

# Statistical Analysis Plan

## Post Approval Study of the Tecnis Symfony® Toric Lenses

NCT Number: NCT03791619

Document date: 26 FEB 2021

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**STATISTICAL ANALYSIS PLAN**

**Post Approval Study of the Tecnis Symfony® Toric Lenses**

**PROTOCOL NUMBER: TIOL-205-STPA**

**SPONSOR**

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**SAP CHANGE HISTORY**

Version	Section(s)	Page(s)	Description of Change(s)	Rationale for Change(s)
1.0	N/A	N/A	Original	N/A

## 1 INTRODUCTION

This document summarizes the statistical methods to be implemented for this post approval study of the Tecnis Symphony® Toric lenses, Models ZXT300, ZXT375 with ZXT150 as the control lens. This study is a 6-month, prospective, multicenter, bilateral, non-randomized open label comparative clinical trial conducted at up to 50 sites. Subjects will be bilaterally implanted with a TECNIS Symphony IOL, either toric (Models ZXT150, ZXT225, ZXT300 or ZXT375) or non-toric (TECNIS Symphony Extended Range of Vision IOL, Model ZXR00). Each eye may have a different TECNIS Symphony IOL implanted, as determined by the surgeon and the TECNIS Symphony Toric IOL calculator; however, at least one eye must be implanted with either a Symphony Toric IOL Model ZXT150 (lower-cylinder group) or a Model ZXT300 or ZXT375 (higher-cylinder group) and the fellow eye must have the same or a lower toric power. The eye with the highest toric power IOL will determine the model group.

The purpose of this post-approval study is to evaluate the rates of bothersome visual symptoms for the higher-cylinder Symphony Toric IOLs, Models ZXT300 and ZXT375, compared to the lower-cylinder Symphony Toric IOL, Model ZXT150. The first primary endpoint is the rate of bothersome visual symptoms [REDACTED] [REDACTED] contained in the Patient-Reported Visual Symptom Questionnaire (PRVSQ). The second primary endpoint will be the rate of those having a lot of difficulty [REDACTED] as measured in the PRVSQ.

Other endpoints are individual visual symptom ratings included in the PRVSQ, rates of IOL repositioning procedures (secondary surgical intervention) due to IOL misalignment, rates of explants due to visual symptoms, distance visual acuities, mean percent reduction in absolute cylinder, mean refractive cylinder, mean refractive cylinder compared to the preoperatively-predicted cylinder, mean spherical equivalent, spherical equivalent compared to the preoperatively-predicted spherical equivalent, percent of eyes with cylinder and spherical equivalent (MRSE) within 0.50 D and within 1.00 D of the preoperatively-predicted spherical equivalent, rates of medical and/or lens findings, and rates of other adverse events.

The key time point for reporting will be at 6 months. however, any subject that undergoes a lens repositioning procedure due to IOL misalignment, or reports "[REDACTED] bother that impacts daily living [REDACTED] at 6 months, will be followed through 1 year postoperatively.

## 2 ANALYSIS POPULATIONS

### 2.1 ANALYSIS POPULATIONS/HANDLING OF MISSING DATA

The higher cylinder group will consist of subjects with a ZXT300 or ZXT375 in at least one eye. To be included in the lower cylinder group a subject must have a ZXT150 in at least one eye and not have a ZXT300 or ZXT375 in the other eye. For the primary endpoints and other questionnaire data, the primary analysis population will be all bilaterally-implanted subjects having available data at the 6-month visit, with data reported separately for the higher- and lower-cylinder groups. For the final report, [REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

In addition, for the primary endpoints, data will also be reported as supportive analysis for all subjects, [REDACTED]

[REDACTED]

In addition to the primary population analyses discussed above, additional analyses will also be performed for the primary endpoints to evaluate the influence of missing data.

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

For other questionnaire items, bilaterally-implanted subjects with available data at six months postoperative will be used for analysis. Refraction, monocular visual acuity, medical/lens findings and adverse event data will be reported for primary eyes (higher cylinder eye or first eye implanted if same IOL model in both eyes) and fellow eyes. Data will be reported separately for the higher-cylinder group and the lower cylinder control group.

For monocular endpoints, data will be presented by primary and fellow eyes. Primary eye of a subject is defined as the eye having a higher toric power. If both eyes have the same Toric lens model, the first eye undergoes surgery will be defined as the primary eye and the second eye will be defined as the fellow eye.

[REDACTED]

## 2.3 DATA CONVENTIONS

Descriptive statistics will typically include sample size (N), mean, standard deviation (SD), median, minimum (Min.), and maximum (Max.) as appropriate for continuous variables. For categorical data, the frequency and proportion will be computed.

### 3 ACCOUNTABILITY/DEMOGRAPHICS

### 3.1 ENROLLMENT/ACCOUNTABILITY

The number of enrolled subjects will be tabulated by site for primary and fellow eyes. Subject accountability will be summarized as a frequency distribution by scheduled visits. A frequency table by IOL will be generated, showing the number of available eyes (those in interval and outside of the interval) and the number of missing and active subjects.

### 3.2 DEMOGRAPHICS

Subject demographic data including age, sex, race, and eye color will be presented by IOL group. Age will be determined at the time of the preoperative visit and will be categorized by less than 60, 60 to 69, 70 to 79, and equal to or older than 80 years old. In addition, age will be summarized with descriptive statistics. The frequency distributions of sex, race, and iris color will also be tabulated.

#### 4 POSTOPERATIVE ANALYSES – PRIMARY ENDPOINTS

There are two primary endpoints for this study, rate of bothersome visual symptoms and rate of difficulty with an activity due to the symptoms at 6-month postoperative. ■■■■

\_\_\_\_\_

- [REDACTED]**

The first primary endpoint is the rate of bothersome visual symptoms, [REDACTED]

\_\_\_\_\_

████████████████████ The second primary endpoint is the rate of reported difficulty with an activity due to one or more visual symptoms, determined by a

“Yes” response to the question “Is there anything you have a lot of difficulty with, or do not do, because of [visual symptom]”) at 6 months postoperative.

The frequency and proportion of subjects with bothersome visual symptoms [REDACTED] and the frequency and proportion of subjects reporting difficulty with an activity due to one or more visual symptoms will be reported along with the two-sided, 95% confidence interval at the 6-month visit.

## **5 POSTOPERATIVE ANALYSIS: OTHER ENDPOINTS**

### **5.1 VISUAL ACUITY ENDPOINTS**

Visual acuity will be reported by high and low cylinder group. The frequency and proportion of eyes achieving each line of visual acuity will be reported.

### **5.2 MANIFEST REFRACTION**

Descriptive statistics of mean percent reduction in cylinder, refractive cylinder, cylinder vs preoperatively-predicted cylinder, spherical equivalent and spherical equivalent vs preoperatively-predicted spherical equivalent will be reported by IOL group. The frequency and proportion of eyes within 0.50 D and within 1.00 D of the preoperatively-predicted values will be reported for refractive cylinder and spherical equivalent. Percent reduction in cylinder will be calculated for each eye using the following formula:

$$100 * ((\text{Postop Ref. Cyl.} - \text{Preop K. Cyl.}) / (\text{Target Ref. Cyl.} - \text{Preop K. Cyl.}))$$

Key: Ref. Cyl.=absolute refractive cylinder; K. Cyl.=keratometric cylinder;

Refractive data will be referred to the corneal plane prior to determining percent reduction in cylinder.

### **5.3 OTHER QUESTIONNAIRE ENDPOINTS**

The frequency and proportion with each response will be reported for the individual visual symptom items on the questionnaire and will be reported by high and low cylinder group for bilateral subjects.

### **5.4 SAFETY ENDPOINTS/MEDICAL/LENS FINDINGS**

The frequency and proportion of medical and lens findings will be reported for primary and fellow eyes of toric subjects. The frequency and proportion of adverse events at any time postoperative will also be reported.

A listing of serious adverse event or device-related events will also be provided for all subjects. Rates of IOL repositioning procedures (secondary surgical intervention) due to IOL misalignments, rates of explants due to visual symptoms will also be reported.

## **5.5 NON-DIRECTED OCULAR/VISUAL SYMPTOMS**

Rates of postoperative non-directed ocular/visual symptoms will be tabulated with the frequency and proportion of eyes with these events reported over time by IOL group.

## **7 SAMPLE SIZE CALCULATIONS**

With a sample size of 240 subjects and assuming a 20% rate of bothersome visual symptoms or difficulty with an activity due to visual symptoms, a two-sided 95% confidence interval will estimate the observed rate of bothersome visual symptoms to within 4.2 percentage points.

To achieve 240 higher-cylinder group subjects and 240 lower-cylinder group subjects evaluable at 6 months, assuming an initial 20% screen-fail rate and a 5% lost-to-follow-up rate, up to 634 total subjects will be enrolled.



## 8.0 REFERENCES

- [REDACTED]  
[REDACTED]
- [REDACTED]  
[REDACTED]

## APPENDIX I: TABLE LISTING

Year	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024	2025	2026	2027	2028	2029	2030	2031	2032	2033	2034	2035	2036	2037	2038	2039	2040	2041	2042	2043	2044	2045	2046	2047	2048	2049	2050	2051	2052	2053	2054	2055	2056	2057	2058	2059	2060	2061	2062	2063	2064	2065	2066	2067	2068	2069	2070	2071	2072	2073	2074	2075	2076	2077	2078	2079	2080	2081	2082	2083	2084	2085	2086	2087	2088	2089	2090	2091	2092	2093	2094	2095	2096	2097	2098	2099	2100																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																										
Population (millions)	11.5	11.6	11.7	11.8	11.9	12.0	12.1	12.2	12.3	12.4	12.5	12.6	12.7	12.8	12.9	13.0	13.1	13.2	13.3	13.4	13.5	13.6	13.7	13.8	13.9	14.0	14.1	14.2	14.3	14.4	14.5	14.6	14.7	14.8	14.9	15.0	15.1	15.2	15.3	15.4	15.5	15.6	15.7	15.8	15.9	16.0	16.1	16.2	16.3	16.4	16.5	16.6	16.7	16.8	16.9	17.0	17.1	17.2	17.3	17.4	17.5	17.6	17.7	17.8	17.9	18.0	18.1	18.2	18.3	18.4	18.5	18.6	18.7	18.8	18.9	19.0	19.1	19.2	19.3	19.4	19.5	19.6	19.7	19.8	19.9	20.0	20.1	20.2	20.3	20.4	20.5	20.6	20.7	20.8	20.9	21.0	21.1	21.2	21.3	21.4	21.5	21.6	21.7	21.8	21.9	22.0	22.1	22.2	22.3	22.4	22.5	22.6	22.7	22.8	22.9	23.0	23.1	23.2	23.3	23.4	23.5	23.6	23.7	23.8	23.9	24.0	24.1	24.2	24.3	24.4	24.5	24.6	24.7	24.8	24.9	25.0	25.1	25.2	25.3	25.4	25.5	25.6	25.7	25.8	25.9	26.0	26.1	26.2	26.3	26.4	26.5	26.6	26.7	26.8	26.9	27.0	27.1	27.2	27.3	27.4	27.5	27.6	27.7	27.8	27.9	28.0	28.1	28.2	28.3	28.4	28.5	28.6	28.7	28.8	28.9	29.0	29.1	29.2	29.3	29.4	29.5	29.6	29.7	29.8	29.9	30.0	30.1	30.2	30.3	30.4	30.5	30.6	30.7	30.8	30.9	31.0	31.1	31.2	31.3	31.4	31.5	31.6	31.7	31.8	31.9	32.0	32.1	32.2	32.3	32.4	32.5	32.6	32.7	32.8	32.9	33.0	33.1	33.2	33.3	33.4	33.5	33.6	33.7	33.8	33.9	34.0	34.1	34.2	34.3	34.4	34.5	34.6	34.7	34.8	34.9	35.0	35.1	35.2	35.3	35.4	35.5	35.6	35.7	35.8	35.9	36.0	36.1	36.2	36.3	36.4	36.5	36.6	36.7	36.8	36.9	37.0	37.1	37.2	37.3	37.4	37.5	37.6	37.7	37.8	37.9	38.0	38.1	38.2	38.3	38.4	38.5	38.6	38.7	38.8	38.9	39.0	39.1	39.2	39.3	39.4	39.5	39.6	39.7	39.8	39.9	40.0	40.1	40.2	40.3	40.4	40.5	40.6	40.7	40.8	40.9	41.0	41.1	41.2	41.3	41.4	41.5	41.6	41.7	41.8	41.9	42.0	42.1	42.2	42.3	42.4	42.5	42.6	42.7	42.8	42.9	43.0	43.1	43.2	43.3	43.4	43.5	43.6	43.7	43.8	43.9	44.0	44.1	44.2	44.3	44.4	44.5	44.6	44.7	44.8	44.9	45.0	45.1	45.2	45.3	45.4	45.5	45.6	45.7	45.8	45.9	46.0	46.1	46.2	46.3	46.4	46.5	46.6	46.7	46.8	46.9	47.0	47.1	47.2	47.3	47.4	47.5	47.6	47.7	47.8	47.9	48.0	48.1	48.2	48.3	48.4	48.5	48.6	48.7	48.8	48.9	49.0	49.1	49.2	49.3	49.4	49.5	49.6	49.7	49.8	49.9	50.0	50.1	50.2	50.3	50.4	50.5	50.6	50.7	50.8	50.9	51.0	51.1	51.2	51.3	51.4	51.5	51.6	51.7	51.8	51.9	52.0	52.1	52.2	52.3	52.4	52.5	52.6	52.7	52.8	52.9	53.0	53.1	53.2	53.3	53.4	53.5	53.6	53.7	53.8	53.9	54.0	54.1	54.2	54.3	54.4	54.5	54.6	54.7	54.8	54.9	55.0	55.1	55.2	55.3	55.4	55.5	55.6	55.7	55.8	55.9	56.0	56.1	56.2	56.3	56.4	56.5	56.6	56.7	56.8	56.9	57.0	57.1	57.2	57.3	57.4	57.5	57.6	57.7	57.8	57.9	58.0	58.1	58.2	58.3	58.4	58.5	58.6	58.7	58.8	58.9	59.0	59.1	59.2	59.3	59.4	59.5	59.6	59.7	59.8	59.9	60.0	60.1	60.2	60.3	60.4	60.5	60.6	60.7	60.8	60.9	61.0	61.1	61.2	61.3	61.4	61.5	61.6	61.7	61.8	61.9	62.0	62.1	62.2	62.3	62.4	62.5	62.6	62.7	62.8	62.9	63.0	63.1	63.2	63.3	63.4	63.5	63.6	63.7	63.8	63.9	64.0	64.1	64.2	64.3	64.4	64.5	64.6	64.7	64.8	64.9	65.0	65.1	65.2	65.3	65.4	65.5	65.6	65.7	65.8	65.9	66.0	66.1	66.2	66.3	66.4	66.5	66.6	66.7	66.8	66.9	67.0	67.1	67.2	67.3	67.4	67.5	67.6	67.7	67.8	67.9	68.0	68.1	68.2	68.3	68.4	68.5	68.6	68.7	68.8	68.9	69.0	69.1	69.2	69.3	69.4	69.5	69.6	69.7	69.8	69.9	70.0	70.1	70.2	70.3	70.4	70.5	70.6	70.7	70.8	70.9	71.0	71.1	71.2	71.3	71.4	71.5	71.6	71.7	71.8	71.9	72.0	72.1	72.2	72.3	72.4	72.5	72.6	72.7	72.8	72.9	73.0	73.1	73.2	73.3	73.4	73.5	73.6	73.7	73.8	73.9	74.0	74.1	74.2	74.3	74.4	74.5	74.6	74.7	74.8	74.9	75.0	75.1	75.2	75.3	75.4	75.5	75.6	75.7	75.8	75.9	76.0	76.1	76.2	76.3	76.4	76.5	76.6	76.7	76.8	76.9	77.0	77.1	77.2	77.3	77.4	77.5	77.6	77.7	77.8	77.9	78.0	78.1	78.2	78.3	78.4	78.5	78.6	78.7	78.8	78.9	79.0	79.1	79.2	79.3	79.4	79.5	79.6	79.7	79.8	79.9	80.0	80.1	80.2	80.3	80.4	80.5	80.6	80.7	80.8	80.9	81.0	81.1	81.2	81.3	81.4	81.5	81.6	81.7	81.8	81.9	82.0	82.1	82.2	82.3	82.4	82.5	82.6	82.7	82.8	82.9	83.0	83.1	83.2	83.3	83.4	83.5	83.6	83.7	83.8	83.9	84.0	84.1	84.2	84.3	84.4	84.5	84.6	84.7	84.8	84.9	85.0	85.1	85.2	85.3	85.4	85.5	85.6	85.7	85.8	85.9	86.0	86.1	86.2	86.3	86.4	86.5	86.6	86.7	86.8	86.9	87.0	87.1	87.2	87.3	87.4	87.5	87.6	87.7	87.8	87.9	88.0	88.1	88.2	88.3	88.4	88.5	88.6	88.7	88.8	88.9	89.0	89.1	89.2	89.3	89.4	89.5	89.6	89.7	89.8	89.9	90.0	90.1	90.2	90.3	90.4	90.5	90.6	90.7	90.8	90.9	91.0	91.1	91.2	91.3	91.4	91.5	91.6	91.7	91.8	91.9	92.0	92.1	92.2	92.3	92.4	92.5	92.6	92.7	92.8	92.9	93.0	93.1	93.2	93.3	93.4	93.5	93.6	93.7	93.8	93.9	94.0	94.1	94.2	94.3	94.4	94.5	94.6	94.7	94.8	94.9	95.0	95.1	95.2	95.3	95.4	95.5	95.6	95.7	95.8	95.9	96.0	96.1	96.2	96.3	96.4	96.5	96.6	96.7	96.8	96.9	97.0	97.1	97.2	97.3	97.4	97.5	97.6	97.7	97.8	97.9	98.0	98.1	98.2	98.3	98.4	98.5	98.6	98.7	98.8	98.9	99.0	99.1	99.2	99.3	99.4	99.5	99.6	99.7	99.8	99.9	100.0	100.1	100.2	100.3	100.4	100.5	100.6	100.7	100.8	100.9	101.0	101.1	101.2	101.3	101.4	101.5	101.6	101.7	101.8	101.9	102.0	102.1	102.2	102.3	102.4	102.5	102.6	102.7	102.8	102.9	103.0	103.1	103.2	103.3	103.4	103.5	103.6	103.7	103.8	103.9	104.0	104.1	104.2	104.3	104.4	104.5	104.6	104.7	104.8	104.9	105.0	105.1	105.2	105.3	105.4	105.5	105.6	105.7	105.8	105.9	106.0	106.1	106.2	106.3	106.4	106.5	106.6	106.7	106.8	106.9	107.0	107.1	107.2	107.3	107.4	107.5	107.6	107.7	107.8	107.9	108.0	108.1	108.2	108.3	108.4	108.5	108.6	108.7	108.8	108.9	109.0	109.1	109.2	109.3	109.4	109.5	109.6	109.7	109.8	109.9	110.0	110.1	110.2	110.3	110.4	110.5	110.6	110.7	110.8	110.9	111.0	111.1	111.2	111.3	111.4	111.5	111.6	111.7	111.8	111.9	112.0	112.1	112.2	112.3	112.4	112.5	112.6	112.7	112.8	112.9	113.0	113.1	113.2	113.3	113.4	113.5	113.6	113.7	113.8	113.9	114.0	114.1	114.2	114.3	114.4	114.5	114.6	114.7	114.8	114.9	115.0	115.1	115.2	115.3	115.4	115.5	115.6	115.7	115.8	115.9	116.0	116.1	116.2	116.3	116.4	116.5	116.6	116.7	116.8	116.9	117.0	117.1	117.2	117.3	117.4	117.5	117.6	117.7	117.8	117.9	118.0	118.1	118.2	118.3	118.4	118.5	118.6	118.7	118.8	118.9	119.0	119.1	119.2	119.3	119.4	119.5	119.6	119.7	119.8	119.9	120.0	120.1	120.2	120.3	120.4	120.5	120.6	120.7	120.8	120.9	121.0	121.1	121.2	121.3	121.4	121.5	121.6	121.7	121.8	121.9	122.0	122.1	122.2	122.3	122.4	122.5	122.6	122.7	122.8	122.9	123.0	123.1	123.2	123.3	123.4	123.5	123.6	123.7	123.8	123.9	124.0	124.1	124.2	124.3	124.4	124.5	124.6	124.7	124.8	124.9	125.0	125.1	125.2	125.3	125.4	125.5	125.6	125.7	125.8	125.9	126.0	126.1	126.2	126.3	126.4	126.5	126.6	126.7	126.8	126.9	127.0	127.1	127.2	127.3	127.4	127.5	127.6	127.7	127.8	127.9	128.0	128.1	128.2	128.3	128.4	128.5	128.6	128.7	128.8	128.9	129.0	129.1	129.2	129.3	129.4	129.5	129.6	129.7	129.8	129.9	130.0	130.1	130.2	130.3	130.4	130.5	130.6	130.7	130.8	130.9	131.0	131.1	131.2	131.3	131.4	131.5	131.6	131.7	131.8	131.9	132.0	132.1	132.2	132.3	132.4	132.5	132.6	132.7	132.8	132.9	133.0	133.1	133.2	133.3	133.4	133.5	133.6	133.7	133.8	133.9










**KEY:** [REDACTED]  
[REDACTED]  
[REDACTED]  
[REDACTED]

**TIME FRAME:** The 6-month postoperative visit is the key timeframe for reporting.

**STATISTICS:** See text portion of the statistical analysis plan for information on inferential statistics for comparisons between IOL group

Signature Page for VTMF-14016391, V-TMF Version: 1.0  
TIOL-205-STPA---Statistical Analysis Plan-25 Feb 2021

Signature Meaning:

To verify that the content is accurate and true to the best of my knowledge.