the need and solutions for a more rational and unified approach to TB drug development.

Regulators and patient organizations:
Interactions and collaboration with the wider TB community are a crucial and active part of the PreDiCT-TB strategy.

Socio-economic:
No truly novel TB drug regimens have been registered for more than thirty years. More effective pre- and early clinical development could accelerate the arrival of new drug combinations that could simplify treatment delivery for TB programmes in high-burden countries, save the lives of thousands more TB patients and reduce global transmission of the disease.

The Duration

PreDiCT-TB is a five year project which started in May 2012.

The Partners

EFPIA member companies:
- GlaxoSmithKline R & D Limited, *United Kingdom*
- Sanofi Research and Development, *France*
- Janssen Infectious Diseases BVBA (Tibotec), *Belgium*

Universities, research organisations, public bodies, non-profit groups:
- University of Liverpool, *United Kingdom*
- Universidad Carlos III Madrid, *Spain*
- Max Planck Institute of Molecular and Cell Biology and Genetics, *Germany*
- Max Planck Institute for Infection Biology, *Germany*
- Erasmus University Medical Center, *Netherlands*
- Health Protection Agency, Porton Down, *United Kingdom*
- Institut Pasteur, *France*
- St George's University, *United Kingdom*
- University of Saint Andrews, *United Kingdom*
- Global Health Institute, *Switzerland*
- University of Leicester, *United Kingdom*
- University College London, *United Kingdom*
- VU University Medical Center, *Netherlands*
- Liverpool School of Tropical Medicine, *United Kingdom*
- Uppsala University - *Sweden*

Small and medium-sized enterprises (SMEs)
- Microsens Medtech, Ltd, *United Kingdom*
- ZF screens – *Netherlands*

The Key Contacts

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