191

Safety and efficacy of Fel d 1 derived peptide immunotherapy in a double-blind, placebo-controlled environmental exposure chamber study

Larché, M[1]; Patel, D[2]; Patel, P[3]; Salapatek, A[2]; Laidler, P[4]; Hafner, R[4]
[1]McMaster University/St. Joseph's Healthcare, Medicine/Firestone Institute for Respiratory Health, Hamilton, Canada; [2]Cetero Research, Mississauga, Canada; [3]AllerPharma, Toronto, Canada; [4]Circassia Limited, Oxford, United Kingdom

Background: Allergic rhinoconjunctivitis is an increasing problem worldwide with a significant impact on quality of life and productivity. Sensitivity to cats accounts for 10-15% of the disease burden. Previous attempts to use peptide immunotherapy with two 27aa peptides were unsuccessful as a result of early and late phase responses. ToleroMune Cat is a mixture of seven T cell epitopes (13-17aa) from Fel d 1. The present study evaluated safety and relationship between dose, dosing regimen and symptom scores in cat allergic subjects with rhinoconjunctivitis after treatment with ToleroMune Cat following standardized allergen challenge in an environmental exposure chamber (EEC).
Method: In a multicentre, double-blind, placebo-controlled clinical trial, subjects attended a central EEC, before and after treatment with 4 different regimens of ToleroMune Cat (4x3nmol 2weeks(w) apart, 4x6nmol 2w apart, 4x3nmol 4w apart, 8x3nmol 2w apart) or placebo. 121 subjects were randomised to one of 4 treatment regimens or placebo. Clinical efficacy was assessed by measurement of changes in Total Rhinoconjunctivitis Symptom Score (TRSS) between Baseline and Post Treatment Challenge. Safety was assessed by observing subjects in the clinic for 1 hour on each dosing day and capturing adverse events (AE) by direct questioning of subjects at each visit.
Result: There were no serious AE on any regimen. Frequencies of all Treatment Emergent Adverse Events (TEAE) in the ToleroMune Cat treatment arms were less than in the Placebo cohort with the exception of the 6nmol cohort which trended slightly higher. Analysis of the respiratory system TEAEs showed no evidence of any safety signal after treatment with ToleroMune Cat. Respiratory system TEAEs, including asthma, dyspnoea and wheezing, occurred at a low frequency in both active and placebo groups, with no obvious difference between the groups. Treatment with ToleroMune Cat showed greater efficacy when dosed over 12-14w than when dosed over 6w. 8x3nmol dose showed a statistically significant reduction in symptoms vs placebo ($p < 0.05$) in subjects who attended the main centre for all their visits. The 6nmol dose showed a trend to be superior to the 3nmol dose, albeit tested in a sub-optimal regimen.
Conclusion: A course of ToleroMune Cat over 12-14 weeks was safe and well tolerated and improved TRSS. Potential for greater treatment benefits by using a higher dose over a three month period should be evaluated in future studies.