Safety and Efficacy Study of Intravitreal Ocriplasmin in Subjects With AMD With Focal VitreomacularAdhesion (MIVI-5)

This study has been completed.

Sponsor:	ThromboGenics
Collaborators:	
Information provided by (Responsible Party):	ThromboGenics
ClinicalTrials.gov Identifier:	NCT00913744

Purpose

The primary objective of the study was to evaluate the safety and preliminary efficacy of intravitreal ocriplasmin in subjects with exudative AMD with focal vitreomacular adhesion

The secondary objective: not provided

Condition	Intervention	Phase
Exudative Age-Related Macular Degeneration Focal Vitreomacular Adhesion	Drug: Ocriplasmin Drug: Sham injection	Phase 2

Study Type: Interventional
Study Design: Treatment, Parallel Assignment, Double Blind (Subject, Investigator), Randomized, Safety/Efficacy Study

Official Title: A Randomized, Sham-Injection Controlled, Double-Masked, Multicenter Trial of Ocriplasmin Intravitreal Injection for Treatment of Focal Vitreomacular Adhesion in Subjects With Exudative Age-Related Macular Degeneration (AMD)

Further study details as provided by ThromboGenics

Primary Outcome Measure:

Proportion of Subjects With Focal Vitreomacular Adhesion (VMA) Release by Day 28 [Time Frame: Day 28][Designated as safety issue: No]

The VMA release was determined by masked Central Reading Center Optical Coherence Tomography (OCT) evaluation

Secondary Outcome Measures:

Vitreomacular adhesion status and PVD status at visits other than day 56 post-injection visit (OCT andultrasound) [Time Frame: Visits other than day 56 post-injection visit (OCT and ultrasound)][Designated as safety issue: No]

Enrollment: 100
Study Start Date: January 2010
Primary Completion Date: December 2012
Study Completion Date: April 2013

Arms	Assigned Interventions
Experimental: Ocriplasmin	Drug: Ocriplasmin Single Ocriplasmin intravitreal injection (125 µg)
Sham comparator: sham injection	Drug: Sham injection Single Sham injection

Detailed Description:

- No data

Eligibility

Ages Eligible for Study: 50 Years and older
Genders Eligible for Study: Both
Accepts Healthy Volunteers: No

Criteria

Inclusion Criteria:

- Male or female subjects aged > 50
- Presence of focal vitreomacular adhesion measured by Optical Coherence Tomography (OCT)
- Diagnosis of active primary or recurrent subfoveal CNV secondary to AMD, including those with predominantly classic, minimally classic or occult lesions with no classic component
- The total area of Choroidal Neovascularization (CNV) (including both classic and occult components) encompassed within the lesion must be > 50% of the total lesion area
- The total lesion area must be < 12 disc areas
- Subjects who have previously received at least three antiangiogenic injections(Lucentis® or Avastin®) in the study eye
- Subjects with visual acuity of 20/32 to 20/200 in the study eye
- Written informed consent obtained from the subject prior to inclusion in the study

Exclusion Criteria:

- Evidence of complete macular Posterior Vitreous Detachment (PVD) in the study eye on biomicroscopy, B-scan ultrasound or OCT prior to planned study drug injection
- Subjects with vitreous haemorrhage which precludes either of the following: visualization of the posterior pole by visual inspection or adequate assessment of the macula by either OCT and/or fluorescein angiography in the study eye or other opacities precluding visualisation of the fundus.
- Subjects who have previously received more than 9 antiangiogenic agent injections (whether Lucentis® or Avastin® or other anti-angiogenic agent) in the study eye
- Subjects with history of rhegmatogenous retinal detachment or proliferative vitreoretinopathy (PVR) in the study eye
- Subjects with high myopia (> 8D) or aphakia in the study eye
- Subjects who have had ocular surgery in the study eye in the prior three months
- Subjects who have had a vitrectomy in the study eye at any time

Contacts and Locations

Locations

United States, California

Retina-Vitreous Associates Medical Group
Beverly Hills, California, United States, 90211

Retinal Consultants Medical Group
Sacramento, California, United States, 95819

United States, Colorado

University of Colorado Denver
Aurora, Colorado, United States, 80045

United States, Florida

Center for Retina and Maculla Disease Winter Haven, Florida, United States, 33880

United States, Georgia

Southeast Retina Center, PC
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United States, South Dakota

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United States, Texas

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Italy

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Sponsors and collaborators
ThromboGenics

More Information

Responsible Party: ThromboGenics
Other Study Id Numbers: TG-MV-005
ClinicalTrials.gov Identifier: NCT00913744
Study First Received: June, 2, 2009
Results First received: April, 2, 2014

EudraCT 2008-004844-35

Health Authority: United States: Food and Drug administration
Belgium: Federal Agency for Medicinal Products and Health Products
Italy: The Italian Medicines Agency
France: Afssaps - Agence française de sécurité sanitaire des produits de santé (Saint-Denis)
Germany: Federal Institute for Drugs and Medical Devices
United Kingdom: Medicines and Healthcare Products Regulatory Agency

Study Results

Participant Flow

Recruitment Details	First subject was enrolled on 29 Jan 2010 and last subject completed the study on 06 Dec 2012

Reporting Groups

	Description
Ocriplasmin	Intravitreal injection (125 µg)
Sham	Sham injection

Overall Study

	Ocriplasmin	Sham
Started	75	25
Completed	70	24
Not Completed	5	1
Adverse Event	2	0
Withdrawal by Subject	2	1
Death	1	0

Baseline Characteristics

Reporting Groups

	Description
Ocriplasmin	Intravitreal injection (125 µg)
Sham	Sham injection

Baseline Measures

	Ocriplasmin	Sham	Total
Number of Participants	74 *	25	99
Age, Continuous [units: Years] Mean (Standard Deviation)	74.5 (8.13)	74.7 (7.16)	74.6 (7.86)
Gender [units: participants]			
Females	39	15	54
Male	35	10	45

* Full Analysis Set (FAS): All randomized subjects who have been administered trial medication and for whom data of at least one post-baseline efficacy assessment is available. One subject (ocriplasmin) was not included in the FAS because the subject withdrew consent after receiving study treatment and refused further contact

Outcome Measures

1. Primary Outcome Measure:

Measure Title	Proportion of subjects With Focal Vitreomacular Adhesion (VMA) Release by day 28
Measure Description	The VMA release was determined by masked Central Reading Center Optical Coherence Tomography (OCT) evaluation
Time Frame	Day 28
Safety Issue?	No

Analysis Population Description

The Full Analysis Set (FAS) was the primary data set for efficacy analysis. Data that were missing for any reason were imputed using the Last Observation Carried Forward (LOCF) method.

	Description
Ocriplasmin	Intravitreal injection (125 µg)
Sham	Sham injection

Measured Values

	Ocriplasmin	Sham
Number of Participants Analyzed	74	25
Proportion of Subjects With Focal Vitreomacular Adhesion (VMA) Release by Day 28 units: percentage of subjects]	24.3	12.0

Statistical Analysis 1 for Proportion of Subjects With Focal Vitreomacular Adhesion (VMA) Release by Day 28

Groups [1]	All groups
Method [2]	Fisher Exact
P Value [3]	0.262
Difference in proportions [4]	12.3
95% Confidence Interval	-3.7 to 28.4

Reported Adverse Events

Time Frame	Adverse Events (AEs)/Serious Adverse Events (SAEs) were collected from injection day up to discontinuation, and for a maximum of 12 months after injection
Additional Description	Safety Set consisted of all subjects who received study treatment and was used for all safety analysis. All subjects were included in the Safety Set: 75 subjects in the ocriplasmin group and 25 subjects in the sham group. AEs and SAEs include ocular events in study eye and non-study eye, as well as non-ocular events.

Reporting Groups

	Description
Ocriplasmin	Intravitreal injection (125 µg)
Sham	Sham injection

Serious Adverse Events

	Ocriplasmin	Sham
Total, serious adverse events		
# participants affected / at risk	**18/75 (24.00%)**	**2/25 (8.00%)**
Cardiac disorders		
Myocardial infarction † 1		
# participants affected / at risk	**1/75 (1.33%)**	**0/25 (0.00%)**
# events	**1**	**0**
Eye disorders		
Retinal detachment † 1		
# participants affected / at risk	**3/75 (4.00%)**	**0/25 (0.00%)**
# events	**3**	**0**
Visual acuity reduced † 1		
# participants affected / at risk	**3/75 (4.00%)**	**0/25 (0.00%)**
# events	**3**	**0**

Blindness transient † 1		
# participants affected / at risk	2/75 (2.67%)	0/25 (0.00%)
# events	2	0
Gastrointestinal disorders		
Rectal haemorrhage † 1		
# participants affected / at risk	1/75 (1.33%)	0/25 (0.00%)
# events	1	0
Hepatobiliary disorders		
Cholecystitis acute † 1		
# participants affected / at risk	1/75 (1.33%)	0/25 (0.00%)
# events	1	0
Infections and infestations		
Urinary tract infection † 1		
# participants affected / at risk	2/75 (2.67%)	0/25 (0.00%)
# events	2	0
Cystitis † 1		
# participants affected / at risk	0/75 (0.00%)	1/25 (4.00%)
# events	0	1
Endophthalmitis † 1		
# participants affected / at risk	1/75 (1.33%)	0/25 (0.00%)
# events	1	0
Urosepsis † 1		
# participants affected / at risk	1/75 (1.33%)	0/25 (0.00%)
# events	1	0
Injury, poisoning and procedural complications		
Femur fracture † 1		
# participants affected / at risk	1/75 (1.33%)	0/25 (0.00%)
# events	1	0
Joint injury † 1		

# participants affected / at risk	1/75 (1.33%)	0/25 (0.00%)
# events	1	0
Vascular pseudoaneurysm † 1		
# participants affected / at risk	0/75 (0.00%)	1/25 (4.00%)
# events	0	1
Investigations		
Intraocular pressure increased † 1		
# participants affected / at risk	2/75 (2.67%)	0/25 (0.00%)
# events	2	0
Musculoskeletal and connective tissue disorders		
Rotator cuff syndrome † 1		
# participants affected / at risk	1/75 (1.33%)	0/25 (0.00%)
# events	1	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)		
Brain cancer metastatic † 1		
# participants affected / at risk	1/75 (1.33%)	0/25 (0.00%)
# events	1	0
Prostate cancer metastatic † 1		
# participants affected / at risk	1/75 (1.33%)	0/25 (0.00%)
# events	1	0
Vocal cord neoplasm † 1		
# participants affected / at risk	1/75 (1.33%)	0/25 (0.00%)
# events	1	0
Nervous system disorders		
Dizziness postural † 1		
# participants affected / at risk	0/75 (0.00%)	1/25 (4.00%)
# events	0	1

Surgical and medical procedures		
Vocal cordectomy † 1		
# participants affected / at risk	**1/75 (1.33%)**	**0/25 (0.00%)**
# events	**1**	**0**
Vascular disorders		
Ateriosclerosis † 1		
# participants affected / at risk	**0/75 (0.00%)**	**1/25 (4.00%)**
# events	**0**	**1**

† Events were collected by systematic assessment
1 Term from vocabulary, MedDRA (14.1)

Other Adverse Events

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

Time Frame	Adverse Events (AEs)/Serious Adverse Events (SAEs) were collected from injection day up to discontinuation, and for a maximum of 12 months after injection.
Additional Description	Safety Set consisted of all subjects who received study treatment and was used for all safety analysis. All subjects were included in the Safety Set: 75 subjects in the ocriplasmin group and 25 subjects in the sham group. AEs and SAEs include ocular events in study eye and non-study eye, as well as non-ocular events.

Reporting Groups

	Description
Ocriplasmin	Intravitreal injection (125 µg)
Sham	Sham injection

Other Adverse Events

	Ocriplasmin	Sham
Total, other (not including serious) adverse events		
# participants affected / at risk	**33/75 (44.00%)**	**11/25 (44.00%)**
Eye disorders		
Visual acuity reduced † 1		
# participants affected / at risk	**12/75 (16.00%)**	**3/25 (12.00%)**
# events	**17**	**5**
Photopsia † 1		
# participants affected / at risk	**9/75 (12.00%)**	**2/25 (8.00%)**
# events	**10**	**2**

Eye pain † [1]		
# participants affected / at risk	**10/75 (13.33%)**	**0/25 (0.00%)**
# events	**10**	**0**
Conjuctival haemorrhage † [1]		
# participants affected / at risk	**7/75 (9.33%)**	**2/25 (8.00%)**
# events	**8**	**3**
Retinal haemorrhage † [1]		
# participants affected / at risk	**3/75 (4.00%)**	**5/25 (20.00%)**
# events	**3**	**6**
Vitreous floaters † [1]		
# participants affected / at risk	**8/75 (10.67%)**	**0/25 (0.00%)**
# events	**9**	**0**
Blepharitis † [1]		
# participants affected / at risk	**4/75 (5.33%)**	**0/25 (0.00%)**
# events	**4**	**0**
Cataract nuclear † [1]		
# participants affected / at risk	**4/75 (5.33%)**	**0/25 (0.00%)**
# events	**4**	**0**
Corneal oedema † [1]		
# participants affected / at risk	**4/75 (5.33%)**	**0/25 (0.00%)**
# events	**4**	**0**
Metamorphosia † [1]		
# participants affected / at risk	**1/75 (1.33%)**	**2/25 (8.00%)**
# events	**1**	**2**
Ulcerative keratitis † [1]		
# participants affected / at risk	**0/75 (0.00%)**	**2/25 (8.00%)**
# events	**0**	**2**

† Events were collected by systematic assessment [1] Term from vocabulary, MedDRA (14.1)

Limitations and Caveats

[Not specified]

More Information

Certain Agreements:

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

There IS an agreement between the Principal Investigator and the Sponsor (or its agents) that restricts the PI's rights to discuss or publish trial results after the trial is completed.

Other disclosure agreement that restricts the right of the PI to discuss or publish trial results after the trial is completed.

Restriction Description: Institution and the Principal Investigator (PI) reserve the right to publish only the results of the work performed by the Principal Investigator pursuant to this Agreement; provided, however, that Institution provides Sponsor a copy of any proposed publication, for review and comment at least sixty (60) days in advance of its submission for publication.

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Publications:

Novack RL, Staurenghi G, Girach A, Narendran N, Tolentino M (2015). Safety of intravitreal ocriplasmin for focal vitreomacular adhesion in patients with exudative age-related macular degeneration. Ophthalmology Apr;122(4):796-802.