Roundtable Proceedings
INNOVATIVE FORMULATION FOR INHALED DRUGS

"Inhalation Vaccines: is it feasible from a formulation point of view?"

June 23, 2021

Welcome

By Stefano Console, Workstream Formulation Ambassador and Advisory Board Member of eu.reca vzw

In his welcome address Stefano Console introduced the European Respiratory Cluster Antwerp (eu.reca), a young ecosystem entirely focused on everything that impacts the human lung. To advance respiratory innovation, eu.reca brings scientific and medical experts together with entrepreneurs and other stakeholders. The network stands for a hands-on approach, not only tackling relevant challenges, but always reaching out to present possible solutions.

As eu.reca's approach is based on the exchange of knowledge to advance innovation, initiatives such as round tables and workshops are important. These proceedings capture the essence of an in depth and relevant discussion on the topic of vaccine delivery.

Acknowledgements

Six technical experts (both industrial and academic) offered an insight into vaccine delivery, into nasal vs pulmonary delivery and into the available technologies. The eu.reca network acknowledges Harro Höfliger and Lonza for their continued support and in particular for their keen interest into this specific topic.

▶ Setting the scene: goals of the workstream

When administering a drug, the routes to successfully reach the target can vary depending on the product and its specificities, as well as the intended effect. For respiratory therapies many options are available. With regard to the current pandemic and the administration of vaccines, the main course of action has been the injection of drugs. Several new vaccines however are aiming to make the difference (and obtain a market position) based on easier administration by inhalation. This session focusses on that topic.

This virtual roundtable discussion was initiated trough a number of questions to which all participants provided their answer. These proceedings capture the essence of the participants' combined answers.

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Discussion

Does it make sense to think about inhalation as a way of delivering vaccines?

In the field of respiratory diseases, vaccination via the mucosal route would be an excellent choice. Nasal administration could be a route considering the fact that the abundance of immune cells in the nasal mucosa are giving a better immune response. However, further research is needed to determine whether clearance via mucosa is not too big of a barrier and the deposit of the RNA vaccine is effective enough.

When the mucosal area is indeed found to be a good place to deposit a vaccine, it would make the delivery much easier and much more convenient for the patient, for it foregoes the use of needles.

However, when there is a need to deposit the vaccine in a systemic way (e.g. lung periphery), it is more complicated to get the vaccines at the right place. Another point of consideration: a stable formulation is necessary, so the product can be handled at room temperature and logistics can be kept cost effective and simple, avoiding the cold chain management.

What is the location where the vaccine needs to be delivered?

There are various routes of administration, each of which has associated advantages and disadvantages. All the routes of drug administration need to be understood in terms of their implications for the effectiveness, immunogenic effects, and the patients' experience.

For example nasal administration has the advantage of a high density of immune cells (presence of APC), while the lung has a much bigger surface.

Needle free administration is the desired route for children but it is difficult to control the effectiveness of the inhalation.

Again stability at room temperature is highly recommended and depending on the availability of excipients and the dose, even a combination of nasal and pulmonary delivery could be an option to be evaluated.

Innovations and new tools & knowledge are required to design products to deliver therapeutic agents to the right target at the right time in the right patients. Taking into account the pharma-economical and compliance factors (stable product, avoiding cold chain supply, less invasive, cost to society, delivery speed and location) which formulation is most suitable for nasal or pulmonary administration?

- Nasal route delivery: RNA vaccines including the targeting ligand (nanoparticles) can migrate to the brain via the olfactory bulb, but the stability of these nanoformulations (colloidal, microbial, chemical) needs to be investigated. Again the same factors need to be considered directly from the beginning for global vaccination: logistics, storage, people, speed of delivery, availability, price. The Single Disposable (and cheap) devices are preferred. There is still a lot of investigation needed about the way of administration, depending on the target: solution or spray or even dry powder (longer residence time, but with a limitation that is the dose)

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- Lung delivery: powder versus nebulisation. When talking about nanoparticles formulations or even peptides or small proteins, the easiest and quickest method is to develop a liquid formulation, but on the other hand, once developed a dry powder platform (with an easier and cheaper storage and shorter incubation time) can be used for any RNA drug formulation. Once again there is a trade-off, depending on the target population: a nebulised solution is more flexible in use in hospitals as long as it is affordable and can be used in urgent intervention, while for mass vaccination dry powder is still the way to go. Some research and development is needed to create platforms, enabling to load with bioactive compounds, but also the industry must mature and be ready to increase production faster when needed.

Devices and excipients

As already highlighted in previous discussions and roundtables, there are not a lot of approved excipients for inhalation. Authorities should streamline and accelerate approvals for new excipients and devices. It might help looking into excipients that are already in clinical phase II/III. E.g. leucine is already used in many studies, but everybody is hesitant to pay the expensive toxicology study.

Another aspect to be considered, is the sustainability of the devices, for example carbon footprint of the devices itself. From the on-set of development companies should be aware of this, but currently the lack of approved biodegradable materials is an innovation barrier. Authorities should pay more attention to these aspects.

Participants

Olivia Merkel has been a Professor of Drug Delivery in the Department of Pharmacy at LMU Munich in Germany since 2015. From 2011 until 2017 she was an Assistant Professor of Pharmaceutics and an Associate Faculty Member of Oncology at Wayne State University, Detroit, MI, USA, where she is also a Scientific Member of the Molecular Therapeutics Program and Faculty in the Cancer Biology Graduate Program at Barbara Ann Karmanos Cancer Institute. She became a Registered Pharmacist in 2005. In 2006, she received a MS in Pharmaceutical Technology from Martin-Luther-Universität Halle-Wittenberg, and in 2009 a PhD in Pharmaceutical Technology from Philipps-Universität Marburg, Germany. She received several awards and is the author of over 90 peer-reviewed articles, 15 book chapters and the editor of two books. From 2020 until 2021, she was the President of the Controlled Release Society German Local Chapter and she has been the Chair of the CRS Focus Group Transdermal and Mucosal Delivery since 2020. Currently her research centres around targeted RNA delivery in cancer, inflammatory diseases and viral infections with a focus on pulmonary administration.

Ulf Krueger, CEO and founder of Pulmotree. His experience in life sciences and especially in managing projects, programs and portfolios is the basis of Pulmotree's business. He also brings his broad industry knowledge of strategic development, product management, R&D and industrialization of inhaled drug delivery products. In his former position as Director – Fox Nebulizer Programs at Vectura, he held responsibility for the entire sector of membrane nebulizers. Previous to that, he held various positions in the research and development department of Pari GmbH. He is a graduate biomedical engineer and a certified senior project manager (IPMA® Level B) and is a member of The Aerosol Society, the European Respiratory Society (ERS) and the International Society for Aerosols in Medicine (ISAM).

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Herbert Chiou is Associate Scientific Director at Moderna. Herbert has been involved in the respiratory field, starting in academia before going into industry then being active across different roles and functions, including analytical, formulation, and device development, for nebulisers, pMDIs and DPIs. His experience spans from start-up to large companies, innovator and generic, as well as sponsor and CDMO, at organizations such as The University of Sydney, 3M, Lupin, Moderna, and Omega Therapeutics.

Paul Hagedoorn is Senior Technologist/Scientist Inhalation and head of the inhalation research laboratory of the Department Pharmaceutical Technology and Biopharmacy, Groningen Research Institute of Pharmacy, University of Groningen, Netherlands. His research focus is developing of drug formulations for the pulmonary route and developing of effective dry powder inhalers. Paul has over 25 years experience in the field of inhalation and is (co) author of more than 100 publications in peer reviewed journals, has 4 patents and is the (co) inventor of several DPI's like the Novolizer, Genuair, Twincer and the Cyclops. He is the scientific advisor and board member of the foundation Inhalation Medication Instruction School (IMIS) in the Netherlands and scientific advisor of the Lung Alliance Netherlands (LAN). He is also a board member of the Inhaler Research Workgroup (IRW) and Medical Aerosol Thinktank in the Benelux. Paul is also author of a patient care atlas, patient care app and author of 3 books about inhalation technology.

Mohit Mehta is Director DPI Consulting at Harro Höfliger, Germany. He obtained a PhD in Pharmaceutical technology from Mumbai university (2013). Subsequently, he joined the Respiratory Centre of Excellence, Cipla R&D and gained extensive experience on respiratory API micronization, particle engineering and formulation development of dry powder inhalers. He led the team in the successful development of Dry Powder Inhalers for key regulated markets. Later he worked with DFE Pharma, Germany, where he was responsible as technical lead and customer support for development of customized Inhalation grade lactose and in exploring new excipients for biologics. Mohit recently joined Harro Höfliger, where he is responsible for managing external consultancy projects related to product development of novel drug delivery systems and dry powder inhalers.

Stefano Console has 27 years of experience in the pharmaceutical and fine chemical business. The broad experience gathered with different CDMOs (Contract Development & Manufacturing Organizations) in Italy and Switzerland covered strategic roles managing a large number of successful projects for big as well as small Pharma partners across EU, USA and Japan. A vibrant passion for business development, organizational innovation and start-up initiatives, together with a relevant expertise in pharmaceutical particle engineering technologies (especially spray drying and micronization) and respiratory products complete the profile. Currently Stefano is Senior Advisor at Oriento SA, the company he founded in 2018, member of the Advisory Board at Eu.reca (European Respiratory Cluster of Antwerp) as well as scientific and business advisor for a number of companies in the life sciences space.

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