CROSS-INDUSTRY Organizations

An introduction to Drugs in the Lungs

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On behalf of Drugs in the Lungs

Drugs in the Lungs Network

The future development of new or improved inhaled medicines, especially those based on new chemical entities or pharmacological modes of action, will require a better understanding of drug disposition after delivery to the lungs. Despite modern capabilities in imaging, analytical and biological sciences, there is still a poor understanding of drug disposition, i.e. absorption, distribution, metabolism and elimination, after deposition in the lungs. The influence of pulmonary pharmacokinetics on drug efficacy and safety are the critical determinants of clinical outcomes. Yet the lung remains a quasi black box with regard to our understanding of the fate of most current inhaled medicines. This begs the question, how can the fate of drugs in the lungs be understood better to allow improvements in current therapy and to expedite the development of new inhaled medicines?

A research network

While many opportunities exist for those interested in inhaler devices and formulation technology to meet, network and engage in scientific debate, researchers interested in the fate of drugs delivered to the lungs have not had a dedicated forum. The Drugs in the Lungs Network was devised with the aim of promoting cross-company collaboration and developing academia-industry consortia. It operates as a subgroup of the Inhalation Focus Group of the Academy of Pharmaceutical Scientists (APS) of Great Britain. The Network aims to provide regular, accessible, supportive fora for technical and scientific (i.e., data-rich) discussions, with the aim of advancing the knowledge and practice of early- to late-stage inhaled product development. Taking into account feedback from previous endeavours, an inaugural meeting was organized in 2010 to discuss topics of interest and, moreover, identify the important challenges alluded to above that are common to all.

Beginnings: Consensus on key issues

The network concept was launched at a meeting hosted by GlaxoSmith Kline, UK, which was attended by 190 delegates from nearly 40 institutions from Europe and the US. The major themes of the meeting were "Dosimetry issues and predicting safety" and "Understanding pharmacokinetics-pharmacodynamics in the lungs." The workshop featured short talks to introduce issues relevant to the theme of each session. This was followed by facilitated breakout sessions to discuss key topics. At the end of the meeting, feedback was provided regarding the consensus formed. All of the original presentations and consensus from the meeting are still freely available by visiting http://www.apsgb.co.uk/FocusGroups/DrugsInTheLungs. A more detailed perspective on the topics discussed and conclusions reached at the meeting was collated in the form of a review: Challenges in inhaled product development and opportunities for open innovation, Advanced Drug Delivery Reviews, 63, 69-87 (2011).

Lung imaging

Last year, the Network meeting was hosted at Novartis and had the theme "Advances in lung imaging and their application in the development of inhaled medicines." The meeting covered the expanding and diversifying role of imaging in inhaled product development. Pre-clinical applications included the visualization and quantification of drug deposition and disposition in the lungs, the study of lung disease, identification of biomarkers and evaluation of animal models of human lung disease. The use of imaging to translate pre-clinical outcomes into the clinical arena was also covered, plus the standardization of established imaging techniques for quantifying drug deposition in humans and the use of imaging to monitor therapeutic efficacy. The presentations from this meeting are also available from the Network website.

Respiratory toxicology

Respiratory toxicology has been identified as the focus for the Autumn meeting in 2012. This is a high priority area across all pharma companies undertaking inhaled drug delivery. The aim is to establish a wide perspective on the common responses seen in the lungs and the regulatory concerns regarding these. Important topics include:

- Baseline findings in normal healthy lungs across different species
- Variability of macrophage responses to inhaled aerosols
- Histochemical methodologies for a consistent approach across companies
- Responses, interpretations, categorization of adverse and non-adverse findings
- Endpoints to aid interpretation in preclinical pathology
- Monitoring adversity (especially macrophages) in patients or healthy volunteers

This meeting will be of interest to all companies with a focus in inhaled pharmaceuticals; contract research organizations; academics with inhaled drug delivery expertise; environmental agencies and regulatory authorities.

In addition, the Network has been invited to host a pre-conference session at DDL23 in Edinburgh, following the precedent established by EPAG in 2010 and ISAM in 2011.

Open innovation

Collaborative research and the pooling of resources and data will advance our knowledge and promote progress in our area of interest. To date, we have explored the potential for such activities in the areas of:

- Toxicokinetics. Study design and interpretation
- In vitro toxicology. Sharing of preclinical data for in vitro/in vivo correlation
- Dosimetry. Opportunities to rationalize the dosimetry requirements in pre-clinical studies

The organizing committee encourages any activity in these areas and will be pleased to provide a platform for reporting progress at future meetings. The committee will support and facilitate any pre-competitive activities within the topic area of the Network and invite expressions of interest, however preliminary these may be.

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