Sponsor Novartis
Generic Drug Name QAX576
Therapeutic Area of Trial Dermatology/ keloids
Approved Indication Investigational

Protocol Number

CQAX576A2206

Title

A post-shave keloid recurrence study in two parts: A biomarker assessment followed by a randomized, double-blind, placebo-controlled evaluation of safety, tolerability, and efficacy of QAX576

Phase of Development

Phase II

Study Start/End Dates

16-Jun-2009 to 04-Nov-2010

The study was terminated early based on the absence of an IL-13 signature in biomarker data from Part I of this study.

Study Design/Methodology

This was a two-part study, with Part I designed to investigate biomarker responses following keloid shave (no investigational drug administered), and Part II designed as a two-arm double-blind, placebo controlled proof of concept (PoC) study investigating QAX576 and placebo treatment responses following keloid shave.

Centres

4 centers in 1 country; USA

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

QAX576 100 mg . Dose: 3 mg/kg was administered via intravenous infusion over 2 hours every 4 weeks (Day 1, Day 29 and Day 57) for a total of 3 doses in Part II.

Statistical Methods

No statistical analysis was performed, since the study was terminated with only 3 patients in part II.

Study Population: Inclusion/Exclusion Criteria and Demographics

Key inclusion criteria included:

- Male and female patients aged 18 to 70 years with keloid formation, and in general good health.
- Two or more keloids were to be present on the trunk or upper extremities or thighs. One of the two keloids (that was to be biopsied) had to measure ≥ 1.5 cm and ≤ 3.5 cm at its base, the other keloid had to measure ≥ 1.0 cm and ≤ 3.5 cm.
- Keloids should have been present for ≥ 1 year, been stable in size and symptoms for at least 6 months.

Key exclusion criteria included:

- History of repeated recurrence of keloid after prior surgical removal (4-5 times removed).
- Keloids for study near to hands, joints, and anogenital areas as recurrence might cause significant problems.
- Unable or unwilling to undergo multiple venipunctures because of poor tolerability or lack or easy access to veins.
- Surgical excision of the test keloid, cryotherapy of test keloid, laser therapy, or radiation therapy in the past 1 year from study start. Chronic systemic or intralesional corticosteroid therapy or silicone gel sheet in the 2 months prior to study start. The following therapies were washed out for 4 weeks or 5 times the half life (whichever was longer) prior to first dose: anticoagulant drugs, fibrinolytic agents (antithrombotic agents), anti-platelet drugs, insulin, or hypoglycemic drugs.
- Smokers that smoke more than 10 cigarettes per day.

Participant Flow

Part I:

	All (no drug) (n=8)	Total (n=8)
Patients		
Completed	8 (100.0%)	8 (100.0%)
Discontinued	0	0

Part II:

	QAX576 (n=2)	Placebo (n=1)	Total (n=3)
Patients			
Completed	0	0	0
Discontinued	2 (100.0%)	1 (100.0%)	3 (100%)
Primary reason for premature discontinuation			
Administrative problems/ Study terminated	2 (100.0%)	1 (100.0%)	3 (100%)

Baseline Characteristics

Part I:

		All (no drug) (n=8)	Total (n=8)
Age (years)	Mean	43	43
	Median	46	46
	Range	22-63	22-63
Age group – n (%)	19–39 years	3 (37.5%)	3 (37.5%)
	40–64 years	5 (62.5%)	5 (62.5%)
	≥ 65 years	0	0
Gender – n (%)	Male	7 (87.5%)	7 (87.5%)
	Female	1 (12.5%)	1 (12.5%)
Race – n (%)	Caucasian	5 (62.5%)	5 (62.5%)
	Black	0	0
	Asian	0	0
	Native American	1 (12.5%)	1 (12.5%)
	Other	2 (25.0%)	2 (25.0%)

Part II:

		QAX576 (n=2)	Placebo (n=1)	Total (n=3)
Age (years)	Mean	38.5	37	38
	Median	38.5	37	37
	Range	32-45	37	32-45
Age group – n (%)	19–39 years	1 (50.0%)	1 (100.0%)	2 (66.7%)
	40–64 years	1 (50.0%)	0	1 (33.3%)
	≥ 65 years	0	0	0
Gender – n (%)	Male	1 (50.0%)	1 (100.0%)	2 (66.7%)
	Female	1 (50.0%)	0	1 (33.3%)
Race – n (%)	Caucasian	1 (50.0%)	0	1 (33.3%)
	Black	1 (50.0%)	0	1 (33.3%)
	Asian	0	1 (100.0%)	1 (33.3%)
	Other	0	0	0

Safety Results

Adverse Events by System Organ Class

Part I:

	All (no drug) N=8 (%)
Renal and urinary disorders	1 (12.5)
Infections and infestations	1 (12.5)
Investigations	8 (100.0)

Part II:

	QAX576 N=2 (%)	Placebo N=1 (%)
Nervous system disorders	1 (50.0)	0 (0.0)
Gastrointestinal disorders	1 (50.0)	0 (0.0)
Vascular disorders	1 (50.0)	0 (0.0)
Immune system disorders	0 (0.0)	1 (100.0)
Investigations	0 (0.0)	1 (100.0)

Most Frequently Reported AEs Overall by Preferred Term n (%)

Part I:

	No drug
Nasopharyngitis	1 (12.5)
Aspartate Aminotransferase Increased	1 (12.5)
Blood Chloride Increased	1 (12.5)
Blood Cholesterol Increased	1 (12.5)
Blood Creatine Phosphokinase Increased	3 (37.5)
Blood Creatinine Increased	1 (12.5)
Blood Glucose Increased	3 (37.5)
Blood Lactate Dehydrogenase Increased	2 (25.0)
Blood Phosphorus Increased	1 (12.5)
Blood Sodium Increased	1 (12.5)
Blood Triglycerides Increased	2 (25.0)
Lipase Increased	1 (12.5)
Lymphocyte Count Increased	1 (12.5)
Neutrophil Count Decreased	1 (12.5)
Urinary Casts	1 (12.5)
Ketonuria	1 (12.5)

Part II:

	QAX576	Placebo
Nausea	1 (50.0)	0 (0.0)
Dizziness	1 (50.0)	0 (0.0)
Orthostatic Hypotension	1 (50.0)	0 (0.0)
Multiple Allergies	0 (0.0)	1 (100.0)
Blood Lactate Dehydrogenase Increased	0 (0.0)	1 (100.0)
Blood Triglycerides Increased	0 (0.0)	1 (100.0)

Serious Adverse Events and Deaths

None

Other Relevant Findings

QAX576 PK parameters after 3 doses of 3mg/kg (2-hour intravenous infusion, q4w)

	Cmax (3^{rd} dose) (µg/mL)	Tmax (hr)	AUCinf (µg*day/mL)	CL (mL/day/kg)	Vss (mL/kg)	T1/2 (day)
One Pt.	97.5	3	NA	NA	NA	NA
One Pt.	173	1.52	2760	1.09	28.9	26.4

Date of Clinical Trial Report 16 March 2012