Short Title

Summary Report for Protocol ILJ466-P003

Long Title

Summary Report: Protocol Post-Market Clinical Investigation of the Clareon® IOL—1 Year Interim Analysis

TITLE PAGE

Operations Unit Number / Name:	96 / Clinical Science
Name of Test Article/ Investigational Product:	Clareon aspheric hydrophobic acrylic monofocal intraocular lens (IOL) Model SY60WF; hereafter referred to as Clareon IOL
Indication Studied/Supported:	This IOL is intended for primary implantation in the capsular bag in the posterior chamber for the visual correction of aphakia secondary to removal of a cataractous lens in adult subjects.
Study Description:	This is a prospective, multicenter, single-arm trial assessing the long-term (3-year) safety and effectiveness of the Clareon IOL in approximately 200 bilaterally implanted adults (≥ 22 years of age) who required bilateral cataract extraction and who met study entry criteria. Subjects will attend 12 study visits (9 post-implantation) over approximately 36 months. The primary objective is to demonstrate the long-term (3 years) favorable visual acuity and adverse event outcomes of the Clareon IOL, and one-year visual acuity and adverse event outcomes are compared to historical SPE rates as reported in EN ISO 11979-7:2014. Interim analyses will be conducted at completion of Visit 4A (Day 120-180 post-implantation from second eye surgery), Visit 5A (Day 330-420 post-implantation from second eye surgery), and Visit 6A (Day 630-780 post-implantation from second eye surgery) in support of the study publication plan.
Name of Sponsor:	Alcon Research, LLC 6201 South Freeway Fort Worth, Texas 76134-2099
Development Phase of Study:	Postmarket

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Approvals:	See last page for electronic approvals.

1 ABBREVIATIONS

Abbreviation	Definition
AAS	All-Implanted Analysis Set
ACD	Anterior chamber depth
ADE	Adverse device effect
AE	Adverse event
BAS	Best-Case Analysis Set
BCDVA	Best corrected distance visual acuity
D	Diopter
DFU	Directions for Use
EN	European Standard
HEMA	2-hydroxyethyl methacrylate
IOL	Intraocular lens
IOP	Intraocular pressure
ISO	International Organization for Standardization
IV	Intravenous
LogMAR	Logarithm of the minimum angle of resolution
LSMean	Least Squares Mean
MRSE	Manifest refraction spherical equivalent
NCS	Not clinically significant
Nd:YAG	Neodymium-doped yttrium aluminum garnet
OD	Right eye
OS	Left eye
OU	Both eyes
PC	Posterior capsulotomy
PCO	Posterior capsule opacification
PT	Preferred term
SAE	Serious adverse event
SAP	Statistical Analysis Plan
SEM	Standard error of the mean
SPE	Safety and Performance Endpoint
UCDVA	Uncorrected distance visual acuity
VA	Visual acuity

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3 SUMMARY

The following report describes clinical outcomes of a 1-year interim analysis of a currently ongoing postmarket clinical investigation of the Clareon IOL.

4 INTRODUCTION

The rationale to conduct this postmarket study is to provide long-term (3 years) safety and effectiveness data on the Clareon IOL in support of Market Access requirements including the development of a product value dossier.

As per the study design, interim analyses will be conducted at completion of Visit 4A (Day 120-180 post-implantation from second eye surgery, TDOC-0056500), Visit 5A (Day 330-420 post-implantation from second eye surgery), and Visit 6A (Day 630-780 post-implantation from second eye surgery) in support of the study publication plan. Final data analysis will be conducted at study completion.

At this time, all continuing subjects have completed Visit 5A (Day 330-420 post-implantation from second eye surgery). This summary report includes the interim analysis of data collected at Visit 5A, and one-year visual acuity and adverse event outcomes compared to historical SPE rates as reported in EN ISO 11979-7:2014.

The study is ongoing.

5 METHODS

5.1 Study Design

This prospective, multicenter, single-arm study includes adults (≥ 22 years of age) who required bilateral cataract extraction and who met study entry criteria. Subjects will attend a total of 12 study visits over a period of approximately 36 months. Of these 12 visits, 1 is a preoperative screening visit (Visit 0) and 2 are operative visits (Visit 00 and Visit 00A). The remaining 9 visits are post-implantation visits (Visits 1-7A), which will occur at the following intervals: Visit 1 and Visit 1A (Day 1-2 post-implantation, first and second eye), Visit 2 and 2A (Day 7-14 post-implantation, first and second eye), Visit 3A (Day 30-45 post-implantation from second eye surgery), Visit 4A (Day 120-180 post-implantation from second eye surgery), Visit 5A (Day 330-420 post-implantation from second eye surgery), Visit 6A (Day 630-780 post-implantation from second eye surgery), and Visit 7A (Day 990-1140 post-implantation from second eye surgery). Visit day calculations for Visits 1 and 2 are based off of the day of the first eye surgery (Visit 00) and calculations for Visits 1A-7A are

based off of the day of second eye surgery (Visit 00A). Unscheduled visits may be conducted if needed for medical attention and safety follow-up.

Primary endpoint data were collected at Visit 5A (330-420 days post-implantation from second eye surgery), and secondary endpoint data will be collected at Visit 5A (330-420 days post-implantation from second eye surgery), Visit 6A (630-780 days post-implantation from second eye surgery), and Visit 7A (990-1140 days post-implantation from second eye surgery). The study will be considered successful if the data at Visit 5A indicate a favorable outcome in relation to the SPE rates for subjects with BCDVA of 0.3 logMAR or better as reported in EN ISO 11979-7:2014.

As per the study design, this interim analysis was conducted at the completion of Visit 5A (Day 330-420 post-implantation from second eye surgery).

Refer to the study protocol for specific methodological details.

5.2 Analysis Plan

5.2.1 Analysis Data Sets

The primary analysis set for effectiveness analyses is the All-Implanted Analysis Set (AAS). The AAS includes all eyes with successful test article implantation. Additional supportive analyses may be conducted using the Best-Case Analysis Set (BAS). BAS includes all eyes successfully implanted with the test article that had:

- at least 1 postoperative visit;
- no preoperative ocular pathology;
- no macular degeneration detected at any time; and
- no previous surgery for the correction of refractive errors.

The Safety Analysis Set includes all eyes with attempted implantation with the test article (successful or aborted after contact with the eye) and is used for the safety analyses.

5.2.2 Interim Analyses

All effectiveness and safety endpoints available at Visit 5A (Day 330-420 post-implantation from second eye surgery) are analyzed as defined in the Statistical Analysis Plan (SAP) (See Section 9.3).

5.2.3 Changes to the Planned Analysis

A clinical verification of the IOL A-constant at Visit 4A (Day 120-180 post-implantation from second eye surgery) was summarized descriptively, and the LSmean for the calculation of the lens power constant using a random effect model was determined. The clinical verification of the IOL A-constant analysis was not part of the planned analysis.

The primary objective was amended to clarify that the comparison of visual acuity and adverse events rates to historical safety and performance endpoint (SPE) rates as reported in EN ISO 11979-7:2014 was to be evaluated at the completion of Visit 5A instead of Visit 7A. Thus, a one-sided exact 95% lower confidence limit for incidence rates observed up to one year of follow-up (ie, after all implanted subjects have completed Visit 5A) was compared to the cumulative and persistent adverse event SPE rates in EN ISO 11979-7:2014. The reason for this amendment was that although study follow-up will continue until Visit 7A is completed for all subjects, the comparison with SPE rates will only be performed at Visit 5A, as the SPE rates in EN ISO 11979-7:2014 were developed from 1-year post-op clinical investigations (ie, the SPE rates are not appropriate for studies with greater than one year of follow up).

There were no other changes to the planned analysis.

6 RESULTS

6.1 Study Subjects

Additional conduct tables and listings are located in Appendix 9, Section 9.1.1.

6.1.1 Disposition of Subjects

A total of 245 subjects were enrolled and 215 subjects were implanted (Table 6-1). Twenty-nine subjects did not meet entry criteria, and 1 subject discontinued due to “other reason” at Visit 00 due to an exclusion at the time of surgery (capsular tear). Of the 215 subjects implanted, 209 subjects were implanted bilaterally; of the 6 subjects implanted in the first eye only, 1 subject (6681.00017) discontinued due to death, 4 subjects (7215.00001, 7926.00002, 7926.00003, and 7926.00007) withdrew, and 1 subject (6441.00004) was re-assessed at the time of surgery and the IOL power for the second eye was no longer within range for the study (Listing 16-2 and Table 9-7). Subject 6441.00004 is continuing in the study for assessments on the first eye only (Table 9-7). Five subjects bilaterally implanted have discontinued due to death, resulting in a total of 10 subjects who have discontinued since implantation in at least one eye. In total, 205 subjects are ongoing.

Of the 215 first eyes and 209 second eyes implanted, total of 199 first eyes (92.6%) and 198 second eyes (94.7%) were available for the 1-year interim analysis (Table 6-2 and Table 6-3). Two subjects, 7813.00011 and 7813.00016, who were last seen at 1 month died by 6 months, and were not "Discontinued" until 1 year. Of the 6 subjects who only had the first eye implanted, 5 subjects discontinued prior to the 1-month visit (6681.00017, 7215.00001, 7926.00002, 7926.00003, and 7926.00007), and 1 subject (6441.00004) is continuing and attended the 1-year visit.

The number of subjects by Investigator is presented in Table 10-17 (All-Implanted), Table 10-18 (Best-Case Analysis Set), and Table 10-19 (Safety Analysis Set). At the 1-year visit, 1 subject developed macular degeneration and was excluded from the Best-Case Analysis Set (Listing 16-7).

Additional disposition details can be found in a listing of subjects with screen failures (Listing 16-1) and a listing of subjects discontinued from the study (Listing 16-2).

Table 6-1 Subject Disposition (All Enrolled Subjects)

	n	(%)
Total enrolled	245	
Discontinued Prior to Attempted Implantation	30	
Screen Failure	29	
Other Reason	1	
Attempted Implantation	215	
Successful Implantation	215	(100.0)
Completed Study	0	(0.0)
Discontinued After Attempted Implantation	10	(4.7)
Adverse Event	1	(0.5)
Death	5	(2.3)
Withdrawal by Subject	4	(1.9)

Total enrolled = Total number of subjects consented.
All percentages are based on the number of subjects with attempted implantation
Discontinuation prior to attempted implantation will comprise screen failure and other reasons for discontinuation
Completed the study indicated by Subject Status on CRF Subject Derivations

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Table 6-2 Subject Status Summary, First Eye (All-Implanted Analysis Set)

Subject Status	N	1 Day n (%)	1 Week n (%)	1 Month n (%)	6 Months n (%)	1 Year n (%)	2 Years n (%)	3 Years n (%)
	215							
Available for Analysis		215 (100.0)	214 (99.5)	207 (96.3)	201 (93.5)	199 (92.6)	0 (0.0)	0 (0.0)
Missing Subjects								
Discontinued		0 (0.0)	1 (0.5)	5 (2.3)	6 (2.8)	9 (4.2)	10 (4.7)	10 (4.7)
Missed Visit		0 (0.0)	0 (0.0)	3 (1.4)	8 (3.7)	7 (3.3)	0 (0.0)	0 (0.0)
Lost to Follow-up		0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Active		0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	205 (95.3)	205 (95.3)
Percent Accountability		(100.0)	(100.0)	(98.6)	(96.2)	(96.6)	(0.0)	(0.0)

Available for Analysis = represents the total number of subjects for whom data are available at the form.
Discontinued = subjects that have discontinued study or treatment prior to the visit
Active = subjects that have not reached the time associated with the visit
Lost to follow-up = subjects that have missed the visit and there is no information available about them
Discontinued and lost to follow-up are cumulative at the visit, other values are not
Percent Accountability = Available for Analysis / (N - Discontinued - Active) x 100

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Table 6-3 Subject Status Summary, Second Eye (All-Implanted Analysis Set)

Subject Status	N	1 Day n (%)	1 Week n (%)	1 Month n (%)	6 Months n (%)	1 Year n (%)	2 Years n (%)	3 Years n (%)
	209							
Available for Analysis		209 (100.0)	204 (97.6)	206 (98.6)	200 (95.7)	198 (94.7)	0 (0.0)	0 (0.0)
Missing Subjects								
Discontinued		0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)	4 (1.9)	5 (2.4)	5 (2.4)
Missed Visit		0 (0.0)	5 (2.4)	3 (1.4)	8 (3.8)	7 (3.3)	0 (0.0)	0 (0.0)
Lost to Follow-up		0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

Subject Status	N	1 Day n (%)	1 Week n (%)	1 Month n (%)	6 Months n (%)	1 Year n (%)	2 Years n (%)	3 Years n (%)
Active		0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	204 (97.6)	204 (97.6)
Percent Accountability		(100.0)	(97.6)	(98.6)	(96.2)	(96.6)	(0.0)	(0.0)

Available for Analysis = represents the total number of subjects for whom data are available at the form
Discontinued = subjects that have discontinued study or treatment prior to the visit
Active = subjects that have not reached the time associated with the visit
Lost to follow-up = subjects that have missed the visit and there is no information available about them
Discontinued and lost to follow-up are cumulative at the visit, other values are not
Percent Accountability = Available for Analysis / (N - Discontinued - Active) x 100

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6.1.2 Protocol Compliance

Protocol deviations continue to be documented throughout the study and are evaluated to assess any potential impact on the study data. Protocol deviations were categorized as related to visual acuity, out of window visit, and "other." Listings of all protocol deviations, including the subject number and the description of the deviation are included in Section 9.4.

The protocol deviations did not result in exclusion from any analysis set.

The following description is a cumulative assessment.

There were 30 deviations related to VA measurement, with deviations related to the VA ETDRS Fast Method being most prevalent and only observed at 2 sites (sites 2203 and 2764). There were 6 deviations reported for BCDVA and 24 deviations reported for UCDVA (Table 9-5).

The Fast ETDRS testing method used in this trial prescribes specific rules for determining where the Investigator needs to instruct the subject to begin reading letters on the ETDRS VA chart for testing. Specifically, the test starts when a subject correctly identifies all 5 letters on a single row and testing stops when 3 or more letters on a row are incorrectly identified.

The Fast ETDRS Method deviations related to errors in *identifying the starting row* (n = 13) were determined to have a negligible impact on VA scores since the Fast Method assumes that any missed letters above the threshold region are false negatives and do not impact the final VA score (Camparini 2001). Site 2203 accounted for the majority of starting row deviations. Additionally, the majority of these deviations affected UCDVA testing (11/13) while the remaining (2/13) affecting BCDVA testing.

Fast ETDRS Method deviations related to errors *when the testing should have continued* (n = 6) resulted in potential underestimation of final VA score (ie VA score reported was worse than the true VA score, resulting in an underestimation of VA performance). All 6 deviations affected UCDVA and none affected BCDVA.

There were 56 protocol deviations related to out of window visit (Table 9-6).

There were 211 deviations considered "other," with the most prevalent related to missed assessment (Table 9-7). The majority of these deviations (48%) were related to a number of sites not been able to record ACD postoperatively at Visits 3A, 4A, or 5A. On further discussion with the sites, it was discovered that certain models of the study biometers are not able to detect the anterior surface of the Clareon IOL, which is a parameter needed by these commercial biometers to assess postoperative ACD. This effect is currently believed to be attributed to the low level of surface haze characteristics of the Clareon IOL that results in the anterior surface of the lens to appear "invisible" to the observer/instrument as compared with other monofocal IOLs.

Nine subjects did not meet inclusion criterion requiring at least 1 eye to have BCDVA worse than 0.20 logMAR, and 4 eyes did not have an IOL implanted that was within the defined parameter of ± 0.5 D spherical equivalent for emmetropia.

6.1.3 Demographics and Other Baseline Characteristics

Demographics for all implanted subjects are summarized in Table 6-4. Demographics by site, for sites with ≥ 10 subjects in the AAS, are presented in Table 10-8a to Table 10-8k.

Baseline characteristics for all implanted first eyes and second eyes are summarized in Table 6-5 and Table 6-6, respectively. Baseline characteristics by site are presented for the first eye in Table 10-11a to Table 10-11k and for the second eye in Table 10-12a to Table 10-12k.

Table 6-4 Demographic Statistics (All-Implanted Analysis Set)

Parameter	(N = 215)
Age (Years), n (%)	
<65	34 (15.8)
≥65	181 (84.2)
Mean (SD)	72.1 (8.07)
Median	72.0
(Min, Max)	(45, 89)
Sex, n (%)	
Female	126 (58.6)
Male	89 (41.4)
Unknown	0 (0.0)
Undifferentiated	0 (0.0)
Race, n (%)	
White	204 (94.9)
Black or African American	3 (1.4)
American Indian or Alaska Native	0 (0.0)
Asian	6 (2.8)
Native Hawaiian or Other Pacific Islander	1 (0.5)
Multi-Racial	0 (0.0)
Other	1 (0.5)
Ethnicity, n (%)	
Hispanic or Latino	17 (7.9)
Not Hispanic or Latino	195 (90.7)
Not Reported	3 (1.4)
Unknown	0 (0.0)

N = Number of subjects in treatment group
n = Number of subjects in specified category
Percentages are calculated as (n/N) * 100
SD = Standard deviation
Min = Minimum
Max = Maximum

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Table 6-5 Baseline Characteristics, First Eye (All-Implanted Analysis Set)

	N = 215
Best Corrected Distance VA (logMAR)	
n	215
Mean (SD)	0.397 (0.2182)
Median	0.34
(Min, Max)	(0.00, 1.70)
Uncorrected Distance VA (logMAR)	
n	215
Mean (SD)	0.690 (0.3133)
Median	0.64
(Min, Max)	(0.12, 1.70)
Intraocular Pressure (mmHg)	
n	214
Mean (SD)	14.977 (2.7874)
Median	15.00
(Min, Max)	(6.00, 23.00)
Axial Length (mm)	
n	215
Mean (SD)	23.556 (0.8661)
Median	23.51
(Min, Max)	(21.30, 26.03)
Axial Length Category	
Total	215
Short (<21 mm)	0 (0.0)
Medium (21-26 mm)	214 (99.5)
Long (>26 mm)	1 (0.5)
Anterior Chamber Depth (mm)	
n	212
Mean (SD)	3.140 (0.3899)
Median	3.12

	N = 215
(Min, Max)	(2.14, 4.32)
Corneal astigmatism = abs (K1-K2)	
n	214
Mean (SD)	0.765 (0.4757)
Median	0.68
(Min, Max)	(0.00, 2.83)

N = Number of subjects in treatment group
n = Number of subjects in specified category
Percentages are calculated as (n/N) * 100
SD = Standard deviation
Min = Minimum
Max = Maximum
VA = Visual acuity
Baseline = Preoperative

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Table 6-6 Baseline Characteristics, Second Eye (All-Implanted Analysis Set)

	N = 209
Best Corrected Distance VA (logMAR)	
n	209
Mean (SD)	0.237 (0.1365)
Median	0.24
(Min, Max)	(-0.14, 0.72)
Uncorrected Distance VA (logMAR)	
n	209
Mean (SD)	0.534 (0.2604)
Median	0.50
(Min, Max)	(0.00, 1.30)
Intraocular Pressure (mmHg)	
n	208
Mean (SD)	15.284 (2.7839)
Median	15.00
(Min, Max)	(6.00, 23.00)
Axial Length (mm)	
n	209
Mean (SD)	23.517 (0.8298)
Median	23.43
(Min, Max)	(21.36, 25.82)
Axial Length Category	
Total	209
Short (<21 mm)	0 (0.0)
Medium (21-26 mm)	209 (100.0)
Long (>26 mm)	0 (0.0)
Anterior Chamber Depth (mm)	
n	206
Mean (SD)	3.117 (0.3693)
Median	3.12

	N = 209
(Min, Max)	(2.07, 4.33)
Corneal astigmatism = abs (K1-K2)	
n	209
Mean (SD)	0.729 (0.4545)
Median	0.63
(Min, Max)	(0.00, 2.43)

N = Number of subjects in treatment group
n = Number of subjects in specified category
Percentages are calculated as (n/N) * 100
SD = Standard deviation
Min = Minimum
Max = Maximum
VA = Visual acuity
Baseline = Preoperative

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6.2 Analysis of Effectiveness

Additional effectiveness tables and listings are located in Appendix 9, Section 9.1.2.

6.2.1 BCDVA of 0.3 logMAR or better

The primary effectiveness endpoint of this study is to evaluate the 1-year favorable visual acuity of the Clareon IOL compared to historical SPE rates as reported in EN ISO 11979-7:2014.

A total of 99.5% of first eyes (197/198 eyes) and 99.5% (197/198 eyes) of second eyes had 0.3 logMAR or better monocular BCDVA at 1 year (Table 6-7 and Table 6-8).

Two eyes (Subject 1696.00006 OD and Subject 6681.00014 OS) failed to achieve BCDVA of 0.3 logMAR or better at 1 year (Table 6-9). Subject 1696.00006 had a loss of 2 lines in the second eye and the event was reported as an AE, but the site was unable to provide a definitive explanation for the VA decrease based on the clinical findings at the visit. The Investigator thought that perhaps conjunctivochalasis (which was present at baseline) could have influenced the decrease in VA (Section 6.2.2). Subject 6681.00014 had multiple vitrectomies in the first eye due to retinal detachment and these SAEs are detailed in Section 6.3.3.1.

Table 6-7 Post-operative Monocular BCDVA of 0.3 logMAR or Better at 1 Year, First Eye (All-Implanted Analysis Set and Best-Case Analysis Set)

Analysis Set		Category	n	%	2-Sided 95% CI	1-Sided 95% Upper CL	SPE rate
All-Implanted Analysis Set	(N = 215)	Total	198				
		0.3 logMAR or better	197	99.5	(97.2, 100.0)	100.0	92.5
Best-Case Analysis Set	(N = 214)	Total	197				
		0.3 logMAR or better	196	99.5	(97.2, 100.0)	100.0	96.7

CL = Confidence Limit
Total = Number of eyes with data
N = Number of eyes in treatment group. n = Number of eyes in specified category.
Percentages are calculated as (n/Total) * 100
SPE = Safety and Performance Endpoint
BCDVA = Best corrected distance visual acuity

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Table 6-8 Post-operative Monocular BCDVA of 0.3 logMAR or Better at 1 Year, Second Eye (All-Implanted Analysis Set and Best-Case Analysis Set)

Analysis Set		Category	n	%	2-Sided 95% CI	1-Sided 95% Upper CL	SPE rate
All-Implanted Analysis Set	(N = 209)	Total	198				
		0.3 logMAR or better	197	99.5	(97.2, 100.0)	100.0	92.5
Best-Case Analysis Set	(N = 209)	Total	198				
		0.3 logMAR or better	197	99.5	(97.2, 100.0)	100.0	96.7

CL = Confidence Limit
Total = Number of eyes with data
N = Number of eyes in treatment group. n = Number of eyes in specified category.
Percentages are calculated as (n/Total) * 100
SPE = Safety and Performance Endpoint
BCDVA = Best corrected distance visual acuity

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Table 6-9 Listing of Monocular Visual Acuity (logMAR) for Eyes Failed to Achieve BCDVA of 0.3 logMAR or Better at 1 Year (All-Implanted Analysis Set)

Subject	Age (y)/Sex	Surgery Eye	Eye	Visit	Days from Surgery	BCDVA
1696.00006	83/M	2nd	OD	Preoperative	-31	0.22
				1 Week	8	0.34
				1 Month	43	0.28
				6 Months	127	0.14
				1 Year	393	0.36
6681.00014	70/F	1st	OS	Preoperative	-10	0.30
				1 Week	7	0.10
				1 Month	71	1.70
				6 Months	142	0.52
				1 Year	381	0.54

BCDVA = Best Corrected Distance Visual Acuity at 4 m
OD = Right eye; OS = Left eye
Surgery was Day 0

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6.2.2 BCDVA

Descriptive statistics for BCDVA are shown in Table 6-10 for the first eye and Table 6-11 for the second eye. Descriptive statistics for BCDVA by site, for sites with ≥ 10 subjects in the AAS, are presented for the first eye in Table 11-9a to Table 11-9k and for the second eye in Table 11-10a to Table 11-10k.Categorical statistics for BCDVA in logMAR are shown in Table 11-21 for the first eye and Table 11-22 for the second eye.

Categorical statistics for BCDVA in Snellen are provided in Table 11-29 for the first eye and Table 11-30 for the second eye.

At the time of writing this report, the study team discovered 2 cases (Subject 7813.00005 and Subject 7813.00015) in which the BCDVA scores captured in the database were incorrect. BCDVA scores for Subject 7813.00005 were incorrectly captured for OU at Visit 5A, and for Subject 7813.00015 at Visit 2A, first eye only. In both cases, the recorded visual acuity scores were recorded as: -0.01 logMAR (ie, a score equal to half a letter) instead of -0.10 logMAR

(a full line score). The study team determined that there is no negative impact to the 1-year safety and efficacy results of the Clareon IOL described in this interim report, and thus unlocking the database to re-run the 1-year interim analysis was not warranted. The study team has worked with the investigator at Site 7813 to make the corrections in the database but the BCDVA tables in this interim report will continue to reflect the incorrect values for Visit 5A. These tables will be updated with the corrected values at the time of the 2-year interim analysis.

Loss of 10 letters or more compared with best postoperative BCDVA at any time during the study occurred in 17 first eyes and 13 second eyes (Table 6-12 and Table 6-13); details are provided in Table 6-14.

- Subject 1696.00006 (second eye) – The investigator assessed the decrease (BCDVA 0.36 logMAR) as NCS at Visit 5 and indicated that perhaps conjunctivochalasis (which was present at baseline) could have influenced the result. However, the investigator reported the decrease in VA as an AE since the loss was not well explained.
- Subject 1793.00001 (second eye) – BCVA was -0.10 logMAR at Visit 3 and 0.12 logMAR at Visit 5. There are no AEs or clinical findings to explain the change.
- Subject 4526.00014 (first eye) – The first eye had macular edema with an onset at Visit 3 (0.46 logMAR) and lasted for approximately 6 weeks. The loss of 10 letters resolved by Visit 4.
- Subject 5956.00007 (second eye) – Site attributed the loss of 10 letters of BCVA at Visit 3 (0.06 logMAR) as possibly due to a headache, which lasted 5 months (3 Aug 2018 – 30 Jan 2019). The patient also experienced negative dysphotopsia from surgery until Visit 5. The loss of VA resolved by 6 months.
- Subject 5956.00008 (second eye) – Subject has died; there was no AE per the Investigator for the VA decrease (0.1 logMAR) patient had no complaints.
- Subject 6441.00012 (first eye) – BCVA was -0.20 logMAR at Visit 3 and Visit 4, and 0.02 logMAR at Visit 5. The decrease in VA was considered NCS at Visit 5 per the Investigator.
- Subject 6660.00010 (second eye) –BCVA was -0.08 logMAR at Visit 2 and 0.12 logMAR at Visit 5. The site was queried at Visit 5 but the query response did not adequately address question of decreased VA. The occurrence was not reported as an AE.

- Subject 6681.00006 (second eye) – BCVA was 0.04 logMAR at Visit 2A and 0.24 logMAR at Visit 3A, and resolved to 0.00 logMAR at Visit 4A. The investigator did not provide any reason clinically to explain the decrease in VA and did not assess the change as meeting the definition of an AE. Clinically non-significant PCO was the only finding reported at Visit 3A.
- Subject 6681.00010 (first eye) – No AEs were reported. A decrease of greater than 2 lines at Visit 4 compared to Visit 2 was noted. At Visit 5, the BCVA decrease had resolved and BCVA was 0.00 logMAR. The eye had clinically nonsignificant PCO.
- Subject 6681.00014 (first eye) – The subject had multiple vitrectomies. The Sponsor considered the loss of 10 letters (0.54 logMAR) clinically significant.
- Subject 6681.00018 (first eye) – BCVA decreased between Visit 3 (0.00 logMAR) and Visit 4 (0.20 logMAR), then was 0.10 logMAR at Visit 5. The decrease in VA was considered NCS at Visit 4 per the Investigator.
- Subject 6681.00019 (first eye) – BCVA was 0.00 logMAR at Visit 3 and 0.22 logMAR at Visit 5. AE was reported for decreased tear break-up, and the subject was prescribed treatment for the condition.
- Subject 7215.00002 (first eye) – There was a 2-line logMAR decrease in BCVA at Visit 5 (0.12 logMAR) compared to Visit 3 (-0.08 logMAR). There were no clinical findings noted on the Visit 5 exams and no AEs have been reported by the investigator.
- Subject 7813.00005 (first and second eye) – The loss of 10 letters (0.16 logMAR and 0.28 logMAR) was attributed to uveitis OU, which was resolved at Visit 4.
- Subject 7813.00006 (first eye) – BCVA was -0.02 logMAR at Visit 2 and was 0.20 logMAR at Visit 5. The VA change was not commented on by the investigator, and no AE was reported.
- Subject 7813.00009 (first and second eye) – BCVA decreased from Visit 2 to Visit 3 (0.16 logMAR), and BCVA at Visit 4 and Visit 5 (0.20 logMAR) remained within 2 letters of BCVA at Visit 3. The VA change OU was considered NCS per the Investigator's assessment at Visit 3.
- Subject 7813.00016 (first eye) – The subject died. The Investigator assessed the loss in VA (0.20 logMAR) at Visit 3 as NCS.
- Subject 7813.00018 (first eye and second) – The first eye had BCVA -0.10 at Visit 4 and 0.20 logMAR at Visit 5. The second eye had BCVA -0.10 logMAR at Visit 3 and 0.30 logMAR at Visit 5. The subject has developed clinically significant PCO OU.

- Subject 7813.00019 (first eye and second eye) – The first eye had BCVA 0.00 logMAR at Visit 3 and 0.30 logMAR at Visit 4 and Visit 5. The second eye had BCVA 0.00 logMAR at Visit 3 and 0.20 logMAR at Visit 4 and Visit 5. Subject has lid margin disease OU.
- Subject 7813.00020 (first eye and second eye) – The first eye had BCVA 0.00 logMAR at Visit 2, 0.20 logMAR at Visit 4, and 0.00 logMAR at Visit 5. The second eye had BCVA 0.00 logMAR at Visit 4 and 0.20 logMAR at Visit 5. The loss in VA was associated with the AE of Adie's pupil in the first eye. The decrease in second eye was assessed as NCS per the Investigator, with a comment that the cause is unknown.
- Subject 7813.0027 (first eye) – BCVA was -0.10 logMAR at Visit 4 and 0.18 logMAR at Visit 5. Subject has developed macular degeneration OD.
- Subject 7925.00001 (first eye) – BCVA was 0.02 logMAR at Visit 4 and 0.22 logMAR at Visit 5. The decrease in VA was assessed as NCS per the Investigator.
- Subject 7936.00001 (second eye) – BCVA was -0.18 logMAR at Visit 2 and 0.06 logMAR at Visit 3. The decrease in VA was considered NCS per the Investigator and was resolved at Visit 4.
- Subject 7936.00003 (first eye) – BCVA was -0.28 logMAR at Visit 2 and -0.06 logMAR at Visit 4. At Visit 5, BCVA was -0.10 logMAR. No assessment/comment was provided by the Investigator.
- Subject 7947.00010 (second eye) – BCVA was -0.08 logMAR at Visit 2 and 0.12 logMAR at Visit 3. The decrease in VA was considered NCS per the Investigator and was resolved at Visit 4.

Table 6-10 Descriptive Statistics for Monocular BCDVA at 4 m (logMAR), First Eye (All-Implanted Analysis Set)

Visit	Statistic	(N = 215)
Preoperative	n	215
	Mean (SD)	0.397 (0.2182)
	Median	0.34
	(Min, Max)	(0.00, 1.70)
	95% CI	(0.368, 0.426)
1 Week	n	212
	Mean (SD)	0.002 (0.1021)

Visit	Statistic	(N = 215)
	Median	0.00
	(Min, Max)	(-0.28, 0.38)
	95% CI	(-0.012, 0.016)
1 Month	n	207
	Mean (SD)	-0.011 (0.1583)
	Median	-0.04
	(Min, Max)	(-0.24, 1.70)
	95% CI	(-0.032, 0.011)
6 Months	n	201
	Mean (SD)	-0.027 (0.0991)
	Median	-0.04
	(Min, Max)	(-0.26, 0.52)
	95% CI	(-0.041, -0.014)
1 Year	n	198
	Mean (SD)	-0.030 (0.1028)
	Median	-0.04
	(Min, Max)	(-0.30, 0.54)
	95% CI	(-0.044, -0.016)
2 Years	n	0
	Mean (SD)	- (-)
	Median	-
	(Min, Max)	-, -
	95% CI	-
3 Years	n	0
	Mean (SD)	- (-)
	Median	-
	(Min, Max)	-, -
	95% CI	-

N = Number of eyes in treatment group
n = Number of eyes at visit

SD = Standard deviation; Min = Minimum; Max = Maximum; CI = Confidence interval
BCDVA = Best corrected distance visual acuity

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Table 6-11 Descriptive Statistics for Monocular BCDVA at 4 m (logMAR), Second Eye (All-Implanted Analysis Set)

Visit	Statistic	(N = 209)
Preoperative	n	209
	Mean (SD)	0.237 (0.1365)
	Median	0.24
	(Min, Max)	(-0.14, 0.72)
	95% CI	(0.218, 0.255)
1 Week	n	203
	Mean (SD)	-0.011 (0.1116)
	Median	-0.02
	(Min, Max)	(-0.30, 0.54)
	95% CI	(-0.026, 0.005)
1 Month	n	204
	Mean (SD)	-0.020 (0.0893)
	Median	0.00
	(Min, Max)	(-0.22, 0.28)
	95% CI	(-0.033, -0.008)
6 Months	n	200
	Mean (SD)	-0.038 (0.0854)
	Median	-0.04
	(Min, Max)	(-0.24, 0.20)
	95% CI	(-0.050, -0.027)
1 Year	n	198
	Mean (SD)	-0.040 (0.0950)
	Median	-0.04
	(Min, Max)	(-0.28, 0.36)
	95% CI	(-0.054, -0.027)
2 Years	n	0
	Mean (SD)	- (-)
	Median	-
	(Min, Max)	-, -
	95% CI	-
3 Years	n	0
	Mean (SD)	- (-)
	Median	-
	(Min, Max)	-, -
	95% CI	-

N = Number of eyes in treatment group
n = Number of eyes at visit

SD = Standard deviation; Min = Minimum; Max = Maximum; CI = Confidence interval
BCDVA = Best corrected distance visual acuity

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Table 6-12 Number of Eyes with a Loss of 10 Letters or More Compared to Best Post-Op BCDVA, First Eye (All-Implanted Analysis Set)

		(N = 215) n (%)
	Total	214
Loss of 10 Letters or More Compared to Best Postoperative BCDVA	**Yes**	17 (7.9)
	No	197 (92.1)

N = Number of eyes in the analysis set. n = Number of eyes in specified category.
Total = Number of eyes with data. Percentages are calculated as (n/Total) * 100
BCDVA = Best corrected distance visual acuity

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Table 6-13 Number of Eyes with a Loss of 10 Letters or More Compared to Best Post-Op BCDVA, Second Eye (All-Implanted Analysis Set)

		(N = 209) n (%)
	Total	209
Loss of 10 Letters or More Compared to Best Postoperative BCDVA	**Yes**	13 (6.2)
	No	196 (93.8)

N = Number of eyes in the analysis set. n = Number of eyes in specified category.
Total = Number of eyes with data. Percentages are calculated as (n/Total) * 100
BCDVA = Best corrected distance visual acuity

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Table 6-14 Listing of Monocular Visual Acuity (logMAR) for Eyes with a Loss of 10 Letters or More Compared to Best Post-Op BCDVA (All-Implanted Analysis Set)

Subject	Age (y)/Sex	Surgery Eye	Eye	Visit	Days from Surgery	BCDVA
1696.00006	83/M	2nd	OD	Preoperative	-31	0.22
				1 Week	8	0.34
				1 Month	43	0.28
				6 Months	127	0.14
				1 Year	393	0.36
1793.00001	46/F	2nd	OS	Preoperative	-56	0.10
				1 Week	14	0.00
				1 Month	39	-0.10
				6 Months	151	-0.06
				1 Year	396	0.12
4526.00014	69/F	1st	OD	Preoperative	-56	0.46
				1 Week	16	-0.04
				1 Month	48	0.46
				6 Months	160	-0.04
				Unscheduled	209	0.00
				1 Year	393	-0.04
4625.00007	72/F	1st	OD	Preoperative	-8	0.42
				1 Week	14	-0.08
				1 Month	74	-0.02
				6 Months	158	0.00
				1 Year	361	0.14
5956.00007	72/M	2nd	OS	Preoperative	-64	-0.08
				1 Week	12	-0.14
				1 Month	39	0.06
				6 Months	166	-0.04
				1 Year	377	-0.10
5956.00008	78/M	2nd	OS	Preoperative	-60	0.02

Subject	Age (y)/Sex	Surgery Eye	Eye	Visit	Days from Surgery	BCDVA
				1 Week	12	-0.10
				1 Month	39	0.10
6441.00012	75/M	1st	OD	Preoperative	-28	0.26
				1 Month	51	-0.20
				6 Months	176	-0.20
				1 Year	372	0.02
6660.00010	84/M	2nd	OD	Preoperative	-35	0.24
				1 Week	9	-0.08
				1 Month	42	-0.04
				6 Months	128	-0.06
				1 Year	337	0.12
6681.00010	67/F	2nd	OD	Preoperative	-24	0.36
				1 Week	11	-0.04
				1 Month	32	0.10
				6 Months	146	0.20
				1 Year	375	0.00
6681.00014	70/F	1st	OS	Preoperative	-10	0.30
				1 Week	7	0.10
				1 Month	71	1.70
				6 Months	142	0.52
				1 Year	381	0.54
6681.00018	67/M	1st	OS	Preoperative	-55	0.44
				1 Week	14	0.00
				1 Month	49	0.00
				6 Months	158	0.20
				1 Year	364	0.10
6681.00019	76/F	1st	OD	Preoperative	-57	0.30
				1 Week	9	0.08
				1 Month	47	0.00

Subject	Age (y)/Sex	Surgery Eye	Eye	Visit	Days from Surgery	BCDVA
				6 Months	168	0.14
				1 Year	362	0.22
7215.00002	75/F	1st	OD	Preoperative	-7	0.38
				1 Week	14	-0.12
				1 Month	106	-0.20
				6 Months	190	-0.08
				1 Year	344	0.12
7813.00005	61/M	1st	OD	Preoperative	-25	0.24
				1 Week	10	-0.04
				1 Month	59	0.16
				Unscheduled	171	0.22
				6 Months	178	0.00
				1 Year	385	-0.01
		2nd	OS	Preoperative	-39	0.20
				1 Week	8	-0.04
				1 Month	45	0.28
				Unscheduled	157	0.16
				6 Months	164	0.00
				1 Year	371	-0.01
7813.00006	73/M	1st	OD	Preoperative	-14	0.44
				1 Week	10	-0.02
				1 Month	57	0.14
				6 Months	192	0.14
				1 Year	364	0.20
7813.00009	71/F	1st	OS	Preoperative	-11	1.62
				1 Week	10	-0.04
				1 Month	57	0.16
				6 Months	193	0.20
				1 Year	441	0.20

Subject	Age (y)/Sex	Surgery Eye	Eye	Visit	Days from Surgery	BCDVA
		2nd	OD	Preoperative	-25	0.68
				1 Week	10	0.00
				1 Month	43	0.16
				6 Months	179	0.20
				1 Year	427	0.20
7813.00016	62/M	1st	OD	Preoperative	-40	0.32
				1 Week	8	-0.08
				1 Month	64	0.20
7813.00018	74/F	1st	OD	Preoperative	-25	0.30
				1 Week	12	-0.10
				1 Month	59	-0.06
				6 Months	189	-0.10
				1 Year	399	0.20
		2nd	OS	Preoperative	-39	0.18
				1 Week	8	0.00
				1 Month	45	-0.10
				6 Months	175	0.00
				1 Year	385	0.30
7813.00019	80/M	1st	OS	Preoperative	-18	0.26
				1 Week	10	0.16
				1 Month	59	0.00
				6 Months	189	0.30
				1 Year	395	0.30
		2nd	OD	Preoperative	-32	0.06
				1 Week	10	0.00
				1 Month	45	0.00
				6 Months	175	0.20
				1 Year	381	0.20
7813.00020	84/M	1st	OD	Preoperative	-18	0.40

Subject	Age (y)/Sex	Surgery Eye	Eye	Visit	Days from Surgery	BCDVA
				1 Week	14	0.00
				1 Month	59	0.10
				6 Months	192	0.20
				1 Year	407	0.00
		2nd	OS	Preoperative	-32	0.14
				1 Week	14	0.00
				1 Month	45	-0.06
				6 Months	178	0.00
				1 Year	393	0.20
7813.00027	75/F	1st	OD	Preoperative	-11	0.32
				1 Week	10	-0.10
				1 Month	56	-0.10
				6 Months	178	-0.10
				1 Year	402	0.18
7925.00001	79/M	1st	OD	Preoperative	-17	0.44
				1 Week	8	0.38
				1 Month	57	0.22
				6 Months	141	0.02
				1 Year	392	0.22
7936.00001	71/F	2nd	OD	Preoperative	-36	0.14
				1 Week	8	-0.18
				1 Month	34	0.06
				6 Months	153	-0.12
				1 Year	356	-0.08
7936.00003	88/F	1st	OD	Preoperative	-57	0.54
				1 Week	6	-0.28
				1 Month	48	-0.08
				6 Months	139	-0.06
				1 Year	368	-0.10

Subject	Age (y)/Sex	Surgery Eye	Eye	Visit	Days from Surgery	BCDVA
7947.00010	76/F	2nd	OD	Preoperative	-14	0.20
				1 Week	12	-0.08
				1 Month	47	0.12
				6 Months	159	-0.10
				1 Year	334	0.00

BCDVA = Best Corrected Distance Visual Acuity at 4 m
OD = Right eye; OS = Left eye
Surgery was Day 0

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6.2.3 UCDVA

Descriptive statistics for UCDVA are shown in Table 6-15 for the first eye and Table 6-16 for the second eye. There was 1 first eye (Subject 6681.00014) that required multiple vitrectomies and presented with a UCDVA of 1.60 logMAR at 6 months and 0.70 logMAR at 1 year.

Descriptive statistics for UCDVA by site are presented for the first eye in Table 11-13a to Table 11-13k and for the second eye in Table 11-14a to Table 11-14k.

Categorical statistics for UCDVA in logMAR are provided in Table 11-25 for the first eye and Table 11-26 for the second eye.

Categorical statistics for UCDVA in Snellen are provided in Table 11-33 for the first eye and Table 11-34 for the second eye.

Table 6-15 Descriptive Statistics for Monocular UCDVA at 4 m (logMAR), First Eye (All-Implanted Analysis Set)

Visit	Statistic	(N = 215)
Preoperative	n	215
	Mean (SD)	0.690 (0.3133)
	Median	0.64
	(Min, Max)	(0.12, 1.70)
	95% CI	(0.648, 0.733)

Visit	Statistic	(N = 215)
1 Day	n	214
	Mean (SD)	0.221 (0.2139)
	Median	0.16
	(Min, Max)	(-0.24, 1.02)
	95% CI	(0.192, 0.250)
1 Week	n	213
	Mean (SD)	0.109 (0.1499)
	Median	0.08
	(Min, Max)	(-0.24, 0.56)
	95% CI	(0.088, 0.129)
1 Month	n	207
	Mean (SD)	0.085 (0.1767)
	Median	0.06
	(Min, Max)	(-0.22, 1.70)
	95% CI	(0.061, 0.109)
6 Months	n	201
	Mean (SD)	0.099 (0.1827)
	Median	0.06
	(Min, Max)	(-0.20, 1.60)
	95% CI	(0.073, 0.124)
1 Year	n	199
	Mean (SD)	0.080 (0.1495)
	Median	0.06
	(Min, Max)	(-0.26, 0.70)
	95% CI	(0.059, 0.101)
2 Years	n	0
	Mean (SD)	- (-)
	Median	-
	(Min, Max)	-, -
	95% CI	-

Visit	Statistic	(N = 215)
3 Years	n	0
	Mean (SD)	- (-)
	Median	-
	(Min, Max)	-, -
	95% CI	-

N = Number of eyes in in the analysis set
n = Number of eyes at visit
SD = Standard deviation; Min = Minimum; Max = Maximum; CI = Confidence interval
UCDVA = Uncorrected distance visual acuity

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Table 6-16 Descriptive Statistics for Monocular UCDVA at 4 m (logMAR), Second Eye (All-Implanted Analysis Set)

Visit	Statistic	(N = 209)
Preoperative	n	209
	Mean (SD)	0.534 (0.2604)
	Median	0.50
	(Min, Max)	(0.00, 1.30)
	95% CI	(0.498, 0.569)
1 Day	n	208
	Mean (SD)	0.199 (0.2056)
	Median	0.16
	(Min, Max)	(-0.18, 0.94)
	95% CI	(0.171, 0.227)
1 Week	n	204
	Mean (SD)	0.090 (0.1604)
	Median	0.06
	(Min, Max)	(-0.30, 0.76)
	95% CI	(0.067, 0.112)
1 Month	n	206
	Mean (SD)	0.057 (0.1358)
	Median	0.04
	(Min, Max)	(-0.24, 0.64)
	95% CI	(0.038, 0.075)

Visit	Statistic	(N = 209)
6 Months	n	200
	Mean (SD)	0.065 (0.1413)
	Median	0.04
	(Min, Max)	(-0.24, 0.56)
	95% CI	(0.045, 0.084)
1 Year	n	198
	Mean (SD)	0.058 (0.1360)
	Median	0.04
	(Min, Max)	(-0.26, 0.50)
	95% CI	(0.039, 0.077)
2 Years	n	0
	Mean (SD)	- (-)
	Median	-
	(Min, Max)	-, -
	95% CI	-
3 Years	n	0
	Mean (SD)	- (-)
	Median	-
	(Min, Max)	-, -
	95% CI	-

N = Number of eyes in the analysis set
n = Number of eyes at visit
SD = Standard deviation; Min = Minimum; Max = Maximum; CI = Confidence interval
UCDVA = Uncorrected distance visual acuity

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6.2.4 Manifest Refraction

At 1-year, the observed mean MRSE was 0.0477 D for the first eye and 0.0713 D for the second eye (Table 6-17 and Table 6-18). Categorical statistics for absolute manifest refraction spherical equivalent (MRSE) are presented in Table 11-53 for first eyes and Table 11-54 for second eyes. Descriptive statistics for MRSE by site are presented for the first eye in Table 11-65a to Table 11-65k and for the second eye in Table 11-66a to Table 11-66k.

The absolute predicted target residual refractive error was 0.5 D or less for 98.6% of first eyes and 99.5% of second eyes (Table 6-19 and Table 6-20). Descriptive statistics for predicted target residual refractive error are presented in Table 11-61 for the first eye and Table 11-62 for the second eye.

Categorical statistics for absolute prediction error are presented in Table 11-57 for first eyes and Table 11-58 for second eyes. Descriptive statistics for prediction error are presented in Table 11-69 for first eyes and Table 11-70 for second eyes.

Table 6-17 Descriptive Statistics for Manifest Refraction Spherical Equivalent (D) at 1 Year, First Eye (All-Implanted Analysis Set)

Visit	Statistic	N = 215
Preoperative	n	215
	Mean (SD)	-0.4820 (2.58326)
	Median	0.000
	(Min, Max)	(-10.000, 4.375)
	95% CI	(-0.8292, -0.1347)
1 Week	n	214
	Mean (SD)	0.0053 (0.39236)
	Median	0.000
	(Min, Max)	(-1.125, 1.500)
	95% CI	(-0.0476, 0.0581)
1 Month	n	207
	Mean (SD)	0.0248 (0.40672)
	Median	0.000
	(Min, Max)	(-1.250, 1.500)
	95% CI	(-0.0310, 0.0805)
6 Months	n	201
	Mean (SD)	0.0367 (0.51989)
	Median	0.000
	(Min, Max)	(-1.375, 4.250)
	95% CI	(-0.0356, 0.1090)
1 Year	n	199
	Mean (SD)	0.0477 (0.45322)
	Median	0.000
	(Min, Max)	(-2.250, 1.875)
	95% CI	(-0.0156, 0.1111)

Visit	Statistic	N = 215
2 Years	n	-
	Mean (SD)	- (-)
	Median	-
	(Min, Max)	(-, -)
	95% CI	(-, -)
3 Years	n	-
	Mean (SD)	- (-)
	Median	-
	(Min, Max)	(-, -)
	95% CI	(-, -)

N = Number of eyes in the analysis set
n = Number of eyes at visit
SD = Standard deviation; Min = Minimum; Max = Maximum; CI = Confidence interval

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Table 6-18 Descriptive Statistics for Manifest Refraction Spherical Equivalent (D) at 1 Year, Second Eye (All-Implanted Analysis Set)

Visit	Statistic	N = 209
Preoperative	n	208
	Mean (SD)	0.1292 (1.94289)
	Median	0.375
	(Min, Max)	(-6.125, 3.750)
	95% CI	(-0.1364, 0.3948)
1 Week	n	204
	Mean (SD)	-0.0098 (0.37885)
	Median	0.000
	(Min, Max)	(-1.000, 2.250)
	95% CI	(-0.0621, 0.0425)
1 Month	n	206
	Mean (SD)	-0.0006 (0.35345)
	Median	0.000
	(Min, Max)	(-1.000, 1.750)

Visit	Statistic	N = 209
	95% CI	(-0.0492, 0.0479)
6 Months	n	200
	Mean (SD)	0.0306 (0.39099)
	Median	0.000
	(Min, Max)	(-1.000, 1.875)
	95% CI	(-0.0239, 0.0851)
1 Year	n	198
	Mean (SD)	0.0713 (0.40485)
	Median	0.000
	(Min, Max)	(-1.000, 1.750)
	95% CI	(0.0146, 0.1281)
2 Years	n	-
	Mean (SD)	- (-)
	Median	-
	(Min, Max)	(-, -)
	95% CI	(-, -)
3 Years	n	-
	Mean (SD)	- (-)
	Median	-
	(Min, Max)	(-, -)
	95% CI	(-, -)

N = Number of eyes in the analysis set
n = Number of eyes at visit
SD = Standard deviation; Min = Minimum; Max = Maximum; CI = Confidence interval

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Table 6-19 Categorical Statistics for Absolute Predicted Target Residual Refractive Error, First Eye (All-Implanted Analysis Set)

Visit	Category	N = 215 n (%)
Surgery	Total	215
	0.25 D or less	176 (81.9)
	0.50 D or less	212 (98.6)
	1.00 D or less	215 (100)
	More than 1.00 D	0 (0.0)

N = Number of eyes in the analysis set
n = Number of eyes in specified category
Total = Number of eyes with data
Percentages are calculated as (n/Total) * 100

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Table 6-20 Categorical Statistics for Absolute Predicted Target Residual Refractive Error, Second Eye (All-Implanted Analysis Set)

Visit	Category	N = 209 n (%)
Surgery	Total	209
	0.25 D or less	175 (83.7)
	0.50 D or less	208 (99.5)
	1.00 D or less	209 (100)
	More than 1.00 D	0 (0.0)

N = Number of eyes in treatment group
n = Number of eyes in specified category
Total = Number of eyes with data
Percentages are calculated as (n/Total) * 100

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6.2.5 Percentage of Eyes Having Nd:YAG Capsulotomy

Two (0.9%) first eyes and no second eyes had an Nd:YAG capsulotomy (Table 6-21 and Table 6-22). One of these eyes had the Nd:YAG capsulotomy at Day 1 postop due to a pre-existing residual posterior subcapsular cataract; the other first eye had an Nd:YAG at

1 year for PCO developed post-implantation (refer to Section 6.3.12 for additional information).

Table 6-21 Number of Eyes with a Posterior Capsulotomy, First Eye (All Implanted Analysis Set)

		(N = 215) n (%)
	Total	215
Posterior Capsulotomy	**Yes**	2 (0.9)
	No	213 (99.1)

N = Number of eyes in treatment group. n = Number of eyes in specified category.
Total = Number of eyes with data. Percentages are calculated as (n/Total) * 100

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Table 6-22 Number of Eyes with a Posterior Capsulotomy, Second Eye (All Implanted Analysis Set)

		(N = 209) n (%)
	Total	209
Posterior Capsulotomy	**Yes**	0 (0.0)
	No	209 (100.0)

N = Number of eyes in the analysis set. n = Number of eyes in specified category.
Total = Number of eyes with data. Percentages are calculated as (n/Total) * 100

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6.2.6 Glistenings

Glistenings were rated with the following scale adapted from Miyata (2001): Grade 0 (0-25 vacuoles/mm^3), Grade 1 (26-75 vacuoles/mm^3), Grade 2 (76-150 vacuoles/mm^3), and Grade 3 (151 > vacuoles/mm^3). At 1 year, there was 1 subject (Subject 7947.00005) with IOL glistenings Grade 1 in the first eye and second eye (Table 6-23, Table 6-24, and Listing 16-34). All other eyes (99.5%) had glistenings Grade 0 at 1 year.

Table 6-23 Summary of IOL Glistenings - Grading for Glistenings, First Eye (All Implanted Analysis Set)

Visit	Category	N = 215 n (%)
Overall	Total	208
	Grade 0	207 (99.5)
	Grade 1	1 (0.5)
	Grade 2	0 (0.0)
	Grade 3	0 (0.0)
1 Month	Total	205
	Grade 0	205 (100)
	Grade 1	0 (0.0)
	Grade 2	0 (0.0)
	Grade 3	0 (0.0)
6 Months	Total	201
	Grade 0	201 (100)
	Grade 1	0 (0.0)
	Grade 2	0 (0.0)
	Grade 3	0 (0.0)
1 Year	Total	199
	Grade 0	198 (99.5)
	Grade 1	1 (0.5)
	Grade 2	0 (0.0)
	Grade 3	0 (0.0)
2 Years	Total	0
	Grade 0	0 (0.0)
	Grade 1	0 (0.0)
	Grade 2	0 (0.0)
	Grade 3	0 (0.0)
3 Years	Total	0
	Grade 0	0 (0.0)
	Grade 1	0 (0.0)

Visit	Category	N = 215 n (%)
	Grade 2	0 (0.0)
	Grade 3	0 (0.0)

Overall = Category represents maximum rating for an eye during the study.
N = Number of eyes in the analysis set. n = Number of eyes in specified category.
Total = Number of eyes with data. Percentages are calculated as (n/Total) * 100

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Table 6-24 Summary of IOL Glistenings - Grading for Glistenings, Second Eye (Safety Analysis Set)

Visit	Category	N = 209 n (%)
Overall	Total	207
	Grade 0	206 (99.5)
	Grade 1	1 (0.5)
	Grade 2	0 (0.0)
	Grade 3	0 (0.0)
1 Month	Total	204
	Grade 0	204 (100)
	Grade 1	0 (0.0)
	Grade 2	0 (0.0)
	Grade 3	0 (0.0)
6 Months	Total	200
	Grade 0	200 (100)
	Grade 1	0 (0.0)
	Grade 2	0 (0.0)
	Grade 3	0 (0.0)
1 Year	Total	198
	Grade 0	197 (99.5)
	Grade 1	1 (0.5)
	Grade 2	0 (0.0)
	Grade 3	0 (0.0)

Visit	Category	N = 209 n (%)
2 Years	Total	0
	Grade 0	0 (0.0)
	Grade 1	0 (0.0)
	Grade 2	0 (0.0)
	Grade 3	0 (0.0)
3 Years	Total	0
	Grade 0	0 (0.0)
	Grade 1	0 (0.0)
	Grade 2	0 (0.0)
	Grade 3	0 (0.0)

Overall = Category represents maximum rating for an eye during the study.
N = Number of eyes in the analysis set. n = Number of eyes in specified category.
Total = Number of eyes with data. Percentages are calculated as (n/Total) * 100

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6.2.7 Estimated IOL A-Constant

As previously reported in Summary Report: Protocol Post-Market Clinical Investigation of the Clareon® IOL—6 Month Interim Analysis (TDOC-0056500), a post-hoc analysis for clinical verification of A-Constant was conducted at Visit 4A (6-months). Descriptive statistics for the Clinical SRK/T A-Constant are summarized in the 6-month report (TDOC-0056500).

6.3 Analysis of Safety

Additional safety tables and listings are located in Appendix 9, Section 9.1.3.

6.3.1 Adverse Events Including Secondary Surgical Interventions

6.3.1.1 Cumulative and Persistent Adverse Events

The primary safety endpoint of this study is to evaluate the 1-year AE rates of the Clareon IOL compared to historical SPE rates as reported in EN ISO 11979-7:2014. The SPE rate was considered not exceeded if the 1-sided 95% lower confidence limit (LCL) for an AE was less than the SPE%. The rate of cumulative and persistent SAEs, including SSIs, for first and second eyes were below the threshold as set forth by ISO 11979-7:2014 (Table 6-25 and

Table 6-26). All LCLs were < SPE%, meeting the ISO requirement and study safety requirement.

SSIs occurred in 3 first eyes and 0 second eyes. All 3 cases (n = 2 intra-ocular injection and n = 1 vitrectomy) were assessed as not related to the IOL (Table 12-61, Table 12-62, Listing 16-19).

Table 6-25 Cumulative and Persistent Serious Adverse Events and SPE Rates at 1 Year, First Eye (Safety Analysis Set)

	(N = 215) n (%)	2-sided 95% CI	1-sided 95% Lower CL	SPE %
Cumulative Serious Adverse Events				
Cystoid macular oedema	3 (1.4)	(0.29, 4.02)	0.38	3.0
Hypopyon	0 (0.0)	(0.00, 1.70)	0.00	0.3
Endophthalmitis	0 (0.0)	(0.00, 1.70)	0.00	0.1
Lens dislocated from posterior chamber	0 (0.0)	(0.00, 1.70)	0.00	0.1
Pupillary block	0 (0.0)	(0.00, 1.70)	0.00	0.1
Retinal detachment	1 (0.5)	(0.01, 2.56)	0.02	0.3
Secondary surgical intervention	3 (1.4)	(0.29, 4.02)	0.38	0.8
Persistent Serious Adverse Events				
Corneal stroma oedema	0 (0.0)	(0.00, 1.70)	0.00	0.3
Cystoid macular oedema	1 (0.5)	(0.01, 2.56)	0.02	0.5
Iritis	0 (0.0)	(0.00, 1.70)	0.00	0.3
Raised IOP requiring treatment	0 (0.0)	(0.00, 1.70)	0.00	0.4

CI = Confidence Interval; CL = Confidence Limit; SPE = Safety and Performance Endpoints
If an eye has multiple occurrences of an AE, the eye is presented only once in the respective eye count column (n) for the corresponding AE. Percentages are calculated as (n/N) * 100.
The SPE rate is considered not exceeded if the 1-sided 95% lower CL for an AE is less than the SPE%
Persistent = Present or ongoing at the final scheduled visit. IOP = Intraocular Pressure

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Table 6-26 Cumulative and Persistent Serious Adverse Events and SPE Rates at 1 Year, Second Eye (Safety Analysis Set)

	(N = 209) n (%)	2-sided 95% CI	1-sided 95% Lower CL	SPE %
Cumulative Serious Adverse Events				
Cystoid macular oedema	0 (0.0)	(0.00, 1.75)	0.00	3.0
Hypopyon	0 (0.0)	(0.00, 1.75)	0.00	0.3
Endophthalmitis	0 (0.0)	(0.00, 1.75)	0.00	0.1
Lens dislocated from posterior chamber	0 (0.0)	(0.00, 1.75)	0.00	0.1
Pupillary block	0 (0.0)	(0.00, 1.75)	0.00	0.1
Retinal detachment	0 (0.0)	(0.00, 1.75)	0.00	0.3
Secondary surgical intervention	0 (0.0)	(0.00, 1.75)	0.00	0.8
Persistent Serious Adverse Events				
Corneal stroma oedema	0 (0.0)	(0.00, 1.75)	0.00	0.3
Cystoid macular oedema	0 (0.0)	(0.00, 1.75)	0.00	0.5
Iritis	0 (0.0)	(0.00, 1.75)	0.00	0.3
Raised IOP requiring treatment	0 (0.0)	(0.00, 1.75)	0.00	0.4

CI = Confidence Interval; CL = Confidence Limit; SPE = Safety and Performance Endpoints
If an eye has multiple occurrences of an AE, the eye is presented only once in the respective eye count column (n) for the corresponding AE. Percentages are calculated as (n/N) * 100.
The SPE rate is considered not exceeded if the 1-sided 95% lower CL for an AE is less than the SPE%
Persistent = Present or ongoing at the final scheduled visit. IOP = Intraocular Pressure

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6.3.1.2 Ocular AEs

No single SAE type had a rate > 1.4% in the first eye and > 0.5% in the second eye to date (Table 6-27 and Table 6-28). All reported SAEs were unrelated to the IOL (Listing 16-13). There was 1 ocular adverse device effect (ADE) in the first eye (visual impairment) (Table 12-6), and 1 in the second eye (visual impairment) (Table 12-7). There were no serious adverse device effects.

In the first eye, dry eye was the most frequently reported nonserious ocular AE (7.0%), followed by posterior capsule opacification (2.3%), corneal edema (1.9%) and punctate

keratitis (1.9%). All other nonserious AEs in the first eye were reported at a rate ≤ 1.4% (Table 6-29). In the second eye, dry eye was the most frequently reported nonserious ocular AE (7.7%), followed by punctate keratitis (4.3%), posterior capsule opacification (2.9%), and corneal edema (2.4%). All other nonserious AEs in the second eye were reported at a rate ≤ 1.4% (Table 6-30).

Table 6-27 Ocular Serious Adverse Events Including Serious Adverse Device Effects, First Eye (Safety Analysis Set)

	(N = 215)		
Preferred Term	**n (%)**	**2-sided 95% CI**	**E**
Vitrectomy	1 (0.5)	(0.01, 2.56)	5
Retinal detachment	1 (0.5)	(0.01, 2.56)	4
Cystoid macular oedema	3 (1.4)	(0.29, 4.02)	3
Intra-ocular injection	2 (0.9)	(0.11, 3.32)	2
Age-related macular degeneration	1 (0.5)	(0.01, 2.56)	1
Intraocular pressure increased	1 (0.5)	(0.01, 2.56)	1
Iridocyclitis	1 (0.5)	(0.01, 2.56)	1

If an eye has multiple occurrences of an AE, the eye is presented only once in the respective eye count column (n) for the corresponding AE. Events are counted each time in the event (E) column.
N = Number of eyes in treatment group; n = Number of eyes with event; E = Number of events; CI = Confidence Interval
Percentages are calculated as (n/N) * 100. Adverse events are coded using MedDRA version 20.0.

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Table 6-28 Ocular Serious Adverse Events Including Serious Adverse Device Effects, Second Eye (Safety Analysis Set)

	(N = 209)		
Preferred Term	**n (%)**	**2-sided 95% CI**	**E**
Iridocyclitis	1 (0.5)	(0.01, 2.64)	1
Posterior capsule rupture	1 (0.5)	(0.01, 2.64)	1

If an eye has multiple occurrences of an AE, the eye is presented only once in the respective eye count column (n) for the corresponding AE. Events are counted each time in the event (E) column.
N = Number of eyes in treatment group; n = Number of eyes with event; E = Number of events; CI = Confidence Interval
Percentages are calculated as (n/N) * 100. Adverse events are coded using MedDRA version 20.0.

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Table 6-29 Ocular Adverse Events (Serious and Non-Serious Combined), First Eye (Safety Analysis Set)

	(N = 215)		
Preferred Term	**n (%)**	**2-sided 95% CI**	**E**
Dry eye	15 (7.0)	(3.96, 11.25)	15
Posterior capsule opacification	5 (2.3)	(0.76, 5.34)	5
Vitrectomy	1 (0.5)	(0.01, 2.56)	5
Corneal oedema	4 (1.9)	(0.51, 4.69)	4
Punctate keratitis	4 (1.9)	(0.51, 4.69)	4
Retinal detachment	1 (0.5)	(0.01, 2.56)	4
Blepharitis	3 (1.4)	(0.29, 4.02)	3
Cystoid macular oedema	3 (1.4)	(0.29, 4.02)	3
Intraocular pressure increased	3 (1.4)	(0.29, 4.02)	3
Visual acuity reduced	3 (1.4)	(0.29, 4.02)	3
Vitreous detachment	3 (1.4)	(0.29, 4.02)	3
Abnormal sensation in eye	2 (0.9)	(0.11, 3.32)	2
Anterior capsule contraction	2 (0.9)	(0.11, 3.32)	2
Intra-ocular injection	2 (0.9)	(0.11, 3.32)	2
Tear break up time decreased	2 (0.9)	(0.11, 3.32)	2
Adverse drug reaction	1 (0.5)	(0.01, 2.56)	1
Age-related macular degeneration	1 (0.5)	(0.01, 2.56)	1
Blepharochalasis	1 (0.5)	(0.01, 2.56)	1
Blepharoplasty	1 (0.5)	(0.01, 2.56)	1
Cataract operation complication	1 (0.5)	(0.01, 2.56)	1
Cataract subcapsular	1 (0.5)	(0.01, 2.56)	1
Conjunctivitis bacterial	1 (0.5)	(0.01, 2.56)	1
Eye inflammation	1 (0.5)	(0.01, 2.56)	1
Eyelid disorder	1 (0.5)	(0.01, 2.56)	1
Eyelids pruritus	1 (0.5)	(0.01, 2.56)	1
Holmes-Adie pupil	1 (0.5)	(0.01, 2.56)	1
Iridocyclitis	1 (0.5)	(0.01, 2.56)	1
Lacrimation increased	1 (0.5)	(0.01, 2.56)	1
Lid parallel conjunctival fold s examination	1 (0.5)	(0.01, 2.56)	1

	(N = 215)		
Preferred Term	**n (%)**	**2-sided 95% CI**	**E**
Meibomianitis	1 (0.5)	(0.01, 2.56)	1
Pterygium operation	1 (0.5)	(0.01, 2.56)	1
Retinal drusen	1 (0.5)	(0.01, 2.56)	1
Trichiasis	1 (0.5)	(0.01, 2.56)	1
Visual impairment	1 (0.5)	(0.01, 2.56)	1
Vitreous floaters	1 (0.5)	(0.01, 2.56)	1

If an eye has multiple occurrences of an AE, the eye is presented only once in the respective eye count column (n) for the corresponding AE. Events are counted each time in the event (E) column.
N = Number of eyes in treatment group; n = Number of eyes with event; E = Number of events; CI = Confidence Interval
Percentages are calculated as (n/N) * 100. Adverse events are coded using MedDRA version 20.0.

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Table 6-30 Ocular Adverse Events (Serious and Non-Serious Combined), Second Eye (Safety Analysis Set)

	(N = 209)		
Preferred Term	**n (%)**	**2-sided 95% CI**	**E**
Dry eye	16 (7.7)	(4.44, 12.13)	16
Punctate keratitis	9 (4.3)	(1.99, 8.02)	9
Posterior capsule opacification	6 (2.9)	(1.06, 6.14)	7
Corneal oedema	5 (2.4)	(0.78, 5.49)	5
Abnormal sensation in eye	3 (1.4)	(0.30, 4.14)	3
Blepharitis	3 (1.4)	(0.30, 4.14)	3
Conjunctival haemorrhage	3 (1.4)	(0.30, 4.14)	3
Eye pruritus	3 (1.4)	(0.30, 4.14)	3
Intraocular pressure increased	3 (1.4)	(0.30, 4.14)	3
Vitreous floaters	3 (1.4)	(0.30, 4.14)	3
Blepharoplasty	2 (1.0)	(0.12, 3.41)	2
Tear break up time decreased	2 (1.0)	(0.12, 3.41)	2
Ulcerative keratitis	2 (1.0)	(0.12, 3.41)	2
Visual impairment	2 (1.0)	(0.12, 3.41)	2

	(N = 209)		
Preferred Term	**n (%)**	**2-sided 95% CI**	**E**
Adverse drug reaction	1 (0.5)	(0.01, 2.64)	1
Anterior chamber cell	1 (0.5)	(0.01, 2.64)	1
Chalazion	1 (0.5)	(0.01, 2.64)	1
Conjunctival irritation	1 (0.5)	(0.01, 2.64)	1
Conjunctivitis bacterial	1 (0.5)	(0.01, 2.64)	1
Corneal erosion	1 (0.5)	(0.01, 2.64)	1
Eye pain	1 (0.5)	(0.01, 2.64)	1
Eyelid oedema	1 (0.5)	(0.01, 2.64)	1
Iridocyclitis	1 (0.5)	(0.01, 2.64)	1
Iris adhesions	1 (0.5)	(0.01, 2.64)	1
Iris atrophy	1 (0.5)	(0.01, 2.64)	1
Lacrimation increased	1 (0.5)	(0.01, 2.64)	1
Lid parallel conjunctival fold s examination	1 (0.5)	(0.01, 2.64)	1
Macular fibrosis	1 (0.5)	(0.01, 2.64)	1
Meibomianitis	1 (0.5)	(0.01, 2.64)	1
Ocular discomfort	1 (0.5)	(0.01, 2.64)	1
Photopsia	1 (0.5)	(0.01, 2.64)	1
Posterior capsule rupture	1 (0.5)	(0.01, 2.64)	1
Pruritus	1 (0.5)	(0.01, 2.64)	1
Pterygium	1 (0.5)	(0.01, 2.64)	1
Retinal haemorrhage	1 (0.5)	(0.01, 2.64)	1
Retinopathy proliferative	1 (0.5)	(0.01, 2.64)	1
Uveitis	1 (0.5)	(0.01, 2.64)	1
Visual acuity reduced	1 (0.5)	(0.01, 2.64)	1
Vitreous detachment	1 (0.5)	(0.01, 2.64)	1

If an eye has multiple occurrences of an AE, the eye is presented only once in the respective eye count column (n) for the corresponding AE. Events are counted each time in the event (E) column.
N = Number of eyes in treatment group; n = Number of eyes with event; E = Number of events; CI = Confidence Interval
Percentages are calculated as (n/N) * 100. Adverse events are coded using MedDRA version 20.0.

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6.3.1.3 Nonocular AEs

The most frequently reported nonocular SAE was myocardial infarction (0.9%). All other nonocular SAEs were reported at a rate of 0.5% (Table 12-11). All nonocular SAEs were assessed as not related to the IOL (Table 12-8).

6.3.2 Deaths

Five deaths were reported during the study to date. They were attributed to non-ocular SAEs, which were not related to the IOL. Refer to Section 6.3.3.3 for narratives on these subjects.

6.3.3 Subject Narratives for SAEs and ADEs

The narratives are as of 14 Jan 2020. All "Days" listed in the narratives are postoperative and relative to the day of surgery (Day 0).

6.3.3.1 Ocular SAEs

Subject 7813.00005: (PT: Iridocyclitis, Increased IOP, Cystoid macular edema)

A 61-year-old African American male was implanted with a Clareon IOL following cataract removal OD and OS (study eyes).

The subject's medical history included diabetes, hypertension, hyperlipidemia, and anxiety.

The subject's baseline fundus observations were unremarkable, and slit-lamp observations showed cataract OU.

On Day 36, the subject was diagnosed with **increased IOP** in OD (moderate severity) of 31 mmHg during slit-lamp exam. During this visit, UCDVA was 0.64 logMAR. The subject was treated with steroid drops and oral acetazolamide. The SAE was resolved on Day 39 and the UCVA was 0.26 logMAR.

On Day 38 OD and Day 24 OS, the subject was diagnosed with **bilateral post-operative uveitis** (severe severity) after the Investigator saw corneal edema, anterior chamber cells, and increased IOP during the slit-lamp exam. The subject was treated with steroids and phenylephrine drops. The subject was not compliant and did not take medication. Three days later on Day 41 OD and Day 27 OS the Investigator noted reduced vision, more anterior chamber cells, and Descements's folds. During this visit UCDVA was 0.68 logMAR OD and 0.86 logMAR OS.

On Day 171, the subject was diagnosed with clinically significant **cystoid macular edema** OD (mild severity), which was observed during fundus exam after the subject presented with foggy vision. The subject was treated with nonsteroidal anti-inflammatory drops. During this visit, UCDVA was 0.30 logMAR and BCDVA was 0.22 logMAR. The subject continues in the study.

The SAE of anterior uveitis OD was recovered/resolved on Day 60 with UCDVA of 0.16 logMAR and BCDVA of 0.16 logMAR.

The SAE of anterior uveitis OS was recovered/resolved on Day 158 with UCDVA of 0.00 logMAR and BCDVA of 0.00 logMAR.

The SAE cystoid macular edema was recovered/resolved on Day 200, and UCDVA was 0.16 logMAR and BCDVA was 0.00 logMAR.

The Investigator and Sponsor assessed the SAEs as unrelated to the IOL but related to the cataract surgery.

Subject 6681.00009: (PT: Posterior capsule rupture, Vitrectomy)

An 80-year-old white female was diagnosed with **capsular tear** (mild severity) in OD during cataract removal. An **anterior vitrectomy** was performed on the same day of surgery. The subject was not implanted with Clareon IOL in the OD and OS. The subject was discontinued from the study.

The subject's medical history included surgical intervention of the heart valve, nonspecific arrhythmia, chronic cardiac insufficiency, arterial hypertension, tonsillectomy, catheterization of the right femoral vein, anxiety, and menopause.

The subject's baseline fundus observations were unremarkable, and slit-lamp observations showed cataract OU.

The Investigator and Sponsor assessed the SAE as unrelated to the IOL but related to the cataract surgery.

Subject 6681.00014: (PT: Retinal detachment x4, Vitrectomy x5)

A 70-year-old white female was implanted with a Clareon IOL following cataract removal OD and OS (study eyes).

The subject's medical history included arterial hypertension, unstable angina, osteoarthritis, dyslipidemia, lumbar hernia intervention, cervical spine intervention, appendectomy, fissure intervention in the colon, and menopause.

The subject's baseline fundus observations were unremarkable, and slit-lamp observations showed cataract OU.

On Day 39, the subject came to the office complaining of visual alterations, loss of vision, stinging, and flies in the vision. The subject was diagnosed with **rhegmatogenous retinal detachment** (severe severity) on OS. On Day 45, a **vitrectomy** was performed. Six days after the vitrectomy on Day 51, the subject went to the clinic complaining of visual loss and flies in the vision and was diagnosed with **re-retinal detachment again.** On Day 53 (2 days after being diagnosed), the subject was treated again with a **vitrectomy**. Eighteen days after the last vitrectomy, the BCDVA and UCDVA were 1.70 logMAR.

On day 77, during a visit to the retinal specialist a **lower retinal detachment** (lower vitreoretinal proliferation, severe severity) OS was diagnosed again. Two days after being diagnosed, on Day 79 a **vitrectomy with silicone** was performed. Fifteen days after the vitrectomy, on day 94, the patient had a follow-up visit and was diagnosed with **inferior retinal detachment again**. Thirteen days later,on Day 107, a **vitrectomy** with peeling of vitreoretinal proliferaiton and macular area was conducted. Thirty-five days after the last vitrectomy, the patient had UCDVA of 1.6 logMAR and BCVA of 0.52 logMAR. Following 196 days after the last vitrectomy, on Day 303, another **vitrectomy was done to remove the silicone**, and 78 days later the patient had UCDVA of 0.7 logMAR and BCDVA of 0.54 logMAR (Visit 5A). Manifest refraction spherical equivalence was 4.250 D at the 6-month visit. The subject continues in the study.

The events have been resolved but waiting for a follow-up visit to assess visual acuity again.

The Investigator and Sponsor assessed the SAEs as unrelated to the IOL or study procedure.

Subject 4625.00014: (PT: Posterior capsule rupture)

A 69-year-old Asian male was implanted with a Clareon IOL following cataract removal OD and OS (study eyes).

The subject's medical history included pre-diabetes, hypertension, cerebral vascular accident, and allergy to penicillin. The subject's baseline fundus observations were unremarkable, and slit-lamp observations showed cataract OU.

During surgery, the subject had **anterior capsule tear** (mild severity) OD. The Investigator used a pupil expander to aid visualization during surgery and completed capsule relaxing incisions to further assist in the placement of the IOL within the bag. The subject continues in the study.

The SAE anterior capsule tear has been recovered/resolved during day of surgery.

The Investigator and Sponsor assessed the SAE as unrelated to the IOL but related to the cataract surgery.

Subject 4526.00014: (PT: Cystoid macular oedema, Intraocular injection)

A 69-year-old white female was implanted with a Clareon IOL following cataract removal OD and OS (study eyes).

The subject's medical history included arterial hypertension, surgery for breast cancer, chronic cardiopathy, hyperuricemia, and mild renal chronic disease.

The subject's baseline fundus observations were unremarkable, and slit-lamp observations showed cataract OU.

On Day 48, the subject was diagnosed with clinically significant **cystoid macular edema** (severe severity) OD. The subject's UCDVA was 0.46 logMAR and BCDVA was 0.46 logMAR. The subject was treated with **intravitreal injection** with steroids. The subject continues in the study.

The SAE cystoid macular edema has been recovered/resolved on Day 90. On Day 160, the subject's UCDVA was 0.36 logMAR and BCDVA was -0.04 logMAR.

The Investigator and Sponsor assessed the SAE as unrelated to the IOL but related to the cataract surgery.

Subject 6441.00014: (PT: Cystoid macular oedema)

A 67-year-old African American male was implanted with a Clareon IOL following cataract removal OD and OS (study eyes).

The subject's medical history included pterygion, adenocarcinoma of the prostate, dyslipidemia, type 2 diabetes, high blood pressure, prostate resection, umbilical hernia, and gastric pain.

The subject's baseline fundus observations were unremarkable, and slit-lamp observations showed cataract OU.

On Day 55, the subject was diagnosed with clinically significant **cystoid macular edema** (moderate severity) OD. The subject's UCDVA was 0.2 logMAR and BCDVA was 0.08 logMAR. The subject was treated with non-steroidal anti-inflammatory drops. The subject is pending a follow-up visit. The subject continues in the study.

The SAE cystoid macular edema has not been recovered/resolved by the 6-month visit.

The Investigator and Sponsor assessed the SAE as unrelated to the IOL but related to the cataract surgery.

Subject 7813.00027: (PT: Age related macular degeneration & intravitreal injection with Eylea [Aflibricept])

A 75-year-old white female was implanted with a Clareon IOL following cataract removal OD and OS (study eyes).

The subject's medical history included tonsilectomy, appendicectomy, bladder surgery general, aneurysm/intracranial clipping, asthma, osteoarthritis, depression, hypercholesterolaemia, Barrett's esophagus, diabetes, sacral, nerve stimulator, vitamin D deficiency, hypertension, and hysterectomy.

The subject's baseline fundus observations showed posterior vitreous detachment OD, and slit-lamp observations showed cataract OU.

On Day 402, the subject was diagnosed with subretinal and sub-retinal pigment epithelium fluid indicating wet **age-related macular degeneration** (moderate severity) OD observed during fundus exam. During this visit UCDVA was 0.24 logMAR and BCDVA 0.18 logMAR. Twelve days after being diagnosed, on Day 414, the patient was treated with intravitreal injection with Aflibricept. The event (macular degeneration) has not been resolved but waiting for a follow-up visit to assess visual acuity again. The subject continues in the study.

The investigator and Sponsor assessed the SAEs as unrelated to the IOL.

6.3.3.2 Ocular ADEs

Subject 5956.00007: (PT: Visual impairment x2)

A 72-year-old white male was implanted with a Clareon IOL following cataract removal OD and OS (study eyes).

The subject's medical history included type II diabetes, obesity, angina pectoris, dry skin, hypertension, and retinal pigment alterations.

The subject's baseline fundus observations were unremarkable, and slit-lamp observations showed cataract OU.

On Day 14, the subject reported feeling like having blinkers (like a horse) since surgery OD. On the same day of surgery, on the OS eye, the subject also reported the same symptoms. The Investigator assessed them as **negative dysphotopsia** (mild severity). On Day 42, the subject's OD UCDVA was 0.16 logMAR and BCDVA was -0.04 logMAR, and the subject's OS UCDVA was 0.10 logMAR and BCDVA was 0.06 logMAR. The subject continues in the study.

The ADEs negative dysphotopsia have not recovered/resolved.

The Investigator and Sponsor assessed the ADEs as related to the IOL and related to the IOL implantation.

6.3.3.3 Nonocular SAEs

Subject 7813.00025: (PT: Osteoarthritis)

An 80-year-old white female was implanted with a Clareon IOL following cataract removal OD and OS (study eyes).

The subject's medical history included menopause, hypertension, osteoarthritis, gastroenteritis, and allergy to DAPA-tabs, Isoptin, and Minipress.

The subject's baseline fundus observations were unremarkable, and slit-lamp observations showed cataract OU.

On Day 16, the Investigator was notified that the subject was hospitalized due to **left knee pain due to worsening of osteoarthritis** (severe severity). The subject was treated with oral nonsteroidal anti-inflammatory medication and discharged the next day. The subject continues in the study.

The SAE worsening of oesteoarthritis was recovered/resolved on Day 17.

The Investigator and Sponsor assessed the SAE as unrelated to the IOL or study procedure.

Subject 6681.00017: Death (PT: Pneumonia, Cardiopulmonary failure)

A 71-year-old white female was implanted with a Clareon IOL following cataract removal OD (study eye). The OS was not implanted.

The subject's medical history included anxiety, rheumatoid arthritis, osteoporosis, chronic obstructive pulmonary disease, menopause, polyps intervention in the throat, and intervention of a lipoma.

The subject's baseline fundus observations were unremarkable, and slit-lamp observations showed cataract OU.

On Day 15, the Investigator was notified that subject had fainted and subsequently **died of bronchopneumonia and acute cardiorespiratory failure** (severe severity) the same day. No other information available.

The Investigator and Sponsor assessed the SAE as unrelated to the IOL or study procedure.

Subject 1696.00003: (PT: Thermal burn)

An 83-year-old white male was implanted with a Clareon IOL following cataract removal OD and OS (study eyes).

The subject's medical history included ocular hypertension, arterial hypertension, benign prostate hypertrophy, and hypercholesterolemia.

The subject's baseline fundus observations were unremarkable, and slit-lamp observations showed cataract OU.

On Day 116, the subject suffered from **a burn injury to the legs, arms, and thorax** (severe severity) while soldering iron. The subject was treated with antibiotics, enzymatic debridement analgesic, cutaneous gels, and antihistamine. The subject continues in the study.

The SAE body burn injury was recovered/resolved on Day 137.

The Investigator and Sponsor assessed the SAE as unrelated to the IOL or study procedure.

Subject 7813.00012: (PT: Colon cancer)

An 80-year-old white male was implanted with a Clareon IOL following cataract removal OD and OS (study eyes).

The subject's medical history included ischaemic heart disease, acute myocardial infarction, stent-coronary, chronic obstructive pulmonary disease, prostatomegaly, hyperlipidemia, lumbar back pain, and hypertension.

The subject's baseline fundus observations were unremarkable, and slit-lamp observations showed cataract OU.

On Day 199, the subject was diagnosed with **bowel cancer** (moderate severity) and treated with surgical intervention. The subject was discharged with diagnosis of colon cancer with advanced Parkinson's Disease. The subject continues in the study.

The SAE of bowel cancer has not been resolved.

The Investigator and Sponsor assessed the SAE as unrelated to the IOL or study procedure.

Subject 6441.00010: (PT: Intensive Care)

An 81-year-old white male was implanted with a Clareon IOL following cataract removal OD and OS (study eyes).

The subject's medical history included prostate cancer, high blood pressure, excision of right scrotum cyst, polyp excision from the left nostril, and knee ligamentoplasty.

The subject's baseline fundus observations were unremarkable, and slit-lamp observations showed cataract OU.

On Day 162**,** the subject was **admitted to the intensive care unit** (severe severity) and was discharged from the hospital apparently due to prostate cancer progression. No other information was obtained. Subject is pending a follow-up visit. The subject continues in the study.

The SAE subject admitted to intensive care unit has been recovered/resolved on Day 199.

The Investigator and Sponsor assessed the SAE as unrelated to the IOL or study procedure.

Subject 5956.00008: Death (PT: Myocardial Infarction)

An 78-year-old white male was implanted with a Clareon IOL following cataract removal OD and OS (study eyes).

The subject's medical history included blepharitis OU, obesity, hypertension, hypercholesterolemia, allergy to grass and mites, panic disorder, agaraphobia, COPD, essential tremor vascular parkinsonism, renal insufficiency, prostate cancer, osteoporosis, vitamin D deficiency, hyperparathyroid, cardiovascular disease, general prutitus, dry skin, cerebrovascular accident, and obstructive sleep apnea syndrome.

The subject's baseline fundus observations were unremarkable, and slit-lamp observations showed cataract OU.

On Day 146, the subject suffered a **heart attack** (severe severity) with fatal outcome. No further details were received.

The Investigator and Sponsor assessed the SAE as unrelated to the IOL or study procedure.

Subject 7813.00011: Death (PT: Multiple organ dysfunction syndrome)

An 89-year-old white male was implanted with a Clareon IOL following cataract removal OD and OS (study eyes).

The subject's medical history included hypertension and myocaldial infarction.

The subject's baseline fundus observations were unremarkable, and slit-lamp observations showed cataract OU.

On Day 162, the subject was hospitalized for **multiorgan failure in setting of ischaemic bowel** (severe severity). A surgical resection of the bowel was performed. The Investigator was notified by the subject's wife that the subject had **died** on Day 165. No other information was provided.

The Investigator and Sponsor assessed the SAE as unrelated to the IOL or study procedure.

Subject 7813.00016: Death (PT: Myocardial Infarction)

A 62-year-old white male was implanted with a Clareon IOL following cataract removal OD and OS (study eyes).

The subject's medical history included coronary artery bypass graft, hypertension, renal failure, hyperlipidemia, left carpel tunner syndrome, and mitral valve endocarditis.

The subject's baseline fundus observations were unremarkable, and slit-lamp observations showed cataract OU.

On Day 110, the Investigator was notified by a nurse that the subject had **died due to a myocardial infarction** (severe severity). No other information was provided.

The Investigator and Sponsor assessed the SAE as unrelated to the IOL or study procedure.

Subject 7947.00013: (PT: Breast cancer, Diarrhea, Hypokalemia, Fall, Biliary sepsis, Cholelitiasis)

A 71-year-old white female was implanted with a Clareon IOL following cataract removal OD and OS (study eyes).

The subject's medical history included chronic kidney disease, pulmonary embolus, osteoarthritis, total knee replacement, cellulitis, pancreatitis, hiatus hernia, and hypothyroidism.

The subject's baseline fundus observations were unremarkable, and slit-lamp observations showed cataract OU.

On Day 78, the subject was diagnosed with **left breast cancer requiring a biopsy** (severe severity). The biopsy was done and on Day 152, treatment with chemotherapy was given, which induced **diarrhea** (moderate severity) and **hypokalemia** (moderate severity). The subject was treated with medication and IV fluids. The subject continues in the study.

On Day186, the subject **fell at home** (moderate severity), an MRI of the head was done and showed no acute findings. The subject was diagnosed with **biliary sepsis** (moderate severity) on the same day and was treaed with IV antibiotics. Also, an ultrasound was performed, which led to the diagnoses of **gallstones** (mild severity) on the same day. The subject continues in the study.

The SAE of left breast cancer has not recovered/not resolved. The SAE for diarrhea and hypokalaemia has recovered/resolved on Day 158.

The SAEs fall and biliary sepsis were recovered resolved on Day 189. Gallstones have not recovered/resolved.

The Investigator and Sponsor assessed the SAE as unrelated to the IOL or study procedure.

Subject 2764.00010: (PT: apoplectic stroke)

A 76-year-old white female was implanted with a Clareon IOL following cataract removal OD and OS (study eyes).

The subject's medical history included hypercoagulability, arrhythmia, splenectomy, mesenteriocaval anastomosis, atrial fibrillation, arterial hypertension, menopause, and allergy to penicillin.

The subject's baseline fundus observations were unremarkable, and slit-lamp observations showed cataract OU.

On day 339, the subject was admitted to the hospital and was diagnosed with **apopectic stroke** (moderate severity) and was treated with medications. The subject continues in the study.

The SAE apoplectis stroke has not been recovered/resolved with sequelae.

The Investigator and Sponsor assessed the SAE as unrelated to the IOL or study procedure.

Subject 7813.00010: Death

An 73-year-old white male was implanted with a Clareon IOL following cataract removal OD and OS (study eyes).

The subject's medical history included hypertension, psoriasis, diabetes, reflux esophagitis, hypercholesterolaemia, chronic kidney disease, and iron deficiency anaemia.

The subject's baseline fundus observations were unremarkable, and slit-lamp observations showed cataract OU.

On day 365, the subject was reported to have died due to **Ischemic Heart Disease** (severe severity).

The investigator and Sponsor assessed the SAE as unrelated to the IOL.

Subject 7947-00010: (PT: Vaginal hysterectomy & colporrhaphy)

A 76-year-old white female was implanted with a Clareon IOL following cataract removal OD and OS (study eyes).

The subject's medical history included scoliosis, breast cancer, mastectomy, uterine prolapse, and cystocele rectocele.

The subject's baseline fundus observations were unremarkable, and slit-lamp observations showed cataract OU.

On Day 199, the subject was admitted to the hospital for a **vaginal hysterectomy** (severe severity) **with anterior and posterior repair (colporrhaphy**, severe severity**).** The subject continues in the study.

The Investigator and Sponsor assessed the SAE as unrelated to the IOL or study procedure.

6.3.4 Device Deficiencies

There was 1 device deficiency reported in a first eye (Table 12-16). The IOL delivery system failed to advance the IOL (Listing 16-20); however, on further inspection, the Investigator was found to have used a non-qualified viscoelastic per the Directions for Use (DFU). This was recorded as a protocol deviation (Table 9-7). There were no device deficiencies reported for second eyes (Table 12-17).

6.3.5 Surgical Problems

There were no surgical problems reported in first eyes (Table 12-18). Surgical problems were reported in 2 second eyes (Table 12-19). One eye (Subject 2764.00011) had corneal epithelial erosion at the incision area, and 1 eye (Subject 4625.00014) had anterior capsular tear and intraoperative loss of pupil dilation (Listing 16-21).

6.3.6 Other Procedures During Surgery

There were no "other surgical procedures" in first eyes (Table 12-20). One second eye had an "other surgical procedure" (Table 12-21). The eye (Subject 4625.00014) had radial relaxing capsulotomy incision following anterior capsule tear during cataract extraction (Listing 16-22).

6.3.7 Intraocular Pressure

An increase in intraocular pressure (IOP) was defined according to Masket (2017) criteria as elevation of IOP by ≥ 10 mmHg above baseline to a minimum of 25 mmHg. An increase in IOP meeting the criteria was observed in 3 first eyes (Table 6-31) and 2 second eyes (Table 6-32).

Table 6-31 Number of Eyes with an Increased Intraocular Pressure based on a Modified Version of AAO Consensus (Masket, 2017), First Eye (Safety Analysis Set)

		(N = 215) n (%)
	Total	215
Increased IOP	**Yes**	3 (1.4)
	No	212 (98.6)

N = Number of eyes in the analysis set. n = Number of eyes in specified category.
Total = Number of eyes with data. Percentages are calculated as (n/Total) * 100

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Table 6-32 Number of Eyes with an Increased Intraocular Pressure based on a Modified Version of AAO Consensus (Masket, 2017), Second Eye (Safety Analysis Set)

		(N = 209) n (%)
	Total	209
Increased IOP	**Yes**	2 (1.0)
	No	207 (99.0)

N = Number of eyes in treatment group. n = Number of eyes in specified category.
Total = Number of eyes with data. Percentages are calculated as (n/Total) * 100

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6.3.8 Slit-lamp Examination

The number of eyes with a slit-lamp abnormality at any time is presented in Table 12-32 for first eyes and Table 12-33 for second eyes. By-subject details are provided in Listing 16-24. SAEs related to slit lamp are in Table 6-28.

6.3.9 IOL Observations

There were no eyes with IOL observations (Listing 16-30).

6.3.10 IOL Position Change

Regarding position change, 1 first eye had an IOL tilted ≥ 1 degree (Table 12-46), which resolved by 6 months, and 1 second eye was decentered ≥ 0.5 mm (Table 12-47), which

resolved 32 days after the 6-month visit (reported during an unscheduled visit). There were no other IOL position changes. A listing of eyes with an IOL position change is provided in Listing 16-31.

6.3.11 Subjective Posterior Capsule Opacification

The frequency of subjective PCO is reported in Table 6-33 for first eyes and Table 6-34 for second eyes. No PCO was reported for 71.6% of first eyes and 70.8% of second eyes. Clinically nonsignificant PCO was reported for 26.5% of first eyes and 26.8% of second eyes. A total of 8 eyes had clinically significant PCO (first eyes: n = 3, 1.4%; second eyes: n = 5, 2.4%); 4 eyes developed PCO at 6 months and 4 eyes developed PCO at 1 year. One first eye (0.5%) had clinically significant PCO requiring Nd:YAG at 1 year; it was first reported at 6 months (Listing 16-32).

Table 6-33 Number of Eyes with Subjective Posterior Capsule Opacification, First Eye (Safety Analysis Set)

		(N = 215) n (%)
	Total	215
Subjective PCO	None	154 (71.6)
	Clinically Nonsignificant	57 (26.5)
	Clinically Significant	3 (1.4)
	Clinically Significant Requiring a YAG	1 (0.5)

Category represents maximum rating for an eye during the study.
N = Number of eyes in treatment group. n = Number of eyes in specified category.
Total = Number of eyes with data. Percentages are calculated as (n/Total) * 100
YAG = Nd:YAG laser treatment

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Table 6-34 Number of Eyes with Subjective Posterior Capsule Opacification, Second Eye (Safety Analysis Set)

		(N = 209) n (%)
	Total	209
Subjective PCO	None	148 (70.8)

		(N = 209) n (%)
	Clinically Nonsignificant	56 (26.8)
	Clinically Significant	5 (2.4)
	Clinically Significant Requiring a YAG	0 (0.0)

Category represents maximum rating for an eye during the study.
N = Number of eyes in treatment group. n = Number of eyes in specified category.
Total = Number of eyes with data. Percentages are calculated as (n/Total) * 100
YAG = Nd:YAG laser treatment

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6.3.12 Posterior Capsulotomy

Two first eyes (Subject 1702.00002 and Subject 5956.00011) had posterior capsulotomy (PC) (Table 12-50). For Subject 1702.00002, the PC was performed at Day 1 postop due to a pre-existing residual posterior subcapsular cataract (recorded in the medical history and AE captured) following cataract surgery, but this was not related to posterior capsular opacification after implantation. For Subject 5956.00011, the PC was performed at 1-year. No second eyes had PC (Table 12-51). One first eye and no second eye had a YAG for PCO developed post-implantation (Listing 16-32).

6.3.13 Dilated Fundus Examination

The number of eyes with a fundus abnormality at any time is presented in Table 12-54 for first eyes and Table 12-55 for second eyes. By-subject details are provided in Listing 16-33. SAEs observations related to dilated fundus examination are in Table 6-27.

6.3.14 Axial length

Descriptive statistics for axial length are provided in Table 11-37 for first eyes and Table 11-38 for second eyes.

6.3.15 Anterior chamber depth

Descriptive statistics for anterior chamber depth are provided in Table 11-41 for first eyes and Table 11-42 for second eyes. Descriptive statistics for anterior chamber depth by site, for sites with ≥ 10 subjects in the AAS, are presented for the first eye in Table 11-41a to Table 11-41k and for the second eye in Table 11-42a to Table 11-42k.

6.3.16 Corneal Astigmatism

Descriptive statistics for corneal astigmatism are provided in Table 11-45 for first eyes and Table 11-46 for second eyes.

7 DISCUSSION

This postmarket clinical study is being conducted to provide long-term (3 years) safety and effectiveness data on the Clareon monofocal IOL Model SY60WF, when used in adult aphakic subjects, in support of Market Access requirements including the development of a product value dossier.

This interim report presents the clinical outcomes of approximately 200 subjects with a 1-year postoperative follow-up.

The primary efficacy objective of this study is to compare the percentage of eyes achieving best-corrected distance visual acuity of 0.3 logMAR or better at 1 Year to the historical post-operative SPE (visual acuity) rates as reported in EN ISO 11979-7:2014. Best corrected visual acuity of 0.3 logMAR or better is observed in 99.5% of first eyes and 99.5% of second eyes implanted. In addition, at 1 year, BCDVA of 0.0 logMAR or better is observed in 80.8% of first eyes and 77.8% of second eyes implanted (Table 11-21 and Table 11-22). UCDVA of 0.3 logMAR or better is observed in 94.0% of first eyes and 95.5% of second eyes implanted (Table 11-25 and Table 11-26). These results support the visual performance criterion of the Clareon IOL compared to historical data.

The primary safety objective is to evaluate the 1-year AE rates of the Clareon IOL compared to historical SPE rates as reported in EN ISO 11979-7:2014. The rate of cumulative and persistent SAEs, including SSIs, for first and second eyes were below the threshold as set forth by ISO 11979-7:2014, thus meeting the ISO requirement and study safety requirement. SSIs occurred in 3 first eyes and 0 second eyes, and all were assessed as not related to the IOL.

Refractive outcomes at 1-year show a mean MRSE of 0.048 D for the first eye and 0.071 D for the second eye (Table 6-15 and Table 6-16), with 95.5% of first eyes and 98.5% of second eyes presenting an absolute MRSE of 1.00 D or less (Table 11-53 and Table 11-54).

As expected, the frequency of subjective PCO at 1 year remains low, with approximately 98% of first eyes and second eyes having no PCO or clinically nonsignificant PCO (Table 6-33 and Table 6-34). One Nd:YAG laser posterior capsulotomy was required for IOL implantation-related PCO.

The addition of a hydrophilic copolymer, HEMA added into the acrylic matrix of the Clareon IOL material is intended to reduce the formation of microvacuoles (glistenings) in the lens. At 1 year, 99.5% of first and second eyes present Grade 0 glistenings, while one subject was reported with Glistenings Grade 1 in both eyes (Table 6-23 and Table 6-24).

There have been no unanticipated AEs reported to date and the incidence of AEs in the study remains low with no serious events related to the IOL at 1 year. This interim analysis does not identify new safety concerns or trends for the Clareon IOL.

8 REFERENCES

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9 APPENDIX

9.1 Tables, Figures, and Listings Referred to but not Included in the Text

9.1.1 Conduct Tables

The tables are located at the end of the document. Table 9-1 provides the complete list of conduct tables.

Table 9-1 Complete List of Conduct Tables

Table 10-1	Subject Disposition | (All Enrolled Subjects)|
Table 10-2	Subject Status Summary, First Eye | (All-Implanted Analysis Set)|
Table 10-3	Subject Status Summary, Second Eye| (All-Implanted Analysis Set)|
Table 10-4	Subject Status Summary, First Eye | (Best-Case Analysis Set)|
Table 10-5	Subject Status Summary, Second Eye | (Best-Case Analysis Set)|
Table 10-6	Subject Accounting for Monocular BCDVA at 4 m, First Eye | (All-Implanted Analysis Set)|
Table 10-7	Subject Accounting for Monocular BCDVA at 4 m, Second Eye | (All-Implanted Analysis Set)|
Table 10-8	Demographic Statistics | (All-Implanted Analysis Set)|
Table 10-8a	Demographic Statistics for Site 1696| (All-Implanted Analysis Set)|
Table 10-8b	Demographic Statistics for Site 2764| (All-Implanted Analysis Set)|
Table 10-8c	Demographic Statistics for Site 4526| (All-Implanted Analysis Set)|
Table 10-8d	Demographic Statistics for Site 4625| (All-Implanted Analysis Set)|
Table 10-8e	Demographic Statistics for Site 5956| (All-Implanted Analysis Set)|
Table 10-8f	Demographic Statistics for Site 6441| (All-Implanted Analysis Set)|
Table 10-8g	Demographic Statistics for Site 6660| (All-Implanted Analysis Set)|
Table 10-8h	Demographic Statistics for Site 6681| (All-Implanted Analysis Set)|
Table 10-8i	Demographic Statistics for Site 7813| (All-Implanted Analysis Set)|
Table 10-8j	Demographic Statistics for Site 7925| (All-Implanted Analysis Set)|
Table 10-8k	Demographic Statistics for Site 7947| (All-Implanted Analysis Set)|
Table 10-9	Demographic Statistics| (Best-Case Analysis Set)|
Table 10-10	Demographic Statistics| (Safety Analysis Set)|
Table 10-11	Baseline Characteristics, First Eye| (All-Implanted Analysis Set)|
Table 10-11a	Baseline Characteristics for Site 1696, First Eye| (All-Implanted Analysis Set)|
Table 10-11b	Baseline Characteristics for Site 2764, First Eye| (All-Implanted Analysis Set)|
Table 10-11c	Baseline Characteristics for Site 4526, First Eye| (All-Implanted Analysis Set)|
Table 10-11d	Baseline Characteristics for Site 4625, First Eye| (All-Implanted Analysis Set)|
Table 10-11e	Baseline Characteristics for Site 5956, First Eye| (All-Implanted Analysis Set)|
Table 10-11f	Baseline Characteristics for Site 6441, First Eye| (All-Implanted Analysis Set)|

9.1.2 Effectiveness Tables

The tables are located at the end of the document. Table 9-2 provides the complete list of effectiveness tables.

Table 9-2 Complete List of Effectiveness Tables

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9.2 Protocol

A copy of the approved protocol starts following Section 9.4.

9.3 Statistical Analysis Plan

The SAP is located at the end of the document.

9.4 Protocol Deviations

Table 9-5 All Protocol Deviations Related to Visual Acuity by Visit

Subject number	PD category	Details/Explanation	Visit	First Eye	Second Eye	UCDVA	BCDVA
2203.00001	VA Fast Method	Starting row identification	Visit 1A		X	X	
2203.00001	VA Fast Method	Starting row identification	Visit 2	X		X	
2203.00001	VA Fast Method	Starting row identification	Visit 3A	X		X	
2203.00001	VA Fast Method	Starting row identification	Visit 3A	X	X		X
2203.00003	VA Lighting deviation	Lighting not measured for VA assessments	Visit 4A	X	X	X	X
2203.00006	VA Fast Method	Starting row identification	Visit 1A		X	X	
2203.00006	VA Fast Method	Starting row identification	Visit 2	X		X	
2203.00006	VA Fast Method	Starting row identification	Visit 3A		X	X	
2203.00007	VA Fast Method	Starting row identification	Visit 1	X		X	
2203.00007	VA Fast Method	Testing should have continued	Visit 2A		X	X	
2203.00007	VA Fast Method	Starting row identification	Visit 4A		X	X	
2203.00008	VA Fast Method	Starting row identification	Visit 4A		X	X	
2203.00010	VA Fast Method	Testing should have continued	Visit 1	X		X	
2203.00010	VA Fast Method	Starting row identification	Visit 3A	X			X
2203.00011	VA Fast Method	Testing should have continued	Visit 2	X		X	
2203.00011	VA Fast Method	Testing should have continued	Visit 4A	X	X	X	
2203.00011	VA Fast Method	Testing should have continued	Visit 4A		X	X	
2764.00001	VA Fast Method	Testing should have continued	Visit 1A		X	X	