



Clinical trial results:

A Multi Center, Randomized, Double-Masked, Active-Controlled, Comparative Clinical Study to Evaluate the Efficacy and Safety of MYL-1701P and Eylea® in Subjects with Diabetic Macular Edema

Summary

EudraCT number	2017-004358-40
Trial protocol	LV HU
Global end of trial date	10 September 2021

Results information

Result version number	v1 (current)
This version publication date	20 September 2022
First version publication date	20 September 2022

Trial information

Trial identification

Sponsor protocol code	MYL-1701P-3001
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03610646
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Mylan Pharmaceuticals Inc.
Sponsor organisation address	1000 Mylan Blvd, Canonsburg, PA, United States, 15317
Public contact	Rajesh Suresh Nachankar, Ph D, Mylan Pharmaceuticals Inc., +91 9148448205, rajesh.nachankar@viatris.com
Scientific contact	Prasanna Ganapathi, MD, Mylan Pharmaceuticals Inc., +91 80 6672 8000, prasannac.ganapathi@viatris.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	23 November 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	10 November 2020
Global end of trial reached?	Yes
Global end of trial date	10 September 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To demonstrate the clinical equivalence of MYL-1701P and Eylea over 8 weeks of treatment at doses and regimen recommended by the Prescribing Information for Eylea, as assessed by change from baseline to week 8 in best corrected visual acuity (BCVA).

Protection of trial subjects:

The study was conducted in compliance with regulatory requirements, the International Conference on Harmonization (ICH) Good Clinical Practice (GCP) guidelines and with the ethical principles of the Declaration of Helsinki. All laboratory specimens, evaluation forms, reports, and other records were identified in a manner designed to maintain patient confidentiality. All records were kept in a secure storage area with limited access. Clinical information was not to be released without the written permission of the patient (or the patient's legal guardian), except as necessary for monitoring and auditing by the sponsor, its designee, regulatory authorities or the IRB/IEC.

The PI (or designee) and all employees and coworkers involved with this study have not disclosed or used for any purpose other than performance of the study any data, record, or other unpublished, confidential information disclosed to those individuals for the purpose of the study.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 August 2018
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: 37
Country: Number of subjects enrolled	Czechia: 43
Country: Number of subjects enrolled	Germany: 11
Country: Number of subjects enrolled	Hungary: 52
Country: Number of subjects enrolled	Latvia: 18
Country: Number of subjects enrolled	India: 77
Country: Number of subjects enrolled	Japan: 41
Country: Number of subjects enrolled	United States: 63
Country: Number of subjects enrolled	Russian Federation: 13
Worldwide total number of subjects	355
EEA total number of subjects	161

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)	207
From 65 to 84 years	148
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study included male or female patients of 18 years or older, who suffered from Diabetic Macular Oedema (DME). Between 27-Jul-2015 and 15-Sep-20, 639 (unique) patients were screened and 355 patients were randomized in sites in 9 countries in Europe (Czech R., Germany, Hungary, Latvia and Poland), USA, Russia, Japan and India.

Pre-assignment

Screening details:

A total of 639 (unique) subjects were screened; total 673 screenings due to 34 rescreenings. 318 subjects were screen failures and 355 patients were randomized.

Period 1

Period 1 title	Study Treatment (Week 52) (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Assessor

Blinding implementation details:

This was a double-masked study. Patient and the investigator(s) who performed safety and efficacy evaluations were masked to study treatment. In each site, there were masked staff members (responsible all study assessments) and unmasked injecting physician (responsible for the injections). In case unmasked injecting physician was unavailable, unmasked pharmacist prepared the injections and handed over injections in the masked form to a masked physician for injection.

Arms

Are arms mutually exclusive?	Yes
Arm title	MYL-1701P

Arm description:

Subjects to receive intravitreal injections of MYL-1701P throughout the 52-week treatment period, with the last dose at 48 weeks. The additional doses may be administered in accordance with the protocol.

Arm type	Experimental
Investigational medicinal product name	Proposed Aflibercept Biosimilar
Investigational medicinal product code	MYL-1701P
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intravitreal use

Dosage and administration details:

MYL-1701P (a proposed biosimilar to Eylea) injection for intravitreal injection is a sterile, preservative-free, aqueous solution in a single-use, glass vial designed to deliver 0.05 mL (50 µL) of proposed aflibercept (40 mg/mL).

All subjects were planned to receive study drug as an intravitreal injection at a dose of 2 mg every 4 weeks for a total of 5 injections, and then every 8 weeks through the remainder of the 52-week treatment period, with the last dose at 48 weeks. In addition to the nine planned doses, study drug may also be administered at Week 20, Week 28, Week 36 and Week 44 based on protocol defined criteria.

Arm title	Eylea
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Arm description:

Subjects to receive intravitreal injections of Eylea throughout the 52-week treatment period, with the last dose at 48 weeks. The additional doses may be administered in accordance with the protocol.

Arm type	Active comparator
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Investigational medicinal product name	Eylea
Investigational medicinal product code	
Other name	Aflibercept
Pharmaceutical forms	Injection
Routes of administration	Intravitreal use

Dosage and administration details:

50 uL injection (40 mg/ml)

Number of subjects in period 1	MYL-1701P	Eylea
Started	179	176
Completed	161	158
Not completed	18	18
Adverse event, serious fatal	2	3
Consent withdrawn by subject	8	9
Physician decision	2	-
Adverse event, non-fatal	5	4
Non-compliance	1	-
Lost to follow-up	-	2

Baseline characteristics

Reporting groups

Reporting group title	MYL-1701P
Reporting group description: Subjects to receive intravitreal injections of MYL-1701P throughout the 52-week treatment period, with the last dose at 48 weeks. The additional doses may be administered in accordance with the protocol.	
Reporting group title	Eylea
Reporting group description: Subjects to receive intravitreal injections of Eylea throughout the 52-week treatment period, with the last dose at 48 weeks. The additional doses may be administered in accordance with the protocol.	

Reporting group values	MYL-1701P	Eylea	Total
Number of subjects	179	176	355
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)	101	106	207
From 65-84 years	78	70	148
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	62.8	61.6	
standard deviation	± 8.37	± 9.93	-
Gender categorical Units: Subjects			
Female	72	67	139
Male	107	109	216

Subject analysis sets

Subject analysis set title	Intent to Treat
Subject analysis set type	Intention-to-treat
Subject analysis set description: The intention-to-treat (ITT) analysis set consists of all randomized subjects.	
Subject analysis set title	Safety analysis set
Subject analysis set type	Safety analysis
Subject analysis set description: The safety analysis set consists of all subjects who received at least one dose of study drug.	

Reporting group values	Intent to Treat	Safety analysis set	
Number of subjects	355	354	
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)	207	206	
From 65-84 years	148	148	
85 years and over	0	0	
Age continuous			
Units: years			
arithmetic mean	62.2		
standard deviation	± 9.18	±	
Gender categorical			
Units: Subjects			
Female	139		
Male	216		

End points

End points reporting groups

Reporting group title	MYL-1701P
Reporting group description: Subjects to receive intravitreal injections of MYL-1701P throughout the 52-week treatment period, with the last dose at 48 weeks. The additional doses may be administered in accordance with the protocol.	
Reporting group title	Eylea
Reporting group description: Subjects to receive intravitreal injections of Eylea throughout the 52-week treatment period, with the last dose at 48 weeks. The additional doses may be administered in accordance with the protocol.	
Subject analysis set title	Intent to Treat
Subject analysis set type	Intention-to-treat
Subject analysis set description: The intention-to-treat (ITT) analysis set consists of all randomized subjects.	
Subject analysis set title	Safety analysis set
Subject analysis set type	Safety analysis
Subject analysis set description: The safety analysis set consists of all subjects who received at least one dose of study drug.	

Primary: Mean Change From Baseline in Best Corrected Visual Acuity (letters) at Week 8

End point title	Mean Change From Baseline in Best Corrected Visual Acuity (letters) at Week 8
End point description: The primary endpoint was the mean change from baseline in Best Corrected Visual Acuity (BCVA) letters after 8 weeks of treatment. All patients included in the intent to treat (all randomized) were analysed. BCVA is measured using an Early Treatment Diabetic Retinopathy Study (ETDRS) chart and is reported as the number of letters read correctly (ranging from 0 to 100 letters) in the study eye. The lower the number of letters read correctly on the ETDRS chart, the worse the vision (or visual acuity). A positive change from baseline indicates an improvement and a negative change from baseline indicates a worsening.	
End point type	Primary
End point timeframe: Baseline to week 8	

End point values	MYL-1701P	Eylea		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	179	176		
Units: BCVA Letter Score				
least squares mean (standard error)	6.60 (\pm 0.548)	6.56 (\pm 0.548)		

Statistical analyses

Statistical analysis title	Comparison of change in BCVA [letters] at week 8
Statistical analysis description: Mixed model for repeated measures analysis	

Comparison groups	MYL-1701P v Eylea
Number of subjects included in analysis	355
Analysis specification	Pre-specified
Analysis type	equivalence ^[1]
Parameter estimate	Mean difference (final values)
Point estimate	0.04
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.4
upper limit	1.47
Variability estimate	Standard error of the mean
Dispersion value	0.73

Notes:

[1] - If the 95% CI was contained in the interval of -3.0 to +3.0 letters, equivalence of MYL-1701P and Eylea could be established.

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Baseline to week 52- Adverse Events were collected from First Patient First Visit (FPFV) until Last Patient Last Visit (LPLV). All Adverse events are reported for all patients from start of treatment till End of study Visit.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
Dictionary version	24.1

Reporting groups

Reporting group title	MYL-1701P
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Reporting group description: -

Reporting group title	Eylea
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Reporting group description: -

Serious adverse events	MYL-1701P	Eylea	
Total subjects affected by serious adverse events			
subjects affected / exposed	31 / 178 (17.42%)	23 / 176 (13.07%)	
number of deaths (all causes)	2	4	
number of deaths resulting from adverse events	2	4	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma gastric			
subjects affected / exposed	0 / 178 (0.00%)	1 / 176 (0.57%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Basal cell carcinoma			
subjects affected / exposed	1 / 178 (0.56%)	0 / 176 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Breast cancer metastatic			
subjects affected / exposed	0 / 178 (0.00%)	1 / 176 (0.57%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Deep vein thrombosis			

subjects affected / exposed	0 / 178 (0.00%)	1 / 176 (0.57%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertensive crisis			
subjects affected / exposed	0 / 178 (0.00%)	1 / 176 (0.57%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombosis			
subjects affected / exposed	0 / 178 (0.00%)	1 / 176 (0.57%)	
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			
Asthenia			
subjects affected / exposed	1 / 178 (0.56%)	0 / 176 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Death			
subjects affected / exposed	1 / 178 (0.56%)	1 / 176 (0.57%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 1	
Respiratory, thoracic and mediastinal disorders			
Respiratory distress			
subjects affected / exposed	0 / 178 (0.00%)	1 / 176 (0.57%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Blood potassium increased			
subjects affected / exposed	1 / 178 (0.56%)	0 / 176 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Contusion			

subjects affected / exposed	0 / 178 (0.00%)	1 / 176 (0.57%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femoral neck fracture			
subjects affected / exposed	2 / 178 (1.12%)	0 / 176 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper limb fracture			
subjects affected / exposed	1 / 178 (0.56%)	0 / 176 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Acute coronary syndrome			
subjects affected / exposed	1 / 178 (0.56%)	0 / 176 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Atrial fibrillation			
subjects affected / exposed	0 / 178 (0.00%)	1 / 176 (0.57%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure			
subjects affected / exposed	2 / 178 (1.12%)	0 / 176 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac arrest			
subjects affected / exposed	0 / 178 (0.00%)	1 / 176 (0.57%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac Failure Chronic			
subjects affected / exposed	1 / 178 (0.56%)	0 / 176 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure congestive			

subjects affected / exposed	0 / 178 (0.00%)	1 / 176 (0.57%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac fibrillation			
subjects affected / exposed	0 / 178 (0.00%)	1 / 176 (0.57%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary artery disease			
subjects affected / exposed	0 / 178 (0.00%)	1 / 176 (0.57%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial infarction			
subjects affected / exposed	0 / 178 (0.00%)	2 / 176 (1.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Nervous system disorders			
Brain stem infarction			
subjects affected / exposed	0 / 178 (0.00%)	1 / 176 (0.57%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Carotid artery stenosis			
subjects affected / exposed	1 / 178 (0.56%)	0 / 176 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Embolic cerebral infarction			
subjects affected / exposed	0 / 178 (0.00%)	1 / 176 (0.57%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Embolic stroke			
subjects affected / exposed	0 / 178 (0.00%)	1 / 176 (0.57%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lumbar radiculopathy			

subjects affected / exposed	0 / 178 (0.00%)	1 / 176 (0.57%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombotic cerebral infarction			
subjects affected / exposed	1 / 178 (0.56%)	0 / 176 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bipolar disorder			
subjects affected / exposed	0 / 178 (0.00%)	1 / 176 (0.57%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear and labyrinth disorders			
Endolymphatic hydrops			
subjects affected / exposed	0 / 178 (0.00%)	1 / 176 (0.57%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Corneal oedema			
subjects affected / exposed	0 / 178 (0.00%)	1 / 176 (0.57%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye haemorrhage			
subjects affected / exposed	1 / 178 (0.56%)	0 / 176 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vitreous detachment			
subjects affected / exposed	0 / 178 (0.00%)	1 / 176 (0.57%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Anal incontinence			
subjects affected / exposed	1 / 178 (0.56%)	0 / 176 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Colitis			
subjects affected / exposed	1 / 178 (0.56%)	0 / 176 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis ischaemic			
subjects affected / exposed	1 / 178 (0.56%)	1 / 176 (0.57%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Duodenal ulcer			
subjects affected / exposed	0 / 178 (0.00%)	1 / 176 (0.57%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower gastrointestinal haemorrhage			
subjects affected / exposed	1 / 178 (0.56%)	0 / 176 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Melaena			
subjects affected / exposed	1 / 178 (0.56%)	0 / 176 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Diabetic foot			
subjects affected / exposed	2 / 178 (1.12%)	1 / 176 (0.57%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Calculus bladder			
subjects affected / exposed	1 / 178 (0.56%)	0 / 176 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Calculus urinary			
subjects affected / exposed	1 / 178 (0.56%)	0 / 176 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Urinary incontinence			
subjects affected / exposed	1 / 178 (0.56%)	0 / 176 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Neuropathic arthropathy			
subjects affected / exposed	1 / 178 (0.56%)	0 / 176 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Synovitis			
subjects affected / exposed	1 / 178 (0.56%)	0 / 176 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Atypical pneumonia			
subjects affected / exposed	1 / 178 (0.56%)	0 / 176 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
COVID-19			
subjects affected / exposed	2 / 178 (1.12%)	0 / 176 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
COVID-19 pneumonia			
subjects affected / exposed	3 / 178 (1.69%)	4 / 176 (2.27%)	
occurrences causally related to treatment / all	0 / 3	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 1	
Cellulitis			
subjects affected / exposed	1 / 178 (0.56%)	0 / 176 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	1 / 178 (0.56%)	0 / 176 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Otitis media chronic			
subjects affected / exposed	1 / 178 (0.56%)	0 / 176 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	2 / 178 (1.12%)	1 / 176 (0.57%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Pyelonephritis chronic			
subjects affected / exposed	1 / 178 (0.56%)	0 / 176 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Diabetic metabolic decompensation			
subjects affected / exposed	1 / 178 (0.56%)	0 / 176 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperglycaemia			
subjects affected / exposed	1 / 178 (0.56%)	0 / 176 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoglycaemia			
subjects affected / exposed	1 / 178 (0.56%)	0 / 176 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypokalaemia			
subjects affected / exposed	1 / 178 (0.56%)	0 / 176 (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	MYL-1701P	Eylea	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	53 / 178 (29.78%)	61 / 176 (34.66%)	
Vascular disorders			
Hypertension			
subjects affected / exposed	16 / 178 (8.99%)	20 / 176 (11.36%)	
occurrences (all)	20	23	
Eye disorders			
Cataract			
subjects affected / exposed	12 / 178 (6.74%)	12 / 176 (6.82%)	
occurrences (all)	17	12	
Diabetic retinal oedema			
subjects affected / exposed	9 / 178 (5.06%)	10 / 176 (5.68%)	
occurrences (all)	9	13	
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	14 / 178 (7.87%)	10 / 176 (5.68%)	
occurrences (all)	19	10	
Metabolism and nutrition disorders			
Diabetes mellitus			
subjects affected / exposed	2 / 178 (1.12%)	9 / 176 (5.11%)	
occurrences (all)	3	10	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
09 June 2020	1) Addition of subjects due to the potential impact related to COVID-19 pandemic. 2) Exclusion criteria Subjects with history of use of intraocular or periocular corticosteroids. 3) Collect smoking history 4) Added text to clarify visit window. 5) All other country specific amendments (applicable for respective country) added in this version 6) Contingency measures implemented due to COVID-19 in Clinical Study Report 7) Added instructions to the investigators to manage COVID-19 pandemic.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
27 March 2020	Except Japan, in all other countries temporary hold on recruitment (Local situation) to reduce risk of exposure to COVID-19.	28 May 2020

Notes:

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Not applicable.

Notes: