10 YEARS OF BREAKTHROUGHS A HEALTHIER FUTURE

TRISTAN TRANSLATIONAL IMAGING IN DRUG SAFETY ASSESSMENT

In vivo models of drug-induced ILD; tools to study and improve drug safety

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Facts & Figures

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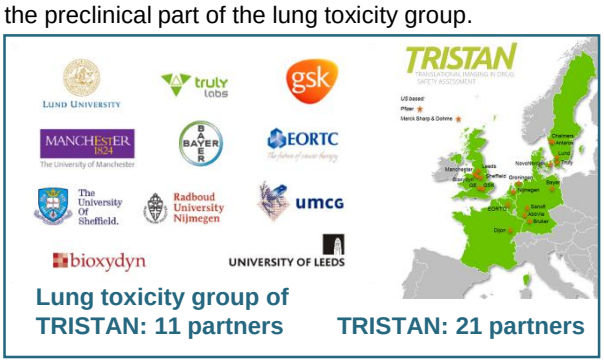
End date:	31/12/2021
Contributions	
IMI funding:	12 000 000 €
EFPIA in kind:	10 448 317 €
Other:	192 733 €
Total Cost:	22 641 050 €
Project website:	www.imi-tristan.eu

Challenge

Adverse effects caused by various drugs may induce lung injury known as drug-induced interstitial lung disease (DIILD) or liver injury (DILI). The outcome is often organ injury in terms of inflammation and fibrosis over time, or even acute organ failure.

Clinical and preclinical studies within the TRISTAN-consortium aim to find translational imaging biomarkers that can indicate progression of DIILD or DILI at an early stage. Lund University and Truly Labs from Lund in Sweden,are two partners from TRISTAN representing the preclinical part of the lung toxicity group.



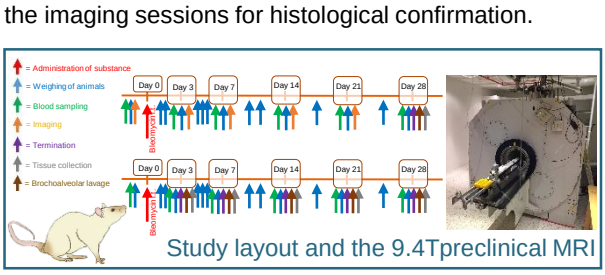
Lung toxicity group of TRISTAN: 11 partners

TRISTAN: 21 partners

Approach & Methodology

We bring together a multidisciplinary team of internationally recognised experts in their fields including; physicians who care for the relevant patients, experts in transporter biology, animal models of lung/liver injury, toxicology, lung MRI and in the labelling of peptides with radionuclide for PET detection.

Animal models are designed to incorporate imaging modalities' MRI, CT and PET and scan animals longitudinally while also terminating animal groups at the imaging sessions for histological confirmation.

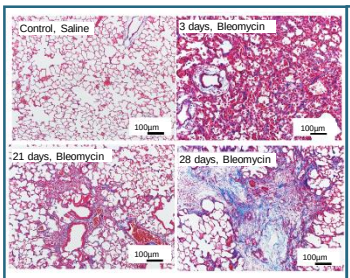


Study layout and the 9.4Tpreclinical MRI

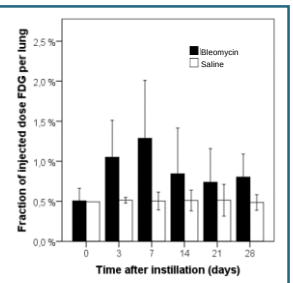
Results

Milestones and deliverables met successfully:

- Lung injury model set-up
- Optimisation of current model (translation and chronic)
- Testing adverse effects of new drugs
- Histological analysis for confirmation
- PET tracers tested and optimised
- MRI signal quantification used for detection of lesions
- Combining PET-CT-MRI techniques longitudinally
- Gene profiling analysis from lung tissue
- Differential and total cell analysis from broncho-alveolar lavage (BAL fluid).

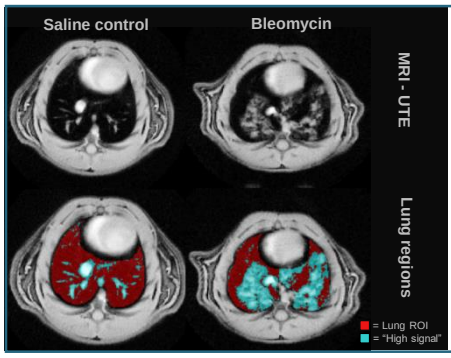


Histological analysis of bleomycin-induced lung injury. Time points presented are day 3, 21 and 28 post-challenge. Day 3-7 post-bleomycin challenge involve inflammation (oedema and immune cell infiltration) while lung fibrosis is present at later time points, day 21-28 (blue = collagen staining).



PET FDG-F^{18} increased uptake in the lung of bleomycin-challenged rats compared to the saline (control). Signal peak at day 7 indicated inflammation.

(FDG = Fludeoxy Glucose, glucose analogue molecule, energy metabolism indicator)



MRI images generated on a small-animal 9.4T magnet. Axial images of a healthy (control) and a bleomycin-challenged rat, applying the Ultra Short Echo (UTE) sequences. Red area is the lung region of interest (ROI) segmented manually. Signal marked with the color cyan represents the lesion and/or increase of signal within the lung ROI. Increased signal in lung was detected by using histogram-based thresholdning method.

Value of IMI collaboration

The consortium aims to develop imaging biomarkers into tools which drug developers can use with confidence in clinical trials of investigational agents, with a demonstrated track record of translating these imaging biomarkers for regulatory drug development and clinical healthcare.

Impact & take home message

The impact that TRISTAN provides is the unique variety of expertise areas and disciplines' able to work in concert for the best intention of the patients.

Finding translational imaging biomarkers that can both be used clinically to assess and follow disease progression, as well as to be used in preclinical models for future drug development and investigations.

imi innovative medicines initiative efpia

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