ClinicalTrials.gov Protocol and Results Registration System (PRS) Receipt
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Subcutaneous Treatment With Icatibant for Acute Attacks of Hereditary Angioedema (HAE) (FAST2)

This study has been completed.

Sponsor:	Shire
Collaborators:	
Information provided by (Responsible Party):	Shire
ClinicalTrials.gov Identifier:	NCT00500656

Purpose

Primary Outcome Measures:

The primary endpoint was the time to onset of symptom relief of the first attack in the double blind phase. H0: λ icatibant/λ tranexamic acid =1 versus H1: λ icatibant/λ tranexamic acid ≠1 Where: λ icatibant refers to the hazard rate under icatibant and λ tranexamic acid refers to the hazard rate under tranexamic acid.

Secondary Outcome Measures:

- Additional efficacy assessments (Time to Almost Complete Symptom Relief)
- Safety and tolerability
- Pharmacoeconomics

Condition	Intervention	Phase
Hereditary Angioedema	Drug: Icatibant Drug: Tranexamic Acid Drug: Oral Placebo Drug: S.C. Placebo	Phase 3

Study Type: Interventional
Study Design: Treatment, Parallel Assignment, Double Blind (Subject, Investigator), Randomized, Efficacy Study
Official Title: Randomised Double Blind, Controlled, Parallel Group, Multicentre Study of a Subcutaneous Formulation of Icatibant Versus Oral Tranexamic Acid for the Treatment of Hereditary Angioedema (HAE)

Further study details as provided by Shire:

Primary Outcome Measure:

- Time to Onset of Symptom Relief. [Time Frame: 2 days] [Designated as safety issue: No]
  The primary efficacy endpoint was Time to onset of symptom relief (TOSR) following treatment with either icatibant or tranexamic acid. The median time to onset of symptom relief for the icatibant group was compared to the the median time to onset of symptom relief for the tranexamic acid group. TOSR was defined as the time between time of injection to time of first documented onset of symptom relief for the three primary symptoms: cutaneous swelling, cutaneous skin, and abdominal pain. The primary symptom was based on the type of attack. For abdominal attacks, the single primary symptom was abdominal pain. For cutaneous attacks, the single primary symptom was either skin swelling or skin pain, whichever was most severe.

Secondary Outcome Measures:

- Time to Almost Complete Symptom Relief [Time Frame: 48 hours] [Designated as safety issue: No]
  Almost complete symptom relief was defined as a score between 0 and 10 mm on the VAS for at least three consecutive measurements for all symptoms.

Enrollment: 85
Study Start Date: March 2005
Primary Completion Date: March 2008
Study Completion Date: March 2008

Arms	Assigned Interventions
Experimental: Randomized controlled - Icatibant Subjects received S.C icatibant+ oral placebo Icatibant Form: solution for injection, 3 mL, 10 mg/mL Single dose: 30 mg (3 mL) Placebo Form: hard capsule Single dose: 2 capsules Frequency: 3 x 2 capsules for 2 days, taken orally, 6 to 8 hours apart	Drug: Icatibant Icatibant: a stable, synthetic decapeptide and specific BK B2 receptor antagonist. Other Names: Brand name, Firazyr® Drug: Oral Placebo hard capsule matched to tranexamic acid Other Names: Placebo
Active Comparator: Randomized controlled- Tranexamic acid Subjects received oral Tranexamic acid+ S.C. placebo Tranexamic acid Form: over encapsulated film tablet Single dose: 1000 mg (2 capsules) Frequency: 3 x 2 capsules for 2 days, taken orally, 6 to 8 hours apart	Drug: Tranexamic Acid over encapsulated film tablet an anti-fibrinolytic agent,is used in some European countries for the treatment of acute oedema episodes and the continuous prophylaxis of HAE. Drug: S.C. Placebo solution for injection, matched to icatibant for injection

Arms	Assigned Interventions
Placebo Form: solution for injection, matched to icatibant for injection Single dose: 3 mL Frequency: one subcutaneous injection in the abdominal region	Other Names: Placebo
Experimental: Controlled Open-label / laryngeal attack Patients with laryngeal symptoms at the baseline were not randomised but treated with icatibant open label during the controlled phase.	Drug: Icatibant Icatibant: a stable, synthetic decapeptide and specific BK B2 receptor antagonist. Other Names: Brand name, Firazyr®
Experimental: Untreated patients at the baseline Patients who were screened and found eligible but did not experience an angioedema attack, or had an attack that was not severe enough to merit treatment while the controlled phase was ongoing were treated in the open label phase with icatibant	Drug: Icatibant Icatibant: a stable, synthetic decapeptide and specific BK B2 receptor antagonist. Other Names: Brand name, Firazyr®

Detailed Description:

This was a Phase III, randomised, double blind, double dummy, multicentre, controlled,parallel group study of a 30 mg s.c. formulation of icatibant for the treatment of patients with moderate to very severe symptoms of cutaneous and/or abdominal symptoms of HAE.

The study consisted of two parts: controlled phase and OLE phase. For the primary endpoint, Efficacy was determined by evaluating the differences in study outcomes using a Visual Analogue Scale for patients treated with icatibant and tranexamic acid.

Eligibility

Ages Eligible for Study: 18 Years and older
Genders Eligible for Study: Both
Accepts Healthy Volunteers: No

Criteria

Inclusion Criteria:

- Age above 18 years;
- Documented diagnosis of HAE Type I or II (confirmed C1-INH deficiency);
- Current edema in the cutaneous, abdominal and/or laryngeal areas;
- Current edema moderate to severe according to the investigator’s Symptom Score.

Exclusion Criteria:

- Diagnosis of angioedema other than HAE,
- Participation in a clinical trial of another investigational medicinal product (IMP)within the past month
- Treatment with any pain medication since onset of the current angioedema attack
- Treatment with replacement therapy, including C1-INH products, less than 3 days before onset of the current angioedema attack
- Treatment with Tranexamic acid replacement therapy within a week before onset of the current angioedema attack
- Treatment with ACE inhibitors
- Contraindications for Tranexamic acid
- Evidence of coronary artery disease based on medical history or Screening examination in particular unstable angina pectoris or severe coronary heart disease
- Congestive heart failure (class 3 and 4)
- Serum creatinine level of ≥ 250 µmol/L
- Serious concomitant illness that the investigator considered to be a contraindication for participation in the trial
- Pregnancy (as assessed prior to treatment) and/or breast-feeding

Contacts and Locations

Locations

Italy

Università degli Studi di Milano, Dipartimento di Medicina Interna

Milano, Italy, 20123

Investigators

Principal Investigator:	Marco Cicardi, Prof. Dr.	Università degli Studi di Milano

More Information

http://www.jerini.com

Results Publications:

Bas M, Bier H, Greve J, Kojda G, Hoffmann TK. Novel pharmacotherapy of acute hereditary angioedema with bradykinin B2-receptor antagonist icatibant. Allergy. 2006 Dec;61(12):1490-2.

Responsible Party:	Shire
Study ID Numbers:	JE049 #2102
Health Authority:	United States: Food and Drug Administration European Union: European Medicines Agency

Study Results

Participant Flow

Pre-Assignment Details	85 patients participated in the study(36 in the icatibant group and 38 in the tranexamic acid group)3 patients with laryngeal symptoms at Baseline.8 Patients were screened and found eligible but did not experience an angioedema attack, or had an attack that was not severe enough to merit treatment while the controlled phase was ongoing

Reporting Groups

	Description
Randomized Controlled -Icatibant	Patients who were randomized to icatibant + Oral placebo (hard capsule matched to tranexamic acid) in the controlled phase after they had an eligible first in-study attack.
Randomized Controlled-Tranexamic Acid	Patients who were randomized to received oral Tranexamic acid + S.C. placebo(solution for injection, matched to icatibant for injection) in the controlled phase after they had an eligible first in-study attack.
Controlled Open-label / Laryngeal Attack	Patients with laryngeal symptoms at the baseline were not randomised but treated with icatibant open label during the controlled phase.
Untreated Patients at the Baseline	Patients who were screened and found eligible but did not experience an angioedema attack, or had an attack that was not severe enough to merit treatment while the controlled phase was ongoing were treated in the open label phase with icatibant

Controlled Phase

	Randomized Controlled -Icatibant	Randomized Controlled-Tranexamic Acid	Controlled Open-label / Laryngeal Attack	Untreated Patients at the Baseline
Started	36	38	3	8
Completed	26	28	2	0
Not Completed	10	10	1	8

Open Label Extension (OLE) Phase

	Randomized Controlled -Icatibant	Randomized Controlled-Tranexamic Acid	Controlled Open-label / Laryngeal Attack	Untreated Patients at the Baseline
Started	23 [1]	21 [2]	2	8 [3]
Completed	16	9	1	6
Not Completed	7	12	1	2

[1] 3 Subjects did not experience an angioedema attack after their first attack in the controlled phase
[2] 7 Subjects did not experience an angioedema attack after their first attack in the controlled phase
[3] Subjects did not experience an angioedema attack during the controlled phase

Baseline Characteristics

Reporting Groups

	Description
Randomized Controlled -Icatibant	Patients who were randomized to icatibant + Oral placebo (hard capsule matched to tranexamic acid) in the controlled phase after they had an eligible first in-study attack.
Randomized Controlled-Tranexamic Acid	Patients who were randomized to received oral Tranexamic acid + S.C. placebo(solution for injection, matched to icatibant for injection) in the controlled phase after they had an eligible first in-study attack.
Controlled Open-label / Laryngeal Attack	Patients with laryngeal symptoms at the baseline were not randomised but treated with icatibant open label during the controlled phase.
Untreated Patients at the Baseline	Patients who were screened and found eligible but did not experience an angioedema attack, or had an attack that was not severe enough to merit treatment while the controlled phase was ongoing were treated in the open label phase with icatibant

Baseline Measures

	Randomized Controlled -Icatibant	Randomized Controlled-Tranexamic Acid	Controlled Open-label / Laryngeal Attack	Untreated Patients at the Baseline	Total
Number of Participants	36	38	3	8	85
Age, Continuous [units: years] Mean (Standard Deviation)	40.4 (13.59)	41.9 (12.36)	35.0 (11.36)	40.6 (13.51)	40.9 (12.8)
Gender, Male/Female [units: participants]					
Female	24	23	1	7	55
Male	12	15	2	1	30
Region of Enrollment [units: participants]					
Austria	3	4	0	1	8
France	3	1	0	2	6
Germany	13	12	0	0	25
Hungary	3	3	0	0	6

	Randomized Controlled -Icatibant	Randomized Controlled- Tranexamic Acid	Controlled Open-label / Laryngeal Attack	Untreated Patients at the Baseline	Total
Ireland	0	1	0	0	1
Israel	4	4	3	4	15
Italy	3	5	0	1	9
Lithuania	1	2	0	0	3
Poland	1	2	0	0	3
Sweden	3	2	0	0	5
Switzerland	2	2	0	0	4

Outcome Measures

1. Primary Outcome Measure:

Measure Title	Time to Onset of Symptom Relief.
Measure Description	The primary efficacy endpoint was Time to onset of symptom relief (TOSR) following treatment with either icatibant or tranexamic acid. The median time to onset of symptom relief for the icatibant group was compared to the the median time to onset of symptom relief for the tranexamic acid group. TOSR was defined as the time between time of injection to time of first documented onset of symptom relief for the three primary symptoms: cutaneous swelling, cutaneous skin, and abdominal pain. The primary symptom was based on the type of attack. For abdominal attacks, the single primary symptom was abdominal pain. For cutaneous attacks, the single primary symptom was either skin swelling or skin pain, whichever was most severe.
Time Frame	2 days
Safety Issue?	No

Analysis Population Description
[Not Specified]

Reporting Groups

	Description
Randomized Controlled -Icatibant	Patients who were randomized to icatibant + Oral placebo (hard capsule matched to tranexamic acid) in the controlled phase after they had an eligible first in-study attack.

	Description
Randomized Controlled-Tranexamic Acid	Patients who were randomized to received oral Tranexamic acid + S.C. placebo(solution for injection, matched to icatibant for injection) in the controlled phase after they had an eligible first in-study attack.

Measured Values

	Randomized Controlled -Icatibant	Randomized Controlled-Tranexamic Acid
Number of Participants Analyzed	36	38
Time to Onset of Symptom Relief. [units: Hours] Median (Inter-Quartile Range)	2.0 (1.0 to 3.5)	12.0 (3.5 to 25.4)

Statistical Analysis 1 for Time to Onset of Symptom Relief.

Statistical Analysis Overview	Comparison Groups	Randomized Controlled -Icatibant, Randomized Controlled-Tranexamic Acid
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	< 0.001
	Comments	[Not specified]
	Method	Other [The Wilcoxon version of the log rank]
	Comments	The median time to onset was calculated using Kaplan Meier methodology. The Wilcoxon version of the log rank test of SAS was used

Method of Estimation	Estimation Parameter	Hazard Ratio (HR)
	Estimated Value	3.475
	Confidence Interval	(2-Sided) 95% 1.901 to 6.355
	Estimation Comments	[Not specified]

2. Secondary Outcome Measure:

Measure Title	Time to Almost Complete Symptom Relief
Measure Description	Almost complete symptom relief was defined as a score between 0 and 10 mm on the VAS for at least three consecutive measurements for all symptoms.

Time Frame	48 hours
Safety Issue?	No

Analysis Population Description

[Not Specified]

Reporting Groups

	Description
Randomized Controlled -Icatibant	Patients who were randomized to icatibant + Oral placebo (hard capsule matched to tranexamic acid) in the controlled phase after they had an eligible first in-study attack.
Randomized Controlled-Tranexamic Acid	Patients who were randomized to received oral Tranexamic acid + S.C. placebo(solution for injection, matched to icatibant for injection) in the controlled phase after they had an eligible first in-study attack.

Measured Values

	Randomized Controlled -Icatibant	Randomized Controlled-Tranexamic Acid
Number of Participants Analyzed	36	38
Time to Almost Complete Symptom Relief [units: Hours] Median (Inter-Quartile Range)	10.0 (2.8 to 23.2)	51.0 (12.0 to 79.5)

Statistical Analysis 1 for Time to Almost Complete Symptom Relief

Statistical Analysis Overview	Comparison Groups	Randomized Controlled -Icatibant, Randomized Controlled-Tranexamic Acid
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	< 0.001
	Comments	[Not specified]
	Method	Other [The Wilcoxon version of the log rank]
	Comments	The median time to almost complete symptom relief was calculated using Kaplan Meier methodology.The Wilcoxon version of the log rank test SAS was used

Reported Adverse Events

Time Frame	An AE was assigned to the controlled phase if the start date of the event was between the first treatment of the first attack and the first treatment in the OLE phase.
Additional Description	[Not specified]

Reporting Groups

	Description
Controlled Phase- Icatibant (Randomized Subjects)	Patients who were randomized to icatibant+ oral placebo in the controlled phase and experienced adverse events while participating in the controlled phase
Controlled Phase- Tranexamic Acid (Randomized Subjects)	Patients who were randomized to Tranexamic acid+ S.C. placebo in the controlled phase and experienced adverse events while participating in the controlled phase.
Controlled Phase- Icatibant (Subjects w/ Laryngeal Attack)	This represents adverse events during the controlled phase that were experienced by Patients with laryngeal symptoms at the baseline and were treated with open label icatibant during the controlled phase.
Open Label Extension Phase- Icatibant (Previously Randomized)	Patients who were randomized to either icatibant+ oral placebo or Tranexamic acid+ S.C. placebo in the controlled phase and experienced adverse events while participating in the open label extension phase.
Open Label Extension Phase (Subjects w/ Laryngeal Attack)	This represents adverse events during the open label extension phase that were experienced by Patients with laryngeal symptoms at the baseline and got treated with open label icatibant during the controlled phase and Open label extension phase.
Open Label Extension Phase(Untreated Patients at the Baseline	This represents adverse events experienced by Patients who were screened and found eligible but did not experience an angioedema attack, or had an attack that was not severe enough to merit treatment while the controlled phase was ongoing.

Serious Adverse Events

	Controlled Phase- Icatibant (Randomized Subjects)	Controlled Phase- Tranexamic Acid (Randomized Subjects)	Controlled Phase- Icatibant (Subjects w/ Laryngeal Attack)	Open Label Extension Phase- Icatibant (Previously Randomized)	Open Label Extension Phase (Subjects w/ Laryngeal Attack)	Open Label Extension Phase(Untreated Patients at the Baseline
	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)
Total	4/36 (11.11%)	1/38 (2.63%)	1/3 (33.33%)	9/44 (20.45%)	1/2 (50%)	0/8 (0%)
Cardiac disorders						
Aortic Value Sclerosis [A] †	0/36 (0%)	1/38 (2.63%)	0/3 (0%)	0/44 (0%)	0/2 (0%)	0/8 (0%)

	Controlled Phase- Icatibant (Randomized Subjects)	Controlled Phase- Tranexamic Acid (Randomized Subjects)	Controlled Phase- Icatibant (Subjects w/ Laryngeal Attack)	Open Label Extension Phase- Icatibant (Previously Randomized)	Open Label Extension Phase (Subjects w/ Laryngeal Attack)	Open Label Extension Phase(Untreated Patients at the Baseline
	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)
Coronary Artery Disease [A] †	0/36 (0%)	0/38 (0%)	0/3 (0%)	1/44 (2.27%)	0/2 (0%)	0/8 (0%)
Congenital, familial and genetic disorders						
Hereditary Angioedema [A] †	2/36 (5.56%)	0/38 (0%)	1/3 (33.33%)	3/44 (6.82%)	1/2 (50%)	0/8 (0%)
General disorders						
Sudden Cardiac Death [A] †	0/36 (0%)	1/38 (2.63%)	0/3 (0%)	0/44 (0%)	0/2 (0%)	0/8 (0%)
Hepatobiliary disorders						
Cholelithiasis [A] †	1/36 (2.78%)	0/38 (0%)	0/3 (0%)	0/44 (0%)	0/2 (0%)	0/8 (0%)
Infections and infestations						
Cystitis [A] †	1/36 (2.78%)	0/38 (0%)	0/3 (0%)	0/44 (0%)	0/2 (0%)	0/8 (0%)
Gastroenteritis [A] †	1/36 (2.78%)	0/38 (0%)	0/3 (0%)	2/44 (4.55%)	0/2 (0%)	0/8 (0%)
Urinary Track Infection Bacterial [A] †	0/36 (0%)	0/38 (0%)	0/3 (0%)	1/44 (2.27%)	0/2 (0%)	0/8 (0%)
Injury, poisoning and procedural complications						
Head Injury [A] †	0/36 (0%)	0/38 (0%)	0/3 (0%)	1/44 (2.27%)	0/2 (0%)	0/8 (0%)
Road Traffic Accident [A] †	0/36 (0%)	0/38 (0%)	0/3 (0%)	1/44 (2.27%)	0/2 (0%)	0/8 (0%)
Wound [A] †	0/36 (0%)	0/38 (0%)	0/3 (0%)	1/44 (2.27%)	0/2 (0%)	0/8 (0%)
Investigations						
Pancreatic Enzymes Increased [A] †	0/36 (0%)	0/38 (0%)	0/3 (0%)	1/44 (2.27%)	0/2 (0%)	0/8 (0%)
Musculoskeletal and connective tissue disorders						
Myalgia [A] †	0/36 (0%)	0/38 (0%)	0/3 (0%)	1/44 (2.27%)	0/2 (0%)	0/8 (0%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)						

	Controlled Phase- Icatibant (Randomized Subjects)	Controlled Phase- Tranexamic Acid (Randomized Subjects)	Controlled Phase- Icatibant (Subjects w/ Laryngeal Attack)	Open Label Extension Phase- Icatibant (Previously Randomized)	Open Label Extension Phase (Subjects w/ Laryngeal Attack)	Open Label Extension Phase(Untreated Patients at the Baseline
	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)
Cervix Carcinoma Stage 0 [A] †	0/36 (0%)	0/38 (0%)	0/3 (0%)	1/44 (2.27%)	0/2 (0%)	0/8 (0%)
Psychiatric disorders						
Suicide Attempt [A] †	0/36 (0%)	0/38 (0%)	0/3 (0%)	1/44 (2.27%)	0/2 (0%)	0/8 (0%)
Renal and urinary disorders						
Renal Failure [A] †	0/36 (0%)	0/38 (0%)	0/3 (0%)	1/44 (2.27%)	0/2 (0%)	0/8 (0%)
Surgical and medical procedures						
Tooth Extraction [A] †	0/36 (0%)	0/38 (0%)	0/3 (0%)	1/44 (2.27%)	0/2 (0%)	0/8 (0%)
Vascular disorders						
Hypertensive Crisis [A] †	1/36 (2.78%)	0/38 (0%)	0/3 (0%)	0/44 (0%)	0/2 (0%)	0/8 (0%)

† Indicates events were collected by systematic assessment.
A Term from vocabulary, MedDRA version 8.1

Other Adverse Events
Frequency Threshold Above Which Other Adverse Events are Reported: 5%

	Controlled Phase- Icatibant (Randomized Subjects)	Controlled Phase- Tranexamic Acid (Randomized Subjects)	Controlled Phase- Icatibant (Subjects w/ Laryngeal Attack)	Open Label Extension Phase- Icatibant (Previously Randomized)	Open Label Extension Phase (Subjects w/ Laryngeal Attack)	Open Label Extension Phase(Untreated Patients at the Baseline
	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)
Total	19/36 (52.78%)	16/38 (42.11%)	1/3 (33.33%)	31/44 (70.45%)	1/2 (50%)	4/8 (50%)
Blood and lymphatic system disorders						
Blood and Lymphatic system disorders [A] †	0/36 (0%)	2/38 (5.26%)	0/3 (0%)	1/44 (2.27%)	0/2 (0%)	0/8 (0%)

	Controlled Phase- Icatibant (Randomized Subjects)	Controlled Phase- Tranexamic Acid (Randomized Subjects)	Controlled Phase- Icatibant (Subjects w/ Laryngeal Attack)	Open Label Extension Phase- Icatibant (Previously Randomized)	Open Label Extension Phase (Subjects w/ Laryngeal Attack)	Open Label Extension Phase(Untreated Patients at the Baseline
	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)
Congenital, familial and genetic disorders						
Hereditary Angioedema [B] †	10/36 (27.78%)	6/38 (15.79%)	1/3 (33.33%)	10/44 (22.73%)	1/2 (50%)	1/8 (12.5%)
General disorders						
Injection Site Reaction [B] †	2/36 (5.56%)	0/38 (0%)	0/3 (0%)	1/44 (2.27%)	0/2 (0%)	0/8 (0%)
Infections and infestations						
Dental Caries [B] †	0/36 (0%)	0/38 (0%)	0/3 (0%)	0/44 (0%)	0/2 (0%)	1/8 (12.5%)
Gingival Infection [B] †	0/36 (0%)	0/38 (0%)	0/3 (0%)	0/44 (0%)	1/2 (50%)	0/8 (0%)
Nasopharyngitis [B] †	2/36 (5.56%)	3/38 (7.89%)	0/3 (0%)	4/44 (9.09%)	0/2 (0%)	0/8 (0%)
Pharyngitis [B] †	0/36 (0%)	1/38 (2.63%)	0/3 (0%)	3/44 (6.82%)	0/2 (0%)	0/8 (0%)
Respiratory Track Infection [B] †	0/36 (0%)	0/38 (0%)	0/3 (0%)	1/44 (2.27%)	0/2 (0%)	1/8 (12.5%)
Urinary Track Infection [B] †	0/36 (0%)	0/38 (0%)	0/3 (0%)	6/44 (13.64%)	0/2 (0%)	0/8 (0%)
Injury, poisoning and procedural complications						
Injury, poisoning and procedual complications [A] †	3/36 (8.33%)	1/38 (2.63%)	0/3 (0%)	3/44 (6.82%)	0/2 (0%)	0/8 (0%)
Musculoskeletal and connective tissue disorders						
Musculoskeletal and connective tissue disorders [C] †	2/36 (5.56%)	1/38 (2.63%)	0/3 (0%)	3/44 (6.82%)	0/2 (0%)	0/8 (0%)
Nervous system disorders						
Dizziness [B] †	0/36 (0%)	0/38 (0%)	0/3 (0%)	0/44 (0%)	0/2 (0%)	1/8 (12.5%)
Headache [B] †	2/36 (5.56%)	2/38 (5.26%)	0/3 (0%)	0/44 (0%)	0/2 (0%)	0/8 (0%)
Skin and subcutaneous tissue disorders						

	Controlled Phase- Icatibant (Randomized Subjects)	Controlled Phase- Tranexamic Acid (Randomized Subjects)	Controlled Phase- Icatibant (Subjects w/ Laryngeal Attack)	Open Label Extension Phase- Icatibant (Previously Randomized)	Open Label Extension Phase (Subjects w/ Laryngeal Attack)	Open Label Extension Phase(Untreated Patients at the Baseline
	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)
Pruritus [B] †	0/36 (0%)	0/38 (0%)	0/3 (0%)	0/44 (0%)	0/2 (0%)	1/8 (12.5%)
Surgical and medical procedures						
Dental Operation [B] †	0/36 (0%)	0/38 (0%)	0/3 (0%)	0/44 (0%)	0/2 (0%)	1/8 (12.5%)

† Indicates events were collected by systematic assessment.
A Term from vocabulary, Organ system
B Term from vocabulary, MedDRA version 8.1
C Term from vocabulary, organ system

Limitations and Caveats

[Not specified]

More Information

Certain Agreements:

Principal Investigators are NOT employed by the organization sponsoring the study.

The only disclosure restriction on the PI is that the sponsor can review results communications prior to public release and can embargo communications regarding trial results for a period that is less than or equal to 60 days from the time submitted to the sponsor for review. The sponsor cannot require changes to the communication and cannot extend the embargo.

Results Point of Contact:

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