Sponsor

Novartis

Generic Drug Name

QAX576

Therapeutic Area of Trial

Fistulizing Crohn's Disease

Approved Indication

Investigational

Protocol Number

CQAX576A2209

Title

A multi-center, randomized, double-blind, active controlled study to assess efficacy, safety and tolerability of the anti-IL13 monoclonal antibody QAX576 in the treatment of perianal fistulas in patients suffering from Crohn's disease.

Study Phase

Phase II

Study Start/End Dates

09-Jun-2011to 19-Mar-2013

Study was terminated early due to slow recruitment.

Study Design/Methodology

This was a randomized, multi-center, parallel group, double-blind, active controlled study in Crohn's disease (CD) patients who had one or more perianal fistula(s). Subjects were randomized to either QAX576 treatment arm or infliximab treatment arm. The study consisted of a 21-day screening period, a single day baseline period, a 6-week treatment period comprising four dose administrations (3 active and 1 dummy), followed by a 46 weeks observational period after last dose on Day 43.

Centers

5 centers in 2 countries: Germany (4), Switzerland (1)

Publication

N/A

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

A single dose of the study drug QAX576, 10 mg/kg diluted in 250 mL glucose/dextrose, was planned to be administered as an intravenous infusion over 2 hours on Day 1, Day 22 and Day 43, or a single dose of the active drug infliximab, 5 mg/kg diluted in 250 mL saline, was planned to be administered as an intravenous infusion over 2 hours on Day 1, Day 15 and Day 43. Subjects on the QAX576 arm received a dummy infusion (saline) on Day 15 and those on the infliximab arm received a dummy infusion on Day 22.

Statistical Methods

The primary variable was the number of patients (responders) achieving complete closure of all perianal fistulas for ≥ 4 weeks (compared to historical placebo rate of ~13%). Secondary variables included clinical assessments of the fistulas and MRI-based activity scores of the fistula tracts.

No formal statistical testing was performed in this study. The interpretation of the results was planned to be based on descriptive statistics which included confidence intervals. However, the study results were not definitive due to the low patient number.

Study Population: Inclusion/Exclusion Criteria and Demographics

Inclusion criteria

- At least one draining enterocutaneous perianal fistula
- Diagnosis of Crohn's disease (CD) must have been established for at least 6 months
- At least one ineffective fistula treatment (but no previously failed anti-TNFα (tumour necrosis factor) antibody treatment)
- Patients should not suffer from any other health problems that may jeopardize their participation in the study.

Exclusion criteria

- Current or recent (within 30 days of enrollment, or 5 half-lives of the compound, whichever is longer) use of anti-TNFα antibody treatment
- Active Crohn's disease (CDAI > 250)
- Recent or pending abdominal or ano-rectal surgery, particularly presence of stricture, or abscess, or retention for which surgery might be indicated
- Previously failed anti-TNFα antibody treatment
- Intercurrent bacterial or viral (intestinal) infection (serologically or microbiologically confirmed)

Other protocol defined inclusion/exclusion criteria applied.

Participant Flow (Safety Analysis Set)

	QAX576 10 mg/kg N=6 n (%)	Infliximab 5 mg/kg N=4 n (%)	Total N=10 n (%)
Subjects			
Completed	3 (50.0)	4 (100)	7 (70.0)
Discontinued	3 (50.0)	0 (0.0)	3 (30.0)
Main cause of discontinuation			
Adverse event(s)	1 (16.7)	0 (0.0)	1 (10.0)
Subject withdrew consent	1 (16.7)	0 (0.0)	1 (10.0)
Administrative reasons	1 (16.7)	0 (0.0)	1 (10.0)

Baseline Characteristics (Safety Analysis Set)

Demographic Variable	Statistic	QAX576 10mg/kg N=6	Infliximab 5mg/kg N=4	Total N=10
Age (years)	n	6	4	10
	mean	29.0	40.5	33.6
	SD	7.62	14.80	11.85
	minimum	20	22	20
	median	29.0	41.5	30.0
	maximum	42	57	57
Height (cm)	n	6	4	10
	mean	171.7	172.5	172.0
	SD	9.77	11.27	9.78
	minimum	160	160	160
	median	172.5	171.5	172.0
	maximum	186	187	187
Weight (kg)	n	6	4	10
	mean	74.28	77.80	75.69
	SD	13.011	24.123	17.068
	minimum	58.5	59.2	58.5
	median	74.30	69.75	71.25
	maximum	92.1	112.5	112.5
Gender - n (%)	Male	3 (50.0)	2 (50.0)	5 (50.0)
	Female	3 (50.0)	2 (50.0)	5 (50.0)
Predominant race - n (%)	Caucasian	6 (100)	4 (100)	10 (100)
Ethnicity - n (%)	Hispanic/Latino	0 (0.0)	1 (25.0)	1 (10.0)
	Other	6 (100)	3 (75.0)	9 (90.0)
BMI (kg/m2)	n	6	4	10
	mean	25.06	25.71	25.32
	SD	2.607	4.750	3.378
	minimum	22.3	20.7	20.7
	median	24.42	24.97	24.97
	maximum	29.4	32.2	32.2

SD: Standard deviation
Age is calculated from date of screening and date of birth.
Weight and height are taken from Screening vital signs evaluations
Body mass index (BMI) [kg/m2] = weight [kg] /(height [m]**2)

Outcome measures

Due to slow recruitment, the study was prematurely terminated before the planned enrollment could have been achieved for a definitive interpretation of result.

Safety Results

Adverse Events by System Organ Class (Safety Analysis Set)

	QAX576 10mg/kg N=6 n (%)	Infliximab 5mg/kg N=4 n (%)	Total N=10 n (%)
Subjects with AE(s)	4 (66.7)	4 (100.0)	8 (80.0)
System organ class			
Infections and infestations	4 (66.7)	3 (75.0)	7 (70.0)
Gastrointestinal disorders	4 (66.7)	2 (50.0)	6 (60.0)
Musculoskeletal and connective tissue disorders	3 (50.0)	3 (75.0)	6 (60.0)
Investigations	1 (16.7)	2 (50.0)	3 (30.0)
Eye disorders	1 (16.7)	1 (25.0)	2 (20.0)
Injury, poisoning and procedural complications	1 (16.7)	1 (25.0)	2 (20.0)
Nervous system disorders	1 (16.7)	1 (25.0)	2 (20.0)
Respiratory, thoracic and mediastinal disorders	2 (33.3)	0 (0.0)	2 (20.0)
Metabolism and nutrition disorders	1 (16.7)	0 (0.0)	1 (10.0)

A subject with multiple occurrences of an AE under one treatment is counted only once in the AE category for that treatment.

A subject with multiple AEs within a primary system organ class is counted only once in the primary system organ class total row.

Arranged in descending order of frequency (in total group) and by system organ class.

Incidence of AEs by preferred term (Safety Analysis Set)

	QAX576 10mg/kg N=6 n (%)	Infliximab 5mg/kg N=4 n (%)	Total N=10 n (%)
Subjects with AE(s)	4 (66.7)	4 (100.0)	8 (80.0)
Preferred term			
Nasopharyngitis	3 (50.0)	2 (50.0)	5 (50.0)
Fistula	2 (33.3)	2 (50.0)	4 (40.0)
Fistula discharge	2 (33.3)	1 (25.0)	3 (30.0)
Abdominal pain	2 (33.3)	0 (0.0)	2 (20.0)
Crohn's disease	2 (33.3)	0 (0.0)	2 (20.0)
Diarrhoea	2 (33.3)	0 (0.0)	2 (20.0)
Procedural pain	1 (16.7)	1 (25.0)	2 (20.0)
Abdominal distension	1 (16.7)	0 (0.0)	1 (10.0)
Abscess	1 (16.7)	0 (0.0)	1 (10.0)
Acute tonsillitis	1 (16.7)	0 (0.0)	1 (10.0)
Anal haemorrhage	0 (0.0)	1 (25.0)	1 (10.0)
Arthralgia	0 (0.0)	1 (25.0)	1 (10.0)
Arthropathy	0 (0.0)	1 (25.0)	1 (10.0)
Blood creatine phosphokinase increased	0 (0.0)	1 (25.0)	1 (10.0)
Blood creatinine increased	0 (0.0)	1 (25.0)	1 (10.0)
Blood potassium increased	0 (0.0)	1 (25.0)	1 (10.0)
Blood triglycerides increased	1 (16.7)	0 (0.0)	1 (10.0)
C-reactive protein increased	0 (0.0)	1 (25.0)	1 (10.0)
Carpal tunnel syndrome	0 (0.0)	1 (25.0)	1 (10.0)
Cough	1 (16.7)	0 (0.0)	1 (10.0)
Episcleritis	0 (0.0)	1 (25.0)	1 (10.0)
Folate deficiency	1 (16.7)	0 (0.0)	1 (10.0)
Frequent bowel movements	1 (16.7)	0 (0.0)	1 (10.0)
Furuncle	0 (0.0)	1 (25.0)	1 (10.0)
Haemoglobin decreased	0 (0.0)	1 (25.0)	1 (10.0)
Intervertebral disc protrusion	0 (0.0)	1 (25.0)	1 (10.0)
Iritis	1 (16.7)	0 (0.0)	1 (10.0)
Musculoskeletal pain	0 (0.0)	1 (25.0)	1 (10.0)
Nausea	1 (16.7)	0 (0.0)	1 (10.0)
Oropharyngeal pain	1 (16.7)	0 (0.0)	1 (10.0)
Respiratory tract infection	1 (16.7)	0 (0.0)	1 (10.0)
Rhinitis allergic	1 (16.7)	0 (0.0)	1 (10.0)
Syncope	1 (16.7)	0 (0.0)	1 (10.0)
Toothache	0 (0.0)	1 (25.0)	1 (10.0)
White blood cell count increased	0 (0.0)	1 (25.0)	1 (10.0)

A subject with multiple occurrences of an AE under one treatment is counted only once in the AE category.

Arranged in descending order of frequency in total group and alphabetically.

Serious Adverse Events and Deaths (Safety Analysis Set)

	Novartis product	Comparator
No. (%) of subjects studied	6	4
No. (%) of subjects with AE(s)	4(66.7)	4(100)
Death	0	0 (0.0)
SAE(s)	0 (0.0)	1 (16.6)
Discontinued due to SAE(s)	0 (0.0)	0 (0.0)

Other Relevant Findings

N/A

Date of Clinical Trial Report

11 September 2013

Date Inclusion on Novartis Clinical Trial Results Database

05 April 2014

Date of Latest Update

27 February 2014