Preservative-Free MK2452 (Tafluprost) for Open-Angle Glaucoma/Ocular Hypertension (MK2452-001) (COMPLETED)

This study has been completed.

Sponsor:
Merck Sharp & Dohme Corp.

Information provided by (Responsible Party):
Merck Sharp & Dohme Corp.

ClinicalTrials.gov Identifier:
NCT01026831

First received: December 2, 2009
Last updated: October 30, 2015
Last verified: October 2015
History of Changes

Purpose

This study was to compare the safety and efficacy of the preservative-free formulation of 0.0015% MK2452 (tafluprost) and preservative-free 0.5% timolol maleate in patients with open-angle glaucoma and ocular hypertension. This study was to demonstrate that the preservative-free formulation of 0.0015% tafluprost is non-inferior to preservative-free 0.5% timolol maleate.

Condition	Intervention	Phase
Open-angle Glaucoma Ocular Hypertension	Drug: Preservative-Free Tafluprost Drug: Comparator: timolol	Phase 3

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

Official Title: A Phase III, Randomized, Active Comparator-Controlled, Twelve-Week, Double-Masked Clinical Trial to Compare the Efficacy and Safety of Preservative-Free MK2452 (0.0015%) and Preservative-Free Timolol Maleate (0.5%) in Patients With Open-Angle Glaucoma and Ocular Hypertension

Resource links provided by NLM:

Genetics Home Reference related topics: early-onset glaucoma

MedlinePlus related topics: Glaucoma High Blood Pressure

Drug Information available for: Timolol Timolol maleate Tafluprost

Genetic and Rare Diseases Information Center resources: Pigment-dispersion Syndrome

U.S. FDA Resources

Further study details as provided by Merck Sharp & Dohme Corp.:

Primary Outcome Measures:

- Mean Intraocular Pressure (IOP) Change From Baseline at All 9 Time Points During the Study (0800, 1000 and 1600 Hrs at Weeks 2, 6, and 12) [Time Frame: Baseline, Weeks 2, 6, and 12.] [Designated as safety issue: No]

  IOP was measured using a Goldmann applanation tonometer. The primary evaluation was based on the study eye (the worse eye based on the 0800 hour IOP baseline or the right eye when both eyes had the same IOP). IOP change from baseline was calculated using the baseline IOP at each time point (0800 hours at baseline to 0800 hours at Week 2, 6, and 12; 1000 hours at baseline to 1000 hours at Week 2, 6, and 12; 1600 hours at baseline to 1600 hours at Week 2, 6, and 12). Lowering elevated IOP is a treatment goal of glaucoma.

Other Outcome Measures:

- Baseline IOP [Time Frame: Baseline] [Designated as safety issue: No]

  IOP was measured using a Goldmann applanation tonometer. The primary evaluation was based on the study eye (the worse eye based on the 0800 hour IOP baseline or the right eye when both eyes had the same IOP).

Enrollment:	643
Study Start Date:	January 2010
Study Completion Date:	September 2010
Primary Completion Date:	September 2010 (Final data collection date for primary outcome measure)

Arms	Assigned Interventions
Experimental: Tafluprost Preservative-free tafluprost	Drug: Preservative-Free Tafluprost One drop of preservative-free vehicle per eye in the morning, and one drop of preservative-free tafluprost (0.0015%) per eye in the evening for 12 weeks Other Name: MK2452
Active Comparator: timolol maleate Preservative-free timolol maleate	Drug: Comparator: timolol One drop of preservative-free timolol maleate (0.5%) per eye twice daily for 12 weeks

Eligibility

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

Criteria

Inclusion Criteria:

- Patient has been diagnosed with primary open-angle glaucoma, pigmentary glaucoma, capsular glaucoma/pseudoexfoliation, or ocular hypertension
- Patient has a mean (or median) IOP of >=23 and =<36 in at least one eye at the 0800 hours time point at the Baseline Visit.
- Patient has <5 mmHg difference in mean (or median) IOP between eyes at each time point (0800 hours, 1000 hours, and 1600 hours) at Baseline.
- Patient is currently using a prescribed ocular hypotensive medication and has been on a stable dose for 30 days prior to screening, or patient is drug-naive (those who have never used or who have not used ocular hypotensive medication for at least 4 weeks prior to screening)
- Patient is able to safely discontinue current ocular hypotensive medication during up to the 4-week washout period
- Patient has vision corrected to 20/80 or better in each eye
- Patient is willing and able to avoid wearing contact lenses from 4 weeks prior to dosing through 24 hour after final dosing
- Patient is willing and able to self-administer or has an able person available on a daily basis to assist with administration of study medications

Patient is not pregnant and not planning to become pregnant during the study

- Patient is male or female ≥18 of age on the day of signing the informed consent

Exclusion Criteria:

- Patient is unable to use study medication in the affected eye(s)
- Patient has a history of inflammatory ocular surface disease or anterior or posterior uveitis in either eye
- Patient has a history of retinal detachment, diabetic retinopathy, or other progressive retinal disease
- Patient has experienced significant visual field loss within the last year
- Patient has had intraocular surgery in either eye in the last 4 months
- Patient has a history of glaucoma surgery or refractive surgery in either eye
- Patient is currently taking two or more anti-glaucoma medications (except Cosopt™ or its generic formulation)
- Patient has previously used tafluprost
- Patient has a history of cardiovascular disorder within 6 months prior to screening
- Patient has a history of bronchial asthma, wheezing, pneumonia, COPD, other pulmonary disease, or abnormal chest x-ray
- Patient has a mean (or median) IOP >36 mmHg in either eye at the Screening Visit or at any time point (0800 hours, 1000 hours, and 1600 hours) of the Baseline Visit.

Contacts and Locations

Choosing to participate in a study is an important personal decision. Talk with your doctor and family members or friends about deciding to join a study. To learn more about this study, you or your doctor may contact the study research staff using the Contacts provided below. For general information, see Learn About Clinical Studies.

Please refer to this study by its ClinicalTrials.gov identifier: NCT01026831

Sponsors and Collaborators

Merck Sharp & Dohme Corp.

Investigators

Study Director: Medical Monitor Merck Sharp & Dohme Corp.

More Information

Publications automatically indexed to this study by ClinicalTrials.gov Identifier (NCT Number):

Chabi A, Varma R, Tsai JC, Lupinacci R, Pigeon J, Baranak C, Noble L, Lines C, Ho TW. Randomized clinical trial of the efficacy and safety of preservative-free tafluprost and timolol in patients with open-angle glaucoma or ocular hypertension. Am J Ophthalmol. 2012 Jun;153(6):1187-96. doi: 10.1016/j.ajo.2011.11.008. Epub 2012 Feb 4.

Responsible Party:	Merck Sharp & Dohme Corp.
ClinicalTrials.gov Identifier:	NCT01026831 History of Changes
Other Study ID Numbers:	2452-001 2009_701
Study First Received:	December 2, 2009
Results First Received:	August 9, 2011
Last Updated:	October 30, 2015
Health Authority:	United States: Food and Drug Administration

Additional relevant MeSH terms:

Glaucoma	Adrenergic beta-Antagonists
Glaucoma, Open-Angle	Anti-Arrhythmia Agents
Hypertension	Antihypertensive Agents
Ocular Hypertension	Cardiovascular Agents
Cardiovascular Diseases	Molecular Mechanisms of Pharmacological Action
Eye Diseases	Neurotransmitter Agents
Vascular Diseases	Pharmacologic Actions
Timolol	Physiological Effects of Drugs
Adrenergic Agents	Therapeutic Uses

Adrenergic Antagonists

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TO TOP

For Patients and Families | For Researchers | For Study Record Managers

HOME RSS FEEDS SITE MAP TERMS AND CONDITIONS DISCLAIMER CONTACT NLM HELP DESK

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Results First Received: August 9, 2011

Study Type:	Interventional
Study Design:	Allocation: Randomized; Endpoint Classification: Safety/Efficacy Study; Intervention Model: Parallel Assignment; Masking: Double Blind (Subject, Investigator); Primary Purpose: Treatment
Conditions:	Open-angle Glaucoma Ocular Hypertension
Interventions:	Drug: Preservative-Free Tafluprost Drug: Comparator: timolol

Participant Flow

Hide Participant Flow

Recruitment Details

Key information relevant to the recruitment process for the overall study, such as dates of the recruitment period and locations
No text entered.

Pre-Assignment Details

Significant events and approaches for the overall study following participant enrollment, but prior to group assignment
No text entered.

Reporting Groups

	Description
Tafluprost	One drop of preservative-free vehicle per eye in the morning, and one drop of preservative-free tafluprost (0.0015%) per eye in the evening for 12 weeks.
Timolol Maleate	One drop of preservative-free timolol maleate (0.5%) per eye twice daily for 12 weeks.

Participant Flow: Overall Study

	Tafluprost	Timolol Maleate
STARTED	**320** [1]	**323** [1]
COMPLETED	**306**	**312**
NOT COMPLETED	**14**	**11**
Adverse Event	**4**	**3**
Lost to Follow-up	**2**	**0**
Physician Decision	**1**	**1**
Protocol Violation	**0**	**2**
Withdrawal by Subject	**7**	**5**

[1] randomized

Baseline Characteristics

Hide 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
Tafluprost	One drop of preservative-free vehicle per eye in the morning, and one drop of preservative-free tafluprost (0.0015%) per eye in the evening for 12 weeks.
Timolol Maleate	One drop of preservative-free timolol maleate (0.5%) per eye twice daily for 12 weeks.
Total	Total of all reporting groups

Baseline Measures

	Tafluprost	Timolol Maleate	Total
Number of Participants [units: participants]	**320**	**323**	**643**
Age [units: years] Mean (Standard Deviation)	**63.3 (11.7)**	**63.3 (11.6)**	**63.3 (11.6)**
Gender [units: participants]			

Female	**183**	**192**	**375**
Male	**137**	**131**	**268**

Outcome Measures

Hide All Outcome Measures

1. Primary: Mean Intraocular Pressure (IOP) Change From Baseline at All 9 Time Points During the Study (0800, 1000 and 1600 Hrs at Weeks 2, 6, and 12) [Time Frame: Baseline, Weeks 2, 6, and 12.]

Measure Type	Primary
Measure Title	Mean Intraocular Pressure (IOP) Change From Baseline at All 9 Time Points During the Study (0800, 1000 and 1600 Hrs at Weeks 2, 6, and 12)
Measure Description	IOP was measured using a Goldmann applanation tonometer. The primary evaluation was based on the study eye (the worse eye based on the 0800 hour IOP baseline or the right eye when both eyes had the same IOP). IOP change from baseline was calculated using the baseline IOP at each time point (0800 hours at baseline to 0800 hours at Week 2, 6, and 12; 1000 hours at baseline to 1000 hours at Week 2, 6, and 12; 1600 hours at baseline to 1600 hours at Week 2, 6, and 12). Lowering elevated IOP is a treatment goal of glaucoma.
Time Frame	Baseline, Weeks 2, 6, and 12.
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.
The Per-Protocol (PP) approach excluded all patients with important protocol violations and was performed for the efficacy endpoints. The PP population excluded patients due to important deviations from the protocol that may have substantially affected the results of the primary endpoints.

Reporting Groups

	Description
Tafluprost	One drop of preservative-free vehicle per eye in the morning, and one drop of preservative-free tafluprost (0.0015%) per eye in the evening for 12 weeks.
Timolol Maleate	One drop of preservative-free timolol maleate (0.5%) per eye twice daily for 12 weeks.

Measured Values

	Tafluprost	**Timolol Maleate**
Number of Participants Analyzed [units: participants]	**299**	**313**
Mean Intraocular Pressure (IOP) Change From Baseline at All 9 Time Points During the Study (0800, 1000 and 1600 Hrs at Weeks 2, 6, and 12) [units: mmHg] Least Squares Mean (95% Confidence Interval)		
Week 2 - 0800 (n=280; n=295)	**-7.1 (-7.5 to -6.8)**	**-6.8 (-7.1 to -6.5)**

Week 2 - 1000 (n=293; n=305)	**-6.8 (-7.1 to -6.5)**	**-6.1 (-6.4 to -5.8)**
Week 2 - 1600 (n=289; n=302)	**-6.2 (-6.5 to -5.9)**	**-5.3 (-5.7 to -5.0)**
Week 6 - 0800 (n=294; n=308)	**-7.3 (-7.6 to -6.9)**	**-7.4 (-7.7 to -7.1)**
Week 6 - 1000 (n=298; n=312)	**-7.0 (-7.3 to -6.7)**	**-6.6 (-6.9 to -6.3)**
Week 6 - 1600 (n=295; n=310)	**-6.3 (-6.7 to -6.0)**	**-5.5 (-5.9 to -5.2)**
Week 12 - 0800 (n=296; n=308)	**-7.4 (-7.8 to -7.1)**	**-7.5 (-7.8 to -7.1)**
Week 12 - 1000 (n=298; n=312)	**-7.0 (-7.4 to -6.7)**	**-6.6 (-7.0 to -6.3)**
Week 12 - 1600 (n=295; n=310)	**-6.2 (-6.5 to -5.9)**	**-5.7 (-6.0 to -5.4)**

No statistical analysis provided for Mean Intraocular Pressure (IOP) Change From Baseline at All 9 Time Points During the Study (0800, 1000 and 1600 Hrs at Weeks 2, 6, and 12)

2. Other Pre-specified: Baseline IOP [Time Frame: Baseline]

Measure Type	Other Pre-specified
Measure Title	Baseline IOP
Measure Description	IOP was measured using a Goldmann applanation tonometer. The primary evaluation was based on the study eye (the worse eye based on the 0800 hour IOP baseline or the right eye when both eyes had the same IOP).
Time Frame	Baseline
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.
The Per-Protocol (PP) approach excluded all patients with important protocol violations and was performed for the efficacy endpoints. The PP population excluded patients due to important deviations from the protocol that may have substantially affected the results of the primary

endpoints.

Reporting Groups

	Description
Tafluprost	One drop of preservative-free vehicle per eye in the morning, and one drop of preservative-free tafluprost (0.0015%) per eye in the evening for 12 weeks.
Timolol Maleate	One drop of preservative-free timolol maleate (0.5%) per eye twice daily for 12 weeks.

Measured Values

	Tafluprost	Timolol Maleate
Number of Participants Analyzed [units: participants]	**299**	**313**
Baseline IOP [units: mmHg] Least Squares Mean (95% Confidence Interval)		
Baseline 0800 timepoint (n=299; n=313)	**26.1 (25.8 to 26.4)**	**26.0 (25.7 to 26.2)**
Baseline 1000 timepoint (n=299; n=313)	**24.8 (24.5 to 25.2)**	**24.6 (24.2 to 24.9)**
Baseline 1600 timepoint (n=296; n=312)	**23.8 (23.4 to 24.2)**	**23.5 (23.2 to 23.9)**

No statistical analysis provided for Baseline IOP

Serious Adverse Events

Hide Serious Adverse Events

Time Frame	No text entered.
Additional Description	No text entered.

Reporting Groups

	Description
Tafluprost	One drop of preservative-free vehicle per eye in the morning, and one drop of preservative-free tafluprost (0.0015%) per eye in the evening for 12 weeks.
Timolol Maleate	One drop of preservative-free timolol maleate (0.5%) per eye twice daily for 12 weeks.

Serious Adverse Events

	Tafluprost	Timolol Maleate
Total, serious adverse events		

# participants affected / at risk	2/320 (0.63%)	7/323 (2.17%)
Cardiac disorders		
atrial fibrillation		
# participants affected / at risk	1/320 (0.31%)	1/323 (0.31%)
# events	1	1
myocardial infarction		
# participants affected / at risk	1/320 (0.31%)	0/323 (0.00%)
# events	1	0
Eye disorders		
retinal detachment		
# participants affected / at risk	0/320 (0.00%)	1/323 (0.31%)
# events	0	1
Gastrointestinal disorders		
colitis		
# participants affected / at risk	0/320 (0.00%)	1/323 (0.31%)
# events	0	1
General disorders		
hernia		
# participants affected / at risk	0/320 (0.00%)	1/323 (0.31%)
# events	0	1
Injury, poisoning and procedural complications		
fracture		
# participants affected / at risk	0/320 (0.00%)	1/323 (0.31%)
# events	0	1
joint dislocation		
# participants affected / at risk	0/320 (0.00%)	1/323 (0.31%)
# events	0	1
tendon rupture		
# participants affected / at risk	0/320 (0.00%)	1/323 (0.31%)
# events	0	1
Respiratory, thoracic and mediastinal disorders		
pulmonary embolism		
# participants affected / at risk	0/320 (0.00%)	1/323 (0.31%)
# events	0	1

Other Adverse Events

Hide Other Adverse Events

Time Frame	No text entered.
Additional Description	No text entered.

Frequency Threshold

Threshold above which other adverse events are reported	5%

Reporting Groups

	Description
Tafluprost	One drop of preservative-free vehicle per eye in the morning, and one drop of preservative-free tafluprost (0.0015%) per eye in the evening for 12 weeks.
Timolol Maleate	One drop of preservative-free timolol maleate (0.5%) per eye twice daily for 12 weeks.

Other Adverse Events

	Tafluprost	Timolol Maleate
Total, other (not including serious) adverse events		
# participants affected / at risk	**0/320 (0.00%)**	**0/323 (0.00%)**

Limitations and Caveats

Hide 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

Hide 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.

Restriction Description: Merck agreements may vary with individual investigators, but will not prohibit any investigator from publishing. Merck supports the publication of results from all centers of a multi-center trial but requests that reports based on single-site data not precede the primary publication of the entire clinical trial.

Results Point of Contact:

Name/Title: Senior Vice President, Global Clinical Development
Organization: Merck Sharp & Dohme Corp.
phone: 1-800-672-6372
e-mail: ClinicalTrialsDisclosure@merck.com

Publications automatically indexed to this study by ClinicalTrials.gov Identifier (NCT Number):

Chabi A, Varma R, Tsai JC, Lupinacci R, Pigeon J, Baranak C, Noble L, Lines C, Ho TW. Randomized clinical trial of the efficacy and safety of preservative-free tafluprost and timolol in patients with open-angle glaucoma or ocular hypertension. Am J Ophthalmol. 2012 Jun;153(6):1187-96. doi: 10.1016/j.ajo.2011.11.008. Epub 2012 Feb 4.

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TO TOP

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