REDUCING VASCULAR MORTALITY IN PATIENTS WITH SUSPECTED ACUTE MI

In this article, Mark Stansfield, Senior Project Manager, and Kambiz Yadidi, Founder and Chief Executive Officer, both of Otitopic, discuss initial results of their pilot Phase I clinical study of dry powder inhalation of aspirin for the treatment of acute myocardial infarction.

Dry powder aspirin inhalation company Otitopic is currently conducting its pilot Phase I clinical study – "*A Phase I, Single-dose, Open-label, Pilot Study to Compare the Pharmacodynamics and Pharmacokinetics of Acetylsalicylic Acid Inhalation Powder with Non-Enteric-Coated Chewable Aspirin in Healthy Adults*".

The level of activity and data observed with the dry powder inhalation of aspirin has been encouraging. At the first on-treatment assessment, all subjects demonstrated 100% inhibition on platelet aggregation in two minutes. All subjects reached a complete 100% arachidonic acid (AA) response in two minutes. In addition, the dry powder inhalation of aspirin continued to demonstrate a satisfying therapeutic and safety profile.

Aspirin is an anti-platelet medicine, which means it prevents blood clotting as easily due to inhibition of platelet function. Platelet aggregation was measured with AA as the platelet aggregating agent (platelet agonist) using light transmittance aggregometry (LTA). When an agonist is added, the platelets aggregate and absorb less light; an increase in transmission occurs and this reaction is detected by the photocell.

Within two minutes of inhalation (37 mg emitted dose), the percentage of platelet aggregation fell below 5% for all subjects. Up to 20 minutes after ingestion, percentage aggregation remained high for some subjects.

Asprihale is a proprietary dry powder inhalation of aspirin formulation delivered via a portable dry powder inhaler. It is designed to be carried by high-risk patients, like an EpiPen. Once the US FDA grants approval, the rapid onset of action indicates a promising role for Asprihale in the treatment of acute thrombotic conditions such as stroke and heart attack.

> "This new method of delivery will allow those at risk to receive the benefits of aspirin without the side effects."

A study conducted by researchers at Harvard University (Cambridge, MA, US), and published this year in JAMA Neurology, found that taking "baby aspirin" is linked to an increased risk of bleeding within the skull for people without heart disease. This prompted the American College of Cardiology and American Heart Association to change their guidelines. The Harvard study presents how at least 29 million people taking daily aspirin should review the guidelines.

Although people without a history of heart problems shouldn't take daily aspirin, it's still recommended for heart attack survivors. Otitopic will seek to persuade the FDA to recommend Asprihale as a pocket-sized rescue drug device delivery system that is easy to use at the time of myocardial infarction (MI) symptoms. High-risk individuals can rapidly inhale Asprihale, and benefit from having rapid onset of action and therapeutic effect.

"TIME IS MUSCLE" DURING MI

The longer the infarct time, the greater the ischaemia and subsequent necrosis of the myocardium. This new method of delivery will allow those at risk to receive the benefits of aspirin without the side effects.

Otitopic believes that the clinical benefits the Asprihale trial has yielded thus far, and the data linking this antiplatelet activity through dry powder inhalation responses, support and confirm

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the mechanism of action and our approach. Otitopic will continue working to advance the clinical study to improve the lives of high-risk patients and individuals who need better treatment options at the time of MI.

The team is excited and looking forward to starting its Phase III clinical trial.

ASPRIHALE CLINICAL RESULTS HIGHLIGHTS

Efficacy data from the evaluable subjects based on AA results:

- All subjects achieved complete AA-induced platelet aggregation inhibition within two minutes (first blood sample timepoint), demonstrating consistent, never-seen-before performance
- These subjects have shown superior AA-induced platelet aggregation response compared with chewable (therapeutic effect 10 times faster than chewable aspirin)
- Platelet aggregation inhibition achieved with 37 mg emitted dose of proprietary aspirin formulation.

ABOUT THE ASPRIHALE CLINICAL STUDY

The Asprihale clinical study, conducted in the US, is an open-label, pilot Phase I trial to assess the PK/PD of aspirin inhalation powder in healthy volunteers, 18-55 years of age.

Platelet aggregation with AA as the platelet agonist using LTA was measured at 10 timepoints.

Pharmacokinetic (ASA and salicylic acid) and PD (adenosine diphosphate- and collagen-induced platelet aggregation inhibition, thromboxane B2 and 6-keto-PGI1α) results are yet to be announced.

ABOUT THE COMPANY

Otitopic is a clinical-stage dry powder inhalation of aspirin company with a track record of success in pharmaceutical product drug delivery and drug device development. Asprihale is a proprietary dry powder inhalation of aspirin formulation delivered via portable dry powder inhaler that is expected to enter the bloodstream faster than oral tablets at the time of MI.

Otitopic is on track with Asprihale to file a US NDA for a novel drug-device combination product in rescue management of suspected acute MI. Otitopic is committed to providing high-risk MI patients with a faster alternative for management of suspected MI. The company is currently assessing non-small-cell lung cancer as an additional indication to the MI indication therapy.

ABOUT THE AUTHORS

Mark Stansfield is Senior Project Manager at Otitopic, with more than 11 years' experience in the development of respiratory medicine and oral drug formulations. He has extensive product development and manufacturing experience, including products for the treatment of asthma, chronic obstructive pulmonary disease, cancer and acute thrombotic conditions such as heart attack and stroke.

Kambiz Yadidi, Founder and Chief Executive Office of Otitopic, is an accomplished entrepreneur in the healthcare industry, is the inventor of the underlying technology for the Asprihale product. With over 28 years of experience, he has created and helped small to medium sized businesses evolve into valuable and enduring companies that have made a difference in the healthcare market. Prior to OtiTopic, he was the founder and Chief Executive Officer of several successful healthcare businesses including Pharmalink Pharmaceutical Inc, Medquip Inc (recently sold to Drive Medical), Respitouch Inc, and General Home Pharmacy, where he created the trademarked brand Sinus Dynamics.