HEX17, A Novel Broad-spectrum Antiviral Intranasal Drug, Demonstrates Efficacy Against Influenza In A Controlled Human Infection Model Conducted In Healthy Adults

Geoff Kitson, Marion Byford1, Lindsey Cass1, David Howat2, Brigitte Köhn1, Douglas Thomson

Research Supported by Pneumagen Ltd, St Andrews, United Kingdom.

Authors relevant interests : Geoff Kitson consultant to Pneumagen Ltd., holds stock options; Douglas Thomson, Pneumagen Ltd Employee, holds stock and stock options (corresponding author)

(Other authors 1 Consultants to Pneumagen Ltd; 2 Former employee of Pneumagen)

Introduction

Viral respiratory tract infection is of enormous global concern, particularly in patients with underlying pulmonary disease (e.g., chronic obstructive pulmonary disease or bronchiectasis), in whom viral infections induce exacerbations of the underlying pulmonary disease. A broad-spectrum anti-viral prophylactic agent will complement the current strategies. HEX17 is a novel, engineered, multivalent, Carbohydrate Binding Module. It acts by binding directly to sialic acid on the host's mucosal surfaces, preventing the virus binding, thus, preventing the entry of the viral pathogen. Due to this mechanism of action, HEX17 has low risk of driving viral resistance. This current study assessed the safety, tolerability, and prophylactic antiviral activity of HEX17 against an H3N2 influenza virus strain challenge, in a controlled human infection model.

Objectives

To evaluate the effect of HEX17 in reducing the incidence of symptomatic influenza infection (quantifiable virus in nasal samples, determined by RT-qPCR and culture) in healthy adult participants between 18 and 55 years of age. The study was powered based on demonstrating a > 50% reduction in the incidence of influenza infection compared to placebo. Based on these positive clinical results, taken together with a pre-clinical data package demonstrating HEX17’s activity against a broad range of viruses, HEX17 will be advanced into further clinical studies.

Methods

This was a double blind, placebo-controlled, Phase 2 study, conducted in healthy adult participants between 18 and 55 years of age, inclusive. Participants were screen up to 93 days before challenge and had to be sero-suitable (HAI titre ≤10). Participants entered quarantine on Day -4 and were randomised to receive one of 3 treatment regimens: HEX17 single dose on Day -3 followed by placebo on Days -2 and -1.

Endpoints

The co-primary endpoints were the effect of symptomatic influenza infection and/or the severity of symptoms after influenza virus challenge, compared to placebo. The study was powered based on demonstrating a difference between the pooled population of HEX17 recipients compared to placebo recipients in the per protocol population.

Results

Participant disposition

A total of 104 participants were randomised to the three treatment groups and constitute the safety analysis set (Table 1). Five participants were withdrawn, with 99 completing the study as per the protocol. For the per protocol population the incidence of infection in the placebo population based on quantifiable RT-qPCR was 50.0% which is in line with the historical data on the infectivity rate of the H3N2 influenza strain challenge. The incidence of symptomatic infection was 40.0% in the placebo group compared to 20.3% in the pooled HEX17 group p=0.0331. Hence, HEX17 significantly reduced the incidence of symptomatic infection compared to placebo.

There were statistically significant reductions in VL-Area Under the Curve (Table 2) and VL peak, as measured by PCR and culture, in the HEX17 treated participants.

Safety

No serious adverse events reported.

No severe adverse events reported in the treatment groups.

Six events were considered moderate. All other adverse events were reported as mild.

Six AEs considered related, 3 in the placebo group

Conclusions

The results demonstrate that HEX17 is well-tolerated, has a safety profile suitable for a prophylactic medication and, compared with placebo, is effective in reducing the incidence and/or the severity of symptomatic influenza infection. Based on these positive clinical results, taken together with a pre-clinical data package demonstrating HEX17’s activity against a broad range of viruses, HEX17 will be advanced into further clinical studies.