A Multicenter Study to Compare Multiple Doses of Intravitreal Microplasmin Versus Sham Injection for Treatment of Patients With Diabetic Macular Edema (DME) (MIVI-II)

TG-MV-002

This study has been completed.

ClinicalTrials.gov Identifier:
NCT00412451

Sponsor:
ThromboGenics

Study Type:	Interventional
Study Design:	Allocation: Randomized; Endpoint Classification: Safety/Efficacy Study; Intervention Model: Parallel Assignment; Masking: Double Blind (Subject, Investigator, Outcomes Assessor); Primary Purpose: Treatment
Condition:	Diabetic Macular Edema
Interventions:	Drug: ocriplasmin Other: Sham injection

Purpose

A multicenter study to compare multiple doses of intravitreal microplasmin for non-surgical PVD induction for treatment of patients with DME.

Condition	Intervention	Phase
Diabetic Macular Edema	Drug: ocriplasmin Other: Sham injection	Phase 2

Study Type: Interventional
Study Design: Allocation: Randomized
Endpoint Classification: Safety/Efficacy Study
Intervention Model: Parallel Assignment
Masking: Double Blind (Subject, Investigator, Outcomes Assessor)
Primary Purpose: Treatment

Official Title: A Randomized, Sham-Injection Controlled, Double-Masked, Ascending-Dose, Dose-Range-Finding Trial of Microplasmin Intravitreal Injection for Non-Surgical Posterior Vitreous Detachment (PVD) Induction for Treatment of DME.

Further study details as provided by ThromboGenics:

Primary Outcome Measures:

- PVD Induction [Time Frame: Day 14 post-injection] [Designated as safety issue: No]

  The primary efficacy variable was the proportion of patients with total posterior vitreous detachment (PVD) on Day 14 as determined by a masked central reading center (CRC) using 4-quadrant B-scan and optical coherence tomography (OCT)

Enrollment: 51
Study Start Date: December 2006
Study Completion Date: March 2010
Primary Completion Date: January 2010 (Final data collection date for primary outcome measure)

Arms	Assigned Interventions
Experimental: Ocriplasmin 25µg 25µg ocriplasmin intravitreal injection versus sham injection	Drug: ocriplasmin Intravitreal injection, single administration Other Name: microplasmin
Experimental: Ocriplasmin 75µg 75µg ocriplasmin intravitreal injection versus sham injection	Drug: ocriplasmin Intravitreal injection, single administration Other Name: microplasmin
Experimental: Ocriplasmin 125µg 125µg ocriplasmin intravitreal injection versus sham injection	Drug: ocriplasmin Intravitreal injection, single administration Other Name: microplasmin
Sham Comparator: sham injection Sham injection	Other: Sham injection Sham intravitreal injection

Eligibility

Ages Eligible for Study: 18 Years and older (Adult, Senior)
Genders Eligible for Study: Both
Accepts Healthy Volunteers: No

Criteria

Inclusion Criteria include:

- patients >18 years of age with Diabetic Macular Edema

Exclusion Criteria include:

- PVD present at baseline
- Vitreous hemorrhage
- Certain vitreoretinal conditions including proliferative disease, rhegmatogenous retinal detachment, and proliferative vitreoretinopathy (PVR)
- Patients who have had a vitrectomy in the study eye at any time

Contacts and Locations

Locations

Belgium

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Germany

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Italy

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Sponsors and Collaborators

ThromboGenics

More Information

Responsible Party:	ThromboGenics
ClinicalTrials.gov Identifier:	NCT00412451
Other Study ID Numbers:	**TG-MV-002**
EudraCT number:	2006-004626-93

Study First Received:	December 14, 2006
Results First Received:	July 4, 2013
Last Updated:	December 2, 2014
Health Authority:	Germany: Federal Institute for Drugs and Medical Devices Belgium: Ministry of Social Affairs, Public Health and the Environment Netherlands: The Central Committee on Research Involving Human Subjects (CCMO) United Kingdom: Medicines and Healthcare Products Regulatory Agency Spain: Ministry of Health

Participant Flow

Recruitment Details

Key information relevant to the recruitment process for the overall study, such as dates of the recruitment period and locations
The first patient was enrolled on 15 December 2006 and the last patient completed the last visit on 19 January 2010. All patients were selected in medical clinics

Pre-Assignment Details

Significant events and approaches for the overall study following participant enrollment, but prior to group assignment
The trial investigated 3 doses: 25, 75 and 125µg in 3 consecutive cohorts. Patients in each cohort were to be randomized to active treatment or sham injection in a 3:1 ratio. Enrolment into the high dose microplasmin groups was to start only after acceptable safety had been achieved with the previous doses as determined by a Study Safety Committee.

Reporting Groups

	Description
Ocriplasmin 25µg	25µg ocriplasmin intravitreal injections versus sham injection
Ocriplasmin 75µg	75µg ocriplasmin intravitreal injection versus sham injection
0criplasmin 125µg	125µg ocriplasmin intravitreal injection versus sham injection
Sham Injection	Sham intravitreal injection

Participant Flow: Overall Study

	Ocriplasmin 25µg	Ocriplasmin 75µg	0criplasmin 125µg	Sham Injection
STARTED	8	15	15	13
COMPLETED	8	15	14	11
NOT COMPLETED	0	0	1	2

Baseline Characteristics

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
No text entered.

Reporting Groups

	Description
Ocriplasmin 25µg	25µg ocriplasmin intravitreal injection versus sham injection
Ocriplasmin 75µg	75µg ocriplasmin intravitreal injection versus sham injection
Ocriplasmin 125µg	125µg ocriplasmin intravitreal injection versus sham injection
Sham Injection	Sham injection Sham injection : Sham intravitreal injection
Total	Total of all reporting groups

Baseline Measures

	Ocriplasmin 25µg	Ocriplasmin 75µg	Ocriplasmin 125µg	Sham Injection	Total
Number of Participants [units: participants]	**8**	**15**	**15**	**13**	**51**
Age [units: years] Mean (Standard Deviation)	**61.6 (9.8)**	**67.3 (8.8)**	**61.7 (13.4)**	**69.9 (6.2)**	**63.9 (11.1)**
Gender [units: participants]					
Female	**5**	**6**	**4**	**4**	**19**
Male	**3**	**9**	**11**	**9**	**32**

Outcome Measures

1. Primary: PVD Induction [Time Frame: Day 14 post-injection]

Measure Type	Primary
Measure Title	PVD Induction
Measure Description	The primary efficacy variable was the proportion of patients with total posterior vitreous detachment (PVD) on Day 14 as determined by a masked central reading center (CRC) using 4-quadrant B-scan and optical coherence tomography (OCT)
Time Frame	Day 14 post-injection
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Intent-To-Treat (ITT), Last Observation Carried Forward (LOCF)

Reporting Groups

	Description
Ocriplasmin 25µg	25µg ocriplasmin intravitreal injection versus sham injection
Ocriplasmin 75µg	75µg ocriplasmin intravitreal injection versus sham injection
Ocriplasmin 125µg	125µg ocriplasmin intravitreal injection versus sham injection
Sham Injection	Sham injection Sham injection : Sham intravitreal injection

Measured Values

	Ocriplasmin 25µg	Ocriplasmin 75µg	Ocriplasmin 125µg	Sham Injection
Number of Participants Analyzed [units: participants]	**8**	**15**	**15**	**13**
PVD Induction [units: percentage of participants]	**0**	**20**	**13.3**	**30.8**

Statistical Analysis 1 for PVD Induction

Groups [1]	Ocriplasmin 25µg vs. Sham Injection
Method [2]	Fisher Exact
P Value [3]	0.131
Odds Ratio (OR) [4]	0.001
95% Confidence Interval	0.001 to 999.999

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	No text entered.
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	No text entered.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.
[4]	Other relevant estimation information:
	No text entered.

Statistical Analysis 2 for PVD Induction

Groups [1]	Ocriplasmin 75µg vs. Sham Injection
Method [2]	Fisher Exact
P Value [3]	0.670
Odds Ratio (OR) [4]	0.562
95% Confidence Interval	0.132 to 2.400

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	No text entered.
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	No text entered.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.
[4]	Other relevant estimation information:
	No text entered.

Statistical Analysis 3 for PVD Induction

Groups [1]	Ocriplasmin 125µg vs. Sham Injection
Method [2]	Fisher Exact
P Value [3]	0.372
Odds Ratio (OR) [4]	0.346
95% Confidence Interval	0.070 to 1.703

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	No text entered.
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	No text entered.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.
[4]	Other relevant estimation information:
	No text entered.

Serious Adverse Events

Time Frame	AEs/SAEs were collected from injection day up to Month 12 post-injection
Additional Description	No text entered.

Reporting Groups

	Description
Ocriplasmin 25µg	25µg ocriplasmin intravitreal injection versus sham injection
Ocriplasmin 75µg	75µg ocriplasmin intravitreal injection versus sham injection
Ocriplasmin 125µg	125µg ocriplasmin intravitreal injection versus sham injection
Sham Injection	Sham injection Sham injection : Sham intravitreal injection

Serious Adverse Events

	Ocriplasmin 25µg	Ocriplasmin 75µg	Ocriplasmin 125µg	Sham Injection
Total, serious adverse events				
# participants affected / at risk	1/8 (12.50%)	4/15 (26.67%)	5/15 (33.33%)	9/13 (69.23%)
Cardiac disorders				
Angina pectoris † [1]				
# participants affected / at risk	0/8 (0.00%)	0/15 (0.00%)	0/15 (0.00%)	1/13 (7.69%)
# events	0	0	0	1
Atrioventricular block complete † [1]				
# participants affected / at risk	0/8 (0.00%)	0/15 (0.00%)	0/15 (0.00%)	1/13 (7.69%)
# events	0	0	0	1
Cardiac arrest † [1]				
# participants affected / at risk	0/8 (0.00%)	0/15 (0.00%)	0/15 (0.00%)	1/13 (7.69%)
# events	0	0	0	1
Myocardial infaction † [1]				
# participants affected / at risk	0/8 (0.00%)	0/15 (0.00%)	0/15 (0.00%)	1/13 (7.69%)
# events	0	0	0	1
Myocardial ischaemia † [1]				
# participants affected / at risk	0/8 (0.00%)	0/15 (0.00%)	0/15 (0.00%)	1/13 (7.69%)
# events	0	0	0	1
Eye disorders				
maculopathy † [1]				
# participants affected / at risk	0/8 (0.00%)	0/15 (0.00%)	0/15 (0.00%)	1/13 (7.69%)
# events	0	0	0	1
Macular oedema † [1]				
# participants affected / at risk	0/8 (0.00%)	1/15 (6.67%)	0/15 (0.00%)	0/13 (0.00%)
# events	0	1	0	0
Optic disc vascular disorder † [1]				
# participants affected / at risk	0/8 (0.00%)	1/15 (6.67%)	0/15 (0.00%)	0/13 (0.00%)
# events	0	1	0	0
Retinal artery occlusion † [1]				
# participants affected / at risk	0/8 (0.00%)	1/15 (6.67%)	0/15 (0.00%)	0/13 (0.00%)
# events	0	1	0	0
Gastrointestinal disorders				
Intestinal obstruction † [1]				
# participants affected / at risk	0/8 (0.00%)	0/15 (0.00%)	0/15 (0.00%)	1/13 (7.69%)
# events	0	0	0	1
Oesophageal varices haemorrhage † [1]				
# participants affected / at risk	0/8 (0.00%)	0/15 (0.00%)	0/15 (0.00%)	1/13 (7.69%)
# events	0	0	0	1
Infections and infestations				
Urosepsis † [1]				
# participants affected / at risk	1/8 (12.50%)	0/15 (0.00%)	0/15 (0.00%)	0/13 (0.00%)
# events	1	0	0	0

Metabolism and nutrition disorders				
Diabetes mellitus inadequate control † 1				
# participants affected / at risk	**0/8 (0.00%)**	**1/15 (6.67%)**	**0/15 (0.00%)**	**0/13 (0.00%)**
# events	**0**	**1**	**0**	**0**
Hyperglycaemia † 1				
# participants affected / at risk	**0/8 (0.00%)**	**0/15 (0.00%)**	**1/15 (6.67%)**	**0/13 (0.00%)**
# events	**0**	**0**	**1**	**0**
Musculoskeletal and connective tissue disorders				
Osteoarthritis † 1				
# participants affected / at risk	**0/8 (0.00%)**	**0/15 (0.00%)**	**0/15 (0.00%)**	**1/13 (7.69%)**
# events	**0**	**0**	**0**	**1**
Nervous system disorders				
Monoparesis † 1				
# participants affected / at risk	**0/8 (0.00%)**	**0/15 (0.00%)**	**1/15 (6.67%)**	**0/13 (0.00%)**
# events	**0**	**0**	**1**	**0**
Vascular disorders				
Haematoma † 1				
# participants affected / at risk	**0/8 (0.00%)**	**0/15 (0.00%)**	**1/15 (6.67%)**	**0/13 (0.00%)**
# events	**0**	**0**	**1**	**0**
Hypovolaemic shock † 1				
# participants affected / at risk	**0/8 (0.00%)**	**0/15 (0.00%)**	**1/15 (6.67%)**	**0/13 (0.00%)**
# events	**0**	**0**	**1**	**0**
Thrombosis † 1				
# participants affected / at risk	**0/8 (0.00%)**	**0/15 (0.00%)**	**1/15 (6.67%)**	**0/13 (0.00%)**
# events	**0**	**0**	**1**	**0**

† Events were collected by systematic assessment
1 Term from vocabulary, MedDRA (12.1)

Other Adverse Events

Time Frame	AEs/SAEs were collected from injection day up to Month 12 post-injection
Additional Description	No text entered.

Frequency Threshold

Threshold above which other adverse events are reported	5

Reporting Groups

	Description
Ocriplasmin 25µg	25µg ocriplasmin intravitreal injection versus sham injection
Ocriplasmin 75µg	75µg ocriplasmin intravitreal injection versus sham injection
Ocriplasmin 125µg	125µg ocriplasmin intravitreal injection versus sham injection
Sham Injection	Sham injection Sham injection : Sham intravitreal injection

Other Adverse Events

	Ocriplasmin 25µg	Ocriplasmin 75µg	Ocriplasmin 125µg	Sham Injection
Total, other (not including serious) adverse events				
# participants affected / at risk	1/8 (12.50%)	4/15 (26.67%)	5/15 (33.33%)	7/13 (53.85%)
Cardiac disorders				
Angina Pectoris † [1]				
# participants affected / at risk	0/8 (0.00%)	0/15 (0.00%)	0/15 (0.00%)	1/13 (7.69%)
Atrioventricular block complete † [1]				
# participants affected / at risk	0/8 (0.00%)	0/15 (0.00%)	0/15 (0.00%)	1/13 (7.69%)
Cardiac arrest † [1]				
# participants affected / at risk	0/8 (0.00%)	0/15 (0.00%)	0/15 (0.00%)	1/13 (7.69%)
Myocardial infarction † [1]				
# participants affected / at risk	0/8 (0.00%)	0/15 (0.00%)	0/15 (0.00%)	1/13 (7.69%)
Myocardial ischaemia † [1]				
# participants affected / at risk	0/8 (0.00%)	0/15 (0.00%)	0/15 (0.00%)	1/13 (7.69%)
Eye disorders				
Maculopathy † [1]				
# participants affected / at risk	0/8 (0.00%)	0/15 (0.00%)	0/15 (0.00%)	1/13 (7.69%)
Macular oedema † [1]				
# participants affected / at risk	0/8 (0.00%)	1/15 (6.67%)	0/15 (0.00%)	0/13 (0.00%)
Optic disc vascular disorder † [1]				
# participants affected / at risk	0/8 (0.00%)	1/15 (6.67%)	0/15 (0.00%)	0/13 (0.00%)
Retinal artery occlusion † [1]				
# participants affected / at risk	0/8 (0.00%)	1/15 (6.67%)	0/15 (0.00%)	0/13 (0.00%)
Infections and infestations				
Urosepsis † [1]				
# participants affected / at risk	1/8 (12.50%)	0/15 (0.00%)	0/15 (0.00%)	0/13 (0.00%)
Metabolism and nutrition disorders				
Diabetes mellitus inadequate control † [1]				
# participants affected / at risk	0/8 (0.00%)	1/15 (6.67%)	0/15 (0.00%)	0/13 (0.00%)
Hyperglycaemia † [1]				
# participants affected / at risk	0/8 (0.00%)	0/15 (0.00%)	1/15 (6.67%)	0/13 (0.00%)
Musculoskeletal and connective tissue disorders				
Osteoarthritis † [1]				
# participants affected / at risk	0/8 (0.00%)	0/15 (0.00%)	0/15 (0.00%)	1/13 (7.69%)
Nervous system disorders				
Monoparesis † [1]				
# participants affected / at risk	0/8 (0.00%)	0/15 (0.00%)	1/15 (6.67%)	0/13 (0.00%)

Vascular disorders				
Heamatoma † 1				
# participants affected / at risk	**0/8 (0.00%)**	**0/15 (0.00%)**	**1/15 (6.67%)**	**0/13 (0.00%)**
Hypovolaemic shock † 1				
# participants affected / at risk	**0/8 (0.00%)**	**0/15 (0.00%)**	**1/15 (6.67%)**	**0/13 (0.00%)**
Thrombosis † 1				
# participants affected / at risk	**0/8 (0.00%)**	**0/15 (0.00%)**	**1/15 (6.67%)**	**0/13 (0.00%)**

† Events were collected by systematic assessment
1 Term from vocabulary, MedDRA (12.1)

Limitations and Caveats

Limitations of the study, such as early termination leading to small numbers of participants analyzed and technical problems with measurement leading to unreliable or uninterpretable data
No text entered.

More Information

Certain Agreements:

Principal Investigators are **NOT** employed by the organization sponsoring the study.
There **IS** an agreement between Principal Investigators and the Sponsor (or its agents) that restricts the PI's rights to discuss or publish trial results after the trial is completed.
The agreement is: ☑ 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**. The sponsor cannot require changes to the communication and cannot extend the embargo. ☐ 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 **more than 60 days but less than or equal to 180 days**. The sponsor cannot require changes to the communication and cannot extend the embargo. ☐ Other disclosure agreement that restricts the right of the PI to discuss or publish trial results after the trial is completed.

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