



## Clinical trial results:

**Randomized parallel-group, multicentre study to evaluate the after-use sensation and safety of carteolol LA 2% versus timolol LA 0.5% in simple intra-ocular hypertension and glaucoma.**

### Summary

EudraCT number	2007-001680-30
Trial protocol	FR PT BE CZ
Global end of trial date	05 May 2009

### Results information

Result version number	v1 (current)
This version publication date	27 August 2020
First version publication date	27 August 2020

### Trial information

#### Trial identification

Sponsor protocol code	529
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#### Additional study identifiers

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

Notes:

#### Sponsors

Sponsor organisation name	Bausch and Lomb
Sponsor organisation address	Brunsbütteler Damm 165-173, Berlin, Germany,
Public contact	Manager Clinical Science, Bausch&Lomb Dr Gerhard Mann chem.-Fabrik GmbH, natasa.orlic-pleyer@bausch.com
Scientific contact	Manager Clinical Science, Bausch&Lomb Dr Gerhard Mann chem.-Fabrik GmbH, Raphaele.SiouMermet@bausch.com
Sponsor organisation name	Bausch and Lomb
Sponsor organisation address	Brunsbütteler Damm 165-173, Berlin, Germany, 13581
Public contact	Manager Clinical Science, Bausch and Lomb, 331 60795083,
Scientific contact	Manager Clinical Science, Bausch and Lomb, 331 60795083,

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	05 May 2009
Is this the analysis of the primary completion data?	Yes
Primary completion date	05 May 2009
Global end of trial reached?	Yes
Global end of trial date	05 May 2009
Was the trial ended prematurely?	No

Notes:

## General information about the trial

Main objective of the trial:

Primary objective: To evaluate the subjective tolerance upon instillation (rate of patients experiencing symptoms of ocular discomfort ) of carteolol LA compared to timolol LA in patients with simple ocular hypertension or POAG (superiority design)

Protection of trial subjects:

This study was conducted in compliance with the protocol and in accordance with Good Clinical Practices (GCPs), as described in the ICH Harmonized Tripartite Guidelines for Good Clinical Practice 1996, applicable local regulations, and the Declaration of Helsinki (2004).

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	08 February 2008
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	Poland: 9
Country: Number of subjects enrolled	Portugal: 21
Country: Number of subjects enrolled	Belgium: 16
Country: Number of subjects enrolled	Czech Republic: 123
Country: Number of subjects enrolled	France: 30
Worldwide total number of subjects	199
EEA total number of subjects	199

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)	111
From 65 to 84 years	83
85 years and over	5

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

After providing informed consent, subjects were screened for inclusion. Subjects with unilateral or bilateral OHT or POAG and whose IOP was being controlled by beta-blocker monotherapy were enrolled in this study. If both eyes were diagnosed with OHT or POAG, both eyes were treated.

### Period 1

Period 1 title	Treatment (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
<b>Arm title</b>	Carteolol LA

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Carteolol LA
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Eye drops
Routes of administration	Ocular use

Dosage and administration details:

Subjects were instructed to instill one drop daily into the conjunctival sac at 8:00 AM.

<b>Arm title</b>	Timolol LA
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Arm description: -

Arm type	Active comparator
Investigational medicinal product name	Timolol LA
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Eye drops
Routes of administration	Ocular use

Dosage and administration details:

Subjects were instructed to instill one drop daily into the conjunctival sac at 8:00 AM.

<b>Number of subjects in period 1</b>	Carteolol LA	Timolol LA
Started	101	98
Completed	97	90
Not completed	4	8
Consent withdrawn by subject	-	4
Adverse event, non-fatal	1	3

Other	1	1
Lost to follow-up	2	-

## Baseline characteristics

### Reporting groups

Reporting group title	Treatment
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Reporting group description: -

Reporting group values	Treatment	Total	
Number of subjects	199	199	
Age categorical			
Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	111	111	
From 65-84 years	83	83	
85 years and over	5	5	
Gender categorical			
Units: Subjects			
Female	134	134	
Male	65	65	

## End points

### End points reporting groups

Reporting group title	Carteolol LA
Reporting group description:	-
Reporting group title	Timolol LA
Reporting group description:	-

### Primary: Number of subjects who felt discomfort upon instillation at 90 days

End point title	Number of subjects who felt discomfort upon instillation at 90 days
End point description:	
End point type	Primary
End point timeframe:	90 days

End point values	Carteolol LA	Timolol LA		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	97	90		
Units: Subjects	18	25		

### Statistical analyses

Statistical analysis title	Comparison of treatment arms
Comparison groups	Carteolol LA v Timolol LA
Number of subjects included in analysis	187
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1354
Method	Cochran-Mantel-Haenszel

### Secondary: Number of subjects who felt discomfort upon instillation at 30 days

End point title	Number of subjects who felt discomfort upon instillation at 30 days
End point description:	
End point type	Secondary
End point timeframe:	30 days

<b>End point values</b>	Carteolol LA	Timolol LA		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	98	93		
Units: Subjects	21	37		

### Statistical analyses

No statistical analyses for this end point

### Secondary: Global subjective tolerance upon instillation at 90 days

End point title	Global subjective tolerance upon instillation at 90 days
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End point description:

End point type	Secondary
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End point timeframe:

90 days

<b>End point values</b>	Carteolol LA	Timolol LA		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	97	90		
Units: Subjects				
Very Bad	1	2		
Bad	2	2		
Good	27	20		
Very Good	67	66		

### Statistical analyses

No statistical analyses for this end point

### Secondary: Global subjective tolerance upon instillation at 30 days

End point title	Global subjective tolerance upon instillation at 30 days
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End point description:

End point type	Secondary
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End point timeframe:

30 days

<b>End point values</b>	Carteolol LA	Timolol LA		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	98	93		
Units: Subjects				
Very Bad	2	0		
Bad	1	4		
Good	31	28		
Very Good	64	61		

### Statistical analyses

No statistical analyses for this end point

### Secondary: Blurry/Dim Vision According to the Glaucoma Symptom Scale at 90 days

End point title	Blurry/Dim Vision According to the Glaucoma Symptom Scale at 90 days
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End point description:

End point type	Secondary
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End point timeframe:

90 days

<b>End point values</b>	Carteolol LA	Timolol LA		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	18	25		
Units: Subjects				
Very Bothersome	0	3		
Somewhat Bothersome	1	1		
A Little Bothersome	1	9		
Not at All Bothersome	16	12		

### Statistical analyses

No statistical analyses for this end point

### Secondary: Blurry/Dim Vision According to the Glaucoma Symptom Scale at 30 days

End point title	Blurry/Dim Vision According to the Glaucoma Symptom Scale at 30 days
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End point description:

End point type	Secondary
End point timeframe:	
30 days	

<b>End point values</b>	Carteolol LA	Timolol LA		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	21	37		
Units: Subjects				
Very Bothersome	0	2		
Somewhat Bothersome	0	5		
A Little Bothersome	5	14		
Not at All Bothersome	16	16		

### Statistical analyses

No statistical analyses for this end point

### Secondary: "Inflammation of eyelids" at external eye examination at 90 days

End point title	"Inflammation of eyelids" at external eye examination at 90 days
End point description:	
End point type	Secondary
End point timeframe:	
90 days	

<b>End point values</b>	Carteolol LA	Timolol LA		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	97	90		
Units: Subjects	3	6		

### Statistical analyses

No statistical analyses for this end point

### Secondary: "Bulbar motility" at external eye examination at 90 days

End point title	"Bulbar motility" at external eye examination at 90 days
End point description:	
End point type	Secondary

End point timeframe:

90 days

<b>End point values</b>	Carteolol LA	Timolol LA		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	97	90		
Units: Subjects	0	1		

### Statistical analyses

No statistical analyses for this end point

### Secondary: Severe 'Lens' abnormality by slit lamp examination by 90 days

End point title | Severe 'Lens' abnormality by slit lamp examination by 90 days

End point description:

End point type | Secondary

End point timeframe:

90 days

<b>End point values</b>	Carteolol LA	Timolol LA		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	97	90		
Units: Subjects	3	3		

### Statistical analyses

No statistical analyses for this end point

### Secondary: Tear film break-up time at 90 days

End point title | Tear film break-up time at 90 days

End point description:

End point type | Secondary

End point timeframe:

90 days

<b>End point values</b>	Carteolol LA	Timolol LA		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	97	90		
Units: Seconds				
arithmetic mean (standard deviation)	13.822 ( $\pm$ 5.048)	13.802 ( $\pm$ 5.558)		

### Statistical analyses

No statistical analyses for this end point

### Secondary: Tear film break-up time at 30 days

End point title	Tear film break-up time at 30 days
End point description:	
End point type	Secondary
End point timeframe:	
30 days	

<b>End point values</b>	Carteolol LA	Timolol LA		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	98	93		
Units: Seconds				
arithmetic mean (standard error)	13.541 ( $\pm$ 5.188)	13.608 ( $\pm$ 5.294)		

### Statistical analyses

No statistical analyses for this end point

### Secondary: Fluorescein staining at 90 days

End point title	Fluorescein staining at 90 days
End point description:	
End point type	Secondary
End point timeframe:	
90 days	

<b>End point values</b>	Carteolol LA	Timolol LA		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	97	90		
Units: Grade				
arithmetic mean (standard error)	0.2 ( $\pm$ 0.5)	0.3 ( $\pm$ 0.6)		

### Statistical analyses

No statistical analyses for this end point

### Secondary: Fluorescein staining at 30 days

End point title	Fluorescein staining at 30 days
End point description:	
End point type	Secondary
End point timeframe:	
30 days	

<b>End point values</b>	Carteolol LA	Timolol LA		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	98	93		
Units: Grade				
arithmetic mean (standard deviation)	0.3 ( $\pm$ 0.5)	0.3 ( $\pm$ 0.7)		

### Statistical analyses

No statistical analyses for this end point

### Secondary: Overall lissamine test result at 90 days

End point title	Overall lissamine test result at 90 days
End point description:	
End point type	Secondary
End point timeframe:	
90 days	

<b>End point values</b>	Carteolol LA	Timolol LA		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	97	90		
Units: Grade				
arithmetic mean (standard deviation)	0.6 ( $\pm$ 1.4)	0.5 ( $\pm$ 1.0)		

### Statistical analyses

No statistical analyses for this end point

### Secondary: Overall lissamine test result at 30 days

End point title	Overall lissamine test result at 30 days
End point description:	
End point type	Secondary
End point timeframe:	
30 days	

<b>End point values</b>	Carteolol LA	Timolol LA		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	98	93		
Units: Grade				
arithmetic mean (standard deviation)	0.7 ( $\pm$ 1.4)	0.5 ( $\pm$ 0.9)		

### Statistical analyses

No statistical analyses for this end point

### Secondary: Result of examination of the macula by fundoscopy at 90 days

End point title	Result of examination of the macula by fundoscopy at 90 days
End point description:	
End point type	Secondary
End point timeframe:	
90 days	

<b>End point values</b>	Carteolol LA	Timolol LA		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	97	89		
Units: Subjects				
Normal	94	86		
Abnormal	3	3		

### Statistical analyses

No statistical analyses for this end point

### Secondary: "Lid Closure" at external eye examination at 90 days

End point title	"Lid Closure" at external eye examination at 90 days
End point description:	
End point type	Secondary
End point timeframe:	
90 days	

<b>End point values</b>	Carteolol LA	Timolol LA		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	97	90		
Units: Subjects	1	2		

### Statistical analyses

No statistical analyses for this end point

### Secondary: "Lid motility" at external eye examination at 90 days

End point title	"Lid motility" at external eye examination at 90 days
End point description:	
End point type	Secondary
End point timeframe:	
90 days	

<b>End point values</b>	Carteolol LA	Timolol LA		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	97	90		
Units: Subjects	2	3		

### Statistical analyses

No statistical analyses for this end point

### Secondary: "Conjunctival injection" at external eye examination at 90 days

End point title	"Conjunctival injection" at external eye examination at 90 days
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End point description:

End point type	Secondary
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End point timeframe:

90 days

<b>End point values</b>	Carteolol LA	Timolol LA		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	97	90		
Units: Subjects	6	3		

### Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

90 days

Assessment type	Non-systematic
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### Dictionary used

Dictionary name	MedDRA
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Dictionary version	NA
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### Reporting groups

Reporting group title	Carteolol LA
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Reporting group description: -

Reporting group title	Timolol LA
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Reporting group description: -

<b>Serious adverse events</b>	Carteolol LA	Timolol LA	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 99 (0.00%)	0 / 95 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	

Frequency threshold for reporting non-serious adverse events: 2 %

<b>Non-serious adverse events</b>	Carteolol LA	Timolol LA	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 99 (1.01%)	2 / 95 (2.11%)	
Eye disorders			
Cataract			
subjects affected / exposed	1 / 99 (1.01%)	2 / 95 (2.11%)	
occurrences (all)	1	2	

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
19 November 2007	Czech Republic only: <ul style="list-style-type: none"><li>• the Exclusion Criterion for pregnant or lactating women was changed so that a urine pregnancy test was required for women of childbearing potential</li><li>• in the Withdrawal of Subjects from Therapy or Assessment section (Section 6.3), a sentence was added stating that women that become pregnant during the study would be discontinued from treatment but would continue to be followed for safety evaluation per the protocol defined visits</li><li>• in the Baseline Visit section, that a urine pregnancy test must be administered if applicable</li></ul>

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported