Sponsor

Novartis

Generic Drug Name

Not Available

Trial Indication(s)

Allergic rhinitis

Protocol Number

CQAX576A2104

Protocol Title

A proof of concept study of the effects of QAX576 (an interleukin-13 monoclonal antibody) on allergic inflammation following out of allergy season repeated nasal allergen challenge in subjects with seasonal allergic rhinitis sensitive to Timothy grass pollen

Clinical Trial Phase

Phase II

Study Start/End Dates

23 Jan 2008 to 07 Aug 2008

Reason for Termination (If applicable)

Not Applicable

Study Design/Methodology

This was a 2-centre, randomized, parallel-group, double-blind study with QAX576 using a placebo control and an open-label active (fluticasone) calibrator group, in subjects sensitive to Timothy grass pollen, performed out of allergy season.

Centers

Germany (1) and United Kingdom (1)

Objectives:

Primary objective:

To assess the ability of QAX576 to inhibit inflammation from nasal allergen exposure (Timothy Grass Pollen) as assessed by Th2-associated cytokines in nasal secretions.

Test Product (s), Dose(s), and Mode(s) of Administration

Subjects were administered QAX576 (6 mg/kg) intravenously.

Statistical Methods

Efficacy: All subjects with evaluable efficacy data were included in the efficacy population. Efficacy data were summarized by descriptive statistics for each treatment group. Mean and median values were plotted over time, where appropriate. All subjects were included in the tables and listings, but only those treated with QAX576 or placebo were included in the inferential analysis. The primary efficacy variable was the IL-5 concentrations from the nasal filter adsorption 6 h post nasal allergen challenge on Day 7.The log transformed IL-5 levels from the QAX576 and placebo group were analyzed using a model with a fixed effect for treatment (QAX576, Placebo). The log transformed IL-5 concentration from the nasal filter adsorption 6 h post the last pre-dose nasal allergen challenge was included in the model as a covariate for baseline adjustment. Estimates for the treatment contrasts “QAX576 – Placebo” on Day 7 are provided together with 90% confidence The peak value after each challenge (Emax), and the average value (AUEC/time range) were determined for the Total Nasal Symptom Score (TNSS), selected nasal cytokines in nasal secretions (IL-5, IL-13), and eosinophils in nasal lavage fluid. These parameters were summarized by descriptive statistics. Day 7 data were analyzed

using the model described above as were Day 7 6 h post NAC values of IL-4, IL-13, eosinophil counts, and the 0.25 h post NAC TNSS. Pharmacokinetics: All subjects with quantifiable PK data were included in the PK population. Pharmacokinetic parameters were not derived if the available data were insufficient to obtain reliable estimates. Plasma drug concentrations were expressed in mass per volume units. Missing data or those below the limit of quantification were labeled as such in the concentration data listings. Concentrations below the limit of quantification were treated as zero in summary statistics and for the calculation of pharmacokinetic parameters. The actual blood sampling times were used for the determination of PK parameters in plasma. Descriptive statistics of pharmacokinetic parameters were expressed as mean, SD, CV, and geometric means except for Tmax which was presented as median and range. Safety: All subjects who received at least part of one dose of study drug were included in the safety and tolerability evaluation. Interim analyses: A first interim analysis was planned when 20 subjects had completed Day 7 assessments. A second interim analysis was planned when all subjects had completed Day 7 assessments. The objective of these analyses was to generate hypotheses for future development and to have the data available early for planning of future studies. Both interim analyses were done as planned by members of the sponsor's clinical trial team who were unblinded to the treatment allocation at interim database lock. Data for nasal symptom scores, cytokines in nasal secretion, eosinophil counts in nasal lavage fluid, and adverse events were reviewed at the interim analysis.intervals.

Study Population: Key Inclusion/Exclusion Criteria

Inclusion criteria:

- Male and female.
- Non-smokers.
- Age between 18-55 years.
- Healthy, but with a history of allergic rhinitis consistent with Timothy grass pollen allergy, determined by skin prick test and symptomatic worsening of nasal symptoms after Nasal Antigen Challenge as assessed by the Total Nasal Symptom Score.

Exclusion Criteria:

- Patients were deemed ineligible for the study if they presented with abnormal nasal structure or polyps, nasal bleeding, nasal surgery or recent respiratory tract infections, were diagnosed with pulmonary disease other than mild intermittent asthma, other significant medical conditions, or used restricted medications.

Participant Flow Table

Patient disposition

Disposition Reason	Total N=36 n (%)	Placebo N=15 n (%)	QAX576 N=16 n (%)	Fluticasone N=5 n (%)
Completed	36 (100%)	15 (100%)	16 (100%)	5 (100%)

Baseline Characteristics

Demographic summary by treatment (Safety population)

		Placebo	QAX576	Fluticasone	All subjects
		N=15	N=16	N=5	N=36
Age (years)	Mean	33	32	39	34
	SD	8.8	9.1	8.6	8.9
	Range	21, 48	20, 47	28, 50	20, 50
Gender – n (%)	Male	14 (93%)	16 (100%)	5 (100%)	35 (97%)
	Female	1 (7%)	0	0	1 (3%)
Race – n (%)	Caucasian	11 (73%)	10 (63%)	4 (80%)	25 (69%)
	Black	2 (13%)	3 (19%)	0	5 (14%)
	Asian	1 (7%)	1 (6%)	0	2 (6%)
	Native Am.	0	1 (6%)	0	1 (3%)
	Other	1 (7%)	1 (6%)	1 (20%)	3 (8%)
Weight (kg)	Mean	78.9	81.7	79.8	80.3
	SD	10.87	9.13	10.13	9.82
	Range	61-95	64-100	67-91	61-100
Height (cm)	Mean	180	181	178	180
	SD	8.4	8.2	8.6	8.2
	Range	159-193	168-195	164-186	159-195
BMI (kg/m^2)	Mean	24.5	24.9	25.3	24.8
	SD	2.94	2.23	3.46	2.65
	Range	19.1-28.4	20.3-28.7	21.4-29.0	19.1-29.0

Summary of Efficacy

Primary Outcome Result(s)

Summary of statistical analysis of IL-5 (pg/ml) 6 h after NAC on Day 7 (Safety analysis set)

			Contrast to Placebo	
Treatment	N	LS geometric mean*	Ratio (90% CI)	P-value
Placebo	15	56.12		
QAX576 6mg/kg	16	46.05	0.82 (0.40, 1.67)	0.32

LS = least squares; CI = confidence interval; *LS mean of log values back-transformed to original scale

Summary of Safety

Safety Results

Adverse events overall and frequently affected system organ classes - n (%) of patients (at least 2 subjects in any treatment group) (safety population)

	Placebo N=15 n (%)	QAX576 N=16 n (%)	Fluticasone N=5 n (%)
Patient with AE(s)	11 (73%)	14 (88%)	4 (80%)
System organ class			
Respiratory, thoracic and mediastinal disorders	6 (40%)	9 (56%)	1 (20%)
Nervous system disorders	5 (33%)	6 (38%)	1 (20%)
Infections and infestations	5 (33%)	5 (31%)	1 (20%)
Musculoskeletal and connective tissue disorders	3 (20%)	2 (13%)	1 (20%)
General disorders and administration site conditions	0	0	2 (40%)

arranged in descending order of frequency in QAX576 group

Serious Adverse Events by System Organ Class

No death, no serious AE and no other significant AE occurred in this study.

Other Relevant Findings

None

Date of Clinical Trial Report

10 Mar 2010