



Clinical trial results:

Efficacy and safety of the biosimilar ranibizumab FYB201 in comparison to Lucentis in patients with neovascular age-related macular degeneration (COLUMBUS-AMD)

Summary

EudraCT number	2015-001961-20
Trial protocol	CZ AT DE HU ES FR GB IT
Global end of trial date	08 June 2018

Results information

Result version number	v1 (current)
This version publication date	13 May 2021
First version publication date	13 May 2021

Trial information

Trial identification

Sponsor protocol code	FYB201-C2015-01-P3
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02611778
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	bioeq GmbH
Sponsor organisation address	Bergfeldstraße 9, Holzkirchen, Germany, 83607
Public contact	Clinical Trial Information Desk, Bioeq GmbH, columbus@bioeq.com
Scientific contact	Clinical Trial Information Desk, Bioeq GmbH, columbus@bioeq.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	08 June 2018
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	08 June 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate and compare functional changes in best corrected visual acuity (BCVA) after 2 months (8 weeks) of treatment with FYB201 or Lucentis, compared to baseline BCVA

Protection of trial subjects:

The study was in compliance with regulatory requirements, the International Conference on Harmonization (ICH) Good Clinical Practice (GCP) guidelines and with the ethical principles of the latest revision of the Declaration of Helsinki as adopted by the World Medical Association. Only subjects that met all inclusion criteria and no exclusion criteria were to enter the study. All patients were free to discontinue their participation in the study at any time.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	19 December 2015
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Italy: 77
Country: Number of subjects enrolled	Ukraine: 14
Country: Number of subjects enrolled	Israel: 147
Country: Number of subjects enrolled	Russian Federation: 19
Country: Number of subjects enrolled	Poland: 122
Country: Number of subjects enrolled	Spain: 57
Country: Number of subjects enrolled	United Kingdom: 30
Country: Number of subjects enrolled	Austria: 11
Country: Number of subjects enrolled	Czech Republic: 81
Country: Number of subjects enrolled	France: 37
Country: Number of subjects enrolled	Germany: 53
Country: Number of subjects enrolled	Hungary: 74
Worldwide total number of subjects	722
EEA total number of subjects	542

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)	82
From 65 to 84 years	554
85 years and over	86

Subject disposition

Recruitment

Recruitment details:

The study included male or post-menopausal or sterile female patients of 50 years or older, who suffered from newly diagnosed subfoveal neovascular age-related macular degeneration (nAMD). Between 19-Dec-2015 and 14-Jun-2017, 712 patients were screened (10 patients were rescreened) in 75 sites in 12 countries in Europe, Russia and Israel.

Pre-assignment

Screening details:

All 712 patients were screened for eligibility before participating in the active treatment phase of the study, resulting in 722 screenings due to 10 rescreenings. Subjects were not to be entered to trial treatment if any of the eligibility criteria were violated. Of the 712 distinct patients, 477 patients were randomized and treated.

Period 1

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

Blinding implementation details:

This study was evaluation-masked, neither the patient nor the investigator(s) who performed evaluations knew, which treatment the patient received. In each site, there were at least 2 masked staff members and 1 unmasked injector who administered the treatment and who performed ophthalmologic pre- and post-injection assessments and questionnaire administration.

Arms

Are arms mutually exclusive?	Yes
Arm title	FYB201

Arm description:

Patients received FYB201 at a dose of 0.5mg (0.05mL of a 10mg/mL solution) as twelve monthly intravitreal injections

Arm type	Experimental
Investigational medicinal product name	FYB201
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravitreal use

Dosage and administration details:

Intravitreal injection of 0.5mg FYB201 (0.05mL of a 10mg/mL solution) given monthly

Arm title	Lucentis
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Arm description:

Patients received Lucentis (ranibizumab) at a dose of 0.5mg (0.05mL of a 10mg/mL solution) as twelve monthly intravitreal injections

Arm type	Active comparator
Investigational medicinal product name	Lucentis
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravitreal use

Dosage and administration details:

Intravitreal injection of 0.5mg Lucentis (0.05mL of a 10mg/mL solution) given monthly

Number of subjects in period 1^[1]	FYB201	Lucentis
Started	238	239
Completed	226	226
Not completed	12	13
Adverse event, serious fatal	2	1
Consent withdrawn by subject	2	8
Adverse event, non-fatal	1	2
Other	2	1
Lost to follow-up	3	1
Need for alternative treatment	1	-
Protocol deviation	1	-

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: Baseline characteristics are based on patients who were randomized after successfully completing the screening period and received at least one injection with the investigational medicinal product.

Baseline characteristics

Reporting groups

Reporting group title	FYB201
Reporting group description:	
Patients received FYB201 at a dose of 0.5mg (0.05mL of a 10mg/mL solution) as twelve monthly intravitreal injections	
Reporting group title	Lucentis
Reporting group description:	
Patients received Lucentis (ranibizumab) at a dose of 0.5mg (0.05mL of a 10mg/mL solution) as twelve monthly intravitreal injections	

Reporting group values	FYB201	Lucentis	Total
Number of subjects	238	239	477
Age categorical			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	25	19	44
From 65-84 years	181	188	369
85 years and over	32	32	64
Age continuous			
Safety set (SAF): The safety set comprised all patients who had received at least one injection with investigational medicinal product (IMP). The safety set was used as general analysis set for all kinds of safety and tolerability data. Patients were analyzed according to the treatment they actually received irrespective of their randomized treatment. If only single injections from the wrong treatment were administered, it was to be decided on a case by case basis how the patient was to be analyzed.			
Units: years			
arithmetic mean	74.9	76.1	
standard deviation	± 8.26	± 7.84	-
Gender categorical			
SAF			
Units: Subjects			
Female	135	134	269
Male	103	105	208

End points

End points reporting groups

Reporting group title	FYB201
Reporting group description:	
Patients received FYB201 at a dose of 0.5mg (0.05mL of a 10mg/mL solution) as twelve monthly intravitreal injections	
Reporting group title	Lucentis
Reporting group description:	
Patients received Lucentis (ranibizumab) at a dose of 0.5mg (0.05mL of a 10mg/mL solution) as twelve monthly intravitreal injections	

Primary: Change from baseline in best corrected visual acuity (BCVA) [letters] after 8 weeks

End point title	Change from baseline in best corrected visual acuity (BCVA) [letters] after 8 weeks
End point description:	
The primary endpoint was the change from baseline in BCVA by Early Treatment Diabetic Retinopathy Study (ETDRS) letters after 2 months (8 weeks) of treatment. All patients included in the full analysis set (FAS_EU) were analysed.	
FAS_EU: The FAS_EU was based on the intention-to-treat principle (i.e., patients were analyzed according to their randomized treatment irrespective of the treatment they actually received) and included all patients who received at least one injection of IMP and for whom BCVA results at least after 1 month were available and who had a screening BCVA between 20/40 and 20/100 Snellen equivalent in the study eye. Overall, 429 subjects were included in the FAS_EU, 215 in the FYB201 treatment group and 214 in the Lucentis treatment group. Of these, 212 patients in the FYB201 and 214 patients in the Lucentis treatment group were still in the study after 8 weeks.	
End point type	Primary
End point timeframe:	
Baseline and Week 8	

End point values	FYB201	Lucentis		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	207 ^[1]	209 ^[2]		
Units: Letters				
arithmetic mean (standard deviation)	5.2 (± 7.75)	6.0 (± 8.42)		

Notes:

[1] - FAS_EU. 5 subjects in the FYB201 group had missing data for the BCVA assessment at Week 8.

[2] - FAS_EU. 5 subjects in the Lucentis group had missing data for the BCVA assessment at Week 8.

Statistical analyses

Statistical analysis title	Comparison of change in BCVA [letters]
Statistical analysis description:	
The hypothesis of biosimilarity of FYB201 and Lucentis was tested with a two-sided equivalence test with an equivalence margin of 3 ETDRS letters. An ANCOVA model was used with the change in BCVA between baseline and Week 8 as the dependent variable, the baseline BCVA as covariate, and the country and the treatment group as fixed effects.	
Comparison groups	FYB201 v Lucentis

Number of subjects included in analysis	416
Analysis specification	Pre-specified
Analysis type	equivalence ^[3]
Method	ANCOVA
Parameter estimate	Difference in least square means
Point estimate	-0.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.3
upper limit	0.9
Variability estimate	Standard error of the mean
Dispersion value	0.8

Notes:

[3] - The confidence interval (CI) for treatment difference (FYB201 - Lucentis) was calculated using Least Square Means. If the 95% CI was completely contained in the interval]-3.5;3.5[ETDRS letters, equivalence of FYB201 and Lucentis could be concluded.

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse Events are collected from First Patient First Visit (FPFV) until Last Patient Last Visit (LPLV). All Adverse events are reported in this record from First Patient First Treatment until Last Patient Last Visit.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	19.0
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Reporting groups

Reporting group title	FYB201
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Reporting group description:

Patients received FYB201 at a dose of 0.5mg (0.05mL of a 10mg/mL solution) as twelve monthly intravitreal injections

Reporting group title	Lucentis
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Reporting group description:

Patients received Lucentis (ranibizumab) at a dose of 0.5mg (0.05mL of a 10mg/mL solution) as twelve monthly intravitreal injections

Serious adverse events	FYB201	Lucentis	
Total subjects affected by serious adverse events			
subjects affected / exposed	19 / 238 (7.98%)	32 / 239 (13.39%)	
number of deaths (all causes)	2	1	
number of deaths resulting from adverse events	2	1	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Benign pancreatic neoplasm	Additional description: Benign pancreatic neoplasm		
subjects affected / exposed	0 / 238 (0.00%)	1 / 239 (0.42%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bladder cancer	Additional description: Bladder cancer		
subjects affected / exposed	1 / 238 (0.42%)	0 / 239 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bladder neoplasm	Additional description: Bladder neoplasm		
subjects affected / exposed	0 / 238 (0.00%)	1 / 239 (0.42%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meningioma benign	Additional description: Meningioma benign		

subjects affected / exposed	1 / 238 (0.42%)	0 / 239 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prostate cancer	Additional description: Prostate cancer		
subjects affected / exposed	0 / 238 (0.00%)	1 / 239 (0.42%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tongue neoplasm malignant stage unspecified	Additional description: Tongue neoplasm malignant stage unspecified		
subjects affected / exposed	0 / 238 (0.00%)	1 / 239 (0.42%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Circulatory collapse	Additional description: Circulatory collapse		
subjects affected / exposed	0 / 238 (0.00%)	1 / 239 (0.42%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertension	Additional description: Hypertension		
subjects affected / exposed	0 / 238 (0.00%)	1 / 239 (0.42%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral artery stenosis	Additional description: Peripheral artery stenosis		
subjects affected / exposed	1 / 238 (0.42%)	0 / 239 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombophlebitis superficial	Additional description: Thrombophlebitis superficial		
subjects affected / exposed	0 / 238 (0.00%)	1 / 239 (0.42%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Chest pain	Additional description: Chest pain		
subjects affected / exposed	0 / 238 (0.00%)	1 / 239 (0.42%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Respiratory, thoracic and mediastinal disorders			
Bronchiectasis	Additional description: Bronchiectasis		
subjects affected / exposed	1 / 238 (0.42%)	0 / 239 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic obstructive pulmonary disease	Additional description: Chronic obstructive pulmonary disease		
subjects affected / exposed	1 / 238 (0.42%)	0 / 239 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Lung disorder	Additional description: Lung disorder		
subjects affected / exposed	0 / 238 (0.00%)	1 / 239 (0.42%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleural effusion	Additional description: Pleural effusion		
subjects affected / exposed	0 / 238 (0.00%)	1 / 239 (0.42%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia aspiration	Additional description: Pneumonia aspiration		
subjects affected / exposed	1 / 238 (0.42%)	0 / 239 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory failure	Additional description: Respiratory failure		
subjects affected / exposed	1 / 238 (0.42%)	2 / 239 (0.84%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Investigations			
Catheterisation cardiac	Additional description: Catheterisation cardiac		
subjects affected / exposed	0 / 238 (0.00%)	1 / 239 (0.42%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Femoral neck fracture	Additional description: Femoral neck fracture		

subjects affected / exposed	1 / 238 (0.42%)	0 / 239 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thoracic vertebral fracture	Additional description: Thoracic vertebral fracture		
subjects affected / exposed	0 / 238 (0.00%)	1 / 239 (0.42%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Atrial fibrillation	Additional description: Atrial fibrillation		
subjects affected / exposed	3 / 238 (1.26%)	1 / 239 (0.42%)	
occurrences causally related to treatment / all	0 / 4	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial flutter	Additional description: Atrial flutter		
subjects affected / exposed	1 / 238 (0.42%)	0 / 239 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure	Additional description: Cardiac failure		
subjects affected / exposed	0 / 238 (0.00%)	1 / 239 (0.42%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure chronic	Additional description: Cardiac failure chronic		
subjects affected / exposed	1 / 238 (0.42%)	0 / 239 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiopulmonary failure	Additional description: Cardiopulmonary failure		
subjects affected / exposed	1 / 238 (0.42%)	0 / 239 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Congestive cardiomyopathy	Additional description: Congestive cardiomyopathy		
subjects affected / exposed	1 / 238 (0.42%)	0 / 239 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial infarction	Additional description: Myocardial infarction		

subjects affected / exposed	1 / 238 (0.42%)	2 / 239 (0.84%)	
occurrences causally related to treatment / all	1 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial ischaemia	Additional description: Myocardial ischaemia		
subjects affected / exposed	0 / 238 (0.00%)	1 / 239 (0.42%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Cerebral haemorrhage	Additional description: Cerebral haemorrhage		
subjects affected / exposed	0 / 238 (0.00%)	1 / 239 (0.42%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebrovascular accident	Additional description: Cerebrovascular accident		
subjects affected / exposed	0 / 238 (0.00%)	1 / 239 (0.42%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Headache	Additional description: Headache		
subjects affected / exposed	0 / 238 (0.00%)	1 / 239 (0.42%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope	Additional description: Syncope		
subjects affected / exposed	1 / 238 (0.42%)	1 / 239 (0.42%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transient global amnesia	Additional description: Transient global amnesia		
subjects affected / exposed	0 / 238 (0.00%)	1 / 239 (0.42%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transient ischaemic attack	Additional description: Transient ischaemic attack		
subjects affected / exposed	1 / 238 (0.42%)	0 / 239 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			

Anaemia	Additional description: Anaemia		
	subjects affected / exposed	0 / 238 (0.00%)	1 / 239 (0.42%)
	occurrences causally related to treatment / all	0 / 0	0 / 1
	deaths causally related to treatment / all	0 / 0	0 / 0
Anaemia macrocytic	Additional description: Anaemia macrocytic		
	subjects affected / exposed	1 / 238 (0.42%)	0 / 239 (0.00%)
	occurrences causally related to treatment / all	0 / 1	0 / 0
	deaths causally related to treatment / all	0 / 0	0 / 0
Lymphadenopathy	Additional description: Lymphadenopathy		
	subjects affected / exposed	0 / 238 (0.00%)	1 / 239 (0.42%)
	occurrences causally related to treatment / all	0 / 0	0 / 1
	deaths causally related to treatment / all	0 / 0	0 / 0
Ear and labyrinth disorders			
	Additional description: Vertigo		
	subjects affected / exposed	0 / 238 (0.00%)	1 / 239 (0.42%)
	occurrences causally related to treatment / all	0 / 0	0 / 1
Eye disorders			
	Additional description: Cataract		
	subjects affected / exposed	0 / 238 (0.00%)	2 / 239 (0.84%)
	occurrences causally related to treatment / all	0 / 0	0 / 2
Iridocyclitis	Additional description: Iridocyclitis		
	subjects affected / exposed	1 / 238 (0.42%)	0 / 239 (0.00%)
	occurrences causally related to treatment / all	1 / 1	0 / 0
	deaths causally related to treatment / all	0 / 0	0 / 0
Gastrointestinal disorders			
	Additional description: Gastric ulcer		
	subjects affected / exposed	0 / 238 (0.00%)	1 / 239 (0.42%)
	occurrences causally related to treatment / all	0 / 0	0 / 1
Intestinal obstruction			
	Additional description: Intestinal obstruction		

subjects affected / exposed	0 / 238 (0.00%)	1 / 239 (0.42%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nausea	Additional description: Nausea		
subjects affected / exposed	0 / 238 (0.00%)	1 / 239 (0.42%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Bile duct stone	Additional description: Bile duct stone		
subjects affected / exposed	0 / 238 (0.00%)	1 / 239 (0.42%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis acute	Additional description: Cholecystitis acute		
subjects affected / exposed	0 / 238 (0.00%)	1 / 239 (0.42%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute kidney injury	Additional description: Acute kidney injury		
subjects affected / exposed	2 / 238 (0.84%)	0 / 239 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hydrourter	Additional description: Hydrourter		
subjects affected / exposed	1 / 238 (0.42%)	0 / 239 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nephrotic syndrome	Additional description: Nephrotic syndrome		
subjects affected / exposed	1 / 238 (0.42%)	0 / 239 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ureterolithiasis	Additional description: Ureterolithiasis		
subjects affected / exposed	0 / 238 (0.00%)	1 / 239 (0.42%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary bladder polyp	Additional description: Urinary bladder polyp		

subjects affected / exposed	0 / 238 (0.00%)	1 / 239 (0.42%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Intervertebral disc protrusion	Additional description: Intervertebral disc protrusion		
subjects affected / exposed	1 / 238 (0.42%)	2 / 239 (0.84%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteoarthritis	Additional description: Osteoarthritis		
subjects affected / exposed	0 / 238 (0.00%)	2 / 239 (0.84%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Bronchitis	Additional description: Bronchitis		
subjects affected / exposed	1 / 238 (0.42%)	0 / 239 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis	Additional description: Cellulitis		
subjects affected / exposed	1 / 238 (0.42%)	0 / 239 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endophthalmitis	Additional description: Endophthalmitis		
subjects affected / exposed	1 / 238 (0.42%)	2 / 239 (0.84%)	
occurrences causally related to treatment / all	0 / 1	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia bacterial	Additional description: Pneumonia bacterial		
subjects affected / exposed	1 / 238 (0.42%)	0 / 239 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Postoperative wound infection	Additional description: Postoperative wound infection		
subjects affected / exposed	0 / 238 (0.00%)	1 / 239 (0.42%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Metabolism and nutrition disorders			
Hyperglycaemia	Additional description: Hyperglycaemia		
subjects affected / exposed	0 / 238 (0.00%)	1 / 239 (0.42%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypokalaemia	Additional description: Hypokalaemia		
subjects affected / exposed	0 / 238 (0.00%)	1 / 239 (0.42%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	FYB201	Lucentis	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	149 / 238 (62.61%)	161 / 239 (67.36%)	
Investigations			
Blood urea increased	Additional description: Blood urea increased		
subjects affected / exposed	4 / 238 (1.68%)	5 / 239 (2.09%)	
occurrences (all)	4	5	
C-reactive protein increased	Additional description: C-reactive protein increased		
subjects affected / exposed	10 / 238 (4.20%)	5 / 239 (2.09%)	
occurrences (all)	11	5	
Intraocular pressure increased	Additional description: Intraocular pressure increased		
subjects affected / exposed	11 / 238 (4.62%)	12 / 239 (5.02%)	
occurrences (all)	20	15	
Visual acuity tests abnormal	Additional description: Visual acuity tests abnormal		
subjects affected / exposed	4 / 238 (1.68%)	5 / 239 (2.09%)	
occurrences (all)	4	6	
Injury, poisoning and procedural complications			
Fall	Additional description: Fall		
subjects affected / exposed	2 / 238 (0.84%)	5 / 239 (2.09%)	
occurrences (all)	2	5	
Vascular disorders			
Hypertension	Additional description: Hypertension		
subjects affected / exposed	3 / 238 (1.26%)	14 / 239 (5.86%)	
occurrences (all)	6	25	

Nervous system disorders			
	Dizziness	Additional description: Dizziness	
	subjects affected / exposed	1 / 238 (0.42%)	5 / 239 (2.09%)
	occurrences (all)	1	5
	Headache	Additional description: Headache	
	subjects affected / exposed	4 / 238 (1.68%)	8 / 239 (3.35%)
	occurrences (all)	5	9
General disorders and administration site conditions			
	Pain	Additional description: Pain	
	subjects affected / exposed	5 / 238 (2.10%)	2 / 239 (0.84%)
	occurrences (all)	9	2
Eye disorders			
	Cataract	Additional description: Cataract	
	subjects affected / exposed	1 / 238 (0.42%)	10 / 239 (4.18%)
	occurrences (all)	1	13
	Choroidal neovascularisation	Additional description: Choroidal neovascularisation	
	subjects affected / exposed	6 / 238 (2.52%)	4 / 239 (1.67%)
	occurrences (all)	6	4
	Conjunctival haemorrhage	Additional description: Conjunctival haemorrhage	
	subjects affected / exposed	14 / 238 (5.88%)	19 / 239 (7.95%)
	occurrences (all)	24	30
	Conjunctival hyperaemia	Additional description: Conjunctival hyperaemia	
	subjects affected / exposed	4 / 238 (1.68%)	6 / 239 (2.51%)
	occurrences (all)	4	6
	Eye pain	Additional description: Eye pain	
	subjects affected / exposed	9 / 238 (3.78%)	6 / 239 (2.51%)
	occurrences (all)	14	8
	Lacrimation increased	Additional description: Lacrimation increased	
	subjects affected / exposed	9 / 238 (3.78%)	2 / 239 (0.84%)
	occurrences (all)	11	2
	Neovascular age-related macular degeneration	Additional description: Neovascular age-related macular degeneration	
	subjects affected / exposed	19 / 238 (7.98%)	22 / 239 (9.21%)
	occurrences (all)	19	24
	Punctate keratitis	Additional description: Punctate keratitis	
	subjects affected / exposed	8 / 238 (3.36%)	12 / 239 (5.02%)
	occurrences (all)	15	25

Retinal haemorrhage subjects affected / exposed occurrences (all)	Additional description: Retinal haemorrhage		
	7 / 238 (2.94%) 9	3 / 239 (1.26%) 3	
Retinal pigment epithelial tear subjects affected / exposed occurrences (all)	Additional description: Retinal pigment epithelial tear		
	2 / 238 (0.84%) 2	6 / 239 (2.51%) 6	
Visual acuity reduced subjects affected / exposed occurrences (all)	Additional description: Visual acuity reduced		
	6 / 238 (2.52%) 6	11 / 239 (4.60%) 13	
Vitreous detachment subjects affected / exposed occurrences (all)	Additional description: Vitreous detachment		
	6 / 238 (2.52%) 7	4 / 239 (1.67%) 4	
Vitreous floaters subjects affected / exposed occurrences (all)	Additional description: Vitreous floaters		
	3 / 238 (1.26%) 3	5 / 239 (2.09%) 5	
Gastrointestinal disorders Diarrhoea subjects affected / exposed occurrences (all)	Additional description: Diarrhoea		
	2 / 238 (0.84%) 2	5 / 239 (2.09%) 5	
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all)	Additional description: Cough		
	5 / 238 (2.10%) 7	5 / 239 (2.09%) 5	
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all)	Additional description: Arthralgia		
	0 / 238 (0.00%) 0	5 / 239 (2.09%) 5	
	Additional description: Back pain		
	5 / 238 (2.10%) 5	8 / 239 (3.35%) 8	
Infections and infestations Bronchitis subjects affected / exposed occurrences (all)	Additional description: Bronchitis		
	8 / 238 (3.36%) 8	5 / 239 (2.09%) 5	
	Additional description: Conjunctivitis		
Conjunctivitis			

subjects affected / exposed	9 / 238 (3.78%)	2 / 239 (0.84%)	
occurrences (all)	10	2	
Influenza	Additional description: Influenza		
subjects affected / exposed	5 / 238 (2.10%)	2 / 239 (0.84%)	
occurrences (all)	7	2	
Nasopharyngitis	Additional description: Nasopharyngitis		
subjects affected / exposed	12 / 238 (5.04%)	16 / 239 (6.69%)	
occurrences (all)	15	17	
Upper respiratory tract infection	Additional description: Upper respiratory tract infection		
subjects affected / exposed	8 / 238 (3.36%)	6 / 239 (2.51%)	
occurrences (all)	10	7	
Urinary tract infection	Additional description: Urinary tract infection		
subjects affected / exposed	3 / 238 (1.26%)	6 / 239 (2.51%)	
occurrences (all)	3	6	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
30 November 2015	Additional sampling points in PK Subgroup, exclusion criterion related to acute treatment need of fellow eye at Visit 1 added
08 March 2017	Harmonization of the primary EU and US endpoint, adaption of sample size, removal of interim analysis and trough level sampling
10 May 2017	Local protocol version for France due to comments from the French Competent Authority.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported