STATISTICAL ANALYSIS PLAN

A Multi Center, Extension Study to Evaluate the Safety and Efficacy of MYL-1701P in Subjects with Diabetic Macular Edema Completed MYL-1701P-3001 Study

Clinical Study Protocol No. AFIL-IJZ-3002

(Version 01, dated 19 Aug 2020)

Sponsored By:

Mylan[redacted]

[redacted]

Prepared By:

[redacted]

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SIGNATURE PAGE

CRO's Signatory		
Department: Biostatistics & Programming		
	Prepared By	**Approved By**
Name	[redacted]	
Designation		
Signature & Date		

Sponsor's Signatory	
Mylan [redacted]	
Approved by	
Name	[redacted]
Designation	
Signature & Date	

Revision History

VERSION	DATE	DESCRIPTION OF REVISIONS	REVISED BY
Version 1.0	23NOV2021	Original	

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List of abbreviations and definition of terms

AE	Adverse Event
ADA	Anti-Drug Antibodies
ATC	Anatomical Therapeutic Chemical
BCVA	Best Corrected Visual Acuity
CI	Confidence Interval
COVID-19	Corona Virus Disease-2019
CPMP	Committee for Proprietary Medicinal Products
CRF	Case Report Form
CRT	Central Retinal Thickness
CSR	Clinical Study Report
CRO	Contract Research Organization
DBL	Database Lock
DME	Diabetic Macular Edema
ECG	Electrocardiogram
ETDRS	Early Treatment Diabetic Retinopathy Study
FAS	Full Analysis Set
FDA	Food and Drug Administration
HR	Heart Rate
ICF	Informed Consent Form
ICH	International Council for Harmonisation

LOCF	Last Observation Carried Forward
MedDRA	Medical Dictionary for Regulatory Authorities
MH	Medical History
MMRM	Mixed Model Repeated Measures
OE	Ophthalmological Examination
OCT	Optical Coherence Tomography
OTC	Over the Counter
PT	Preferred Term
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
SAS	Statistical Analysis System
SD	Standard Deviation
SOC	System Organ Class
TEAE	Treatment Emergent Adverse Event
TLFs	Tables, Listings & Figures
USA	United Sates of America
WHO-Drug Global	World Health Organization-Drug Global

1. Introduction to the Statistical Analysis Plan

This Statistical Analysis Plan (SAP) provides a thorough description of statistical analysis methods and presentation of the study data from the clinical trial described in Study Protocol AFIL-IJZ-3002, (Version no. 01) dated 19 Aug 2020.

The SAP includes details of data handling procedures and statistical methodology.

SAP will be finalized prior to Database Lock (DBL) and statistical methods described in this document supersede the statistical section mentioned in the study protocol.

Table, Listing & Figure (TLF) shells are only for template purpose and modifications might be done in the final TLF as identified during the review of data.

The following documents were reviewed in preparation for the SAP:

- Case Report Form (CRF) (Version 1.0, dated 30 Oct 2020)
- Protocol (Version 01, dated 19 Aug 2020)

2. Objective of the Study

The objectives of this study are:

Primary Objective:

The primary objective is to evaluate the safety and tolerability of MYL-1701P in subjects with DME who completed study MYL-1701P-3001.

Secondary Objectives:

The secondary objective is to compare the group that switched from Eylea to MYL-1701P in the extension study with the group that continued MYL-1701P from the parent study regarding the following:

- Efficacy of MYL-1701P as measured by change from baseline (Day 1 of parent study) in BCVA at Week 20.
- Efficacy of MYL-1701P as measured by change from baseline (Day 1 of parent study) in CRT at Weeks 8, 16 and 20.
- Efficacy of MYL-1701P as measured by change from baseline (Day 1 of parent study) in BCVA at Weeks 8 and 16.
- Safety, tolerability, and Immunogenicity of MYL-1701P.
- Impact of immunogenicity on efficacy and safety.

3. Investigational Plan

3.1 Overall Study Design and Plan-Description

This is a multi-center, extension clinical study of the parent study MYL-1701P-3001.

Up to one hundred (100) subjects will be enrolled in the study who meet all the following criteria: participated and completed Week 52 visit of the parent study MYL-1701P-3001 from India, provide informed consent, and meet all the eligibility criteria for the extension study.

The first dose of the extension study will be administered on Day 1 which will be scheduled 8 weeks (±7 days) from the last dose (Week 48 ± 7 days) of administration of the randomized study medication of the parent study. If the dosing at the Week 48 visit of the parent study was missed due to unforeseen reasons, the first dose in the extension study can be scheduled as soon as possible after the Week 52 visit (parent study).

Eligible subjects who provide written informed consent to participate in the extension study will be screened during the end of study visit of the parent study.

Clinical evaluations will be performed at the following study visits:

- Visit 1 – Screening visit (Week 52/ End of study visit of the parent study)
- Visit 2 – Enrollment visit (Day 1 of extension study)
- Visit 3 – Week 8 (± 7 days)
- Visit 4 – Week 16 (± 7 days) End of treatment
- Visit 5 – Week 20 (± 7 days) End of study visit & Early termination

Screening visit for the extension study may occur on the same day as the end of study (visit 16/Week 52) visit of the parent study. If assessments are performed on different days then vital signs must be repeated and all the other assessments of EOS (visit 16/Week 52) visit of parent study can be used. If required additional visit can be performed between end of study visit of the parent study and enrollment visit of extension study based on Investigator's discretion.

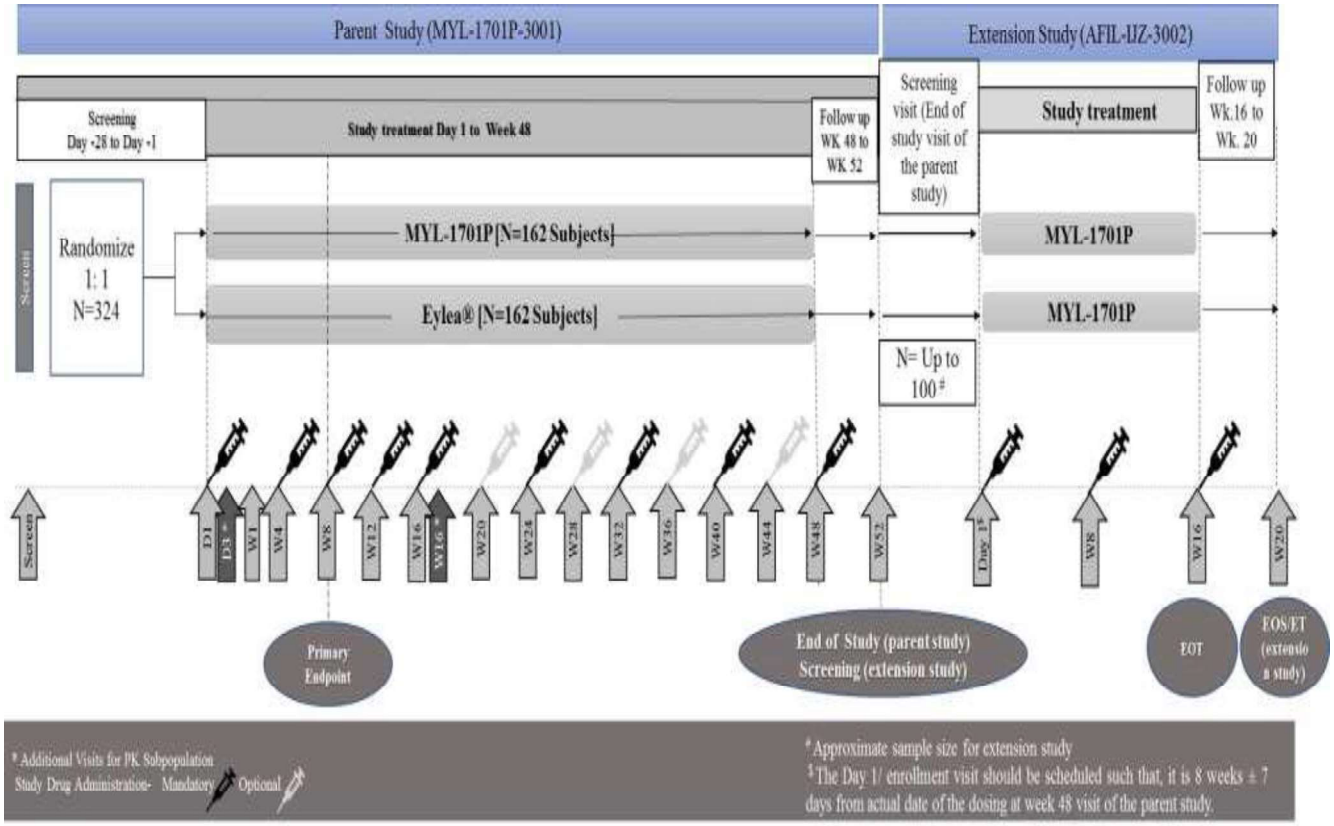
Note: The nomenclature used in this document for denoting the visits for the extension study as mentioned in below table.

Extension study	Parent study (MYL-1701P 3001)
Visit 1 (screening)	Week 52
Visit 2 (enrollment)	Week 56

Visit 3 (Week 8)	Week 64
Visit 4 (Week 16)	Week 72
Visit 5 (Week 20)	Week 76

Extension clinical study duration from screening to end of study would be up to 6 months (24 weeks) approximately.

Figure 1: Study Diagram



3.2 Investigational Medicinal Product:

MYL-1701P (a proposed biosimilar to Eylea) injection for intravitreal injection.

3.3 Randomization and Unblinding Procedure

As this is an open-label study, masking will not be applicable in this study.

Unblinded randomization schedule with treatment information of the parent study (MYL-1701P-3001) will be shared with [redacted] team for performing statistical analyses for this extension study (AFIL-IJZ-3002).

3.4 Schedule of Events

The study visit schedule can be found on Section 1 (page 20-21) of the final protocol (Version 01: 19 Aug 2020).

3.5 Sample Size Justification

There is no formal sample size estimation. The extension study is open for all subjects from India who completed the parent study MYL-1701P-3001. It is expected that up to 100 subjects will be considered for participation in the extension study.

For a mean change from baseline (Day 1 of parent study) in BCVA at Week 20, the point estimate for the difference between the group of subjects that switched from Eylea in parent study and those continued on MYL-1701P should be within the range of [redacted] letters, which is a recommended similarity margin for a 1-year endpoint. The following table gives power with which this can be achieved for expected numbers of subjects per group, assuming a treatment regimen difference of 0 and a standard deviation of 10.5 letters:

Table 1: Power with Expected Number of Subjects per Group

	Number of subjects per group
[redacted]	
Power	

3.6 Change to Analysis from Protocol

There is no change to the analysis from that described in the study protocol.

3.7 Analysis Population

3.7.1 All enrolled Population

All enrolled population includes all subjects who are enrolled in the extension study.

3.7.2 Safety Population

The safety population includes all subjects who received at least 1 dose of MYL- 1701P in the extension study.

3.7.3 Full Analysis Set (FAS) Population

The Full Analysis Set (FAS) includes all subjects in the safety set who have at least one post-dosing Best Corrected Visual Acuity (BCVA) assessment.

3.8 Population Derivation

Conditions for the population derivation:

1) Informed consent form sign date is not missing.
2) Subject ID should not be missing.
3) Subjects who received at least 1 dose of MYL-1701P in the extension study.

Subjects satisfy conditions # 1 to 3 will be considered in safety population.

4) Subjects in the safety set who have at least one post-dosing BCVA assessment.

Subjects who are in the safety population and satisfy conditions # 4 will be included in the FAS population.

4. Safety and Efficacy Variables

4.1 Primary Endpoint

- Incidence of treatment emergent adverse events (TEAEs).

4.2 Secondary Efficacy Endpoint

- Mean change from baseline (Day 1 of parent study) in BCVA as assessed by Early Treatment Diabetic Retinopathy Study (ETDRS) letters at Week 20.
- Mean change from baseline (Day 1 of parent study) in CRT as determined by spectral-domain-optical coherence tomography (SD-OCT) at Weeks 8, 16 and 20.
- Mean change from baseline (Day 1 of parent study) in BCVA as assessed by ETDRS letters at Weeks 8 and 16.
- Proportion of subjects who gained ≥5 letters, ≥10 letters and ≥15 letters from baseline in BCVA, assessed by change from baseline (Day 1 of parent study) in ETDRS letters at Weeks 8, 16 and 20.
- Mean change in BCVA from Day 1 of extension study at Week 20.
- Mean change in CRT from Day 1 of extension study at Week 20.

Note: For all the efficacy endpoints, Day 1 of parent study will be considered as baseline unless otherwise specified.

4.3 Safety and Tolerability Variables

Safety and tolerability will be assessed over time, based on the following evaluations:

- Vital signs
- Targeted physical examination.
- Complete ophthalmological examination (OE).
- Safety labs (serum chemistry, hematology, and urinalysis)
- Twelve-lead electrocardiograms (ECGs)

4.4 Immunogenicity Variables

- Anti-Drug Antibodies to aflibercept: occurrence, titer, and neutralizing capacity.

5. Statistical Considerations

5.1 General Considerations

- All statistical analyses and data presented (table and data listing) will be generated using SAS® version 9.4 (SAS Institute Inc., Cary, North Carolina USA). SDTM IG version 3.2 and ADaMIG Version 1.1 will be used for preparing CDISC data set.
- Statistical significance will be tested at the 5% alpha level, unless specified otherwise. A p-value less than 0.05 will be considered statistically significant.
- Continuous variables like age will be summarized by Number of subjects, mean, median, standard deviation (SD), minimum and maximum. Categorical variables like sex will be presented using Number of subjects and percentages.
- Day 1 of parent study will be considered as baseline unless otherwise specified.
- Some minor modifications may be necessary to the planned design of tables, figures, and listings to accommodate data collected during the actual study conduct.
- Data of unscheduled visits will be presented in listings only; no summary table will be provided for the same.
- Statistical Analysis Plan (SAP) will be finalized before database lock (DBL). Any further change from final SAP will be reflected in the Clinical Study Report (CSR).

5.2 Derived Variables

Below mentioned formula will be used for derivation of the respective parameters and same formula will be displayed in footnote of respective tables.

- Change from baseline = Post-Baseline value – Baseline value

- AE duration = AE End Date – AE Start Date +1
- Prior Medication = Medications taken from end of study visit (parent study) to enrollment visit in the current study will be documented as a prior medication.
- Concomitant Medication = Medications taken after the first dose of study medication in the current study will be documented as concomitant medications.
- Prior & Concomitant Medication = Medication taken from end of study visit (parent study) to enrollment visit (extension study) and ongoing/stops during the treatment period
- Compliance (%) = 100 × (Number of doses of study drug received / Number of doses of study drug expected during the study period).
- Exposure week = ((date of last dose of study drug received – date of first dose of study drug received)/365)*52.

5.3 Site Pooling

Data of all sites will be pooled together for final statistical analysis.

5.4 Reporting Precision

All outputs will be generated based on the specifications mentioned in the document of Mock TLFs.

Summary statistics will be presented to the following degree of precision:

Statistics	**Degree of Precision**
Mean, Median	One more decimal place than the raw data
Minimum and Maximum	Same as the raw data
Standard deviation	Two more decimal places than the raw data
Percentage	Two decimal places
p-value	Four decimal places or as <0.0001

Examples for the Decimal Places:

If percentage value is 0 or 100, it will be reported as ‘0’ and ‘100’ respectively.

Ratios and/or Confidence Interval (CI) will be reported as percentages with at least 2 decimal places (e.g. xx.xx, (xx.xx, xx.xx)).

Rounding of data will be followed as mentioned in below examples (if required):

Requirement	Original values	Rounded values
4 decimal points	0.07542	0.0754
2 decimal points	0.75462	0.75
1 decimal point	0.75462	0.8

5.5 Multiple Comparison/ Multiplicity

Multiple comparison/ multiplicity adjustment is not applicable for this study.

5.6 Handling of Drop out or Missing Data

Missing data will be imputed as follows: Missing post-baseline values will be imputed using the last observation carried forward (LOCF) before calculating the proportions of subjects who gained or lost letters. For the MMRM analyses, missing data will not be imputed. No imputation will also be employed for the descriptive summaries and listings.

Imputation of partial dates:

If the medication end date is missing or partially known, the following algorithm will be used to determine whether the medication is "prior or concomitant:

- The latest possible date matching the partially known date will be imputed. That is, if the year and month are known, the last day of this month will be imputed;

  E.g. If the available Date is “JAN2019” then imputed date will be “31JAN2019”.

- If the only year is known, consider minimum between last month of that year or month of participation and then the last day of the same month will be imputed.

  E.g. 1: If available Date is “2016” and date of participation is “13NOV2017” then imputed date will be “31DEC2016”.

  E.g. 2: If available Date is “2018” and date of participation is “13APR2018” then imputed date will be “31APR2018”.

- The medication will be considered as concomitant if this imputed end date is on or after the date of the first use of the study medication in the extension study.

- If end date is unknown, the medication will be considered concomitant.

- In case AE start date is missing then, “Date of enrollment” will be considered for start date.

- Additionally, if AE end date is before enrollment then AE start date will be consider "Date of ICF signed".
- If AE end date is missing then "Date of last contact" is considered for AE duration calculation.

5.7 Interim Analysis

There is no interim analysis planned for this study.

6. Statistical Analysis

6.1 Subject Disposition and Withdrawals

Frequency of following categories will be displayed:

- Number of Subjects screened
- Number of screened failure subjects
- Reason for screen failure

The following frequencies (number and percent) will be displayed by treatment for all the enrolled subjects:

- Subjects in the Safety Population
- Subjects in the FAS Population
- Subjects who completed the study
- Subjects who discontinued early, as well as reasons for subject discontinuation

The denominators for the percent calculations will be the number of all enrolled subjects.

Subjects' discontinuation status will be listed and will include subject id, Date of completion or discontinuation and specific reason for discontinuation (if reason for discontinuation will be "Lost to follow-up" then "Date of last contact" will be listed).

6.2 Demographic and Baseline Characteristics

Age, height, weight, BCVA and CRT will be summarized using descriptive statistics: number of subjects (n), mean, standard deviation, median, minimum, maximum; sex, ethnicity, race and smoking history will be presented using number of subjects(n) and percentages based on safety and FAS population. BCVA score at baseline of parent study (Day 1) and enrollment into extension study will be summarized for study eye and fellow eye. CRT score at baseline of parent study (Day 1) and enrollment into extension study will be summarized for study eye and fellow eye. Demographic and Baseline Characteristics data will also be listed.

6.3 Primary Endpoint

The primary endpoint analysis is described in Section 6.4.3.

6.4 Secondary Endpoints

6.4.1 Efficacy

The Efficacy endpoint are as follows,

- Mean change from baseline (Day 1 of parent study) in BCVA as assessed by Early Treatment Diabetic Retinopathy Study (ETDRS) letters at Week 20.
- Mean change from baseline (Day 1 of parent study) in CRT as determined by spectral-domain-optical coherence tomography (SD-OCT) at Weeks 8, 16 and 20.
- Mean change from baseline (Day 1 of parent study) in BCVA as assessed by ETDRS letters at Weeks 8 and 16.
- Proportion of subjects who gained ≥5 letters, ≥10 letters and ≥15 letters from baseline in BCVA, assessed by change from baseline (Day 1 of parent study) in ETDRS letters at Weeks 8, 16 and 20.
- Mean change in BCVA from Day 1 of extension study at Week 20.
- Mean change in CRT from Day 1 of extension study at Week 20.

Note: For all the efficacy endpoints, Day 1 of parent study will be considered as baseline unless otherwise specified.

The efficacy endpoints will be compared between the following groups:

- Subjects who switch from Eylea in parent study to MYL-1701P in extension study
- Subjects who continue on MYL-1701P

The analysis of the mean change from baseline in BCVA will be based on a mixed model repeated measures (MMRM) analysis with terms for group (switch from Eylea to MYL-1701P or continue on MYL-1701P), visit, and group by visit interaction, together with baseline BCVA as a covariate. The within subject variance-covariance matrix will be assumed to be unstructured, estimation will use restricted maximum likelihood, and the denominator degrees of freedom will use the Kenward-Roger estimate. This model will provide estimates, standard errors, and 90% two-sided CIs for the group difference at Week 8, Week 16 and Week 20.

The mean change from baseline in CRT and the mean change from Day 1 in extension study in BCVA or CRT will be analyzed in a similar manner. Covariates will be adjusted accordingly.

Sample SAS code:

[redacted]

The proportion of subjects who gained ≥ 5, 10, or 15 letters from baseline in BCVA assessed by change from baseline (Day 1 of parent study) in ETDRS letters at Weeks 8, 16 and 20 will be presented by group (switch from Eylea to MYL-1701P or Continue on MYL-1701P). For each time point, the summary table will present the number of subjects in each group, the proportions by group, the difference in proportions, and the 95% CI for the difference. These estimates will be unadjusted for covariates.

All analyses will be performed on the FAS Population and All Enrolled Population.

6.4.2 Subgroup Analyses

For mean change from baseline (Day 1 of parent study) in BCVA as assessed by ETDRS letters at Week 20, the analysis described in Section 6.4.1 will be also performed for the following subgroups (with applicable definitions in parentheses):

- Baseline (Day 1 of parent study) BCVA (73-55, 54-38)
- Age (<55, ≥55 - <65, ≥65 - <75, ≥75)
- Gender (male, female)

6.4.3 Adverse Events

TEAE: An AE will be defined as a treatment emergent adverse event (TEAE) if the first onset (or worsening, in the case of pre-existing disease) is after the first administration of MYL-1701P after enrolment visit through EOS visit of this extension study.

Listing of AEs will include subject id, AE/SOC/PT, start and end date/time, AE duration (Days), relationship to study drug, severity grade, action taken with study drug, serious/seriousness criteria, outcome, caused study discontinuation medication or treatment given for this AE.

All tables will be generated using safety population.

Adverse Events (AEs) will be coded using the Medical Dictionary for Regulatory Activities (MedDRA) dictionary Version 24.1.

6.4.3.1 Overall summary of AEs, TEAEs and SAE

Following categories will be displayed considering Adverse Event, TEAE and SAE.

- Total number of AE/TEAE/SAE (Counts only)
- Number of subjects with at least one TEAE/SAE
- Number of subjects with at least one treatment related TEAE/SAE
- Subjects discontinued due to TEAE/SAE
- Number of deaths

6.4.3.2 Summary of TEAEs by SOC, PT

Incidences of TEAE will be presented by number and percentages of subjects experience the TEAE and total number of events for SOC & PT by treatment.

If a subject has more than one occurrence of the same preferred term (PT) for an AE then the PT will be counted only once for that subject under the SOC at which it was experienced.

6.4.3.3 Summary of SAE by SOC, PT

A summary of number and percent of subjects who experienced at least one serious AE or TEAE as well as the number of events, number and percent of subjects who experienced each specific SOC and PT will be presented by treatment.

If a subject has more than one occurrence of the same preferred term (PT) for an AE then the PT will be counted only once for that subject under the SOC at which it was experienced.

6.4.3.4 Summary of SAEs and TEAE leading to discontinuation by SOC, PT

Incidences of SAEs and TEAE leading to discontinuation will be presented by number and percentages of subjects experienced SAEs, TEAE and total number of occurrence.

6.4.3.5 Summary of incidence of TEAE by relationship to study drug

All TEAE will be presented by relationship categories (i.e. Definitely, Probably, Possibly Unlikely, Unrelated/Not related) in case any adverse event observed more than once in same subject then closest relationship only will be counted once for that subject and TEAE. Table for TEAE and Serious TEAE will be presented by relationship categories, SOC and PT.

6.4.3.6 Summary of incidence of TEAE by Severity to study drug SOC and PT

All TEAE will be presented by severity categories, in case any AE observed more than once in same subject then highest severity only will be counted once for that subject and TEAE. The count and percentage for all TEAE will be presented by severity categories.

6.4.3.7 Summary of incidence of SAEs and TEAE by outcome

All SAEs and TEAE will be presented by outcome categories. Table will be presented for TEAE and Serious SAEs.

6.4.4 Vital Signs

Systolic blood pressure, diastolic blood pressure, body temperature and pulse rate will be listed and descriptively summarized (N, mean, standard deviation, minimum and maximum) by group (switch from Eylea to MYL-1701P or continue on MYL-1701P) and visit. Baseline (defined as the pre-dose value collected at Day 1 of extension study) and changes from baseline will be similarly summarized.

Listing of all vital signs data will include subject id, visit, vital signs parameters, results and interpretation.
Vital signs will be analyzed for safety population.

6.4.5 Laboratory Parameters

Descriptive summaries of observed values and change from baseline (defined as the value collected at the screening visit in the extension study) will be presented for clinical laboratory evaluations (serum chemistry and hematology) by group. Assessments of laboratory variables according to clinical relevance will be tabulated by visit and group (switch from Eylea to MYL-1701P or continue on MYL-1701P) for each clinical laboratory parameter in frequency tables. Additionally, for each laboratory parameter, shifts in value from baseline to all post-baseline visits will be presented by group in shift tables.

The assessment of categorical urinalysis variables will be tabulated by visit for each urine parameter by group (switch from Eylea to MYL-1701P or continue on MYL-1701P) in frequency tables. Additionally, for each of the urine parameters, shifts in assessments from baseline (defined as the value collected at the screening visit in the extension study) to all post-baseline visits will be presented for each group in shift tables.

All laboratory parameters will be listed by visit (if applicable) with appropriate date of examinations /time of collection, units, reference range, and results.

6.4.6 Physical examination

Physical examination performed throughout the study will be listed. Listing will include subject id, visit, examination performed, date of physical examination, body systems and interpretation.

6.4.7 Ophthalmological examination

Ophthalmological examination (slit lamp examination, indirect ophthalmoscopy and intraocular pressure measurement) performed throughout the study will be summarized and listings will be

provided. Listing will include subject id, visit, date and time of ophthalmological examination, eye, category and result.

6.4.8 12-lead electrocardiograms (ECGs)

ECG data; QT, QTc (Fridericia's), heart rate (HR), QRS duration, PR and RR interval will be listed and descriptively summarized (N, mean, standard deviation, minimum and maximum) by group (switch from Eylea to MYL-1701P or continue on MYL-1701P) and visit. Listing will include subject id, visit, method of ECG, date and time of ECG performed, parameters, and interpretation.

6.5 Immunogenicity

Occurrence, titer, and neutralizing capacity of ADA will be summarized by count and percentage at each scheduled sampling time.
Listing of Immunogenicity will be presented. Listing will include subject id, visit, date/time of sample collection, number of blood sample collected and kit number.

6.6 Exposure Duration and Treatment Compliance

There are in total 3 doses of the study drug (intravitreal injection) planned (expected) for this study. The number of doses of the study drug (intravitreal injection) received and missed are summarized using frequency and percentage. Exposure week and compliance are summarized using summary statistics. The exposure week and compliance will be calculated as below:
Compliance (%) = 100 × (Number of doses of study drug received / Number of doses of study drug expected during the study period).
Exposure week = ((date of last dose of study drug received – date of first dose of study drug received)/365)*52.

6.7 COVID - 19 related assessment

The number of subjects with missed or delayed visits and the reason for the miss or delay will be summarized by visit.

6.8 Protocol Deviation (PD)

The PDs will be classified as 'Major' and 'Minor ' in Clinical Trial Management System depending on the severity of deviation.

The list of major PDs will be finalized prior to DBL. All PDs, including major PD, will be reviewed by DM and study team throughout the conduct of the study in accordance with study deviation rules document.

A list of all PDs will be produced. A summary of PDs will also be produced as frequency and percentages. In tables and listings, major protocol deviations will be referred to as 'key/important' protocol deviations and minor protocol deviations as 'non-key/unimportant' protocol deviations.

6.9 Medical, Surgical, Ophthalmic and Smoking History

Medical history will include surgical, ophthalmic and smoking history. Medical, surgical, ophthalmic and smoking history, and current medical conditions and medications will be listed by subject and coded using the MedDRA (version 24.1) and will be summarized.

Listing of medical history will include the parameters subject id, medical and surgical term, start and end date of the term, ongoing and medication ongoing of the term.

6.10 Prior and Concomitant Medication

Any medication other than study drug, either prescription drug or OTC will be treated as a concomitant medication.

Medication/Therapy and indication code terms will be coded to preferred name and anatomical therapeutic chemical (ATC) classification of ingredients using the WHO-Drug Global (Version Sep 2020).

Listing of medication will include subject id, visit, Medication name or therapy, Indication, Frequency, Route of administration, Dose, Start and End dates (wherever applicable), Study day and Categorization of the medication(prior/concomitant medication)
Identifications of prior and concomitant medications are explained in the derived section.

7. Summary of analyses

Endpoint(s)	Analyses	Population(s)
Primary Endpoint: Incidence of treatment emergent adverse events (TEAEs)	• Frequency (n) & Percentage (%)	Safety Population
Secondary Endpoints: Mean change from baseline (Day 1 of parent study) in BCVA as assessed by Early	• Summary Statistics • MMRM & 90 % CI	FAS Population and All enrolled population.

Endpoint(s)	Analyses	Population(s)
Treatment Diabetic Retinopathy Study (ETDRS) letters at Week 20		
Proportion of subjects who gained ≥5 letters, ≥10 letters and ≥15 letters from baseline in BCVA, assessed by change from baseline (Day 1 of parent study) in ETDRS letters at Weeks 8, 16 and 20	• Frequency (n), Percentage (%) • 95 % CI •	FAS population and All enrolled population.
Other Secondary Efficacy Endpoints	• Summary Statistics • 90% CI (Using MMRM)	FAS Population and All enrolled population.
<u>Safety Variables:</u> Adverse events Twelve-lead electrocardiograms	• Frequency (n), Event (e) & Percentage (%) • Frequency (n) & Percentage (%) • Summary Statistics	Safety Population
Laboratory parameters, Vital signs, Disposition	• Summary Statistics • Frequency (%)	Safety Population
Disposition	• Frequency (%)	All screen subject.
Demographic and Baseline characteristics	• Summary Statistics, • Frequency (%)	FAS Population, Safety Population and All enrolled population.

8. Data management considerations

All data collected in the Case Report Forms (CRFs) will be entered into the clinical study database using validated Code Angelo Version 2.0. Prior to performing the analyses, a series of Validation checks will be performed to identify missing data, inconsistent data and errors in the database. PDs will be identified. All reported AEs and MH will be coded to standard 'Preferred terms' and

'System Organ Class' using the Medical Dictionary for Regulatory Activities (MedDRA) version 24.1. Concomitant medications will be coded using the WHO-Drug Global (Version Sep 2020) dictionary.

After all data issues are resolved and updated in the database, PDs identified, AEs, MH and CM are coded, the database will be locked. All requests to modify the database after treatment assignment is added, will require the written approval of the sponsor, statistician and medical monitor responsible for the study.

9. Tables, Listings

The TLs shells for this study are provided in a separate document "SAP Mock TLs". These shells may not be reflective of every aspect of this study but are intended to show the general layout of the Tables and Listings that will be included in the final report.

TLs are numbered following the ICH E3 "Structure and Content of Clinical Study Report".

10. References

- ICH E3: Structure and Content of Clinical Study Reports, July 1996, CPMP.
- ICH E9: Statistical Principles for Clinical Trials, September 1998, CPMP.
- FDA Guidance on Conduct of Clinical Trials of Medical Products during COVID-19 Pandemic: Guidance for Industry, Investigators, and Institutional Review Boards, 27 March 2020
- New Drugs and Clinical Trials Rules, 2019 (Ministry of Health and Family Welfare, Notification, New Delhi, the 19th Mar, 2019).

11. Appendix

Not Applicable