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

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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 to minimal 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, assessed by RT-qPCR measurements, reported on 2 or more independent nasal samples over 2 days and any symptoms of grade 2 or more at a single time point) and/or in reducing the severity of symptoms after influenza viral challenge, compared to placebo.

Evaluate effect of HEX17 on symptoms, viral load (as determined by RT-qPCR and culture) .

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 screened 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, HEX17 three doses or placebo three doses, on days -3 to -1 and were inoculated with influenza virus on Day 0. Participants remained in quarantine until Day 8. Efficacy assessments were collected during the quarantine period, including total symptom scores [TSS], and nasal samples for viral load [VL], were analysed from Day 1 to 8. Participants returned on Day 28 for the end of study visit.

Endpoints

The co-primary endpoints were the effect on the incidence of symptomatic influenza infection and/or the severity of symptoms after influenza viral 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 60.0% which is in line with the historical data on the infectivity rate or the H3N2 influenza challenge strain.

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 (Fig 1).

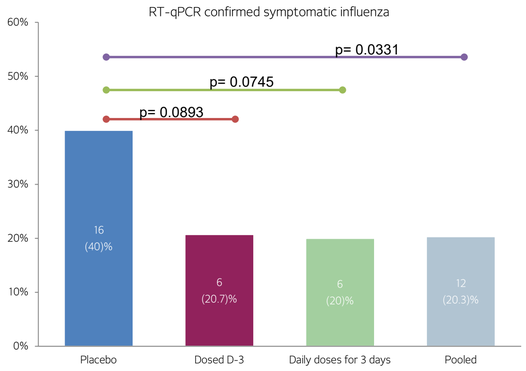
There was a statistically significant reduction in median peak TSS in the HEX17 single dose arm vs the placebo arm (p=0.0192).

Table 1: Demographic characteristics (safety analysis set)

	Treatment Arm			
	Placebo (N=41)	HEX17 Single Dose on Day -3 (N=31)	HEX17 Three Daily Doses (N=32)	Pooled HEX17 (N=63)
Sex n (%)				
Male	27 (65.9)	22 (71.0)	23 (71.9)	45 (71.4)
Female	14 (34.1)	9 (29.0)	9 (28.1)	18 (28.6)
Age (years				
Mean (SD)	31.05 (8.82)	30.32 (7.06)	31.22 (6.79	30.78 (6.88
Median (Min, Max)	27.00 (20.0, 51.0)	29.00 (21, 48)	28.50 (22.0, 48.0)	29.00 (21.0, 48.0)
Ethnicity n (%)				
Hispanic/Latino	2 (4.9)	2 (6.5)	1 (3.1)	3 (4.8)
Not Hispanic Latino	39 (95.1)	29 (93.5)	31 (96.9)	60 (95.2)
Race n (%)				
White	33 (80.5)	22 (71.0)	21 (65.6)	43 (68.3)
Black or African American	4 (9.8)	5 (16.1)	0	5 (7.9)
Asian	1 (2.4)	1 (3.2)	3 (9.4)	4 (6.3)
Other	3 (7.3)	3 (9.7)	6 (18.8)	9 (14.3)
Multiple	0	0	2 (6.3)	2 (3.2)

Max=maximum; min=minimum; SD=standard deviation.

Fig 1 Incidence of RT-qPCR confirmed symptomatic infection



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.

Table 2 comparison of Area under the curve of viral load as assessed by RT-qPCR

Parameter	Placebo N=40	Dosed D-3 N=29	Daily doses for 3 days N=30	Pooled N=59
Area under curve of viral load by RT-qPCR Median (IQR) log 10 copies/mL x day	17.24 (27.64)	8.60 (19.88)	9.96 (20.01)	9.39 (20).00)
p-value based on median		0.1369	0.0304	0.0382

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.

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