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<b>Study No.:</b> FFR100688	
<b>Title:</b> Clinical Evaluation of GW685698 for Perennial Allergic Rhinitis -Long-Term Safety Study -	
<b>Rationale:</b> This study was designed to evaluate the safety to 12 weeks' treatment with intranasal once-daily Fluticasone Furoate (FF), which is being developed as Japan's first once-daily adrenocortical steroid nasal spray, 110g in patients with perennial allergic rhinitis. The efficacy was also assessed as the secondary objective.	
<b>Phase:</b> III	
<b>Study Period:</b> 21 June 2005 to 12 October 2005	
<b>Study Design:</b> A multicenter, open-label, no-comparative study	
<b>Centres:</b> Two centres in Japan	
<b>Indication:</b> Perennial allergic rhinitis	
<b>Treatment:</b> Subjects were administered once daily (QD) FF nasal spray 110g f or 12 weeks.	
<b>Objectives:</b> The primary objective of this study was to assess the safety to 12 weeks' treatment with intranasal once-daily FF 110 g in patients with perennial allergic rhinitis. The efficacy was also assessed as the secondary objective.	
<b>Primary Outcome/Efficacy Variable:</b> Safety	
<b>Secondary Outcome/Efficacy Variable(s):</b>	
<ul style="list-style-type: none"> <li>• Mean change and mean percent change from baseline in 3 Total Nasal Symptom Score (3TNSS*).</li> <li>• Mean change and mean percent change from baseline in 4 Total Nasal Symptom Score (4TNSS**).</li> <li>• Mean changes from baseline in individual nasal symptom (sneezing, rhinorrhea, nasal congestion, nasal itching) scores.</li> <li>• Mean change from baseline in Total Ocular Symptom Score*** (TOSS).</li> <li>• Mean change from baseline in disturbance to daily life score.</li> </ul> <p>*3 TNSS is the sum (0-9) of three individual symptom scores for sneezing, rhinorrhea and nasal congestion where each symptom is scored on a scale of 0 to 3 in the nasal diary.</p> <p>**4TNSS is the sum (0-12) of four individual symptom scores for sneezing, rhinorrhea, nasal congestion and nasal itching where each symptom is scored on a scale of 0 to 3 in the nasal diary.</p> <p>***TOSS is the sum (0-9) of three individual symptom scores for eye itching and burning, eye tearing and watering, and eye redness where each symptom is scored on a scale of 0 to 3 in the nasal diary.</p>	
<b>Statistical Methods:</b> The safety analysis data set was Safety Population (SP). For safety assessment, all AEs occurring during the study period were summarized. The primary efficacy analysis data set was Full Analysis Set (FAS). For the efficacy endpoints, data were summarized and summary statistics were calculated for each assessment period.	
<b>Study Population:</b> The patients enrolled in the study were outpatients aged 16 years or older who had perennial allergic rhinitis diagnosed, who had positive allergy tests [consisting of a) skin test or serum IgE antibody assay, b) nasal mucosa test, and c) nasal discharge eosinophil count test, should be performed to confirm that the subject is positive for a) and positive for at least either b) or c)], and who had the average of 3TNSS (for sneezing, rhinorrhea, and nasal congestion) in the consecutive 4 days just prior to Visit 2 (start date of study medication) more than 4.0.	
<b>Number of Subjects:</b>	
Planned, N	60

Enrolled, N	65			
Completed, n (%)	59(91)			
Total Number Subjects Withdrawn, n (%)	6(9)			
Withdrawn due to Adverse Events, n (%)	1(2)			
Withdrawn due to Lack of Efficacy, n (%)	0			
Withdrawn for other reasons, n (%)	5(8)			
<b>Demographics</b>				
N (SP/FAS/PPS)	65/64/60			
Females: Males	28:37			
Mean Age, years (SD)	27.9(9.08)			
East/Southeast Asians, n (%)	65(100)			
<b>Primary Efficacy Results: -</b>				
<b>Secondary Outcome Variable(s):</b>				
Mean change and mean percent change from baseline in 3TNSS (FAS)				
Period	n	3TNSS	Mean change from baseline in 3TNSS	Mean percent change from baseline in 3TNSS
		Mean (SD)		%, Mean (SD)
Baseline	6 4	6.0(1.27)	-	-
Week 3-4	6 3	3.4(1.48)	-2.6(1.72)	-42.1(23.79)
Week 7-8	6 2	3.0(1.45)	-3.0(1.73)	-48.1(23.78)
Week 11-12	5 9	2.6(1.39)	-3.4(1.71)	-55.2(23.04)
Mean change and mean percent change from baseline in 4TNSS (FAS)				
Period	n	4TNSS	Mean change from baseline in 4TNSS	Mean percent change from baseline in 4TNSS
		Mean (SD)		%, Mean (SD)
Baseline	6 4	7.6(1.77)	-	-
Week 3-4	6 3	4.2(1.91)	-3.4(2.13)	-44.3(22.81)
Week 7-8	6 2	3.7(1.92)	-3.9(2.18)	-50.7(23.72)
Week 11-12	5 9	3.1(1.79)	-4.4(2.10)	-58.2(22.31)
Mean changes from baseline in individual nasal symptom scores: sneezing (FAS)				
Period	n	Score	Mean change from baseline	
		Mean (SD)		
Baseline	6 4	1.8(0.59)		-
Week 3-4	6 3	1.0(0.52)		-0.7(0.71)
Week 7-8	6 2	0.9(0.48)		-0.9(0.71)
Week 11-12	5 9	0.8(0.50)		-1.0(0.70)
Mean changes from baseline in individual nasal symptom scores: rhinorrhea (FAS)				

Period	n	Score	Mean change from baseline
		Mean (SD)	
Baseline	6 4	2.1(0.52)	-
Week 3-4	6 3	1.2(0.52)	-1.0(0.66)
Week 7-8	6 2	1.1(0.50)	-1.1(0.71)
Week 11-12	5 9	0.9(0.49)	-1.2(0.69)
Mean changes from baseline in individual nasal symptom scores: nasal congestion (FAS)			
Period	n	Score	Mean change from baseline
		Mean (SD)	
Baseline	6 4	2.1(0.56)	-
Week 3-4	6 3	1.2(0.72)	-0.9(0.59)
Week 7-8	6 2	1.1(0.73)	-1.0(0.62)
Week 11-12	5 9	0.9(0.66)	-1.2(0.58)
Mean changes from baseline in individual nasal symptom scores: nasal itching (FAS)			
Period	n	Score	Mean change from baseline
		Mean (SD)	
Baseline	6 4	1.5(0.80)	-
Week 3-4	6 3	0.7(0.63)	-0.8(0.68)
Week 7-8	6 2	0.6(0.64)	-0.9(0.75)
Week 11-12	5 9	0.5(0.54)	-1.0(0.71)
Mean change from baseline in TOSS (FAS)			
Period	n	TOSS	Mean change from baseline
		Mean (SD)	
Baseline	6 4	2.5(1.71)	-
Week 3-4	6 3	1.5(1.59)	-1.0(1.20)
Week 7-8	6 2	1.1(1.38)	-1.3(1.41)
Week 11-12	5 9	0.9(1.17)	-1.6(1.47)
Mean change from baseline in disturbance to daily life score (FAS)			
Period	n	Score	Mean change from baseline
		Mean (SD)	
Baseline	6 4	1.5(0.66)	-
Week 3-4	6 3	0.8(0.64)	-0.7(0.65)
Week 7-8	6 2	0.8(0.64)	-0.7(0.67)

Week 11-12	5 9	0.8(0.61)	-0.8(0.64)
<b>Safety Results:</b> [Primary endpoint]. Safety population (SP)			
AEs reported after the start of treatment (treatment period + post-treatment period)			
AE(s)	N=65 Subjects with AE(s), n (%)		
Total	29(45)		
Nasopharyngitis	8(12)		
Headache	7(11)		
Upper respiratory tract inflammation	3(5)		
Pharyngolaryngeal pain	2(3)		
Stomach discomfort	2(3)		
Diarrhoea	2(3)		
Blood cortisol decreased	2(3)		
Pyrexia	2(3)		
Bronchitis	1(2)		
Infectious mononucleosis	1(2)		
Cough	1(2)		
Productive cough	1(2)		
Epistaxis	1(2)		
Rhinalgia	1(2)		
Somnolence	1(2)		
Nausea	1(2)		
Toothache	1(2)		
Blood potassium decreased	1(2)		
Blood bilirubin increased	1(2)		
White blood cell count increased	1(2)		
Joint sprain	1(2)		
Arthropod sting	1(2)		
Arthropod bite	1(2)		
Foot fracture	1(2)		
Dermatitis acneiform	1(2)		
Pruritus	1(2)		
Rash	1(2)		
Abnormal sensation in eye	1(2)		
Eustachian tube obstruction	1(2)		
Menstruation irregular	1(2)		
<b>Serious Adverse Events - On-Therapy</b>			
<b>n (%) [n considered by the investigator to be related to study medication]</b>			
Subjects with non-fatal SAE(s), n (%)	0		
Subjects with fatal SAE(s), n (%)	0		
<b>Serum cortisol</b>			
Period	n (SP)	Serum cortisol (g/ dL)	Mean change from baseline ( g/dL)
		Mean (SD), Normal range: 4.5-21.1g/ dL	
Baseline	65	12.40(4.512)	-
Week 4	62	12.68(4.783)	0.20(4.750)
Week 8	58	13.28(4.518)	0.68(5.340)
Week 12/early withdrawal	58	13.45(4.412)	0.72(5.104)

The serum cortisol level showed no obvious changes from baseline to Week 4, 8 or 12/early withdrawal. Blood cortisol decreased was reported as an AE in two subjects. Both cases were mild in intensity. For both cases, relationship to the study drug was ruled out because the cortisol level showed a recovery without any medical treatment during the treatment period.

**Conclusion:**

- In this open-label study, intranasal once-daily FF 110 g was well-tolerated in patients 16 years or older with PAR when treated up to 12 weeks. The two leading adverse events, nasopharyngitis and headache, were similar to those reported in the one-year FF safety study, FFR102123. Overall, AM cortisol levels remained stable through the 12 week treatment period compared to baseline.
- Intranasal once-daily FF 110 g improved patients' symptoms. F or 3TNSS and 4TNSS, patients reported a mean % reduction from baseline in symptoms scores ranging from 42-55% and 44-58% respectively for weeks 4 through 12.

**Publications:** No publication

Date updated: 5-Sep-2008