



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 |
|-----------------------|----------------|

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 |
|------------------|-------|

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 |
|----------|-------------------|

| | |
|--|------------------|
| 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 (± 0.548) | 6.56 (± 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 |
|-----------------|------------|

Dictionary used

| | |
|--------------------|--------|
| Dictionary name | MedDRA |
| Dictionary version | 24.1 |

Reporting groups

| | |
|-----------------------|-----------|
| Reporting group title | MYL-1701P |
|-----------------------|-----------|

Reporting group description: -

| | |
|-----------------------|-------|
| Reporting group title | Eylea |
|-----------------------|-------|

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: