CONFERENCE REPORT

DRUG DELIVERY TO THE LUNGS 22 (DDL 22)

DECEMBER 7-9, 2011, EDINBURGH, SCOTLAND, UK

Drug Delivery to the Lungs 22 (DDL 22) was held in Edinburgh, Scotland, UK on December 7-9, 2011. Gay Furness, Publisher of ONdrugDelivery, attended the meeting and here he reports some of the highlights.

The Drug Delivery to the Lungs conference, organised by a voluntary sub-committee of the Aerosol Society, takes place over three days each December at the Edinburgh International Conference Centre (EICC), in the Scottish capital. It is established as a major event in the pulmonary and nasal drug delivery industry calendar; an event where one gets the feeling that the key people in almost the entire inhalable drug delivery community are present.

I attend DDL regularly and, for me, what sets this event apart is the way in which the conference programme consistently reflects the fact that pharma industry, and perhaps particularly the inhalable delivery field, is powered by cutting-edge science being done by first-class scientists both in industrial and academic research labs around the world. These are the people I saw presenting at DDL 22, and one gets a real sense of a thriving and healthy working relationship between industry and academia in the field of inhalable drug delivery.

A balance was struck at DDL 22 whereby even the most academic of academics, whilst presenting the very latest, pioneering scientific techniques, discoveries and developments in the field, always related his or her talk back to unmet clinical needs or opportunities for industry; and, likewise, even the most commercially-minded businessperson presenting never talked purely on “partnering” or “marketing”. These factors came up regularly at DDL 22, but never without being presented in the context of science; fully grounded in the scientific research that underpins the product or technology that is to be partnered or marketed.

In addition to this sense of striking the right science-commerce balance – or perhaps as a result of it – I was also very aware at DDL 22 that this conference really was bang up to date. In fact, on hearing from one presenter why he had had to make some frantic changes to his slides minutes before he took to the stage, I jotted down in my notes: “You know a conference is at the cutting edge when speakers in the afternoon are having to update their slides in light of what they heard that morning!”

Another attractive characteristic of the DDL conferences is that there is just one track of talks all running consecutively in one presentation hall. For attendees, this makes following the proceedings simple and somehow more relaxed, with no parallel sessions and no resultant rushing to and fro between different rooms. A single track in one hall allows more time and space to listen to and digest the content of every presentation. This is precisely what I did, and here is a summary of a few of my key DDL 22 observations and highlights.

The conference opened with The DDL Lecture, entitled “New Drugs and Targets for COPD”, given by Peter Barnes, FRS, FMedSci, Professor of Thoracic Medicine and Head of Airway Disease at the National Heart and Lung Institute, Imperial College (London, UK). Professor Barnes provided some stark facts about COPD – which he said would soon be the third-commonest cause of death worldwide, with incidence in women increasing rapidly of late to equal that in men. COPD now kills more women than breast cancer in the UK.

He described the particularly unpleasant nature of the disease’s slow progression and its terrible effect on the lives of patients, against which there is no treatment. The disease pathology relates directly to symptoms, Barnes said, and current treatment is for symptoms, the mainstay of drug therapy being long-acting bronchodilators, which are generally either long-acting ß-agonists (LABAs) or long-acting muscarinic antagonists (LAMAs).

Improvements in LABA and LAMA therapies included the development of new molecules with longer durations of action, and the development of LABA + LAMA combinations was the most exciting, he said, highlighting QVA-149, an indacaterol + glycopyrronium bromide combination under development by Novartis, which had performed very well in clinical trials. A triple combination inhaler, TrioHale (tiotropium + formoterol + ciclesonide) from Cipla, was on the market, he added.

The focus of Professor Barnes’ research is on understanding the cellular and molecular mechanisms of COPD in order to enable novel therapeutic approaches in the future, importantly including drugs that prevent disease progression. He said that many mediators are involved and so drugs that block these individually are unlikely to work. Possibly promising active molecules mentioned by Professor Barnes and in early development were: neutrophil chemokine receptor (CXC-R2) blockers; selective matrix metalloproteinase 9 (MMP9) inhibitors; and phosphodiesterase 4 (PDE4) inhibitors. An important target he mentioned was nuclear factor erythroid-derived 2-related factor 2 (Nrf2). Activation of the Nrf2 pathway turns on anti-oxidant genes.

In terms of drug delivery challenges in COPD, Professor Barnes pointed out that new treatments for COPD – both bronchodilators and anti-inflammatories – would likely need to be given by inhalation to reduce systemic toxicity. Delivery to the peripheral airways and lung parenchyma was difficult in the presence of airway obstructions of the sort common in COPD and more attention needed to be focused on this challenge he said. Deposition studies in COPD were extremely rare. He could only find one study when he searched, he said, and described this specific area of research as having been neglected.

In addition to respiratory diseases such as COPD and of course asthma, applications of inhalable drug delivery technologies in other indications featured prominently at the meeting. The main focus stayed on diseases of the lung such as respiratory infection and lung cancer though, rather than systemic delivery via the lung.

A particularly powerful presentation on the threat from TB came from David Barros Aguirre, PhD, of the GSK Tres Cantos Medicines Development Campus (Madrid Spain). My notes on his delivery read: “If I was
Mycobacterium tuberculosis, I would not want to be up against this passionate scientist.”

Dr Barros Aguirre described a formidable enemy. He outlined the serious nature of the global TB epidemic (the bacterium infects a third of the world’s population and kills 1.7 million people per year). He described the complex lifecycle of the mycobacterium, the emergence of multi-drug resistance (MDR), and then extensive drug resistance (XDR), and the resulting current treatment strategies, which often included expensive, complex and increasingly toxic regimens of 6-8 drugs, some injected. Other obstacles to the development of effective treatments include the high incidence of co-infection of TB with HIV because the two infections are synergistic and TB drugs interact significantly with HIV drugs.

The size and complexity of the problem, and the severe unmet need for a solution, mean that all of the large pharma companies have established major anti-TB R&D programmes, GSK included. Barros Aguirre described GSK’s TB pipeline and how the company – well aware that one organisation has no chance of defeating TB on its own – is pursuing a collaborative strategy, including an open-innovation approach, and the establishment of the Tres Cantos Open Lab Foundation with funding and lab space for visiting scientists and mechanisms for sharing IP and dividing royalties.

It was in this context that he discussed a rationale for the pulmonary delivery of TB treatments, listing the various benefits (including the possibility of inhaled therapeutics being taken up by infected macrophages and rescuing them from alternative activation) as well as disadvantages (poorly aerated areas of the tubercular lung provide poor access for inhaled medicines) that the route has in this indication.

One problem, explained Dr Barros Aguirre, was that GSK’s drug discovery efforts are focused on generating once-daily oral medications but this strategy is falling down due to human dosing projections of >1g. This was a key challenge that pulmonary drug delivery could perhaps provide a solution for. He ended his dramatic talk with a simple question for the pulmonary delivery scientists that filled the DDL hall: “Can you help us?”

Systemic drug delivery via the lung was the topic of only one talk at DDL22, perhaps indicating that this exciting area of R&D, which has had its setbacks over the past decades, is yet to re-emerge as a major, confident force in the drug delivery business.

Donald Kellerman, PharmD, Vice-President of Clinical Development at MAP Pharmaceuticals (Mountain View, CA, US), reported results from pivotal Phase III clinical trials of LEVADEX, the company’s inhalation aerosol formulation of dihydroergotamine mesylate for the treatment of migraine. The trial included a double-blind, placebo-controlled efficacy portion in 794 migraine sufferers, and an open-label, long-term pulmonary safety extension in 638 patients. In the efficacy portion, LEVADEX met all four primary endpoints (pain relief at 2hrs; photophobia free at 2hrs; phonophobia free at 2hrs; nausea free at 2hrs), and was well tolerated. The pulmonary safety section of the trial revealed no clinically meaningful effect on lung function.

At the time of DDL22, MAP Pharma had recently submitted an NDA to the US FDA for LEVADEX. Since the conference, the company has received a “Complete Response” letter from the FDA which raised issues relating to CMC, facility inspection, and its review of inhaler usability information. The company, which has a meeting with the FDA scheduled for the second quarter of this year, noted that neither clinical efficacy nor clinical safety were cited in the Agency’s letter.

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The above report represents only a selection of the material that was presented at DDL 22, which also included a number of presentations tackling human factors and the development of patient-centric devices, and various presentations covering inhalable drug delivery in paediatrics. Other talks of note included: an interesting and entertaining presentation of “The Case for DPIs” from David Harris, PhD, Principle Consultant at Team Consulting (Cambridge, UK); and the intriguingly titled talk, “Tappiwhacky and the Golden Device”, from James Tibbats, PhD, Managing Director of Concept Flow (Cambridge, UK).

DDL 22 was attended by around 450 delegates who were treated to a total of 36 oral presentations and 65 posters. Additionally, there were 70 companies exhibiting at the event.

The next conference, Drug Delivery to the Lungs 23 (DDL 23) takes place at the EICC, Edinburgh, Scotland, UK, December 5-7, 2012.

www.ddl-conference.org.uk