Clinical trial results:
A Randomized, Multicenter, Double-Masked, Parallel-Group Clinical Safety and Efficacy Evaluation of Loteprednol Etabonate Ophthalmic Gel, 0.5% Versus Vehicle for the Treatment of Inflammation and Pain Following Cataract Surgery

Summary

EudraCT number	2010-019246-11
Trial protocol	GB
Global end of trial date	03 September 2010

Results information

Result version number	v1 (current)
This version publication date	02 January 2020
First version publication date	02 January 2020

Trial information

Trial identification

Sponsor protocol code	577

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01060072
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Bausch & Lomb Incorporated
Sponsor organisation address	1400 North Goodman St., Rochester, NY, United States, 14609
Public contact	Director of Clinical Operations, Bausch & Lomb Incorporated, 011 9733606389, tuyen.ong@bausch.com
Scientific contact	Director of Clinical Operations, Bausch & Lomb Incorporated, 011 9733606389, tuyen.ong@bausch.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	03 September 2010
Is this the analysis of the primary completion data?	Yes
Primary completion date	03 September 2010
Global end of trial reached?	Yes
Global end of trial date	03 September 2010
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objectives of this study were to compare the safety and efficacy of loteprednol etabonate ophthalmic gel, 0.5% to vehicle for the treatment of inflammation and pain following cataract surgery.

Protection of trial subjects:

This study was conducted in compliance with the protocol and in accordance with Good Clinical Practice (GCP), as described in the International Conference on Harmonisation (ICH) Harmonized Tripartite Guidelines for Good Clinical Practice 1996 Food and Drug Administration (FDA) regulations 21CFR Parts 50, 54, 56, and 312, 42 USC 282(j), applicable local regulations, and the Declaration of Helsinki.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	19 February 2010
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United States: 391
Country: Number of subjects enrolled	Germany: 16
Worldwide total number of subjects	407
EEA total number of subjects	16

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	122
From 65 to 84 years	272
85 years and over	13

Subject disposition

Recruitment

Recruitment details:

This study was conducted at 22 enrolling sites; 2 in the European Union (EU) and 20 in the United States (US). First participant was enrolled on 2/19/2010 and last participant completed the study on 9/3/2010.

Pre-assignment

Screening details:

A total of 407 participants, who were candidates for routine, uncomplicated cataract surgery, were enrolled in the study, 400 participants completed the study.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	Loteprednol etabonate

Arm description:

Loteprednol etabonate 0.5% ophthalmic suspension

Arm type	Experimental
Investigational medicinal product name	Loteprednol etabonate
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Eye drops, suspension
Routes of administration	Ophthalmic use

Dosage and administration details:

Topical administration of loteprednol etabonate ophthalmic suspension 1-2 drops in study eye four times a day (QID), postoperative day 1-14.

Arm title	Vehicle

Arm description:

Vehicle of loteprednol etabonate ophthalmic suspension.

Arm type	Placebo
Investigational medicinal product name	Vehicle of Loteprednol Etabonate
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Eye drops, suspension
Routes of administration	Ophthalmic use

Dosage and administration details:

Topical administration of vehicle of loteprednol etabonate ophthalmic suspension 1-2 drops in study eye QID, postoperative day 1-14.

Number of subjects in period 1	Loteprednol etabonate	Vehicle
Started	206	201
Completed	204	196
Not completed	2	5
Physician decision	-	2
Acute cholecystitis	1	-
Adverse event, non-fatal	1	1
Excluded Medications	-	1
Protocol deviation	-	1

Baseline characteristics

Reporting groups	
Reporting group title	Loteprednol etabonate
Reporting group description:	
Loteprednol etabonate 0.5% ophthalmic suspension	
Reporting group title	Vehicle
Reporting group description:	
Vehicle of loteprednol etabonate ophthalmic suspension.	

Reporting group values	Loteprednol etabonate	Vehicle	Total
Number of subjects	206	201	407
Age categorical Units: Subjects			

Age Continuous			
Intent to treat Population (ITT)			
Units: years			
arithmetic mean	68.3	69.4	
standard deviation	± 9.66	± 9.56	-
Gender, Male/Female Units: Subjects			
Female	124	109	233
Male	82	92	174
Region of Enrollment Units: Subjects			
United States	198	193	391
Germany	8	8	16

End points

End points reporting groups

Reporting group title	Loteprednol etabonate
Reporting group description: Loteprednol etabonate 0.5% ophthalmic suspension	
Reporting group title	Vehicle
Reporting group description: Vehicle of loteprednol etabonate ophthalmic suspension.	

Primary: Resolution of anterior chamber cells at Visit 5

End point title	Resolution of anterior chamber cells at Visit 5
End point description: Participants with complete resolution of anterior chamber cells (ACC). ITT population.	
End point type	Primary
End point timeframe: Visit 5 (Postoperative Day 8)	

End point values	Loteprednol etabonate	Vehicle		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	206	201		
Units: participants	64	28		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Loteprednol etabonate v Vehicle
Number of subjects included in analysis	407
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [1]
Method	Chi-squared

Notes:

[1] - p-value obtained from Pearson chi-squared statistic. Pearson value was the primary outcome and Grade 0 (no) pain was only tested if complete resolution of cells was significant at the 0.05 level.

Primary: Grade 0 pain at Visit 5

End point title	Grade 0 pain at Visit 5
End point description: Participants with no pain, graded on a 0-5 scale, 0=no pain and 5=severe pain. ITT population.	
End point type	Primary
End point timeframe: Visit 5 (Postoperative Day 8)	

End point values	Loteprednol etabonate	Vehicle		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	206	201		
Units: participants	206	201		

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Difference in percentages and 95% CI were based on asymptotic normal approximations.

Comparison groups	Loteprednol etabonate v Vehicle
Number of subjects included in analysis	407
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [2]
Method	Chi-squared
Parameter estimate	Difference in percentage
Point estimate	30
Confidence interval	
level	95 %
sides	2-sided
lower limit	20.4
upper limit	39.5

Notes:

[2] - p-value obtained from Pearson chi-squared statistic. Pearson value was the primary outcome and Grade 0 (no) pain was only tested if complete resolution of cells was significant at the 0.05 level.

Secondary: Resolution of anterior chamber cells at Visit 4-7

End point title	Resolution of anterior chamber cells at Visit 4-7

End point description:

Participants with complete resolution of anterior chamber cells (ACC). Cells were graded on a 0-4 scale, where 0=no cells and 4=>30 cells. ITT population.

End point type	Secondary

End point timeframe:

Visit 4-7 (postoperative Day 3-18)

End point values	Loteprednol etabonate	Vehicle		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	206	201		
Units: participants				
Visit 4 (Postoperative Day 3)	8	7		
Visit 5 (Postoperative Day 8)	64	28		

Visit 6 (Postoperative Day 15)	116	61		
Visit 7 (Postoperative Day 18)	114	59		

Statistical analyses

No statistical analyses for this end point

Secondary: Grade 0 pain at Visit 4-7

End point title	Grade 0 pain at Visit 4-7

End point description:

Participants with no pain, graded on a 0-5 scale, 0= no pain and 5=severe pain. ITT population.

End point type	Secondary

End point timeframe:

Visits 4-7 (Postoperative Days 3-18)

End point values	Loteprednol etabonate	Vehicle		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	206	201		
Units: participants				
Visit 4 (Postoperative Day 3)	139	93		
Visit 5 (Postoperative Day 8)	156	92		
Visit 6 (Postoperative Day 15)	160	89		
Visit 7 (Postoperative Day 18)	151	79		

Statistical analyses

No statistical analyses for this end point

Secondary: Resolution of anterior chamber flare

End point title	Resolution of anterior chamber flare

End point description:

Complete resolution of flare, scored on a scale of 0-4 were 0=none and 4=very severe. ITT population.

End point type	Secondary

End point timeframe:

Visit 4-7 (postoperative Day 3-18)

End point values	Loteprednol etabonate	Vehicle		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	206	201		
Units: participants				
Visit 4 (Postoperative Day 3)	93	64		
Visit 5 (Postoperative Day 8)	134	72		
Visit 6 (Postoperative Day 15)	162	90		
Visit 7 (Postoperative Day 18)	143	75		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
14 Days	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	12.0

Reporting groups	
Reporting group title	Vehicle
Reporting group description:	
Vehicle of loteprednol etabonate ophthalmic suspension.	
Reporting group title	Loteprednol etabonate
Reporting group description:	
Loteprednol etabonate 0.5% ophthalmic suspension	

Serious adverse events	Vehicle	Loteprednol etabonate	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 201 (0.50%)	3 / 206 (1.46%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			
Cardiac disorders			
Myocardial infarction			
subjects affected / exposed	0 / 201 (0.00%)	1 / 206 (0.49%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Diverticulitis			
subjects affected / exposed	0 / 201 (0.00%)	1 / 206 (0.49%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis			
subjects affected / exposed	0 / 201 (0.00%)	1 / 206 (0.49%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Dehydration			

subjects affected / exposed	1 / 201 (0.50%)	0 / 206 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypokalemia			
subjects affected / exposed	1 / 201 (0.50%)	0 / 206 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Vehicle	Loteprednol etabonate	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	24 / 201 (11.94%)	10 / 206 (4.85%)	
Eye disorders			
Anterior Chamber Inflammation			
subjects affected / exposed	14 / 201 (6.97%)	7 / 206 (3.40%)	
occurrences (all)	14	7	
Eye Pain			
subjects affected / exposed	10 / 201 (4.98%)	3 / 206 (1.46%)	
occurrences (all)	10	3	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
12 March 2010	Key changes for the amendment were related to the addition of 4 investigative sites in the European Union. The approximate number of participants to be enrolled by each investigator was changed from 20 to 17 participants. All other changes involved specification of personnel, definitions of terms, product labeling, sites for the return of unused product, etc.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported